



Abstract Book

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Oral Presentations



Lecture 1

Retinopathy Of Prematurity as a Cause Of Blindness In Children



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Globally there are 1.4 million children who are blind, almost $\frac{3}{4}$ of whom live in developing countries. The prevalence and causes of blindness are largely determined by levels of socioeconomic development and the provision of effective health care systems.

Retinopathy of prematurity is emerging as a very important cause of blindness in children in the middle income countries of Latin America and Eastern Europe, where it can account for more than 50% of all causes. Retinopathy of prematurity is also being increasingly reported from cities in Asian countries, particularly India and China, where it is likely to become a more important cause of blindness in children as these economies improve and services for the care of premature babies expand. Globally at least 50,000 children are blind from ROP, and an additional unknown number will be visually impaired or blind in one eye.

The characteristics of babies with severe ROP in middle and low income countries show that these babies have a much wider range of gestational ages and birth weights than is currently the case in industrialized countries. Possible reasons for this “third epidemic” of ROP will be discussed.

Lecture 2

Classification Of ROP

CLASSIFICATION OF ROP

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Classification of ROP includes assessment of four parameters including severity, location, and extent of the retinopathy at the border between vascular and avascular retina, as well as determination of the presence of peripapillary vessel abnormalities characterized as plus disease. The classification was "revisited" in 2005 with no change in the basic parameters assessed, but the revision documented a more virulent form of retinopathy and also noted that peripapillary vascular abnormalities may be abnormal without qualifying as plus disease.

Severity of disease

The retinopathy at the vascular/avascular junction is described in five stages. The normally vascularizing retina fades gently from translucent vascular retina to a graying, relatively opaque avascular retina.

Stage 1 is characterized by the presence of a flat, white line (demarcation line) separating the vascular and avascular retina. The vessels end abruptly at the demarcation line and do not extend beyond it.

In Stage 2 ROP, a ridge with height and volume develops in the region demarcation line. The ridge is generally white or gray and may have tiny bud-like vascular abnormalities called "popcorn" just posterior it.

The hallmark of Stage 3 ROP is development of new vessels from the ridge into the vitreous. The neovascularization usually extends up into the vitreous, but may also extend backwards over the surface of the retina.

Retinal detachment characterize the last two stages of ROP with subtotal detachment designated Stage 4. This stage is subdivided based on macular involvement with Stage 4A representing partial detachment not involving the fovea and Stage 4B a partial detachment involving the foveal region.

Stage 5 is a total retinal detachment that is further characterized by the appearance of the anterior and posterior region of the detachment. The funnel is described as open or closed anteriorly and posteriorly.

Location of disease

For the purposes of classification, the retina has been divided into three zones with the optic disc as the central point. The peripheral border of the most posterior zone, zone I, is defined by a circle that has as its radius twice the distance from the disc to the fovea. Zone II is shaped like a doughnut and extends from zone I to an outer border than is defined by a circle with the disc to direct nasal ora serrata. Zone III, the most peripheral zone, is crescent-shaped and extends from the superior-nasal border of zone II around to the inferior-nasal border of zone II. Thus, zone III disease is far peripheral disease and can be seen in both the temporal and nasal quadrants as shown in the figure 7.

Since the fovea is not well defined in the newborn baby, a good approximation of the extent of zone I can be determined by using a 25 or 28 diopter condensing lens and placing the edge of the optic disc at the edge of the field. The approximate limit of zone I is directly across

at the opposite edge of the lens. In addition, that circumferential disease must, by definition, be located in either zone I or zone II. It is also generally safer to assign the retinopathy to the more posterior zone if the examiner cannot precisely determine the zone.

Extent of disease

Disease extent is defined in terms of 30-degree sectors of involvement. Using the clock face as a guide, sector involvement is noted with the boundary between sectors at the clock hour position. For example, involvement of ROP in the 3 o'clock sector extends from 3 o'clock to the 4 o'clock position. Retinopathy occurring in this sector would be located nasally in the right eye and temporally in the left.

Plus disease

As the active phases of ROP progress, involvement of the eye extends beyond the region between the vascular and avascular retina. Signs indicating more severe retinopathy include venous dilation and arteriolar tortuosity of the peripapillary vessels, as well as iris vascular engorgement, poor pupillary dilation, and vitreous haze. In the 1984 classification, abnormal dilation and tortuosity of the posterior pole vessels sufficient to be designated "plus disease" was defined a sample clinical photograph. A less severe example of plus disease was selected as demonstrating the minimum vascular abnormality sufficient for diagnosing plus disease for subsequent multicentered treatment trials. In addition, the diagnosis of plus disease required the presence of sufficient vascular dilation and tortuosity in at least two quadrants. In general, a "+" symbol or the word "plus" is added following the ROP stage number to designate the presence of plus disease, i.e. stage 3 ROP combined with sufficient posterior vascular dilation and tortuosity would be written "stage 3+ ROP".

Pre-plus disease

One of the contributions of the recent "Classification Revisited" is the recognition that plus disease does not evolve suddenly, but rather the abnormal dilation and tortuosity of the posterior pole vessels progresses from normal appearing vessels to the severe form designated plus disease. The spectrum between clearly normal posterior pole vessels and plus disease is designated "pre-plus disease" in which the arterioles and veins of the posterior pole are more dilated (arterioles) and tortuous (veins) than normal, but that abnormality is insufficient to be called plus disease. Such vascular abnormalities in the posterior pole may be quite important since digital imaging of the posterior pole is generally much easier to accomplish and quantification of images may ultimately define whether an eye has a high likelihood of developing serious disease. The presence of pre-plus disease may alert the clinician to increase frequency of screening or to examine the periphery again for serious ROP. The presence of pre-plus disease can be noted beside the stage, e.g. stage 2 with pre-plus disease.

Aggressive posterior retinopathy of prematurity

In the smallest, most premature babies, an uncommon form of ROP, "aggressive posterior ROP" or AP-ROP, may not follow the usual time course and may progress very rapidly to retinal detachment. AP-ROP is characterized by its posterior location and the prominence of plus disease with the retinopathy itself rather unimpressive. (Figure 13) AP-ROP occurs most frequently within zone I, but may be seen in posterior zone II, but the key to making the diagnosis of AP-ROP is the prominent posterior vessels abnormality that is out of proportion to the extent and severity of the peripheral retinopathy. AR-ROP almost always is a circumferential retinopathy. Due to the extensive vascular changes, distinguishing between arterioles and veins is usually quite difficult in AP-ROP. Hemorrhage may occur at the junction between the vascular and avascular retina.

The retinopathy may be observed to progress through the stages of ROP and may appear as a "deceptively featureless" neovascular network at the junction of vascular and avascular retina. (Figure 14) Unless the examiner is attuned to the importance of the posterior vascular changes, AP-ROP might easily be overlooked.

Resolution of ROP

In general, Stages 1 and 2 regress without obvious sequelae while higher stages usually lead to some degree of retinal scarring. These changes include both vascular and retinal abnormalities and can occur in the posterior pole region or in the retinal periphery

ICROP Committee: International classification of retinopathy of prematurity. Arch Ophthalmol 102:1130-1134, 1984.

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RATES OF SEVERE RETINOPATHY OF PREMATURE IN RIO DE JANEIRO, BRAZIL: FINDINGS FROM A 2 YEAR PROSPECTIVE STUDY IN 6 GOVERNMENTAL NEONATAL INTENSIVE CARE UNITS

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Background: There is wide variation in the incidence of severe retinopathy of prematurity (ROP) in different studies. Possible explanations that will be explored include variation in case mix, neonatal outcomes and/or the levels of neonatal care. The overall aim of our ongoing study is to determine optimal screening criteria for neonatal units in Rio de Janeiro, Brazil. Data presented in this paper relate to the incidence and severity of retinopathy of prematurity (ROP) in infants with birth weights (BW) < 1,500g examined by one observer in 6 governmental neonatal intensive care units between January 2004 and April 2006.

Methods: Prospective observational study of babies with birth weight <1501 g. All babies were examined according to a standard protocol. All data were recorded on a standardised recording sheet, and entered into a database. Data on the number of babies admitted with BWs <1,501g, and their survival rates were also recorded, as were the number of trained nurses per incubator.

Results: Rates of ROP needing treatment (i.e. prethreshold type 1 or worse) varied from 3.7% to 12.5%. The mean BW of affected babies ranged from 860g to 1126g, and mean gestational age ranged from 28 to 30 weeks. Survival rates ranged from 53% to 90%. The number of trained nurses/incubator ranged from 1:2 to 1/17.

Conclusions: Rates of ROP vary between units, as do neonatal outcomes. Possible reasons will be discussed.

THE PREVALENCE OF RETINOPATHY OF PREMATURE IN VERY LOW BIRTH WEIGHT NEWBORN INFANTS IN VERONA (1999-2005)

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Objective: To evaluate the incidence of retinopathy of prematurity and the risk factors affecting very low birth weight infants at a neonatal intensive care unit. **METHODS:** A cross-sectional study investigating all newborn infants with birth weights $< \text{or} = 1,500 \text{ g}$ and/or gestational ages $< \text{or} = 32$ weeks, admitted to the NICU at the Universital Hospital GB Rossi Verona, from January 1999 to December 2005. Patients underwent indirect binocular ophthalmoscopy of the fundus from four to six weeks postpartum. Infants who progressed to threshold disease were given laser therapy.

Results: Four hundred and sixty four newborn infants were studied. Two hundred eighty four patients were not diagnosed with retinopathy of prematurity, one hundred eighty had retinopathy of prematurity. The incidence of retinopathy of prematurity was 39% affecting one hundred eighty newborn infants (180/464), and the incidence of retinopathy of prematurity progressing to threshold disease was 19%, affecting thirty four patients (34/180). Retinopathy of prematurity was confirmed in 66% of the infants born at gestational ages of less than 28 weeks or with birth weights below 1,000 g. Gestational age and birth weight were significantly lower among patients with retinopathy of prematurity than among those without.

Conclusions: Although the results of this study demonstrate that the observed incidence was similar to that described in literature, this ROP frequency remains elevated among very low birth weight infants. The development of retinopathy of prematurity was inversely proportional to weight and gestational age at birth.

RETINOPATHY OF PREMATURITY IN SOUTH AFRICA: A SITUATION ANALYSIS OF NEEDS, RESOURCES AND REQUIREMENTS FOR SCREENING PROGRAMS

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Retinopathy of prematurity is a major cause of childhood blindness in middle-income countries. A study of neonatal intensive care units in South Africa was done to look at the survival of babies at risk, nursery practices, and the findings of ROP screening programmes, in order to estimate the likely magnitude of the problem of ROP. A sample of neonatal nurseries, private and public, was visited to study the infrastructure, staffing and policies and practices regarding ventilation and oxygen administration. Data was also collected on ROP screening policies, practices, and results of screening. Data on prematurity rates and survival was ascertained from published literature, reports and the nurseries visited. Infrastructure in South Africa is adequate to provide care for babies above 1000g and over 90% of them survive. 91.4% of very low birth weight babies (1000-1500 g) survive and 91.3% of all low birth weight babies (<2500 g). Extremely low birth weight babies below 1000 g are not routinely ventilated in the public sector but 53.4% still survive in secondary and tertiary care units.

Continuous oxygen saturation monitoring is done on most ventilated babies in intensive care units, but babies on other modes of oxygen delivery in high care units are often not monitored continuously. ROP screening was being done in a minority (4/14) of public sector units visited. In hospitals where the results of screening are available sight threatening ROP is low (0.6-2.9%) as also the over all incidence of ROP (any stage), 6.7% - 25.6%. Most babies needing treatment have been below 1200 grams.

A model was made to calculate the likely numbers of children with ROP blindness. ROP is likely to be 4-10% of the blindness in the population under 15 and 10 -30% of blindness in under-fives at present. It is likely to increase as neonatal care becomes available to the majority of the population. Screening programmes need to be instituted in all institutions with individualized screening guidelines. For this an increase in trained manpower is required.

RETINOPATHY OF PREMATURITY IN INFANTS WITH EXTREMELY LOW BODY WEIGHT AT BIRTH

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The improvement of neonatal care in developed countries has led to a progressive decrease of the death rate of premature infants with extremely low birth weight (ELBW). It is generally known that the lower the birth weight and the shorter the gestational age, the higher is the risk of retinopathy of prematurity (ROP). Therefore, we consider it necessary to analyze the frequency, particular features of ROP clinical course and evaluate the efficacy of laser treatment of active retinopathy in infants with body weight at birth less than 1000 g.

The study was realized in the first-rate Russian center of neonatology, where 60% of infants born prematurely in our city are nursed to health, and the survival index for premature infants with ELBW is high (78-82%) and stable.

From January, 2002 to December, 2005 under our supervision were 119 infants with weight at birth from 660 g to 999 g and gestational age from 24 to 29 weeks. The first signs of the disease develop at the age of 32-34 weeks PCA, therefore we performed the first ophthalmic examination of at-risk infants no sooner than at the 33rd week PCA and continued to monitor them until the completion of retinal vascularization, i.e. up to 40-42 weeks.

The examination included: direct and indirect binocular ophthalmoscopy with 20 and 30 D lenses. Satisfactory mydriasis was reached in 40 minutes after twice, with 15-minute interval repeated instillation of short-acting mydriatics - 0.5-1% Mydriacyl (Tropicamide). But in cases of steady pupillary rigidity, 0.1% atropine solution was used.

From the beginning of 2006, in the ROP diagnosis we use a retinal pediatric camera - RetCamII. Our own experience allows us to establish that this technology considerably reduces the time of retinopathy of prematurity diagnosis, excludes subjective interpretation of the state of the retina in an infant.

In the investigated group, retinopathy was found in 75 (63%) infants and distributed according to the degree of disease severity according to the International ROP Classification. Initial disease stages (I,II) were found in 48 infants (64%) with subsequent spontaneous regression without obvious abnormal changes on the eye fundus. In 27 cases (36%), ROP progressed to the III stage, including progression up to threshold stage in 23 infants (30.6%), what turned out to be an indication to carry out retinal photocoagulation. Mean body weight at birth of operated infants was 894 ± 201 g, gestational age 26 ± 2 weeks.

The efficacy of this treatment was 78.3%. But in 5 infants, that made 6.7% of the total number of infants with ROP, the disease had unfavorable outcomes - further progression up to terminal stages (IV-V).

Thus, low frequency (6.7%) of ROP unfavorable outcomes in the group of infants with ELBW was caused by high level of neonatal care, rendered in our center. It is one of the reserves for infant blindness prevention provided the perfection of ophthalmological care to this category of children.

CAN OPHTHALMOLOGISTS PREVENT SEVERE ROP AND VISUAL IMPAIRMENT? ROP IN PRETERM INFANTS BORN IN MATERNITY HOSPITAL LJUBLJANA, SLOVENIA - A COMPARISON OF TWO TIME PERIODS (1990-1999 VS. 2000-2004)

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Purpose: to compare the rate of ophthalmic morbidity in preterm babies born in tertiary perinatal centre in two time periods (1990-1999 vs. 2000-2004), especially with relation to risk factors and neonatal intensive care measures.

Methods: Group 1 consisted of 759 preterm infants with birth weight < 1500 g and gestational age < 31 weeks born in MH Ljubljana, Slovenia between January 1990 and December 1999. Group 2 were preterm babies with the same birth weight and gestational age limits, born in the same MH between January 2000 and December 2004. All were examined according to contemporary paediatric ophthalmologic recommendations. In group 1, 594 children with high neonatal risk factors for ROP were followed-up 7-16 years and 198 children from group 2 at least 1.5-5 years, to determine ophthalmic outcome. Influence of gender, gestational age, birth weight, diseases (respiratory distress syndrome, bronchopulmonary dysplasia, systemic infection, severe intraventricular haemorrhage, hyperbilirubinaemia), and procedures (artificial ventilation, blood transfusion) on ROP and visual impairment were analysed. The results between both groups of children were compared, especially regarding neonatal care of restrictive oxygen policy.

Results: In group 1, 7 infants (all with GA < 28 weeks and BW < 1000 g), altogether 0.95% developed threshold ROP and needed retinal cryo or laser therapy. Three of the treated babies (2 with GA < 26 weeks and BW < 600 g, 1 with GA 27 weeks and BW 760 g) are legally blind. All of them had neonatal sepsis. Another baby (GA 28 weeks, BW 1580 g) also blinded, due to congenital toxoplasmosis, treated postnatally, but not ROP. In 5.6% babies prethreshold ROP was observed. 2.1% of followed-up children had cortical visual impairment (b.c.v.a. =, < 0.3) with optic nerve atrophy. Higher refractive error, predominantly myopia was found in 5.9% children, 12.7% children were strabismic. Group 2 children had no threshold ROP and none of them needed treatment. Prethreshold ROP was diagnosed in 2.6% of babies (GA 26.1 weeks +, - 1.79 and BW 752 g +, - 197). None of them had severe visual impairment due to ROP per se, but 2% of followed-up children were visually impaired because of visual pathway damage with optic disc pallor. Higher refractive error, and/or strabismus were found in 13.6% of group 2 children. In group 1 low gestational age and low birth weight, need for artificial ventilation, septicaemia, at least one exchange transfusion have shown significant correlation with ROP. Group 2 children with ROP were also born with significantly lower GA and BW, needed more transfusions, but other associated pathology did not show statistically important difference.

Conclusions: Ophthalmologists must continue with refined ROP screening and treatment regimen and take care of any ophthalmic factors causing visual impairment. Team approach with neonatologists and individualised intensive neonatal care tends to reduce the risk of ROP and visual impairment.

THE INCIDENCE OF RETINOPATHY OF PREMATURITY IN BEIJING

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Objective: Since 'the guideline of prevention and treatment of ROP' was issued in China in 2004 little was known about the incidence of ROP in China. This study is designed to determine the incidence of retinopathy of prematurity (ROP) among preterm infants in Beijing

Methods: Neonates with birth body weight (BW) \leq 2000 gm or gestational age (GA) \leq 34 weeks who admitted to 6 neonatal intensive care units in Beijing during 2005 were enrolled and underwent ophthalmologic examination. Ophthalmologic examinations were started at 4 weeks and followed until resolution. The international classification of ROP was used to describe various stages of ROP.

Results: Of the neonates with \leq 2000 g birth weight or \leq 34 weeks gestational age, admitted to 6 neonatal intensive care units, 91% (732/804) survived. Retinopathy of prematurity was detected in 10.8% of 639 neonates who had eye examinations. 3.6% of infants were treated for threshold ROP or type 1 ROP. The mean gestational age and birth weight of treated infants were 1273.91 ± 263.53 g and 30.26 ± 2.14 w respectively. 17% of treat infants were with gestational age greater than 30 weeks and birth weight larger than 1500g. There was significant difference in birth body weight, gestational age between ROP and Non-ROP groups.

EVALUATION FOR MATERNAL RISK FACTORS FOR RETINOPATHY OF PREMATURITY IN PREMATURE BABIES BORN AT MATERNIDADE DARCY VARGAS DURING THE PERIOD 1992 - 1999 - JOINVILLE - SC

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Objectives: Identify the maternal factors that cause a predisposition to Retinopathy of Prematurity in mothers and evaluate the interdependence between the maternal factors identified.

Method: At the Maternity Darcy Vargas, during the period 1992 - 1999, 286 premature babies and 269 mothers were selected. In a preliminary study that served as a basis for this study, group 1 was separated comprising of premature babies with ROP and group 2 comprised of premature babies with ROP and an evaluation of the factors related to them was carried out. In this study, the maternal factors and their correlation with ROP were analyzed. Next, an analysis of the controlled maternal factors most significant in premature babies was carried out. The results were evaluated statistically using the Qui-Squared or Fisher Exact tests. Margin of error considered was 5%.

Results: The factors most involved with ROP in relation to mothers were: Smoking ($p=0,0015$), multiple pregnancy ($p=0,0027$) and educational level ($p=0,0049$). Multiple pregnancies presented an interdependency with serious infection in the premature baby ($p=0,0146$). It did not present this interdependency with any other significant factor in the premature baby. Smoking during pregnancy did not present any interdependency with any other significant factor of the premature baby.

Conclusion: The maternal factors of greatest statistical significance in the development of ROP was: smoking, level of education and the number of conceptions. Smoking during pregnancy is the most significant independent factor in this study.

RETINOPATHY OF PREMATURITY INCIDENCE DATA IN KAUNAS MEDICINE UNIVERSITY HOSPITAL IN 1999 - 2004

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Purpose: The aim of this study was to analyze the results of screening for retinopathy of prematurity (ROP) in Kaunas Medicine University Hospital between 1999 and 2004.

Methods: Between 1999 and 2004, 3754 infants with a gestational age <36 weeks and birth weight less than 2500 g were examined. All prematures were followed-up until full retinal vascularization. Cryocoagulation treatment was performed after threshold was reached, according to Cryo-ROP study. All infants after cryocoagulation treatment were followed-up until stable retinal situation.

Results: There were 68 ROP cases in 1999 (9.7% from all prematures with birth weight less than 2500g), 64 in 2000 (9.1%), 48 in 2001 (8.1%), 37 in 2002 (6.1%), 29 in 2003 (4.8%), and 14 in 2004 (2.6%). The ROP incidence between lowest birth weight (<999 g) infants was 33.3% in 1999, 47.6% in 2000, 42.3% in 2001, 25.4% in 2002, 29.6% in 2003, and 5.6% in 2004. ROP incidence in birth weight 1000 - 1499 g group was 29.5% in 1999, 24.8% in 2000, 27.5% in 2001, 23.5% in 2002, 12.9% in 2003 and 13.1% in 2004. ROP incidence in birth weight >1500 g group was 1.8% in 1999, 1.3% in 2000, 0.2% in 2001, 1.1% in 2002, 0.2% in 2003 and none in 2004. ROP incidence in gestational age 22 - 27 weeks group was 34.6% in 1999, 42.0% in 2000, 26.0% in 2001, 24.7% in 2002, 19.8% in 2003, and 10% in 2004. ROP incidence in gestational age 28 - 31 weeks group was 19.6% in 1999, 15.7% in 2000, 17.0% in 2001, 11.9% in 2002, 10.1% in 2003, and 5.8% in 2004. ROP incidence in gestational age 32 - 36 weeks group was 0.2% in 1999, 0.4% in 2000, 0.1% in 2001, 0.2% in 2002, and no cases in 2003 - 2004. Cryocoagulation treatment was performed in 7 ROP cases in 1999 (10.3% from all ROP cases), 14 in 2000 (21.9%), 3 in 2001 (6.25%), 8 in 2002 (16.2%), 3 in 2003 (10.3%), and 4 in 2004 (28.6%).

Conclusions:

1. The rate of incidence of ROP was constantly decreasing in a period of last 5 years, showing improved quality of neonatology care in Kaunas Medicine University Hospital.
2. The mean incidence of ROP is similar to other center data.
3. Our data give clues to consider revising screening criteria in our hospital, excluding from screening infants with gestational age more than 32 weeks.

SCREENING FOR RETINOPATHY OF PREMATURITY AT CIPTO MANGUNKUSUMO HOSPITAL, JAKARTA, INDONESIA - A PRELIMINARY REPORT

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Background: To report the incidence of retinopathy of prematurity (ROP) at Cipto Mangunkusumo Hospital, Indonesia, and its relation to several risk factors. The results of treatment are also reported.

Materials and Methods: A hospital-based prospective-cohort study in 33 infants in the neonatology ward Cipto Mangunkusumo Hospital, Jakarta, Indonesia, who were referred for ROP screening from December 2003 to December 2004 was performed. Risk factors such as gestational age (GA) at birth ≤ 32 weeks, birth weight (BW) ≤ 1500 g, duration of oxygen (O₂) therapy of more than 7 days, gender, birth status, presence of clinical sepsis, respiratory distress syndrome (RDS), apnea, asphyxia, and maternal pre-eclampsia/eclampsia were analyzed using Chi-square test and multivariate analysis.

Results: Of the total 33 cases, ROP at any stage of disease was found in 30.3% of cases. Infants with ROP were significantly smaller (mean \pm SD of 1397 ± 153.5 g vs. 1610 ± 218.8 g, $p=0.009$), but not significantly younger (mean \pm SD of 31.7 ± 2 weeks vs. 33.3 ± 2 weeks, $p=0.058$) than infants without ROP. Logistic regression showed that low birth weight was not a significant risk-factor for ROP. Asphyxia was found to be the only significant risk factor for the occurrence of ROP ($p=0.021$, OR=13,525). Laser photocoagulation or cryotherapy was performed in 2 out of 3 threshold ROP cases, but the outcomes were still unsatisfactory.

Conclusions: Our results is similar to those reported from previous studies in other developing countries, although in this study young gestational age and low birth weight were not associated with the risk of ROP. Further studies in a larger sample size is required, to confirm these findings and to establish effective screening guidelines.

ANALYSIS OF MATERNAL AND NEONATAL RISK FACTORS FOR RETINOPATHY OF PREMATURITY(ROP) IN 88 PRETERM BABIES IN A TERTIARY HOSPITAL IN SOUTH INDIA

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Aim: To determine the maternal and neonatal risk factors in the development of ROP in premature infants and to study the effect of Laser on threshold ROP

Materials and Methods: Eighty-eight babies who were born <36week gestational age were enrolled into this prospective study. The infants were analyzed for maternal risk factors like Diabetes mellitus(DM) Pregnancy Induced Hypertension (PIH), complications during delivery. Neonatal risk factors like gestational age, birth weight, oxygen supplementation, apnoea, sepsis, use of formula feeds and turbulent neonatal period were also recorded.

All babies underwent complete ophthalmologic examination with scleral depression at 4 weeks after birth or at the time of discharge from neonatal intensive care unit (NICU), whichever was earlier. Babies with threshold ROP were treated with laser and those that progressed to stage IV and V were treated surgically.

Results: The incidence of ROP in our study population was 19 out of 88 (21.59%) The average gestational age of ROP baby was 29.8week. The average gestational age of non-ROP baby was 32.8 weeks. The average birth weight of ROP baby was 1443.6gm. The average birth weight of non-ROP baby was 1751.769 gm. Of the 19 babies with ROP 17 had a turbulent neonatal period. Two babies who were exclusively formula fed developed ROP.

Of the 19 babies with ROP 11 progressed to threshold ROP. Ten of these babies underwent laser therapy and 8 regressed well. Two babies progressed to stage V ROP and underwent vitreous surgery.

Conclusion: The incidence of ROP in developing countries like India is quite high 21.59% in our study.

The development of ROP is significantly increased when there are multiple risk factors.

No important maternal risk factors were identified in our study.

Laser was effective in regressing ROP.

Breast milk may have a protective effect on the developing retina.

FREQUENCY AND RISK FACTOR ANALYSIS FOR RETINOPATHY OF PREMATURITY: A MULTIVARIATE STATISTICAL ANALYSIS

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Purpose: To report the frequency and postnatal risk factors of retinopathy of prematurity (ROP) at a tertiary level hospital, Ankara, Turkey.

Methods: Data from the medical records of neonates with a gestational age ≤ 34 weeks and who were examined for ROP between March 1999 and September 2005 analyzed for frequency and postnatal risk factors of ROP. Logistic regression analysis was used to determine the predictors on the development of ROP.

Results: The frequency of ROP was 37.1% for any stage and 7.2% for stage 3 or greater. Of the neonates with ROP, 80.5% had mild (64 stage 1, 31 stage 2) and 19.5% had severe ROP (23 stage 3 or greater). Nineteen neonates (16.1%) developed threshold ROP. There was no statistically significant difference between groups for gender and mother's age ($p=0.56$, $p=0.90$; respectively). Presence of oxygen therapy, mechanical ventilation, respiratory distress syndrome, blood transfusion, sepsis, and multiple birth were found to be higher in neonates with ROP in addition to birth weight and gestational age. However, only oxygen therapy, gestational age ≤ 32 weeks, birth weight < 1250 g, and sepsis were determined as the independent risk factors in multivariate analysis.

Conclusion: Gestational age ≤ 32 weeks, birth weight < 1250 g, sepsis, and oxygen therapy are independent risk factors for ROP. Screening should be intensified on the neonates with these risk factors.

RETINOPATHY OF PREMATURITY; INCIDENCE AND RISK FACTORS IN IRAN

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Purpose: To determine the incidence of ROP and to evaluate possible neonatal risk factors in Iran.

Materials and Methods: ROP was screened in 186 neonates with gestation age (GA) \leq 32 weeks or birth weight (BW) \leq 1500 grams referred to Farabi Eye Hospital , a tertiary care center in Tehran, during 2004-2006.

Results: ROP was present in 56(30.1%) neonates.(threshold in 23.1%). Mean GA and mean BW was 30 weeks and 1385 g respectively. Univariate analysis revealed an association between ROP and respiratory distress syndrome (RDS), bronchopulmonary dysplasia BPD, transfusion and oxygen therapy.

In a multivariate regression analysis, however, only gestational age, birth weight, BPD and phototherapy were significantly associated with ROP.

Conclusion: ROP incidence seems to be increasing in Iran. This may be in part due to advances in NICU equipment and surveillance that leads to survival of very premature neonates and subsequently higher incidence of ROP. Prematurity per se seems to be the strongest risk factor for ROP in Iran.

COMPARISON OF THRESHOLD ROP IN SOUTHERN INDIA AND SOUTHERN CALIFORNIA

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Purpose: With improvement in Cardio- pulmonary support of the very premature neonate, we have witness a rising incidence of aggressive zone 1 disease in the micro-preemie. Some also manifest a significant delayed of retinal vascular maturation and a new ROP variant of predominantly zone III dry and fibrotic traction, also known as smoldering ROP. In developing nations, the incidence of ROP is also on the rise but often differs in clinical features. We explore clinical aspects of ROP occurring in two disparate populations.

Methods: Retrospective case- control study. We compared the clinical features and photographs of two consecutive series 50 neonates who reached threshold ROP and were managed at two major pediatric retina referral centers , Childrens hospital Los Angeles and the Aravind Eye Hospital of Coimbatore, India. We compared gestational age, birth weight, age at threshold, severity of plus, location and extent of neovascularisation, ocular and systemic co-morbidities, need for surgical procedures including peripheral ablation and vitreo- retinal surgery, anatomic outcome, and qualitative features of the retinal vascular configuration as seen on RetCam imaging and fundus drawings.

Results: For preemies reaching threshold, the mean gestational age in Los Angeles was 24.5 weeks and mean birth weight was 766 grams, as opposed to 33.8 weeks and 1521 grams in Coimbatore. Threshold tended to occur around 37 weeks post conceptual age in both groups, with a mean post -natal age of 12 weeks in Los Angeles group and 4 weeks in Coimbatore. Neonates in Southern California more often presented with Zone 2 extra-retinal neovascularisation or Zone 1 flat neovascularisation. Those in Southern India more often manifested plus disease with arterio- venous loops and shunts with capillary drop out but less severe neovascularisation. They also tended to have less weight gain over the first 12 weeks of life, especially during the 2 weeks preceding the diagnosis of threshold. Both groups had patients requiring more than one procedure, with repeat laser occurring more often in the Coimbatore group and lens - sparing vitrectomy occurring more often in the Los Angeles group.

Conclusions: We postulate that nutritional and genetic factors as well as neonatal intensive care unit practice patterns may account for part of this difference in ROP presentation.

THE CONJUNCTIVAL TISSUE GAS MONITOR - A METHOD TO REDUCE RETINOPATHY OF PREMATURITY?

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Background: If we had better control of the concentration of oxygen and other gases reaching the eye, could we reduce the frequency and/or severity of Retinopathy of Prematurity? Two of the top 3 causes of pediatric blindness in developed countries are somewhat oxygen related - retinopathy of prematurity and hypoxic brain damage. In 1983, Isenberg and Shoemaker published the first human trial of conjunctival monitoring (Am. J. Ophthalmol 95: 803-806) measuring only oxygen. Many studies were subsequently conducted on this device, including the effect of Phenylephrine eye drops, systemic hypertension, smoking, sickle cell disease, monitoring critically ill helicopter transported trauma victims, estimating cerebral blood flow, and diabetes. We studied the oxygen monitor in 10 neonates for up to 2 hours and found a strong correlation between conjunctival O₂ and pulse oximetry ($p < 0.001$) (J Perinatology 22:46-49, 2002).

Methods: The new Conjunctival Tissue Blood Gas Monitor was developed which is less invasive and measures all blood (tissue) gas parameters: oxygen, carbon dioxide, pH, bicarbonate, and temperature. It was tested in animals and adult humans.

Results: Animal studies: Dogs, pigs, and sheep were studied in various physiological conditions, including bradycardia, tachycardia, shock, and ECMO (Extra Corporeal Membrane Oxygenation). The conjunctival values paralleled systemic changes.

Human studies: Twelve adult patients were studied with 10 undergoing cardiac bypass. The sensor was applied from 4 to 6 hours or to end of case. A total of 70 hours of monitoring was performed with no evidence of any eye injury (2,356 data points). Conjunctival pH was stable and measured between 7.06 and 7.10 over all phases of bypass. Conjunctival CO₂ increased during bypass by 4.3 mm Hg (13%) and then reversed off bypass ($P < 0.001$ as a quadratic function). During bypass, loss of pulsatile blood flow to the brain (relative hypoperfusion) caused increased CO₂. After bypass, better perfusion forced accumulated CO₂ from the tissue bed. Conjunctival oxygen decreased during bypass from 79.5 mm Hg to 31.3 mm Hg ($p < 0.001$). There was much variation due to manipulation of heart, aortic cross clamping, and blood transfusion. The lowest O₂ values occurred in a patient who exhibited neurological deficits following surgery. The conjunctival temperature cooled during bypass to $33.0^{\circ}\text{C} + 0.3$ and then warmed to $36.0^{\circ} + 0.1$ off bypass as a quadratic function ($p < 0.001$).

Conclusions: The conjunctival blood gas monitor detected physiologic changes during animal testing, and then during different phases of human cardiac bypass. By mixed model analysis, pH remained constant, CO₂ and temperature assumed a quadratic function, while oxygen decreased linearly with time. The values were stable within each phase. The monitor was found to be safe and non-invasive. Fiberoptic technology was found to produce a very rapid (< 6 seconds) response time and correlated to other perfusion markers.

The device holds great promise to reveal tissue blood gases, especially oxygen, of the retina by measuring non-invasively from the conjunctiva. This may allow better control of these gases by modulating external delivery. Further testing in premature neonates is warranted.

Lecture 3

The Next Level In ROP Care: an Analysis and Response to Failures Among Infants Receiving Ideal ROP Care In The Chicago Area



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This paper reviews the variety of failures after standard laser treatment provided by very experienced observers and surgeons using standard screening and monitoring protocols in the Chicago region. Failures result from ocular hypotony, progression despite laser treatment, unexpected ROP associated with dysmorphia, and late reactivation. Particular techniques to reduce failures will be discussed. In particular, our approach for identification and treatment of failures will be presented as well as a discussion of our recent experience with anti-VEGF therapy and surgery.

Lecture 4

Pharmacologic Management Of ROP



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The effect of VEGF in pediatric retinal vascular disease is most well known and appreciated in retinopathy of prematurity. In retinopathy of prematurity, the act of premature birth creates an environment with increased VEGF that results in retinal neovascularization, increased permeability, and reduction in apoptotic involution of the tunica vasculosa lentis and hyaloid system, contributing to the cell bolus that leads to tractional retinal detachment.

The treatment of retinopathy of prematurity until recently has been centered on destruction of avascular retina, which leads to a hypoxic state and increases VEGF production. With the advent of anti-VEGF pharmacologic therapy, testing in regards to treatment of retinopathy of prematurity has been undertaken. Measurement of vitreous VEGF levels in 27 eyes with vascularly active ROP, vascularly inactive ROP, and congenital cataract were used as controls. The dosing, the treatment patterns, and results will be presented.

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RETINOPATHY OF PREMATURITY: A NEW TREATMENT

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Methods: We retrospectively analysed three patients with retinopathy of prematurity: two with stage 3, zone II, plus disease and one with stage 3, zone I, plus disease, unresponsive to laser; were treated with at least one intravitreal injection of bevacizumab 0,75 mg in 0,03 ml, in the worst eye. The second eye was treated with laser photocoagulation. These eyes were clinically controlled with indirect ophthalmoscope examination at baseline and follow-up visits.

Results: All injected eyes showed rapid regression of the tunica vasculosa lentis, engorgement of iris vessels and disappearance of iris rigidity. Also plus disease along with ROP began to regress. There were no systemic or local complications secondary to the injection.

Comments: The treatment of two eyes with retinopathy of prematurity, stage 3, zone II and one eye with stage 3, Zone I, not responsive to laser, all of them with plus disease, iris vessels dilatation and persistence of tunica vasculosa lentis, did not reveal any short-term safety concerns. Intravitreal bevacizumab resulted in a dramatically regression of the tunica vasculosa lentis, of the plus disease and of the retinal neovascularization. The number of patients and complexity of this pathology, in this pilot study was very limited and the follow-up is too short to make any specific treatment recommendation, but the very favourable short-term results, without any apparent complication, suggest further studies are needed to prove the benefit of this therapy in ROP, alone or associate with a laser photocoagulation.

Lecture 5

VEGF-Targeted Therapies For ROP



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The initial, superficial layer of the dog retinal vasculature forms by vasculogenesis, formation of blood vessels by differentiation and aggregation of vascular precursors or angioblasts. This is similar to the process by which the initial retinal vasculature develops in fetal human eye. When the one-day old (postnatal day 1 or P1) dog is exposed to 100% O₂ for four days, vasculogenesis ceases and vaso-obliteration or destruction of the developing retinal vasculature occurs, the first phase of retinopathy of prematurity (ROP). Overall, there is a 60% decrease in percent vascular area by the end of the four day exposure to hyperoxia and only large vascular channels appear to remain intact. When the animals are returned to room air, the vasoproliferative phase of oxygen-induced retinopathy (OIR) begins. By P21, retinal vessels in the posterior pole become tortuous and florid tufts of intravitreal neovascularization (NV) have formed. The NV persists to at least P45 resulting in tractional retinal folds, tented intravitreal vascularized membranes, and severe vitreous synechias. Therefore, the end stage of canine oxygen-induced retinopathy (OIR) shares many features with human ROP.

VEGF has been implicated in both retinal vasculogenesis and angiogenesis, as well as the pathological NV that occurs in OIR. We have investigated two reagents directed against VEGF that might be useful in treating OIR or ROP. The first is a chimeric antibody from ImClone Systems against VEGF receptor-2 (VEGFR-2). The antibody (150 or 300 ug) or nonimmune IgG were incorporated in ELVAX 40 slow release polymers, which were surgically implanted in vitreous of air control and hyperoxia-exposed animals at P6. Effect of treatment on both preretinal NV and retinal vasculature were analyzed at P21. Anti-VEGFR-2 pellets did not affect the vasculogenesis in air controls but significantly inhibited growth of preretinal NV. Unfortunately, the antibody also inhibited the regrowth of retinal blood vessels in OIR, resulting in a large avascular area in peripheral retina (McLeod et al. Invest. Ophthalmol. Vis. Sci. 2002;43:474-482).

The second agent evaluated was the VEGF Trap from Regeneron Pharmaceuticals, a receptor-based fusion protein that binds all isoforms of VEGF-A. VEGF Trap (5, 25, or 250 ug) was injected in one eye and human Fc control in the fellow eye of air control and oxygen-treated dogs on P6. In air controls, the density of the superficial vascular plexus was reduced in eyes injected with 25 or 250 ug VEGF Trap and the deep capillary network was absent, while the eyes that received the 5 ug dose were indistinguishable from control Fc injected eyes. In OIR animals, all eyes injected with VEGF Trap had significantly less preretinal neovascularization

than in Fc-injected fellow eyes, irrespective of the dose of Trap administered. The retinal vascular area was also significantly reduced in eyes injected with 25 and 250 ug of the Trap, while the 5 ug dose did not appear to inhibit revascularization of the retina.

In the context of OIR and ROP, the desired profile of an antiangiogenic inhibitor would be to inhibit pathologic NV, without altering developmental vasculogenesis or revascularization of the retina after hyperoxia-induced vaso-obliteration. Pharmacological inhibition of VEGF signaling appears to be a reasonable approach to treating ROP, in that both reagents tested inhibited formation of preretinal NV in the dog OIR model. However, the higher doses of VEGF Trap and both doses of anti-VEGFR-2 evaluated also inhibited revascularization of retina, resulting in a large avascular peripheral retina. In contrast, the lowest dose of VEGF Trap blocked intravitreal NV without appreciably affecting vasculogenesis, or retinal revascularization. Therefore, in considering the use of VEGF-targeting agents for the treatment of proliferative ROP, dose selection is likely to be a critical variable.

Lecture 6

Primary Prevention - Evidence From Clinical Trials



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Introduction:

Retinopathy of Prematurity (ROP) or Retrolental fibroplasia (RLF) first appeared in 1942 and was a frustrating mystery until 1953. The results of one of the first multicenter randomized trials done in pediatrics showed that the unmonitored use of prolonged oxygen increased the risk of vision loss from ROP(RLF). Since then, we have learned a great deal more from clinical trials in ROP.

Clinical Trials in Preventing ROP

- Oxygen and ROP
 - Early studies on liberal vs conservative use of oxygen
 - Transcutaneous monitoring to test vigorous vs routine oxygen monitoring
 - Retrospective Evidence of the effect of different oxygen saturation targets
- Light and ROP
 - Trials from the 1950s to the 1990s. Light is not the answer.
- Antioxidants and Others
 - Vitamin E
 - d-penicillamine
 - myo-Inositol

Clinical Trials in Treating ROP

- CYRO-Therapy: Testing

Peripheral ablation

The International Classification of ROP (ICROP)

- Laser-Therapy
 - Comparing lasertherapy and cryotherapy
- Oxygen Supplements
 - Can established ROP be treated with oxygen supplements?
- Early Treatment
 - Earlier treatment is better, but how many?

Where to Next? Potential Pitfalls and Promise in the use of anti-angiogenic agents

- The growing vasculature in the human eye
- Where vascular growth goes wrong in ROP
- Where to intervene? Do we dare?

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RETINOPATHY OF PREMATURITY: IS GENETIC PREDISPOSITION AN IMPORTANT RISK FACTOR?

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Background: Retinopathy of prematurity (ROP) is the leading cause of blindness among children in Poland. Not all ROP risk factors have been identified. Probably the most important in ROP development are: constriction of immature retinal vessels after birth due to relative (in comparison to the intrauterine life) or true hyperoxia, and new vessels formation induced by peripheral avascular part of the retina. Oxygen toxicity is connected with excessive formation of free radicals. One of the system involving in cleavage of free radicals is homocysteine-methionine system. Activity of the system is strongly depended on remethylation of homocysteine to methionine. The C(+677T) transition in the 5,10-methylenetetrahydrofolate reductase (MTHFR) gene changes enzyme activity and can potentially affects antioxidant function of the system.

In response to hypoxia, retinal cells produce vascular growth factors. Experimental data suggest that VEGF (vascular endothelial growth factor) and TGFβ-1 (transforming growth factor) are the most important factors inducing vascular growth in response to hypoxia.

Recently, factor such Insulin-like growth factor 1 (IGF-1) has been studied in pathogenesis of ROP and seems to be oxygen independent mediator involved in neovascularization of the retina. Several genetic polymorphisms of growth factors genes were identified, but their clinical significance is unclear.

Aim: Assessment of the genetic risk factors of ROP, particularly the analysis of the association of polymorphisms of VEGF, TGFβ-1, IGF-1 and MTHFR genes and the risk of proliferative ROP.

Method: 123 newborns with mean birthweight 1070g and mean gestational age 28.3 weeks were included into prospective study.

Molecular studies of TGFβ-1 (G(-800A), C(-509T), T(+10C), G(+25C)), VEGF (T(-460C) and G(+405C)) and MTHFR C(+677T) polymorphisms were performed with PCR-RFLP and RG-PCR methodology. The number of CA repetitions in promotor region and CT repetitions in the 2nd intron of IGF-1 gene were based on direct gene sequencing. The infants were divided into 2 groups: A) no ROP or ROP not requiring treatment (n=87) and B) ROP requiring laser or cryotherapy (n=36).

Results: The frequency of all TGFβ-1, IGF-1 and MTHFR polymorphisms were similar in both groups.

The frequency of VEGF -460 TT allele was insignificantly higher in the group B than in the group A (35 vs 24%; p=0,1). The frequency of VEGF +405CC allele was also insignificantly higher (14 vs 5%; p=0.07) in the group B.

VEGF -460TT/+405CC haplotype was more prevalent in the group B than in the group A (21 vs 2%; p=0.016).

Conclusion: Based on our data we can speculate that VEGF -460TT/+405CC haplotype state can be associated with the higher risk of progressive ROP.

HIGH BIRTH WEIGHT PREMATURE INFANTS WITH ROP

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Purpose: To bring to attention the possibility of ROP developing in High Birth Weight Premature neonates.

Methodology: Retrospective case note analysis.

Results:

Case 1. 31 week infant born to diabetic mother with anaemia and weighing 2320 gms was found to have stage 3, zone 2 ROP, which regressed spontaneously.

Case 2. 32 week neonate weighing 2110 gm born to a 32 year old mother was found to have developed stage 3 zone 3 ROP possibly secondary to fetal maternal transfusion syndrome. ROP regressed spontaneously.

Conclusions: Prolonged intra uterine ischemia due to any cause can lead to development of ROP and hence these premature infants should be screened for ROP irrespective of the birth weight.

ABERRANT PERICYTES AND SMOOTH MUSCLE CELLS UNDERLY PATHOGENESIS OF PLUS DISEASE IN RETINOPATHY OF PREMATURITY (ROP)

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Purpose: Dilated and tortuous vessels (plus disease) in ROP is a grim prognostic indicator of visual outcome. Our aim was to determine whether alterations in mural cells, pericytes and smooth muscle cells (SMCs), are associated with the pathogenesis of ROP, including Plus Disease.

Methods: Kittens were exposed to either 4 days (standard obliterative model) or 2 days (modified model) of hyperoxia resulting in vaso-obliteration or localised vessel regression respectively and returned to room air. The modified model more closely resembles human ROP. Desmin and α -smooth muscle actin (SMA) immunohistochemistry and lectin labelling were used to label mural cells and vessels. The desmin ensheathment ratio (DER), a quantitative measure of vessel stability was determined.

Results: In the neovasculature of the standard model and surviving vasculature of the modified model, radial arterioles and venules were dilated and SMCs attenuated. SMA expression on venules was decreased and the difference in desmin expression normally observed between arterioles and venules lost, indicating altered SMC differentiation. DER was reduced in both ROP models, consistent with highly unstable vascular plexuses, receptive to angiogenic and vascular regression signals.

Conclusion: Our results provide compelling evidence of significant changes in arteriolar and venular SMCs in both experimental models of ROP. The delayed differentiation and apparent dedifferentiation of SMCs during the hypoxic phases would result in impaired ability to regulate blood flow, contributing to the vaso-dilatation and tortuosity, hallmarks of Plus Disease. Vessel tortuosity was only seen in the non-obliterative model, suggesting that tortuosity may be due to increased capillary resistance resulting from capillary closure.

INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN-3 INHIBITS RETINOPATHY

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Our previous studies have demonstrated that low levels of serum insulin-like growth factor-1 (IGF-I) in children born preterm are strongly associated with retinopathy of prematurity (ROP). However in serum IGF-I is bound to IGF binding protein-3 (IGFBP-3). This article presents IGFBP-3 as a new modulator on vascular survival and re-growth both in the retina in the mouse model of oxygen-induced retinopathy and in a clinical study.

Methods: To evaluate the effect of high IGFBP-3 on vessel re-growth C57 Bl/6 mice were exposed to 75% oxygen (postnatal day (P)7- P12), then given 60g /d IGFBP-3 or vehicle (P12-P14). Retinas were isolated at P15 for isolation of total RNA or analysis of area of revascularization. To evaluate the effect of low IGFBP-3 on vessel re-growth IGFBP-3 null and wt sibling mice were exposed to oxygen P7-P12 and area of vessel re-growth evaluated at P17. Serum IGF-I was measured in IGFBP-3 null sibling mice. To evaluate the effect of IGFBP-3 on vessel loss with oxygen exposure IGFBP-3 null and wt sibling mice were exposed to oxygen from P7-P8 for 18 hours and retinas evaluated for vessel loss. Serum IGF-1 was measured in IGFBP-3+/+, IGFBP-3/, and IGFBP-3+/- mice. To investigate the possibility to translate these findings to human ROP we prospectively measured IGFBP-3 plasma levels weekly after birth and co-ordinately examined retinas in all premature infants born at gestational ages <32 weeks at high risk for ROP (n=79). For our studies, ROP stages 3> (n=13) were defined as proliferative ROP and ROP stage 0 (n=38) as no ROP.

Results: There was no difference in serum IGF-I levels between IGFBP-3+/+, IGFBP-3/, and IGFBP-3+/- mice. At P15 there was a 40% increase in vessel re-growth in C57Bl/6 mice treated with IGFBP-3 compared to vehicle control treated mice indicating that IGFBP-3 promotes vessel re-growth. At P17 there was a 31% decrease in retinal vessel re-growth ($P<0.005$) in the IGFBP-3/ compared to IGFBP-3+/+ mice indicating decreased vessel re-growth with decreased IGFBP-3, confirming the result with high IGFBP-3. IGFBP-3 treatment was associated with a 20% suppression of endothelial nitric oxide synthase (eNOS) mRNA expression in retina. At P 8 after oxygen exposure there was an IGFBP-3 dose dependent increase in survival with increasing IGFBP-3 in wtIGFBP-3+/- mice. In patients with proliferative ROP (n=13) the mean \pm SEM level of IGFBP-3 at 30-33 weeks postmenstrual age for infants with proliferative ROP was $802 \pm 66 \mu\text{g/L}$ and for infants with no ROP (n=38) was $974 \pm 41 \mu\text{g/L}$ indicating a significant difference between the three groups in 'mean IGFBP-3' at this time point ($p=0.03$).

Conclusions: IGFBP-3 appears to help prevent oxygen-induced vessel loss and to promote vascular re-growth after vascular destruction. In premature infants increased levels of IGFBP-3 are associated with reduced risk of proliferative retinopathy. The effect on vessel survival and re-growth is consistent with eNOS mRNA suppression. Treatment with IGFBP-3 in ROP or diabetes is consistent with promotion of retinal vessel survival and prevention of proliferative retinopathy.

RELATIONSHIP BETWEEN IGF-1 LEVELS AT 32 AND 34 WEEKS OF GESTATIONAL AGE AND THRESHOLD RETINOPATHY OF PREMATURITY STAGE

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Background: Recent data indicate that serum IGF-I levels in premature infants can predict the proliferative stage in retinopathy of prematurity (ROP).

Objective: Assess the changes in serum IGF-1 in premature infants between 32 and 34 weeks of gestational age and its relation with threshold ROP.

Material and Method: Between July 2005 and March 2006, 30 premature patients, gestational age (GA) < 32 weeks, who attended the Children's Hospital 'Sor Maria Ludovica' NICU, the Hospital 'General San Martin' and Hospital Espanol, La Plata, Argentina without ocular malformations and who survived and finished the screening for ROP were selected. IGF-1 serum value with DSL-5600 active Insulin-like Growth Factor -1 Coated tube IRMA Kit in ng/ml was measured at 32 and 34 weeks of GA. ROP stages were classified according to the International Classification ICROP. Babies were examined and treated following the same protocol. The management for oxygen-therapy was implemented according to the National Guidelines for O₂ saturation control to prematures (National Health Ministry, June 2004). Data on GA, birth weight (BW), Nervous Central System (NCS) damage, and ROP stage were recorded. This study was approved by the Ethics Committee of the Institute for Pediatric Development and Research; written consent was obtained from parents. The percentage of IGF-1 increase was recorded and analyzed by the Chi-square test and Yate's correction, if necessary.

Results: In all 30 patients BW ranged from 600 to 1.620 g (mean BW, 1.067g), GA ranged from 26 to 32 weeks (mean, 29 weeks), days of O₂ ranged from 2 to 64 (mean, 20 days), 12 presented normal NCS ultrasound. In the 6 patients with threshold ROP, mean BW and GA were 919g and 28.6 weeks, mean O₂ was 20.1 days, and CNS damage was present in 5. This patients showed a 7% IGF-1 increase between the first and second serum sample, whereas non-threshold patients (n=24) (mean BW, 1100 g; mean GA, 29.6 weeks, CNS damage 15/24; and mean O₂ days, 15.5) presented a 57% IGF-1 increase in the same period (p=0.03).

Conclusion: These results may suggest that the low increasing percent of serum IGF-I concentrations between 32 and 34 weeks of GA in prematures would be associated with later development of threshold ROP. Further studies would be needed to support this hypothesis.

MULTIFACTORIAL RISK FACTORS ENVIRONMENT FOR RETINOPATHY OF PREMATURITY

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Background. The advances in perinatal and neonatal care have contributed to the survival of immature infants who are in increased risk for developing of retinopathy of prematurity (ROP) as following visual disability and blindness from ROP. Mentioned status might be prevented with timely determined diagnosis, respectively due to the risk factors applied appropriate treatment for particular infant. The goal of our research to combine the optimal clinical and epidemiological markers for ROP risk tool creation.

Methods. The retrospective research was provided in Vilnius University Childrens hospital, centre of neonatology. Research combined examination of immature neonates epidemiological and clinical characteristics born in 2005 years and ROP protocols analysis. Multifactorial risk factors environment for ROP pathological process was created. Statistical data analysis modules were used for the data processing: cluster analysis method; Student t test; Pearson correlation coefficient; linear regression analysis. P values less than 0.05 were considered as statistically significant. Artificial neural networks were applied for classification purpose, i.e. neonate is at high risk for ROP development, moderate risk or low risk for ROP development.

Results. The age of onset of ROP was four to six weeks. The mean gestational age was 28.1 0.9 weeks (range 25-35 weeks) and the mean birth weight was 1250 214 g (range 780-2250 g). Infants at greatest risk of ROP were 1500 g or less at birth ($p < 0,001$), or 30 weeks gestational age or younger ($p < 0,05$). An inverse relationship existed between the incidence and severity of ROP and birth weight and gestational age ($r_1 = -0,8$; $r_2 = -0,7$; $p < 0,01$). Low Apgar scale rates positively associated with ROP stage accordingly high ROP risk level ($r_3 = 0,9$; $p < 0,001$). Delivery and pregnancy failure are higher ROP pattern as following infections and bleeding during delivery are the leading pathological status elevating ROP stage. Oxygen therapy persists in all ROP stages. Adjacent neonate pathologies range within moderate to high risk level for ROP development while infant heart and vascular pathologies overpass high risk level for ROP development ($p < 0,001$).

Conclusions. Upon artificial neural networks based tool has the potentiality to identify risk level for ROP development process with high sensitivity considering positive and negative predictive values. In perspective, this integrated approach could present potential of targeted treatment scheme creation for particular immature neonates.

EVALUATION OF FOVEAL MORPHOLOGY AND THICKNESS USING OPTICAL COHERENCE TOMOGRAPHY IN CHILDREN TREATED FOR RETINOPATHY OF PREMATURITY

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Objectives: To describe the foveal morphology and determine the foveal thickness of children treated for threshold retinopathy of prematurity {ROP} using optical coherence tomography {OCT3}. To compare the OCT3 findings with a normal group consisting of children with no history of prematurity or ROP, and a premature group consisting of children with a history of prematurity but no clinically significant ROP.

Design: A prospective longitudinal controlled clinical study.

Participants: A cohort of 19 infants treated with cryotherapy for threshold ROP between 1984 and 1995 by one of the authors {WES} was followed for at least 7 years.

Methods: OCT3 of the macula was performed including foveal morphology and measurement of foveal thickness and the outcomes compared with 2 groups: a normal group consisting of children with no history of prematurity or ROP, and a premature group consisting of children with a history of prematurity but no clinically significant ROP requiring treatment. In addition, the optic disc to fovea distance was measured using colour fundus photography.

Outcome Measures: Three primary outcome measures: foveal morphology, foveal thickness, and disc-fovea distance.

Results: The ROP and premature groups displayed an abnormal foveal morphology characterized by absence of the normal foveal depression and retention of the inner retinal layers at the fovea. The mean foveal thickness {combined OS/OD} in both the ROP group and the premature group was significantly increased, $234.62\mu\text{m}$ and $220.36\mu\text{m}$ respectively, compared with $156.18\mu\text{m}$ in the normal group {p value < 0.0001}. No statistical difference was found between the ROP group and the premature group { $234.62\mu\text{m}$ versus $220.36\mu\text{m}$ p value = 0.1262}. The mean optic disc-fovea distance in the ROP group measured 2.97 disc diameters {DD} compared with 2.25 DD in the normal group {p value 0.0332} and 2.053 in the premature group {p value 0.0094}, both results reaching statistical significance. Although the mean disc-fovea distance was decreased in the premature group {2.053DD} compared with the normal group {2.25 DD}, it was not significant.

Conclusions: OCT3 demonstrated absence of the normal foveal curvature with retention of the inner retinal layers at the fovea and significantly increased foveal thickness in both the ROP and premature groups compared with the normal group. The clinical significance of the absence of the foveal pit and increased foveal thickness should be interpreted in the context of the variable visual acuities achieved in the ROP group, which ranged from 6/5 to no perception of light. Normally, the foveal pit continues to deepen after birth until 15 months of age due to both the peripheral-ward migration of ganglion cells and neurons of the inner nuclear layer, and the central-ward migration of cones of the photoreceptor layer. However, in our cohort of ROP and premature children, OCT3 findings suggest an incomplete remodulation of the foveal micro-structure resulting in a degree of foveal hypoplasia in childhood. This is a unique finding not previously described.

SEVERE ROP AFTER MATERNAL USE OF ACE INHIBITORS DURING PREGNANCY - A CASE REPORT

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Background: In the renin-angiotensin system, angiotensin converting enzyme (ACE) converts angiotensin I to angiotensin II which elevates blood pressure through vasoconstriction and aldosterone mediated expansion of extra-cellular volume. Angiotensin II is also a growth factor, which stimulates the production of vascular endothelial growth factor (VEGF) and endothelial and vascular smooth muscle cell proliferation.

ACE inhibition is associated with a reduction in proliferative diabetic retinopathy and a role in the prevention of proliferative ROP has been suggested.

Treatment with ACE inhibitors during the second and third trimester is known to cause oligohydramnios, anuria, prolonged hypotension, intrauterine growth restriction, skull hypoplasia, pulmonary dysplasia and neonatal death. To our knowledge, no ocular side effects have been reported.

Case report: A 37 year old woman with a history of chemo- and radiotherapy-treated mediastinal B-cell lymphoma, who was diagnosed with dilated cardiomyopathy when 8 weeks pregnant with twins, was treated with ACE inhibition from gestational week (GW) 10 to 27 and with an angiotensin II receptor antagonist from GW 27 to GW 32 when two girls were delivered by caesarean section.

Both girls (birth weights 1545 g and 1475 g respectively) were anuric and needed peritoneal dialysis for several months and were treated for low blood pressure during the first weeks of life. Twin 2 developed intraventricular haemorrhage grade IV and hydrocephalus.

At the first eye examination at postmenstrual age 41(+5) weeks, both girls had pre-plus disease and retinal vasculature ending in zone II. They both developed proliferative ROP and were treated with laser and cryo-therapy. Twin 1 also had lens sparing vitrectomy. In her right eye ROP progressed to stage 5 and in her left to stage 4A. In twin 2, ROP regressed after treatment in her right eye where the optic disc was atrophic, while progression to stage 5 occurred in her left eye. At 7 months of age, twin 1 reacted to light but could not fix and follow. She had gross nystagmus. Twin 2 gave no reaction to visual stimuli and died shortly after.

Discussion: ROP is a two-stage disease with a first stage characterized by impaired retinal vascularisation and a second stage of uncontrolled proliferative vessel growth. ACE inhibition has been suggested as a treatment to prevent proliferative disease. The twins presented here were exposed to ACE inhibition during a period when growth of retinal vessels normally takes place to meet the demands of the maturing neurons, promoted by local hypoxia and production of VEGF. ACE inhibition down-regulates VEGF and both twins had impaired vascularisation of their retinas suggesting an important role for the renin-angiotensin system in the normal retinal vascularisation as well as in the development of ROP.

HAS ROP ANTENATAL RISK FACTORS?

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Background: Retinopathy of prematurity (ROP) is a disease affecting the formation of retinal blood vessels in the premature infant's retina. Retinopathy of prematurity occurs when there is the cessation of normal retinal vascularization.

Aim of the study - to present unusual case of retinopathy of prematurity like changes found 26 hours after the birth of premature infant.

Material and methods: Pathohistological examination of the two eyes of autopsied premature infant (GA - 31 weeks, BW - 1600 grams) was performed. Baby died 26 hours after the delivery. Mother was diabetic, treated with insulin for many years.

Results: Histological pictures of the peripheral retina are presented.

In the nasal retina spindle shaped cells, cystoid spaces surrounded by Müller's cells, were seen towards periphery. Neither spindle shaped cells nor cystoid spaces were found in vascular retina.

Two active zones in the nerve fibre layer in the temporal retina were seen:

1) thickening of the anterior (a vanguard retina) - proliferation of primitive spindle shaped cells,

2) a rearward zone with primitive endothelial cells.

Pathologic changes of retina corresponding to the stage I ROP were identified 26 hours after the premature birth.

Conclusion: We speculate that the development of ROP is determined not only by postnatal but also by certain antenatal factors.

THE EFFECT OF ANEMIA ON THE DEVELOPMENT AND PROGNOSIS OF RETINOPATHY OF PREMATURITY

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Anemia is common in the first three months of life of newborns and premature babies. There are very few studies about the effect of anemia on the incidence or severity of ROP in the literature, whereas blood transfusions are considered to be one of the main risk factors of ROP. Recently, anemia has been discussed as a potential etiological factor of ROP in relation to the decrease in the number of blood transfusions in premature infants.

The aim of this study is the evaluation of the influence of anemia on the development and prognosis of retinopathy of prematurity.

In retrospective study the average hemoglobin, hematocrit ratio and the amount of erythrocytes were analysed in 210 children.

This cohort was divided into four groups according to severity of ROP.

Group 0 - 60 children without retinopathy symptoms, average birth weight was 1091 ± 172 g.

Group I - 55 children with retinopathy not requiring treatment, average birth weight was 1055 ± 209 g.

Group II - 50 children with retinopathy where cryotherapy or diode laserotherapy were done according to classic International Classification of Retinopathy of Prematurity criteria. In this group retinal changes progressed slowly from stage to stage, with localisation in II or III zone, with 'mild' plus disease. Average birth weight was 1028 ± 216 g.

Group III - 45 children with severe and rapidly progressing retinopathy, with localisation in zone I, big, considerable arteriolar tortuosity and venous dilatation (severe plus disease in zone I), without stages I to II revealed during earlier ophtalmological examinations - cryotherapy or diode laserotherapy were done. Average birth weight was 1022 ± 197 g.

In the III group the average hemoglobin concentration, hematocrit ratio and amount of erythrocytes were significantly lower in comparison with the other groups. They were statistically lower during the first 28 days of life, from the 29th day of life to the end of observation, and calculated for the whole period of observation. The period of observation was statistically equal in groups I, II and III.

Conclusions: The low, average hemoglobin concentration, hematocrit ratio and amount of erythrocytes can be considered a risk factor for severe, bad prognostic retinopathy of prematurity.

ROP AND CARBON DIOXIDE TENSION

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Background: Retinopathy of prematurity (ROP) is a serious complication threatening vision of the child. The most important risk factor of ROP is premature birth, but other risk factors have been widely studied. As carbon dioxide tension (PCO₂) may have some effects on blood vessels, we determined to study the relationship of PCO₂ and ROP.

Methods: This was a prospective cohort study of infants under 34 weeks of gestation or under 1500 g birth weight that needed artificial ventilation in their first week of life. Daily mean, highest and lowest PCO₂ of each child were recorded for two weeks or till the neonate was extubated and an eye exam was performed between 4-6 weeks of life.

Results: Hypocapnia (PCO₂<35 mmHg) is a relevantly frequent event in ventilated preterm babies and 52% of our infants showed hypocapnia in their course of study. All stages of ROP were seen in 10 infants (19%), and stage 3, 4 ROP needing interventional therapies was seen in 2 (4%) infants. There was no significant relation between PCO₂ tension, sex, duration of ventilation, phototherapy and ROP incidence in our study.

Conclusion: As there was no association between high and low PCO₂ tensions and ROP, we recommend ventilating infants with more gentle techniques and allowing higher PCO₂s to reduce lung and brain injuries without affecting the eyes.

ADVANCED SpO₂ ALARM AND MONITORING SYSTEM FOR BETTER OXYGEN THERAPY IN NEONATOLOGY

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Background: The pathogenesis of Retinopathy of Prematurity in premature infants is related to the level and variation of arterial oxygen saturation. Oxygen saturation is measured with a pulse-oximeter (SpO₂). To prevent periods of low or high levels of SpO₂, the nursing staff manually adjusts the inspired fraction of oxygen (FiO₂) in the supplied air.

Automatic control of the FiO₂ may reduce the risk of disorders caused by low or high levels of SpO₂, as well as the number of false alarms and the workload of the nursing staff. Automatic FiO₂ control, however, is unsafe when the measured SpO₂ value is unreliable. Currently, no such controller is used in clinical practice. In this study, we made an inventory of problems occurring in automatic FiO₂ control and investigated the reliability of the SpO₂ measurement.

Methods: Literature was used to make an inventory of factors that could influence automatic FiO₂ control. To make an overview of clinical situations that can occur in relation to SpO₂ monitoring, we observed daily practice for 8 weeks, and performed surveys amongst nursing staff. We obtained 74 hour of data (SpO₂, plethysmographic waveform, pulsatile-flow-indicator and heart rate obtained by the pulse oximeter, FiO₂, and ECG) from premature infants to investigate the reliability of SpO₂ measurements. With the information obtained, we have developed a method that copes with the inaccurate measurements of the pulse-oximeter and is more informative than current alarm systems.

Results: Literature showed that one of the main obstacles in automatic FiO₂ control is the reliability of the SpO₂ measurement. The pulse oximeter is influenced by movement artefacts and has a low accuracy (+/-3%) with respect to the preset alarm limits (+/- 4%). This causes a high rate of false alarms that may lead to a reduced attention of the nursing staff. Furthermore, the relation between SpO₂ and PaO₂ is unpredictable due to changes in e.g. temperature, pH, fetal haemoglobin and infections. Also, the control of SpO₂ itself is difficult and time consuming. The SpO₂ level changes frequently and is unpredictable due to the underdevelopment of the lungs and brain. Finally, there is still no consensus about the safe levels of SpO₂ in premature infants.

The developed method determines reliability of the SpO₂ value by combining several parameters. For instance, when the plethysmographic waveform is not periodic or the pulsatile-flow-indicator is low, a specific alarm is given. When the measurement is accurate and if the SpO₂ value lies between preset limits, the FiO₂ can be adjusted automatically.

Conclusions: The method we have developed determines reliability of the SpO₂ value obtained by the pulse oximeter and identifies the causes of the alarms with respect to the SpO₂ monitoring. Our system allows for safe automatic control of FiO₂ in case of a reliable SpO₂ measurement. This reduces the number of false alarms and the workload of the nursing staff.

Lecture 7

RetCam and ROP



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National guidelines for screening for acute ROP define who and when should be screened. For an overview see¹. Because of country-specific risks related to local socioeconomic and health care conditions, guidelines have to be adapted to specific needs. Screening for ROP requires a high degree of expertise with eventually treatment-requiring ROP. Due to the relative rarity of treatment-requiring ROP digital photography and evaluation in an expert reading centre via telemedicine appear to have the potential of optimising screening quality and minimizing the risk of unfavourable functional visual outcome in all prematures at risk because of timely diagnosis². Image analysis allows documentation and quantification of the retinal pathologies^{3, 4}. This has the potential of uniform evaluation in clinical studies and effective teaching of students and residents.

Several groups are investigating the benefits and drawbacks of using the RetCam 120 for imaging ROP²⁻¹⁴. The paper discusses the results in view of the author's own experiences.

The Bavarian ROP Telemedicine Program

In the Bavarian prospective study the RetCam120 is used for ROP screening in five Bavarian NICUs since 2001. By 2005, more than 600 infants at risk have been examined. Four of these NICUs are peripheral sites, with ROP screening performed by general ophthalmologists. All images were transferred to the Reading Centre at the University of Regensburg for evaluation. The objective of this screening program was targeted at detection of the need for a specialist consult to make the final treatment decision in the presence of referral-warranted ROP and thereby ideally eliminate late referrals. Thus, the sensitivity to detection of inconsequential disease was not at issue. Digital imaging using the RetCam 120 was successful in detecting all referral warranted ROP stages with no incidents where treatment-requiring disease was missed or referred late, and with no false negative and false positive results in a subset of patients where digital imaging and BIO were directly compared i.e. the sensitivity and the specificity to detect referral-warranted ROP were both 100%². Limitations recognized so far were lower contrast and resolution of the digital images compared to binocular indirect ophthalmoscopy BIO, difficulty to image the far periphery, and two-dimensional view compared to three-dimensional BIO. Being familiar with both, the fundusoscopic aspect and the RetCam image is considered crucial for correct interpretation of the images. The transmission of image data and paediatric data usually caused no problems. Trouble in data delivery generates an

error message, making it necessary to send the data for a second time. Problems making data delivery impossible, even after a couple of trying, next to never occurred. Acceptance of the program was excellent among paediatricians and families. The continuous build-up of a digital image atlas allows rapid education and information of students, residents and fellows about the various disease stages and the disease course.

At present, additional images are sent from various institutions and former short-time exchange fellows from abroad who in the meantime have started their own screening programs with the RetCam120. Tele-consulting allows rapid exchange of opinions and discussion of treatment options to the benefit of the infants at risk for serious visual handicap from ROP.

Conclusion

Worldwide, ROP is still a major cause of childhood blindness and severe visual impairment. Implementation of adequate screening programs in all countries is mandatory. Digital wide-field imaging allows timely capture and standardized evaluation of the various disease stages. Precise and objective monitoring of the disease course is essential to further improve the chances of favourable visual outcome in premature infants.

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Lecture 8

Retinal and Retinovascular Development In Preterm Infants - Without and With ROP



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The opportunity to image the neonatal retina has been an exciting recent development. It has permitted for the first time, the quantification of retinal and retinovascular growth in babies born prematurely. Here, the results four recent studies are presented.

Methods

Since 1998, digital retinal images have been obtained during routine screening for retinopathy of prematurity (ROP) by RetCam 130 ® and entered onto a database.

Results

1. Optic Disc Size and Optic Disc-Fovea Distance

Most optic disc morphometric studies in infancy have utilised post mortem material. We measured optic disc dimensions and centre-to-centre distance between optic disc and fovea in 51 infants at 32 to 50 weeks postmenstrual age (PMA). Optic disc height and width were, $1.41 \pm 0.19\text{mm}$ and $1.05 \pm 0.13\text{mm}$ respectively (adult: height $1.88 \pm 0.19\text{mm}$, width $1.77 \pm 0.19\text{mm}$) and the optic disc foveal distance = $4.4 \pm 0.4\text{mm}$ (adult $4.9 \pm 0.3\text{mm}$). Thus, optic nerve head diameter increases by over 50% after birth to reach adult dimensions, whereas optic disc-fovea distance increases only by about 10%.

2. ROP Location and Ocular Growth

The concept that vascular development is centrifugal and symmetrical is the basis of retinal zones and fundamental to ROP classification. However, measuring ROP location in 49 eyes demonstrated considerable asymmetry with retinopathy in the nasal retina being closer to the optic disc than temporal. Most interesting, while the distance between the nasal and temporal retinopathy increased by 20-34 pixels per week, the degree of asymmetry remained constant.

3. Emergent Angle Between the Major Temporal Vessels

The angle between the major temporal retinal vessels is used in the evaluation of the structural integrity of the macular region, and narrowing of this angle is used as a sign of macular ectopia. We measured the temporal retinal vessel angle in 164 eyes of 82 babies. The range was right eye $59-106^\circ$, and left eye $69-97^\circ$, and mean 82° for babies near term, with 95% data above 63° for the right and 67° for the left eye. There was a high degree of

interocular symmetry, but there was no major effect on the angle by either the degree of prematurity or the presence of acute phase ROP.

4. Retinal Vessel Branching

We measured first segment length ([FSL] optic disc to first bifurcation). In infants <28 weeks GA, arteriolar, but not venular, FSL was significantly longer in stage 3 vs no, or mild ROP (stages 1 & 2).

Conclusions

These studies are in agreement with the notion that most growth in the globe occurs in the peripheral retina where ROP occurs, and that growth in the highly organized and visually critical region of the central retina is kept to a minimum. Asymmetry of the temporal retinal vessel angle indicates macular distortion but mild degrees of bilateral macular distortion may not be simple to detect. Severe ROP disrupts arteriolar, but not venular development. As the first arteriolar branch develops early in gestation, before survival is possible, the question arises of whether arteriolar development in preterm babies is affected before and/or after birth, the latter implying the loss of pre-existing branches.

Lecture 9

The Differential Diagnosis Of Retinopathy Of Prematurity



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A. High Risk Babies for Progressive ROP

1. Less than 1000 grams birthweight (means 800 grams)
2. 26-28 weeks gestation
3. Zone I ROP
4. Marked plus disease

B. Long Term Follow Up

1. 70% are myopic
2. Myopia less than 4 diopters – better chance for 20/50 or better vision
3. Myopia greater than 4 diopters – visual acuity less than 20/50 is more likely
4. Average degree of myopia with cryo – 5 diopters
5. Average degree of myopia with laser – 3 diopters

C. Differential Diagnosis of ROP

1. Inheritance
 - a. Autosomal dominant (locus on long arm of chromosome 1)
 - b. X-linked FEVR: 1 mutation to Norrie Disease Protein Gene (NDP)
 - c. 80% asymptomatic (peripheral avascular retina)
 - d. Traction RD

D. Incontinentia Pigmenti

1. X-linked dominant inheritance
2. Fundus findings
 - a. Peripheral avascular retina
 - b. Absence of normal foveal avascular zone
 - c. Retinal folds
 - d. Retinal detachment
 - e. Retinal dysplasia
 - f. Cortical blindness due to occipital lobe infarction

3. Systemic Findings

- a. Incomplete dentition
- b. Vesicular skin eruptions (infancy)
- c. Alopecia at the vertex of the skull

E. X-Linked Retinoschisis-Gene localized to distal short arm of X-chromosome (Xp.22.1-p.22.3)

- 1. Nerve fiber layer dehiscence
- 2. Stellate maculopathy
- 3. Vitreous hemorrhage
- 4. Retinal detachment

F. Stickler Syndrome (Hereditary Artho-Ophthalmology)

- 1. Autosomal dominant inheritance
 - a. Gene mutation – Type II procollagen (COL2A1)
- 2. Eye findings
 - a. High myopia
 - b. Optically empty vitreous
 - c. Perivascular lattice
 - d. Retinal detachment
 - e. Cataract
 - f. Glaucoma
- 3. Systemic findings
 - a. Arthritis (epiphyseal dysplasia)
 - b. Marfanoid appearance
 - c. Loss of hearing
 - d. Flattened faces
 - e. High arched or cleft palate

G. Management of Cataract in Adult Retinopathy of Prematurity Patient

- 1. Purpose: Many adult ROP patients develop visually significant cataracts. In this study the visual results and complications after cataract surgery were reviewed.
- 2. Case Material
 - a. 17 patients, 24 eyes
 - b. Females 12, males 5
 - c. Age range 16 to 47 years (average 37)
- 3. Preoperative Work Up
 - a. Nuclear sclerosis most common type of cataract
 - b. Anterior segment and fundus findings
 - c. Previous retinal surgery
- 4. Phacoemulsification vs. ECCE
 - a. Lenses often hard
 - b. Phaco predominant method
- 5. Postoperative Complications
 - a. May have multiple posterior breaks
 - b. Many require YAG

Patients with ROP and cataracts benefit from cataract surgery when visually compromised. Visual outcomes are frequently limited by previously existing fundus changes due to the ROP. All ROP patients undergoing cataract surgery need to know about the potential complications of retinal detachment.

Lecture 10

Screening For ROP



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ROP is one of the few causes of childhood blindness, which in most cases is preventable if treatment is performed at an adequate time. To detect ROP, prematurely-born infants need to be examined regularly in the neonatal period. Screening for ROP has been shown to be cost-effective. It also full-fills WHO's criteria for screening (Wilson & Jugner 1968), i.e. the disease is well defined, has a well-known natural history, a rather easy method of examination is available and treatment is possible in most cases.

The aim of screening for ROP is to identify severe ROP and to initiate treatment at an adequate time. For that purpose, local guidelines ought to be elaborated. Such guidelines must take into account the local organisation and quality of health care and neonatal care and also the socio-economic circumstances of the society (Gilbert et al –05). National screening programs for ROP are available in many countries today. Such programs should preferably be based on studies on the incidence of ROP in the country per se. Screening for ROP is expensive and also stressful for the infant. Further, there is a continuous improvement of neonatal care. It is therefore important to follow the incidence of ROP in the country, to be able to adjust and modify such screening criteria, to include only infants at risk of severe ROP. In Sweden, we are working on a web-based national register for ROP-screening, which will be initiated in the autumn 2006. This will hopefully help us to optimize our national guidelines for screening.

Finally, improvements in neonatal care have resulted in a new population of extremely immature babies. These babies are at risk of developing a very aggressive and quickly progressing ROP, the so called "AP-ROP", i.e. "aggressive posterior ROP" (Arch Ophthalmol –05). Further, criteria for treatment of ROP have recently been revised (ET-ROP –Arch Ophthalmol –03). Both these facts must also be taken into account in the design of screening programs for ROP.

A successful screening involves many practical aspects. Most ophthalmologists use indirect ophthalmoscopy and 20, 25 and 30 dioptre lenses. The most important fact is, however, to use a method with which the examiner is confident. The examination should be as atraumatic as possible and speculum and indentation used only if necessary. A good communication between ophthalmologist and neonatologist is necessary. Examinations must start in due time. It is of utmost importance to avoid postponement of further examinations and treatment. When treatment is decided upon, it should be performed within 48 hours. Finally, when an

infant is transferred to another ward, another hospital or to their home, it is important to get in touch with their "new" ophthalmologist or to arrange an appointment in your own hospital!

ROP is most often an avoidable cause of blindness. To reduce the risk of visual sequelae, adequate national and local screening programs and routines are required. Such programs ought to have a priority in every society and are recommended in the program of WHO for 2020 – "Vision 2020 – The right to sight"!

IMPACT OF RETINOPATHY OF PREMATURITY SCREENING EXAMINATION ON CARDIO-RESPIRATORY INDICES: A COMPARISON OF INDIRECT OPHTHALMOSCOPY AND RETCAM IMAGING

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Purpose: A prospective (non randomised) interventional study to compare the impact of Retinopathy of Prematurity (ROP) screening examination between digital fundus camera (Retcam) and conventional binocular indirect ophthalmoscopy (BIO), using cardio-respiratory indices as a measure of distress.

Methods: 86 preterm infants with a birthweight of ≤ 1500 g or gestational age ≤ 32 weeks undergoing ROP screening were included. ROP screening examination with BIO or Retcam was performed. Cardiovascular indices were recorded prior to, at the end of, and 1 hour subsequent to examination. Race, birthweight, gender, twin status, duration of exam, gestational age (GA) and post-conceptual age (PCA) were recorded.

Results: 34 infants underwent indirect ophthalmoscopy, while 52 underwent Retcam examination. The main outcome measures were the heart rate (HR), oxygen saturation (SaO₂), the respiratory rate (RR) and the blood pressure (BP). The increase in HR and RR was significantly higher in the indirect ophthalmoscopy group compared to Retcam group ($P < 0.05$). There was a significant increase in HR and BP, decrease in SaO₂ and increase in RR during examination for the whole group ($P < 0.05$). No clinically significant response persisted at 1 hour. Retcam examination took significantly longer ($P < 0.001$).

Conclusions: Screening for ROP with the Retcam is associated with a significantly lower stress related response than conventional indirect ophthalmoscopy.

RETINOPATHY OF PREMATURITY SCREENING AND TREATMENT SOFTWARE (ROPSATS): A TEACHING TOOL FOR THE DEVELOPING WORLD

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Retinopathy of prematurity (ROP) may be found in approximately two-thirds of all babies with birth weights less than 1251g. It accounts for up to 18% of registered blindness in children in industrialized countries. Although figures for developing countries are harder to obtain there is some evidence that it may account for up to 25% of blindness in children in Eastern Europe and nearly 40% in Cuba.

Both the Trial of Cryotherapy for Retinopathy of Prematurity (CRYO-ROP) and the Early Treatment for Retinopathy of Prematurity (ETROP) studies have demonstrated the significant anatomical and functional value of screening at risk infants. Laser treatment of ROP remains one of the most cost effective ophthalmic procedures in any age group.

Despite this the skills necessary to provide optimal care for ROP can be time consuming and costly to obtain. This is especially so in developing countries where the need may be greatest. It can be difficult for many to be able to take the time out of busy practices or service commitments to undertake fellowships or sabbaticals to work with experienced clinicians. In addition these opportunities are becoming quite competitive and in many cases expensive. Books are available but can be costly, cumbersome and given the times involved in getting to print can be outdated quickly. Books by their nature are also constrained to providing static pictures and text and cannot provide more dynamic content such as videos. Video tapes can provide valuable information but are linear in delivery and it can be time consuming and difficult to get to the area of interest which may be at the end of the tape.

We present a computer program that provides an interactive exploration of retinopathy of prematurity with particular emphasis on the practicalities of screening and treatment. This format allows quick access to the areas of interest when reviewing topics. Tips and traps that have been discovered over a number of years are shared. Versions have been produced to be used in the training of junior ophthalmologists and also to be available as a reference for treating doctors in developing countries. The software is being made available on CD and DVD (with additional content) so that it can be scaled to the needs of the various developing regions. Personal communication has demonstrated that the minimum computer requirements are met by most of the contacted centers. Funding can usually be sought from charitable organizations for areas that do not have the necessary equipment at present. Personal communication has also established that this would be a welcomed and useful aid for those screening and treating ROP in countries where other methods of skills transfer may be less readily available.

LONGITUDINAL POSTNATAL WEIGHT AND IGF-I MEASUREMENTS IMPROVE PREDICTION OF ROP

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Objective: ROP screening guidelines are based on perinatal factors. However, postnatal growth and development may also influence ROP but are not considered.

Design: We have developed an algorithm to predict for individual infants the risk of later ROP development requiring treatment based on the postnatal longitudinal systemic factors IGF-I, IGFBP-3 and postnatal weight gain. We tested the algorithm with 79 preterm infants considered at risk for ROP by standard criteria, (gestational age 23.6-31.7 weeks) in a longitudinal study measuring weight gain and serum IGF-I and IGFBP-3 weekly from birth until discharge from the hospital. We monitored deviations from the reference model (those that developed no or minimal ROP) for weight and IGF-I, which could indicate treatable ROP by ETROP criteria.

Results: This monitoring method detected 100% of infants in this cohort who required treatment for ROP with a warning signal at least 5 weeks before requiring treatment and at least 3 weeks before the onset of ROP stage 3. The majority (61 of 73) of infants requiring no treatment also were correctly identified.

Conclusions: The measurements of the postnatal factors of weight gain and IGF-I and IGFBP-3 significantly enhance the clinicians ability to identify patients who will require treatment.

ACCURACY AND RELIABILITY OF REMOTE RETINOPATHY OF PREMATURITY DIAGNOSIS

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Objective: To determine the accuracy and reliability of Retinopathy of Prematurity (ROP) diagnosis using remote digital image review by three masked ophthalmologist readers.

Methods: 64 low birth-weight infants who met ROP examination criteria underwent two consecutive procedures at the neonatal intensive care unit bedside: dilated examination by an experienced pediatric ophthalmologist, and digital retinal imaging with a commercially-available wide-angle camera (RetCam-120; Clarity Medical Systems, Pleasanton, CA). 410 images from 163 eyes were reviewed independently by three trained ophthalmologist readers, who classified each eye into one of four categories: no ROP, mild ROP, type-2 prethreshold ROP, or treatment-requiring ROP. Sensitivity and specificity for detection of mild or worse ROP, type-2 prethreshold or worse ROP, and treatment-requiring ROP were determined, compared to a reference standard of dilated ophthalmoscopy. Receiver operating characteristic (ROC) curves were generated by calculating values for each reader at three diagnostic cutoff levels: mild or worse ROP (i.e., reader was asked whether image sets represented mild or worse ROP), type-2 prethreshold or worse ROP (i.e., reader was asked whether image sets represented type-2 prethreshold or worse ROP), and treatment-requiring ROP.

Results: Sensitivity/specificity of diagnosis of mild or worse ROP were 0.845/0.910 for the first reader, 0.816/0.955 for the second reader, and 0.864/0.493 for the third reader. Sensitivity/specificity of diagnosis of treatment-requiring ROP were 0.850/0.960 for the first reader, 0.850/0.973 for the second reader, and 0.900/0.953 for the third reader. Area under ROC curves ranged from 0.747-0.896 for detection of mild or worse ROP, 0.905-0.946 for detection of type-2 prethreshold or worse ROP, and 0.941-0.968 for detection of treatment-requiring ROP. When ROP was classified into ordinal categories, the overall weighted kappa for inter-reader reliability was 0.743. Intra-reader reliability for detection of type-2 prethreshold or worse ROP was 100% for all readers.

Conclusions: The accuracy, inter-reader reliability, and intra-reader reliability of remote ROP interpretation based on digital imaging are substantial for detection of treatment-requiring ROP, but less so for detection of mild or worse ROP.

OCULAR FINDINGS IN HIGH RISK NEONATES ADMITTED TO NEONATAL INTENSIVE CARE UNIT

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Many ocular disorders could be related to prematurity and low birth weight .ROP is a retinal disorder of low birth weight premature infants. This retrospective study included 100 neonates who were admitted and discharged throughout a study period of one year to the neonatology department. Cairo university We aimed to detect ocular abnormalities that could be related to neonatal clinical status and/or management .The results of this ophthalmologic screening showed that 10 neonates had variable stages of ROP (10%). Other complications such as strabismus anterior and posterior segment anomalies were recorded and evaluated Significant risk factors of ROP were : birth weight , gestational age , duration of oxygen therapy, and respiratory disorders. It was concluded that routine ophthalmic screening of prematures at predetermined schedule is of utmost importance during and post hospitalization.

HOW GOOD ARE THE PROPOSED INCLUSION CRITERIA SET BY CROATIAN GUIDELINES FOR RETINOPATHY OF PREMATURITY (ROP) SCREENING?

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Objective: To assess the validity of recruitment criteria in screening programs for retinopathy of prematurity (ROP) proposed in the national guidelines and to report the incidence of ROP and the need for intervention in our cohort of patients.

Study design: Retrospective analyses using perinatal database, a review of patient charts and eye examination reports.

Patients: A total of 138 prematurely born children were included in screening program for early detection of ROP during a four year period (January 1, 2001 through December 31, 2005). Of these infants, 103 (74.6%) met the proposed criteria for eye examination, i.e. birth weight (BW) equal or less than 1500g and/or gestational age (GA) equal or less than 32 weeks.

Results: The incidence of ROP was 26.8% (37/138) for any stage and 10.9% (15/138) for severe ROP requiring therapy (threshold stage 3 or greater). In the group of infants who fulfilled both criteria for recruitment, i.e. BW \leq 1500g and GA \leq 32 weeks (69 children), the incidence of ROP was the highest - 46.4% (32/69). If only one criterion was met, either BW \leq 1500g or GA \leq 32 weeks (34 children), the incidence of ROP was much lower (11.8%, 4/34). Only one child with BW and GA above the given limits developed ROP and it required therapy, but was included in the screening due to unstable clinical course.

Conclusion: To our experience, the proposed inclusion criteria in screening program for ROP proved to be of satisfactory value. The fact that somewhat bigger and more mature babies with an unstable peri- and postnatal clinical course could also develop ROP should not be overlooked, and such children have to be included in the screening program.

RETINOPATHY OF PREMATURITY: THE EXPERIENCE OF THE LAST DECADE.

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Purpose: To present the results of screening and treatment of Retinopathy of prematurity (ROP).

Design and Methods: Retrospective analyses of clinical reports from newborns admitted to the Neonatal Intensive Care Unit (NICU) between 01/01/1996 and 31/05/2006 screened for ROP [birth weight (BW) less than or equal to 1500g and/or gestational age (GA) less than or equal to 32 weeks (W)]. Fundus observation was performed during the 4th-5th weeks of life and then every 2 weeks or weekly if ROPs diagnosis. The sample was divided into 2 groups (A: without ROP or ROP stage 1; B: ROP stage 2 or superior). ROP was categorized according to the International Classification for ROP.

Results: From the 2878 newborns admitted to NICU, 920 had criteria for screening. The population examined with a long follow-up had a median GA of 29,16+/-2,50W and a median BW of 1221+/-465g. ROP stage 2 or superior was diagnosed in 31 infants (6,6%) from whom 10 (32,3%) were submitted to cryotherapy. The incidence of ROP stage 2 or superior in newborns less than or equal to 1000g was 14,0% and 1,8% for newborns less than or equal to 1250g. Only 1% of newborns more than 1250g developed ROP stage 2 or superior. No ROP above stage 2 was found in infants more than 32W or 1300g. Of all infants requiring cryotherapy, 80% were less than or equal to 1000g and none had a GA above 28W.

Conclusions: This study shows low incidence of ROP clinically important and ROP requiring treatment but ROP continues to be an important problem in our population. ROP stage 2 or superior was not found in newborns above 32W or 1300g.

RETINOPATHY OF PREMATURITY: IS IT TIME TO CHANGE SCREENING LIMITS IN LITHUANIA?

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Background: National guidelines of screening for ROP in Lithuania were published in 1998. The upper limits were: gestational age - 35 weeks and / or birth weight - 2500 grams. The aim of the study: to determine the possibility of restricting the inclusion criteria for screening. Study design - retrospective.

Material and methods: The study cohort comprised 664 prematures of gestational age (GA) ≥ 35 weeks and / or BW ≤ 2500 grams, hospitalized to Vilnius University Children's Hospital in the period 01 of January 2000 - 31 of December 2002. Retinopathy of prematurity was found in 148 (22,3%) infants. 65 infants (9,8%) reached threshold disease and underwent cryo therapy and/or laser therapy.

Results: All cases of threshold ROP were confined to infants with gestational ages ≤ 33 weeks or birth weights ≤ 1920 g. Restricting the inclusion criteria for screening to ≤ 1500 g would only have reduced the total number of screenings and could have allowed us to miss 7 of our threshold cases. If ROP screening is limited to infants with GA of ≤ 28 weeks, 20 infants (30,8 %) would not have been screened and would not have been treated in 2000-2002 years.

Conclusions: Based on our results it seems appropriate to include into screening program all infants with gestational ages ≤ 33 weeks and/or birth weights ≤ 2000 g. At the moment the worldwide recommendations of screening for ROP are still not suitable enough in our county.

ROP DOES OCCUR IN BABIES WITH GESTATIONAL AGE AND BIRTH WEIGHT OUTSIDE WESTERN SCREENING GUIDELINES - ROMANIAN EXPERIENCE

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Background: In 2002 in our institution a regional ROP screening and laser treatment programme was initiated on a systematic basis in Romania. The aims of this present study were to:

- assess the incidence of ROP in infants with gestational age (GA) and birthweight (BW) outside classical screening guidelines, including severe forms of the disease.
- assess whether significant differences existed in perinatal factors between infants with ROP that comply with classical screening criteria vs those outside these criteria.
- present several relevant cases with severe ROP in babies with GA and BW outside western screening criteria, documented with RetCam II.

Method: Infants born Sept 2002 - Dec 2005 with GA \leq 32 weeks and BW \leq 1500 g (group A), and infants with GA $>$ 32 weeks and BW $>$ 1500 g with perinatal complicated progress (group B) were included in study. Comparisons between the two groups were made to investigate differences with respect to perinatal risk factors, incidence of ROP and ROP outcome.

Results: Of the 884 preemies screened, 693 (78,4%) had GA \leq 32 wks and 544 (61.5%) had BW \leq 1500 g (group A); 188 (21.2%) had GA $>$ 32 wks and 338 (38.2%) had BW $>$ 1500 g (group B).

Of the total sample, 50.5% had ROP, 13.8% with severe ROP requiring laser. Among those with ROP, 10.7% had GA $>$ 32 weeks and 25.3% had BW $>$ 1500 g. Similarly, of those 122 with severe ROP, 5.7% had GA $>$ 32 weeks and 24.6% had BW $>$ 1500 g.

Infants in group B had less hours of FiO₂ $>$ 40%, less hours of ventilation - with significant differences only with respect to BW $>$ 1500 g, $p = 0,018$; they had also less ruptured membranes $>$ 24 hrs, less surfactant use and anemia, EPO, dopamine and vitamin E doses, in accordance with their higher GA.

The incidence of ROP was, unsurprisingly, significantly higher in infants in group A - GA \leq 32 wks (57.1% vs 26.6%, OR 3.7, $p < 0.001$) and BW \leq 1500 g (61.2% vs 34%, OR = 3.06, $p < 0.001$). A higher percentage of the former required laser (28.7% vs 16%, OR = 2.1, $p = 0.036$, by GA, but 27.3% vs 26.9%, $p = \text{NS}$, by BW). The incidence of unfavourable outcome was 15.6% in infants with GA \leq 32 wks vs 0% in those in group B and 14.9% in those with BW \leq 1500g vs 13.3% ($p = \text{NS}$).

Several relevant cases from group B documented with RetCam II will be presented.

Conclusions: Although the incidence of perinatal risk factors and of ROP was significantly lower in infants outside the classical screening criteria, ROP, including severe cases, did occur in this population. In order not to miss these patients and thus expose them to the risk of blindness, we suggest that screening criteria should be adapted to the local population.

IMPLEMENTATION IMPACT OF A SCREENING PROGRAM ON ROP IN CALI, COLOMBIA

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Introduction: ROP is first cause of children blindness in Cali and spite of enough scientific and technical information on how to evaluate these children, there are not government programs for addressing this problem.

Objective: To show how important is to increase screening coverage and treatment for ROP with appropriate systems and good strategies for decreasing rates for this disease and to reduce children blindness in Cali.

Methods: Medical charts from the service of pediatric ophthalmology in the University Hospital were reviewed. Newborns weighting under 1500 g and or younger than 32 weeks of gestational age, born between January 1st 2001 until December 31st 2005 hospitalized at unit CIRENA. The intervention program works with all staff members, medical and paramedical, teaching them to be aware of the ROP problem, to personalize the children for instance, telling them by mother's first name of those one than are studying now in the blind school, and some important messages like to be alert for screening and treatment if necessary and so on.

Results: 78 patients out of 266 (29.3%) were screened in 2001 with a rate of treatment of 18%; in 2002 were screened 45.6% (140/307) with rate of treatment of 15.7% and in 2003 the rate of screening was 89.7% (297/331) and treatment of 7.4%. in 2004 the rate of screening was 86.51 % (295/340) and treatment of 5.4% and Finally in 2005 the rate of screening was 98.9% (364/368) and treatment of 4.9%.

Discussion: Trends for the rate of screened newborns grew from 29.3% to 98.9% in last five years. Simultaneously the rate of children requiring treatment decreased from 18% to 4.9% in same period. This is result of early screening plus education and sensibilization in the management of newborns by paramedical staff.

Greater commitment to prevention of ROP from the personnel working at the neonatal intensive care unit is facilitated when they are provided with names of the children who were born in the unit they work in and are now studying in institutions for low vision children and also when they are shown the statistics, as severe as these might seem. Knowledge of the disease as one of the ways of providing quality neonatal care makes the staff reflect on how well they are performing their duties and gives scientific bases with which to improve their performance.

Conclusions: The staff at the NICU responds more positively to special childcare when exposed to educational and awareness promoting activities.

Establishing protocols that indicate which patients are at risk and how often they should be monitored helps in increasing the rate of screened infants and decreasing the rate of patients with severe ROP that merit treatment.

When the program becomes stable, coverage increases and the need for treatment is reduced.

RETINOPATHY OF PREMATURITY IN COSTA RICA: 1982-2005

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Purpose: To describe the screening program and the visual outcomes for retinopathy of prematurity (ROP) in Costa Rica for the period 1982-2005.

Methods: Every child born at < 36 weeks gestation and/or a birth weight of < 1500 gr was referred for ROP screening. Classification was according to the International ROP Classification. If threshold was reached, the patient was treated with cryotherapy. In 2003 treatment with indirect laser photocoagulation was instituted.

Results: In 1982, 169 patients were screened for ROP and 25 of them were diagnosed with ROP. Of these 7 reached threshold and were treated with cryotherapy. In 2004, 322 patients were screened for ROP and 156 of them were diagnosed with ROP. Of these 49 reached threshold and were treated with laser photocoagulation. The incidence of ROP has ranged from a low of 14.8% in 1982 to a high of 57% in 2002. Blindness secondary to ROP has been reduced from a high of 42.3% in 1982 to 3.2% in 2005.

Conclusion: Blindness from ROP can be diminished with a good screening program even in developing countries such as Costa Rica.

ROP SCREENING IN OMAN - MY EXPERIENCE

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My experiences of ROP screening in Omani population is shared. A total of 205 premature babies were screened at SCBU of two tertiary care centres in Muscat over a period of 5 years since october 2000. All infants born at or before 30 weeks of gestational age or with birth weight less than 1500 grams were screened. All infants with ROP stage 3 Threshold were considered for Argon Laser treatment. The results of ROP screening shall be discussed. Overall ROP incidence is found to be 34.15% in this series. No ROP was seen in 65.85% of the babies. Stage 1, 2 & stage 3 Prethreshold ROP was seen in 24.39% of babies and stage 3 Threshold ROP was seen in 9.75% of babies requiring treatment. Risks factors involved shall be discussed. ROP regressed spontaneously in 71.42% cases with ROP. Argon Laser treatment was done in 28.58% of babies with ROP. All babies treated with Laser did well on follow up examination. Thus sincere screening & timely treatment can prevent blindness in premature babies.

Racial Differences in The Occurrence of Retinopathy of Prematurity in a University Hospital Level 3 Neonatal Unit in East London

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Background: The rates of Occurrence of Retina Of Prematurity (ROP) are higher in the smallest and most premature infants. It has been demonstrated by the Cryotherapy for Retinopathy of Prematurity Cooperative Group that severe ROP occurs less frequently in African-American infants than in white infants. There is little recent data regarding UK infants of Asian origin. Anecdotally, however, there is a belief that severe ROP occurs more frequently in Asian than white infants. This difference has previously been ascribed to better survival.

Methods: Retrospectively, case notes of all infants admitted to the 31 cot, level three unit at Homerton Hospital, London for ROP screening were reviewed over the three year period, January 2003 to December 2005, to test this hypothesis.

Results: A total of 330 infants were identified to meet the screening criteria and 251 were screened. Of those not screened, 28 infants died prior to starting or during ROP screening, a mortality rate of 8.5%, and 52 infants were transferred to other units before starting screening. Overall, ROP was detected in 76 of the 251 screened (30.3%). Retinopathy of prematurity developed in 24 out of 83 (28.9%) white infants; 33 out of 114 (28.9%) black/African/Caribbean infants; 7 out of 26 (26.9%) Asian infants and 3 out of 11 (27.3%) mixed race infants. Ethnic data was not available for 19 infants, of whom 9 developed ROP.

27 infants out of 251 screened (11%) required retinal laser therapy. By racial origin, treatment was needed by: 7 of 83 (8.4%) white infants, 6 of 114 (5.2%) black/African infants, 6 of 26 (23.1%) asian infants, 1 of 11 (9%) mixed race infants and 7 of 19 in whom no ethnic data was available.

None of the infants required re-treatment and no infants progressed to stage 4 or 5 ROP. No infant born weighing >1000g or with a gestational age of >30 weeks required treatment for ROP.

Conclusions: This unit serves a multi-ethnic community in East London. The rates of ROP development do not differ significantly between infants admitted from different racial groups. However, in those for whom ROP has been detected, a much greater percentage of Asian babies (86 %) will go on to develop threshold disease compared to either white infants (29%), or black infants (18%). Consequently, any Asian baby in whom ROP has been detected should be carefully observed as they are at high risk of requiring treatment.

Lecture 11

*Vasculogenesis VS Angiogenesis: In Prematurity (ROP)
Eyes. A Clinical & Pathological Study*



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Purpose: In its most severe form, Retinopathy of Prematurity (ROP) is located in posterior retina and affects the smallest, most premature infants. We hypothesize that depending on whether vasculogenesis (de novo formation of new vessels via transformation of vascular precursor cells) or angiogenesis (budding from existing vessels) is perturbed, it results in significant differences in clinical presentation and therapeutic outcome observed in Zone 1 versus Zone 2 ROP.

Design: The study is a retrospective analysis of the difference in outcome between zone 1 and zone 2 ROP after cryo and laser therapy.

Methods: A review of the clinical presentation of Zone 1 & 2 ROP correlating this with the topography of formation of human retinal vasculature via vasculogenesis and angiogenesis.

Results: Presented are population data on susceptible infants, and outcome statistics of clinical trials. Digital images showed a correlation between ROP in Zone 1 with the region of the retina vascularized via vasculogenesis.

Conclusion: Zone 1 ROP is correlated with vessel development by vasculogenesis, relative insensitivity to laser/ cryo therapy and poorer anatomical and visual outcomes. This suggests that if the vasculogenic process is perturbed, it results in a distinct clinical presentation, poorer response to therapy and poorer visual outcome. When the current International Classification was developed knowledge of the processes of human retinal vascular development was incomplete. The work presented here provides a framework for the development of a modification incorporating these ideas without sacrifice of the essential elements of ICROP.

RETINAL VASCULARISATION IN EXTREME PREMATURE

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Purpose: To investigate the morphology of the shunt and quality of vascularisation in extreme prematurity at threshold.

Method: Fundus fluorescein angiography and colour photography was performed on infants with a gestational age of less than 26 weeks GA and threshold disease prior to treatment with a diode laser.

Results: We demonstrated a morphological lesion non-compliant with international guidelines for treatment. Poor development of the vascular bed in vascularised retina.

Conclusion: Posterior pole congestion is the most reliable indicator for treatment in these cases. Findings may explain the clinical morphology and worse prognosis.

FLUORESCEIN ANGIOGRAPHIC FINDINGS IN ZONE I ROP

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Purpose: to evaluate fluorescein angiographic findings in zone I ROP undergoing laser treatment and compare with laser outcomes.

Methods: starting from Dec'04 RETCAM digital fluorescein angiography (Massie Lab. , Pleasanton, CA) became available for ROP screening in the neonatal intensive care unit at the Catholic University Hospital in Rome. More than 80 inborn preterm with gestational age (GA) 32 wks and/or a birth weight (BW) 1500gr were screened for ROP. The mean BW was 1098.9 gr. (range 565-2100gr.) and the mean GA was 29.00 wks (range 24-33wks). ROP was diagnosed in 38 infants (mean BW 921.6gr., GA 27.3wks). 10 babies (mean BW 835.0 gr., mean GA 25.7wks) were classified type1 zone 1 pre-threshold ROP and consequently underwent laser photocoagulation of avascular retina. In all cases digital fluorescein angiography was performed before treatment.

Results: fluorescein angiography allow to visualise shunt, revascularization and leakage at the junction between vascular and avascular retina. In many cases small non perfused area and/or leakage inside the vascularised retina were observed.

Conclusion: Fluorescein angiography was useful to distinguish the deceptively featureless zone 1 junction between vascularized and non-vascularized retina. This study helps to understand the role of vascular abnormalities observed in zone 1 vascularized retina.

Lecture 12

Treatment Of Acute Retinopathy Of Prematurity



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Retinopathy of prematurity (ROP) has been recognized as one of the main causes of blindness and low vision in children since the middle of the last century. Its incidence and severity have been decreasing in developed countries and increasing in pure and middle income countries over the past decades.

World health organization's "Vision 2020" program has identified ROP as an important cause of blindness in both high and middle income countries due to increased survival rates of low and very low birth weight premature infants.

Retinopathy of prematurity is the disease of prevention and timely and proper treatment is the key to success in the fight against this disaster.

ROP cryotherapy multicenter trial showed that peripheral retinal cryotherapy could reduce the frequency of adverse structural and functional outcomes.

Data obtained over recent years have shown that lasertherapy is at least as effective as cryotherapy or even superior, especially in aggressive posterior ROP (Zone I disease).

Aim: to present our modified treatment modalities for Zone II and Zone I ROP treatment.

Methods: Modified cryotherapy for Zone II ROP consists of two rows of cryoapplications:

- a) one row of cryoapplications –on the ridge,
- b) the other row – anterior to the ridge (in avascular retina).

Not the whole area of anterior avascular retina up to ora serrata is covered by cryoapplications.

Modified laser-cryotherapy for aggressive posterior disease (Zone I ROP) consists of:

- 1) cryocoagulation in anterior avascular zone,
- 2) diode laser coagulation applied anterior and posterior to the ridge (or presumed ridge),
- 3) supplemental diode laser applications on the vascular nets up to clear retina.

Results:

Modified Cryotherapy for Zone II ROP was used in 475 eyes.

Favorable structural (anatomical) outcome was achieved in 100% of consecutive eyes over the period of 10 years.

Structural outcome of modified laser - cryotherapy for Zone I ROP was favorable in consecutive 48 eyes treated over 4 years.

Conclusion: Modified therapies for Zone II and Zone I ROP clearly show that blindness caused by retinopathy of prematurity can be completely prevented.

SLIT-LAMP ARGON-LASER PHOTOCOAGULATION FOR THE TREATMENT OF THRESHOLD RETINOPATHY OF PREMATURITY

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Purpose. To determine the effectiveness of slit-lamp argon-laser photocoagulation in eyes with threshold retinopathy of prematurity.

Materials and methods. Between 2003 and 2005 slit-lamp argon-laser photocoagulation was performed in 22 eyes (16 children) with threshold retinopathy of prematurity (ROP): 17 eyes with classic ROP and 5 eyes with plus-disease.

Gestational age ranged from 25 to 33 weeks. Birth weight ranged from 780 to 1600 g. Threshold stage of ROP was developed within 6-11th week of the child life (mean 9,2 weeks), that corresponded to 34-41st week of postconceptual age (mean 38 weeks).

Complex monitoring system consists of standard ophthalmologic examinations, digital retinoscopy by means of RetCam-120 (Massie Laboratories, Inc., USA), retinal vessels measurement method (the analysis of digital RetCam-120 images of eye posterior pole by software Panorama), optical coherence tomography (OCT) (OCT Stratus-3000, Carl Zeiss, Germany).

Laser technique. Tropicamide eye drops (1%), irifrin eye drops (10%), and 0.05 ml mesatoni 1% solution subconjunctively were used to achieve mydriasis. Slit-lamp argon-laser photocoagulation was performed with use of argon laser Coherent Radiation (Novus-2000, USA) (wave length - 514 nm) by means of Goldman's pediatric triple-mirror lens.

Laser photocoagulation parameters were the follows: power - 100-250 mW, impulse duration - 0,1-0,15 sec, spot size - 350-500 mm, laser burns total amount - 250-550. Laser burns were put on a line of demarcation ridge and further in a direction to orra serrata in chessboard order.

Results. The monitoring of the posterior pole vessels diameter alterations was carried out. An analysis of the diameter alterations with use of Wallis-Moor criterion showed statistically significant veins diameter decreasing after laser photocoagulation when ROP regressing (@ < 0,05). Mean veins diameter before photocoagulation was 166,39+6,25 microns, and after photocoagulation it decreased up to 99,85+4,82 microns within 6 weeks. The similar tendency in point of arteries was not found.

In 4 eyes (23,5 %) with threshold stage of classic ROP and in 5 eyes (100 %) with plus-disease OCT revealed significant macular area edema with severe change of fovea profile and serous neuroepithelium detachment. Retina thickness in the fovea center was 530 ± 5 microns. Serous neuroepithelium detachment looked like prominent hyperrefletive contour with optical transparent zone between neuroepithelium and retinal pigment epithelium. Within 6 weeks after photocoagulation macular edema completely regressed. Tomograms showed reduction of retina thickness up to 135 ± 5 microns, with subsequent restoration of the fovea profile.

Conclusions. Slit-lamp argon-laser photocoagulation is the effective method for the treatment of threshold retinopathy of prematurity. Dosed laser influence, minimal invasiveness, clear visual control during slit-lamp argon-laser photocoagulation allow to put 'target' laser burns with necessary 'therapeutic' power in the pathological process site.

LASERPHOTOCOAGULATIONTHROUGHASLIT-LAMPFORRETINOPATHY OF PREMATURITY.

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Purpose: To present our results of slit-lamp laser photocoagulation with sedation and analgesia in the treatment of retinopathy of prematurity (ROP).

Material and methods: Between March 1999 and May 2005, 62 premature infants (125 eyes) with threshold ROP were consecutively treated with argon laser photocoagulation delivered through a conventional table mounted slit-lamp and a pediatric wide field quadraspheric contact lens, under 3 doses of 1-2 mg/kg/IV ketamine each, every twenty minutes. Among them, 39 infants (77 eyes) that had 3 months of post-treatment follow-up or more were included in the present study.

Results: 27 eyes had a zone I disease, and 50 a zone II disease. Mean post-treatment follow-up was 12.3 months (r= 3-59 months). Complete resolution of the disease without apparent sequel was observed in 72 eyes (94.5 %) of the cases. Two eyes developed a stage V disease, 2 eyes a retinal fold involving the macula, and 1 case a late vitreous haemorrhage, all of them having had extensive stage III within zone I disease. All the unfavourable outcomes occurred unilaterally. Ketamine provided a good sedation during the procedure. Only 2 infants needed transient endotracheal intubation because of respiratory depression during the procedure. No other significant systemic complication was observed. Neither cataract nor iris burn or posterior synechia were observed during the follow-up period.

Conclusions: Laser photocoagulation through a slit-lamp and a quadraspheric lens may be performed comfortably, accurately and safely under sedation and analgesia with systemic ketamine in the treatment of ROP.

SLITLAMP-DELIVERED LASER PHOTOCOAGULATION OF ROP UNDER GENERAL AND TOPICAL ANAESTHESIA

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Background. Cryocoagulation or binocular indirect laser photocoagulation for ROP is frequently carried out under general anaesthesia or topical anaesthesia with sedation because it is considered a painful procedure, due in part to scleral indentation. In premature infants the peripheral retina can be visualised up to the ora serrata without scleral indentation using slitlamp binocular indirect ophthalmoscopy with a contact lens. We retrospectively studied slitlamp-delivered laser photocoagulation for the treatment of threshold ROP using general anaesthesia and topical anaesthesia with sedation.

Methods. Thirty eyes of 15 premature babies (mean gestational age 26,1 weeks; mean birth weight 814,4 g) with threshold ROP in zone II were treated with slitlamp-delivered 532 nm laser photocoagulation using a contact lens. The infants were swaddled and held in lateral decubitus by an experienced neonatal nurse. Tight scatter photocoagulation was applied to the avascular retina from the vascular ridge to the ora serrata without the use of scleral indentation. Ten babies were treated under general anaesthesia (desflurane) in the operating room (group A). Five babies were treated in the neonatal intensive care unit (group B) using topical anaesthesia after sedation with chloral hydrate, oral sucrose and a dummy. One infant in group B needed supplemental treatment 13 days later because of bilateral progression of threshold ROP.

Results. In no case treatment had to be interrupted because of systemic complications. After surgery respiratory support in group A was unchanged in 5 infants, the 5 other cases needed increased support for a mean of 53 hours (range 1,5 to 120 hours); in group B respiratory support remained unchanged. The time to regain full enteral nutrition was 27,4 hours in group A. In group B in the first 3 cases full enteral nutrition was re-established after 15 hours in 2 infants, the other baby received total parenteral nutrition; in the 3 most recently treated cases enteral nutrition was not interrupted. Postoperative analgesia (paracetamol) was administered in 7 cases in group A (once in 4 cases, and for a mean of 28 hours in the other 3 cases), and in no cases in group B. In 3 eyes minor retinal haemorrhages developed during treatment. In all eyes ROP regressed.

Conclusions. Slitlamp-delivered laser photocoagulation can be a safe and effective method to treat threshold ROP even under topical anaesthesia. Omitting scleral indentation may be one of the reasons for the smooth postoperative recovery observed in this series.

THE RESULTS OF DIODE LASER TREATMENT FOR POSTERIOR RETINOPATHY OF PREMATURITY

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Purpose. To assess the effectiveness of diode laser therapy for Posterior Retinopathy of Prematurity

Methods. In our unit from January 2000 to the month of October 2005 we have treated 50 eyes of 25 children of comprised gestational age from 23 to 31 weeks, birth weight between 610 and 1200 g., to laser photocoagulation for ROP stage 3 plus zone II and 3 for ROP zone 1 plus (A.P. ROP).

Results and Conclusions.

4 eyes (8%) of 4 infants are evolved to the stage 4A

4 eyes (8%) of 2 infants are evolved to 5 the stage

42 (84%) eyes have had a good outcome with regression of disease.

The diode laser therapy is the treatment of choice in posterior ROP.

TREATMENT OF ZONE 1 RETINOPATHY OF PREMATURITY (ROP): OUR EXPERIENCE

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Background: To describe the outcome of threshold and pre-threshold Zone 1 ROP.

Methods: We performed a retrospective analysis of 6 premature babies (12 eyes) with zone 1 ROP observed and treated between January 1997 and May 2006.

Results: 8 eyes with threshold ROP had an unfavorable outcome despite argon or diode laser treatment.

1 eye with pre-threshold ROP had an unfavorable outcome despite laser treatment and surgery.

3 eyes with pre-threshold ROP had good anatomic outcome: 2 just had laser treatment and 1 had an intravitreal injection of bevacizumab after the laser treatment.

Conclusion: ROP located in zone I has a distinct clinical presentation, poor response to therapy and poor anatomic and visual outcome even when treated at pre-threshold. We think that anti-VEGF drugs have promising potentialities in the treatment of ROP.

RETINOPATHY OF PREMATURITY ZONE I - A CONSTANT CHALLENGE. ROMANIAN EXPERIENCE

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Background: our study aimed to evaluate if there were any differences between pre- and postnatal data of premature babies with ROP in zone I with plus disease and that of those with threshold ROP in zone II, the specific features of laser treatment and post-treatment ROP outcome.

Methods: between 2003-2006, 122 premature neonates were treated for severe ROP in our institution. Comparisons were made between those with ROP zone I with plus disease (group A) and those with threshold ROP in zone II (group B) with respect to their perinatal features (GA and BW), maternal pathology during pregnancy, head ultrasound in the early postnatal period, laser photocoagulation data and postlaser outcome.

Results: 73 eyes from group A (37 babies) and 155 eyes (85 babies) from group B were treated with laser. Maternal pathology was similar in the two groups. GA and BW were lower for group A than B ($p=0.029$ for GA, $p=0.054$ for BW).

Laser photocoagulation was applied at 35.8 weeks postconceptional age (group A) and 37.8 weeks (group B) - $p=0.001$.

No significant differences were noted between the two groups with respect to the need for mechanical ventilation, oxygen therapy with $FiO_2 >40\%$ and the incidence of abnormalities of head ultrasound in the early postnatal period.

Postnatal pathology (anemia, sepsis, prolonged jaundice) were also similar for the two groups.

The number of laser spots was higher in group A than in group B (1885 vs 1155), $p<0.001$, and so was the energy used (median 500 mW for group A and 350 mW for group B, $p<0.001$).

A second session of laser treatment was necessary for 43.2% neonates from group A and only for 17.1% neonates from group B ($p=0.006$).

A favorable outcome was observed in 70.2% of the babies from group A and in 87.9% in those from group B ($p=0.001$).

RetCam II images show the different features of ROP zone I from II (the absence of fibrovascular ridge in the former is significant).

Conclusions: The premature babies with lower GA and BW are more liable to develop ROP zone I with plus disease. The incidence of unfavorable outcome of severe ROP is higher in the preemies with ROP located in zone I than in zone II. No significant differences were recorded between the pre- and postnatal data of the premature babies from the two groups.

RETINOPATHY OF PREMATURITY (ROP) SCREENING AND TREATMENT EXPERIENCE AT A THIRD LEVEL HOSPITAL IN MEXICO CITY

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Purpose: To report the experience on diagnostic and treatment of ROP in Hospital 'Dr. Manuel Gea Gonzalez' over a 5 year period.

Methods: A retrospective review of patients screened and treated for ROP at the intensive care unit of the Hospital 'Dr. Manuel Gea Gonzalez' including premature patients born from June 2000 to June 2005. We included all patients with complete register and searched for: gestational age, birth weight, age at the evaluation, diagnostic, treatment and evolution.

Results: 438 patients were included founding: a mean age at birth of 32.61 weeks, 1228 grams of weight and the screening was performed at 35 days after birth; of those patients reviewed we found: 185 without ROP, 107 with ROP I, 87 with ROP II, 56 with ROP III and 3 with ROP IV. 90 eyes were treated with argon laser and 28 with cryotherapy; 8 eyes needed re treatment; the complications were: eyelid edema, uveal effusion, glaucoma and 3 eyes progressed.

Conclusions: Advances in neonatal care have increased the survival of very low birth weight premature patients. Opportune detection and treatment of ROP improve the life quality of premature patients and with fewer complications on the laser treated group.

RESULTS OF SCREENING AND TREATMENT OF RETINOPATHY OF PREMATURITY OVER A 10 YEAR PERIOD

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Objective: To report the results from the screening and treatment of ROP over a period of 10 years at the Specialized Eye Hospital, Varna, Bulgaria.

Method: Retrospective case note review, between 1996 and 2005, of 686 premature babies screened for ROP in the Specialized Eye Hospital with birth weight below 2050 gr. and gestational age less than 35 weeks. Those with severe ROP were treated with cryotherapy. In 2001 regular screening rounds were introduced in the neonatal unit. The results for 1996-2000 and for 2001-2005 are compared.

Results: The overall incidence of ROP was 20.8%, increasing from 17.92% in the period 1996-2000 to 23.3% in the second period 2001-2005. The number of babies requiring screening increased from 318 in 1996-2000 to 368 in 2001-2005. The incidence of ROP increased from 17.92% in the first period to 23.37% in the second but there was no significant difference in the incidence of severe ROP requiring treatment. The unfavorable outcome after treatment, based on early anatomical outcome, decreased significantly during the second period from 41.56% to 13.51%. The favorable outcome increased during the last 5 years from 71.43% to 93.53%.

Conclusion: The number of babies surviving in our unit has increased as has the incidence of ROP but our treatment outcomes have improved. Regular screening and earlier treatment are important in improving the outcome for babies with ROP.

OUTCOMES OF DIODE LASER TREATMENT OF RETINOPATHY OF PREMATURITY

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Background: Currently the method of first choice treatment in the threshold active phase of ROP is the laser photocoagulation of primary nonvascularized retina. The successful anatomical results are achieved in 81 to 100 %. The purpose of the study was to evaluate the outcomes of diode laser treatment of active phase of retinopathy of prematurity.

Patients and method: We have studied 590 premature infants since January 2003 to March 2006. In 102 premature infants (204 eyes - 17,3 %) ROP was found. Birth weight varied from 650 to 1680g (mean 1110g) and gestational age ranged from 23 to 33 weeks (mean Hbd 28,1). In 30 premature infants (52 eyes - 25,5%) stage 1 ROP was in III zone and in 24 children (48 eyes - 23,5%) - stage 2 ROP was observed in III zone. In these cases retinopathy has regressed without treatment. 52 premature infants (104 eyes - 50,9%) with threshold ROP (stage 3a) in II zone (12 eyes) and in II and III zone (40 eyes) were treated by using the diode laser photocoagulation. Birth weight ranged from 650 to 990 g (mean 799,23 g) and gestational age from 23 to 28 weeks (mean Hbd 26,2).

Results: Good anatomical results were obtained in 49 cases (98 eyes - 94,23 %), in 3 cases (6 eyes - 6,12%) total retinal detachment occurred. In these cases the progression of retinopathy was likely associated with a poor general condition and a extremely low birth weight and gestational age. In addition in 2 eyes we observed uveitis as a complication of laser treatment.

Conclusions: The diode laser treatment of active phase of ROP provides good anatomical results. The outcomes of treatment depend on the other chronic diseases of premature infants.

LIMITED LASER ABLATION FOR SEVERE RETINOPATHY OF PREMATURITY

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Purpose: To assess the safety and efficacy of limited, segmental laser photocoagulation as interdictive treatment of eyes with stage 3+ ROP in zone II or III.

Design: Retrospective review of eyes receiving limited, segmental laser ablation for ROP.

Participants: Between March, 2000 and May, 2006, 161 eyes of 91 patients underwent limited laser treatment of severe ROP in lieu of standard 360° ablative treatment to the entire avascular retina. 37 of the 161 eyes treated with limited laser were excluded from this review because of inadequate follow-up. Follow-up to at least 44 weeks post menstrual age (PMA) was available on 124 eyes of 73 patients. The mean birth weight of this group was 753 g (range: 420-1420) and the mean gestational age at birth was 25.4 weeks (range: 23-30).

Intervention: Laser photocoagulation was performed to the avascular retina adjacent to areas of stage 3 ROP in eyes with Type I ROP in zone II or in select eyes with stage 3+ ROP in zone III. Near-confluent diode laser photocoagulation (810 nm) was placed only in areas adjacent to the stage 3 disease without treating the entire avascular retina. In eyes with Type I ROP in zone II that had only stage 2+ ROP, the photocoagulation treatment was applied solely adjacent to the areas of the stage 2 ROP. The avascular retina adjacent to stage 1 ROP was not treated. The avascular retina adjacent to stage 2 ROP without plus disease was left untreated.

Outcome measures: Anatomic appearance of the posterior retina at 44 weeks post-menstrual age (PMA) or the development of retinal detachment.

Results: 124 eyes of 73 patients are included in this review. 118 eyes (95%) were treated for zone II disease and 6 eyes (5%) had zone III disease. The mean age at the time of treatment interdiction was 38.4 weeks PMA (range: 33.9 - 46.9) and the mean number of clock hour sectors of stage 3 disease at the time of the treatment was 3.8 (range: 1-9). 88 eyes (71%) had contiguous stage 3 ROP and 36 eyes (29%) had non-contiguous stage 3. Outcome measures on all eyes were made at e 44 weeks post menstrual age or at the time of noting retinal detachment. One eye (.8%) developed a stage 4A retinal detachment. No eyes developed a tractional retinal fold or observable macular dragging.

Conclusions: Limited laser photocoagulation treatment of severe ROP in zone II or III is safe and effective in causing involution of the active neovascular disease and preventing adverse anatomic outcomes in a group of eyes at high risk to retinal detachment from ROP. Limiting the extent of peripheral ablative treatment should help preserve better peripheral vision in these eyes than those that receive standard, 360° ablative treatment.

ROP THRESHOLD - CRYOTHERAPY LONG TERM RESULTS

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Purpose: To analyze and present the follow-up of our ROP cases that underwent cryotherapy.

Material And Methods: Between 1996 and 2006, 920 newborns had criteria for screening for ROP (birth weight equal or less than 1500g and/or gestational age equal or less than 32 weeks). 10 of them (20 eyes) achieved ROP threshold stage, requiring treatment, and were submitted to cryotherapy.

Results: In 70% of the eyes that underwent cryotherapy (14 eyes), the disease regressed and they developed normal vision. In the others, the disease progressed: 2 eyes to stage IV A and 2 eyes to stage IV B (with visual acuity reduced to light perception), and 2 eyes achieved stage V, with no light perception.

Conclusion: Emphasis should be placed on a rigorous follow-up, to permit an early diagnosis and successful treatment.

RE-TREATMENT FOR ACTIVE RETINOPATHY OF PREMATURITY. WHEN, WHERE AND HOW.

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Background: The structural success of treating stage 3 retinopathy of prematurity has improved markedly from 75% CryoROP study (1988) to 91% ETROP study (2003). However despite appropriate treatment failures still occur. What more can be done to improve the structural and functional outcome?

Method: Retrospective analysis of infants treated with laser for stage 3 ROP was performed. 141 premature babies were treated 1991-2006 and the details of those requiring further treatment was analysed. Re-treatment was performed because of persistent plus and active stage 3 or an elevated fibrovascular shunt, or a large neovascular frond overlying the treated avascular area or a shallow tractional retinal detachment.

Results: 17 cases were re-treated (12.1%). In 15 both eyes were re-treated, in 2 cases only one eye. Mean gestational age 24.5 weeks, treated initially at mean post menstrual age (PMA) of 36.82 weeks (range 33-41) and re-treated at mean of 40 weeks PMA (range 36-44). An average of 23 days between initial and re-treatment.

All were initially treated with near confluent laser, apart from one eye of one infant who had 749 diode laser burns and the treatment completed with cryotherapy because of a breakdown with the laser machine.

Re-treatments were completed using either cryotherapy alone (4) or laser alone (11) or a combination of cryotherapy and laser (2).

The re-treatment strategy varied depending on the individual case. This included filling-in any untreated gaps, cryotherapy straddling the active shunt and laser applied posterior to the ridge in vascularised retina.

Re-treatment was successful in maintaining a flat retina in 26 eyes. However a macula fold occurred in 2, stage 4A in 2 and stage 5 in 2. The average days between treatments in those that failed was 30.6. Late referral was a factor in one case.

Conclusions: Re-treatments can be an effective way of improving the success rate of treatment. Failure was associated with a delay in instituting additional treatment. Laser posterior to the ridge proved successful in walling off the tractional retinal detachment which then resolved with good long-term functional outcome.

Lecture 13

Influence Of Clinical Trials On Management Of Retinopathy Of Prematurity



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I. History of ROP, 1942 to present

II. CRYO-ROP Study: 3 parts

- The Multicenter Trial of Cryotherapy for Retinopathy of Prematurity
- Natural history study of ROP
- The Outcome Study of cryotherapy and ROP

Incidence of ROP, 1250g or Less

- 2/3 developed ROP of any degree
- 6% developed threshold ROP
- In the category less than 750g, 16% reached threshold
- 1000-1250g BW, only 2% reached threshold

Long-term outcome

- Prospective follow-up for 15 years
- 254/291 returned for examination
- Studied incidence of new retinal detachments/macular folds
- The last cohort of untreated threshold eyes.

Unfavorable acuity (20/200) from age 3 to age 15

Years age	Control %	Treated %
• 3 ½	58	47
• 5 ½	62	47
• 10	62	44
• 15	64	45

Acuity Difference, Rx Vs Control

<u>Years age</u>	<u>Percent reduction UF</u>
• 3 ½	11
• 5 ½	15
• 10	18
• 15	20

Cases of New Retinal Fold/ Detachment

in eyes without these findings at 10 years:

<u>Treated eyes</u>	<u>Control eyes</u>
6 (4.5%)	7 (7.7%)

III. Multicenter ROP Prevention Trials

- Cooperative study of RLF and the use of oxygen (1956)
- PaO₂ Levels and RLF (1977)
- LIGHT-ROP: Light Reduction in Retinopathy of Prematurity (1998)
- STOP-ROP: Supplemental Therapeutic Oxygen for Prethreshold Retinopathy of Prematurity (2000)

IV. Major clinical therapy trials in ROP

- **CRYO-ROP**: Coined “**Prethreshold**” disease:
Zone I - any stage of ROP
Zone II - stage 2+ or 3

Onset of Prethreshold at median 36 wks postmenstrual wks

- **ETROP**: Early Treatment for High-risk Prethreshold Retinopathy of Prematurity (2003)
- Compared standard treatment vs at a milder disease state
- Earlier treated eyes were selected as eyes predicted to need treatment later
- Prediction based on risk data from the CRYO-ROP study

Unfavorable Fundus Outcomes:

- Conventional group of eyes = 15.6%
- Selected earlier treated eyes = 9.1%
- (P < .001)

New clinical indicators for Rx

- Treat prethreshold eyes that develop Plus Disease
(specific degree of dilatation and tortuosity of vascular tree)

Exceptions:

Zone I – treat stage 3 without plus
Zone II – add stage “1+”
Zone III – rarely, if ever, treat

V. Future trial is needed for

Stage 4 (retinal detachment):

- Choice of intervention between scleral buckling and vitrectomy
- Timing of intervention
- Possible neovascular inhibitors

Lecture 14

Management Of Stage 4 and 5 ROP



Tatsuo Hirose

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Stage 4 ROP or partial retinal detachment is usually tractional with a small degree of exudative component in nature. Though retinal detachment is a serious complication of ROP, not all stage 4 requires treatment particularly when the detachment is shallow and is not associated with neovascularization. Indications and the methods of treatment are still controversial. Treatment choice is cryopexy, scleral buckling, closed vitrectomy with or without lens saving and open sky vitrectomy. In the first study, among 36 eyes with stage 4 ROP, 22 eyes underwent SB while 14 eyes were watched in non-randomized fashion.

In 13 of 22 SB eyes (59%), the retina reattached while the retina in 9 of 22 (41%) progressed to stage 5. In the observed group, 6/14 eyes (43%) either stabilized spontaneously reattached completely while 8/14 eyes (57%) progressed to stage 5. In both groups (SB and observation) the severity of the plus disease is a significant factor in predicting the progression to stage 5. In the presence of plus disease, the eyes, which underwent SB, did significantly better than those left alone. Though the study was not randomized and was biased, the results indicate that the significant numbers of Stage 4 regressed spontaneously particularly when there was no plus disease. SB will be ineffective in the posterior zone ROP in which the detachment is limited to the posterior zone with the ridge located much posterior to the equator and the anterior avascular retina not detached.

Subset of the stage 4 is 8 eyes of 6 patients showing posterior zone stage 4 ROP. The detachment showed unique features. The location of the retinal detachment in this group (RD) was nasal to the disc without detachment in the temporal to the disc including the macula in 5/8 eyes. Another unique feature of this group is retinal detachment without macula involved (Stage 4a) in which the major retinal arcade was pulled superiorly and inferiorly making the macula stretched apart making the vision very poor in spite of the attached macula. 4/8 eyes with severe plus disease all progressed to stage 5. 4/8 eyes showed no plus disease. Among those 4, one had lens saving closed vitrectomy (CV), with reattachment, two had lensectomy and CV with reattachment in both. The last one was watched and the retina was spontaneously reattached.

Stage 5 or total retinal detachment is not uniform in its severity. The retina still can reattach spontaneously but by the time it reattaches, the retina usually becomes atrophic and no useful vision results. The wide open-open funnel detachment can be treated by SB with

external drainage of subretinal fluid alone. In cases in which the membrane is not very dense or extensive and retina is very well visible by ophthalmoscopic examination, closed vitrectomy with or without lensectomy may be considered. Those cases with white pupil with no view of the detached retina can be operated upon by open sky vitrectomy with anatomical reattachment of the retina and ambulatory vision. The author will discuss the indications, the operative procedures, anatomical and functional results of over 900 cases with stage 5 ROP accumulated for the past 25 years.

Lecture 15

Treatment Of Retinal Detachment In ROP



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Background: Retinal detachment is the main cause of severe visual loss of in children with ROP. Cryo- and laser therapy of stage 3 have reduced but not eliminated the occurrence of these stages of ROP. The treatment of retinal detachment in ROP is still the greatest challenge for the ophthalmologists treating children with this disease.

Aim: The aim of this paper is to present functional results in children with untreated ROP stage 4a, 4b and 5, possibilities of surgical treatment of these stages of ROP and the results obtained after the surgery.

Material and method: One hundred children with ROP stage 4 and 5 not treated surgically and 660 operated patients with the same stages of disease were observed by the author in years 1996 – 2006. All these children have been treated according to the guidelines developed by the author (Table I). Children with stages 4a have been observed and if retinal detachment was impending macula segmental scleral buckling was performed. This type of surgery was performed in 14 premature infants with stage 4a. In stage 4b with moderate extraretinal proliferation segmental scleral buckling was performed if there was no tendency for spontaneous reattachment (16 premature infants). In 28 children with stage 4b and the most extensive extraretinal proliferation and temporal traction the 180° sclera resection (20 cases of full-sclera and 8 cases of partial-sclera resection) was used. In patients with stage 5 with moderate extraretinal proliferation (90 children) the modified encircling buckling (silicone band lengthening of 6 mm after 6 months and its removal after 12 months) was performed. In patients with open funnel configuration and more extensive extraretinal proliferation (12 children) lens-sparing vitrectomy was used. In patients with closed funnel configuration and the most severe extraretinal proliferation (500 children) limbal approach vitrectomy was performed.

In all patients the clinical course of the disease, visual acuity and binocular vision (if possible) were examined during follow-up. Visual acuity was measured with the use of Lea preferential looking cards, figures optotypes, single figures cards, Lea optotypes, HOTV optotypes and Landolt rings.

Results: In unoperated group with stage 4a spontaneous reattachment was observed in 27%, the disease progressed to stage 5 in 45% and temporal falciform fold developed in 28% of premature infants. In stage 4b spontaneous reattachment occurred in 15%,

progression to stage 5 in 55% and falciform fold was seen in 30% of children. In stage 5 spontaneous reattachment was observed only in 6%, in 8% total but flat retinal detachment with moderate extraretinal proliferation developed and in 86% of infants disease progressed to open or closed funnel configuration of retinal detachment. Visual acuity was: no light perception in 50%, light perception in 15%, 0,01-0,08 in 12%, 0,1-0,5 in 16% and 1,0 in 7% of children in stage 4a, no light perception in 60%, light perception in 25% and 0,1 > in 15% of children in stage 4b and no light perception in 76%, light perception in 20% and finger counting in 4% of children in stage 5. After segmental scleral buckling in children with stages 4a and 4b retinal reattachment was obtained in 60% of operated patients and visual acuity of 0,3 was observed in 47%, 0,02-0,2 in 27% and less than 0,02 in 26% of patients. After full- or partial sclera resection retinal reattachment was seen in 80% and visual acuity of 0,1 was found after the operation in 57% and 0,08 – 0,02 in 43% of these children. In the group operated with the use of modified encircling buckling total retinal reattachment was observed in 52% and partial reattachment in 24,5% of premature infants. The surgery failed to reattach the retina in 23,5%. Visual acuity was: no light perception in 56,1%, light perception to 0,02 in 24,5% and 0,02 to 0,2 in 19,4% of children. In patients after vitrectomy retinal reattachment was seen in 21% of them but vision of 0,01 to 0,03 was observed only in 4%. Lens sparing vitrectomy produced better results: retinal reattachment in 42% and visual acuity of finger counting to 0,07 in 33% of operated children but it was group of patients with less severe extraretinal proliferation than in vitrectomy group.

Conclusions: Occurrence of retinal detachment in ROP is associated with extremely poor prognosis for vision in the involved children if left untreated. The obtained results of the treatment indicate that retinal and vitreoretinal surgery can reattach retina and improve visual function in some patients with active stages 4a and 4b and even in selected cases of stage 5. The results of treatment of retinal detachment with severe extraretinal proliferation in regressed ROP with the use of vitrectomy are disappointing in prevailing majority of children. Performance of this surgery is nowadays the most controversial point in the treatment of ROP but it is still in use in some countries in the world. Therefore, our main goal of therapy must be the prevention of any amount of retinal detachment. However, if retinal detachment occurs segmental or encircling scleral buckling and sclera resection can be an effective treatment in re-attaching the retina in some patients with ROP stages 4 or 5. Up-to-now it is the only possible method of saving at least part of vision in these children although the functional results of therapy are not always satisfactory both for treated children, their parents and paediatric ophthalmologists.

TABLE I

Guidelines of surgery of retinal detachment in active stages 4 and 5 of retinopathy of prematurity

4 a -

observation and segmental buckling in the area of the greatest retinal traction if retinal detachment is impending the macula

4 b -

segmental buckling or 180° full-(partial) sclera resection in the area of the greatest retinal traction if no tendency for spontaneous reattachment after 2 – 3 weeks

5 with moderate extraretinal proliferation -

encircling scleral buckling (band lengthening of 6 mm after 6 months and its removal after 12 months) if no tendency for spontaneous reattachment after 2 - 3 weeks

5 with open funnel configuration -

lens sparing vitrectomy

5 with closed funnel configuration -

limbal approach vitrectomy

Abstract: 056

OPTICAL COHERENCE TOMOGRAPHY IN ACUTE PHASE RETINOPATHY OF PREMATURITY

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We describe a method of obtaining OCT scans in premature babies and present the preliminary findings of using this novel approach. We present information that could facilitate more accurate staging of the disease and discuss how OCT could be used to guide vitreoretinal surgeons contemplating surgical treatments.

EARLY VTREOUS SURGERY FOR AGGRESSIVE POSTERIOR RETINOPATHY OF PREMATURITY

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Background: aggressive posterior retinopathy of prematurity (ROP) rapidly progresses to a closed funnel of tractional retinal detachment within 1 to 2 weeks if left untreated. Retinal photocoagulation or cryopexy is sometimes effective for stabilizing aggressive posterior ROP; however, it sometimes cannot stop the progression to retinal detachment. We assessed the efficacy of early vitrectomy for aggressive posterior ROP to stop progression of retinal detachment.

Methods: Twenty-two eyes (15 patients) with aggressive posterior ROP underwent vitrectomy with or without lens sparing, because retinal photocoagulation failed to stop progression of fibrovascular proliferation, despite being performed early, densely, and with early retreatment. We assessed the status of retinal attachment and foveal formation ophthalmoscopically and the presence or absence of fixation of visual behavior.

Results: Follow-up ranged from 6 to 12 months (mean, 9). Six eyes (100%) in which a lens-sparing vitrectomy was performed developed a large tractional retinal detachment. In contrast, the retinas were completely reattached in 16 eyes (100%) in which vitrectomy with lensectomy was performed, nine eyes had foveal configuration, and 14 eyes had steady fixation.

Conclusions: These results suggest that early vitrectomy is effective for preventing retinal detachment in aggressive posterior ROP.

ANATOMICAL RESULTS AFTER EARLY VITRECTOMY FOR ADVANCED STAGES OF RETINOPATHY OF PREMATURITY

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The aim was to present anatomical outcomes following early vitrectomy (ppv) for advanced stages of retinopathy of prematurity.

Patients and Methods: Consecutive case series of 8 eyes 7 patients (mean birth weight: 750gramm, 560-980, mean gestational age at birth: 26 weeks, 23-28; mean postnatal age at ppv: 15 weeks, 11-18). Six eyes underwent diode laser coagulation for aggressive posterior retinopathy. Vitreous hemorrhage was the indication for vitrectomy in 4 eyes. Vitrectomy was performed due to stage 4B or 5 in another 4 eyes.

Results: Lens sparing vitrectomy occurred in eyes with vitreous hemorrhage caused by advanced stage 3 - 4A ROP. The proliferative tissue could be removed during the peeling of posterior hyaloid surface, the retina remained attached. The lens could not be preserved in the other 4 eyes with stages 4B and 5, funnel shaped retinal detachment developed.

Conclusions: Early vitrectomy could be a useful tool in the prevention of total retinal detachment in selected cases.

VITRECTOMY FOR STAGE 4 RETINAL DETACHMENT IN INFANTS WITH ZONE I RETINOPATHY OF PREMATURITY

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Purpose: To study the treatment outcomes after surgical intervention using vitrectomy to treat stage 4 retinal detachment in a series of infants with zone I Retinopathy of Prematurity (ROP).

Methods: Eighteen eyes of 13 preterm infants with zone I ROP that developed retinal detachment were surgically treated using vitrectomy. Fourteen eyes had stage 4A and 4 had stage 4B retinal detachments. A three port approach was used in all cases. Seven eyes were operated using a lens-sparing vitrectomy technique and 11 had a vitrectomy-lensectomy performed. Either 20 or 25 gauge instrumentation were used.

Results: Mean birth weight was 835,9 grams and mean gestational age was 25,5 weeks. Ten out of 14 (71.4%) infants with stage 4A and 3 out of 4 (75%) with stage 4B had a favorable outcome. In the lens-sparing group 6 out of 7 eyes (85.7%) a favorable result.

Conclusions: Vitrectomy is an effective intervention to treat stage 4 retinal detachment in infants with zone I ROP.

LENS SPARING VITRECTOMY IN STAGE 4A OR 4B RETINOPATHY OF PREMATURITY: INDICATIONS AND OUTCOME

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Purpose: to assess the anatomic success after two port lens sparing vitrectomy in stage 4A and 4B tractional retina detachments due to retinopathy of prematurity

Methods: a retrospective, non comparative consecutive case series of 10 eyes (10 patients) with tractional stage 4 ROP underwent a two port lens sparing vitrectomy (8 eyes were in stage 4A and 2 in stage 4B) All the babies were treated with laser previously and 2 babies (stage 4B) were outborn

Results: 7 of 8 stage 4A were completely reattached after a single procedure(87.5%) 1 progress to a complete detachment (stage 5). 2 eyes in 4B stage remained detached.

Conclusions: This study support the hypotesis that a early vitrectomy stops the evolution of 4A ROP stage.

ANATOMICAL AND FUNCTIONAL OUTCOME OF OF VITRECTOMY IN STAGE 4B OR 5 RETINOPATHY OF PREMATURITY

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Methods: Retrospective study of all ROP patients treated with vitrectomy for stage 4B or 5 in our institution from january 1998 to october 2005. Patients stage 3 or under, or not operated on were excluded . Data concerning gestational age, birth weight , initial eye and fundus examination, ultrasound examination, prior laser treatment, surgical procedure, post-operative complications, anatomical outcome were collected and analysed.

Results: Fifty three patients were included in the study : 32 eyes of 39 patients were operated for stage 5 ROP, and 11 eyes of 14 patients were treated for stage 4B ROP. Mean gestational age and birthweight were respectively 27.1 weeks and 989.5 g. Surgery consisted in all cases in three port lensectomy, extensive membrane peeling and gas tamponade, performed by a single surgeon. Open sky vitrectomy was performed in 3 cases presenting with central corneal opacification. Follow-up ranged from 6 to 48 months, and patients lost of follow-up were considered anatomical failures. Twenty eyes (62.5%) had flattened retina at the posterior pole at the end of follow-up in stage 5 cases, and 8 cases (72%) in stage 4B eyes. Secondary glaucoma was observed in 8 eyes, and treated with topical medication.

Conclusion: Good anatomical outcome can be achieved by surgical treatment in a high proportion of patients presenting with severe retinal detachment secondary to stage 4B or 5 ROP. In case of success, functional outcome is correlated to the vascular status of the retina and the absence of secondary glaucoma.

Lecture 16

Late Ocular Manifestations Of Retinopathy Of Prematurity



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The late manifestations of retinopathy of prematurity present a variable refractive and fundus appearance. Most commonly there is a degree of myopia. Intermediate changes in the retina produce a challenging problem in diagnosis that these changes are from prematurity. Hallmarks of the appearance of the fundus in these cases will be emphasized. The severe late form of vitreo-retinal changes will be outlined with emphasis on the challenge in management if a retinal detachment develops in these patients.

Lecture 17

Low Birth Weight Infant: a Long-term Medical and Social Responsibility



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Many premature children, especially those with very low birth weight, have serious long term problems both ophthalmologically and systemically. Some have major neuro-developmental disabilities, including cerebral palsy, mental retardation, visual impairment, and deafness. Ophthalmologically, they are at increased risk for refractive errors, strabismus, amblyopia, nystagmus, glaucoma, cataracts, optic atrophy, and cosmetic problems. This results in a subset of these premature children spending a life time in the ophthalmologist's office for a variety of reasons. Their eye evaluation will supply crucial information for appropriate school placement.

LONG-TERM OPHTHALMOLOGICAL OUTCOME IN PREMATURELY-BORN CHILDREN

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Preterm children have an increased risk of ophthalmological problems. In the neonatal period they may develop retinopathy of prematurity (ROP), while later they have an increased risk of various visual dysfunctions. Visual impairment may occur due to sequelae of ROP or to cerebral problems. Visual perceptual problems may also occur. Further, comparisons with normal populations reveal an increased risk of refractive errors, strabismus, visual field defects and reduced contrast sensitivity in prematurely-born children. The results from a long-term Swedish population-based study on prematurely-born children at 10 years of age will be reported and compared with children born at term in the same population.

The various visual dysfunctions require long-term ophthalmological follow-up of prematurely-born children and will be discussed.

PROGRESS OF VISION IN ROP BABIES - COMPARISON BETWEEN TREATED AND UNTREATED BABIES

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Purpose: To compare the progress of visual resolution and visual acuity between a group of non treated and a group of treated ROP babies.

Methods: A group of 114 untreated ROP children and a group of 28 treated with cryotherapy (according to ET study guidelines) ROP children, participated in this study. The visual resolution and / or the visual acuity (where possible) was evaluated 8 and 30 months since birth, using the LEA grating cards and the Kay pictures visual acuity test. Babies with severe neurological problems were excluded.

Results: In both groups the gestational age of the babies was less than 32 weeks and the birth weight less than 1500 gr. In the first group, during the first assessment, 2.2% appeared with BCVR equal to 0.43cpd, 5.14% appeared with $0.43 < \text{BCVR} < 1.75\text{cpd}$ and 92.66% appeared with $\text{BCVR} > 1.75\text{cpd}$. In the same group during the second assessment: 1.47% appeared with BCVR equal to 6/60, 8.82% appeared with $6/60 < \text{BCVR} < 6/18$ and 89.71% appeared with $\text{BCVR} > 6/18$.

In the second group, during the first assessment: 2.21% appeared with BCVR equal to 0.43cpd, 3.68% appeared with $0.43 < \text{BCVR} < 1.75\text{cpd}$ and 94.11% appeared with $\text{BCVR} > 1.75\text{cpd}$. In the same group during the second assessment: 1.47% appeared with BCVR equal to 6/60, 3.68% appeared with $6/60 < \text{BCVR} < 6/18$ and 89.71% appeared with $\text{BCVR} > 6/18$.

Conclusion: The visual acuity between the two groups seems to progress in almost the same way. Also, the majority of the ROP children, appear with good visual acuity, either treated or non treated for ROP.

THE LONG-TERM FUNCTIONAL RESULTS IN THRESHOLD RETINOPATHY OF PREMATURITY (ROP) TREATED INFANTS: CRYOTHERAPY VERSUS LASER

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Aim: to audit the visual and refractive outcome of consecutively treated babies with a minimum follow-up of 10 years, comparing cryotherapy (1989-1991) to laser (1992-1994) using the CryoROP outcomes as a benchmark.

Method: 69 infants were treated for stage 3 threshold ROP between 1989-1994. twenty eight infants were excluded for the following reasons; 9 infants died, 12 failed to attend for follow-up but had regressed disease and flat retina at last examination, 7 were blind due to stage 5 (5 cryo, 2 laser treated). The remaining 41 (77eyes) had 10 or more years follow-up.

Results: Twelve of the 20 (60%) cryo treated children, mean age follow-up 13.25 years, mean refractive error (mean spherical equivalent MSE) -8.96 right, -8.73 left had a visual acuity better than or equal to 6/12 (20/40).

Sixteen of 21 (76%) laser treated children, mean age follow-up 11.48 years, mean refractive error (MSE) -2.77 right, -3.21 left, had a visual acuity better than or equal to 6/12.

There was a strongly statistically significant difference in myopic refractive error between the 2 groups for right eyes cryo versus laser $p = 0.004$, for left eyes $p = 0.023$ (Mann-Whitney U test) but no statistical difference in the visual outcome $p = 0.732$, and $p = 0.274$ right and left respectively, though a tendency for better visions in the laser treated group.

Conclusion: The visual results were better than the CryoROP 10 year outcome for both groups where only 25% had visual acuity better than or equal to 6/12 (20/40). Laser treated eyes were more likely to have an acuity of better than or equal to 6/12 than cryo treated but it did not reach statistical significance. The refractive error was strongly significant with cryo treated eyes much more myopic. Differences in disease severity between the 2 groups cannot be excluded but as the cases are consecutive it was not felt to be a major factor in affecting the outcome results.

COMPARISON OF THE RESULTS OF TREATMENT FOR RETINOPATHY OF PREMATURITY WITH DIODE LASER PHOTOCOAGULATION AND CRYOTHERAPY - FOUR YEARS OBSERVATION

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Background. The aim of the study was to compare functional and structural outcomes of treatment for retinopathy of prematurity with diode laser photocoagulation and cryotherapy.

Material and methods. We examined 111 children aged 4 years, treated for retinopathy of prematurity with transpupillary diode laser photocoagulation or cryotherapy. Both functional (visual acuity, orthoptic status) and structural (anterior segment and fundus examination) results were evaluated. The cycloplegic refraction was examined in all cases.

Results. Favorable functional result occurred in 87.8% of eyes in patients after cryotherapy and in 97.4% of eyes in patients after diode laser photocoagulation. Structural outcome was favorable in 87.8% of eyes treated with cryotherapy and in 96.6% of eyes treated with diode laser photocoagulation.

Conclusion. Diode laser photocoagulation is an optimal method of treatment for active stages of retinopathy of prematurity.

ANATOMICAL AND VISUAL OUTCOMES AFTER TRANSPUPILLARY LASER COAGULATION TREATMENT FOR STAGE 3+ RETINOPATHY OF PREMATURITY (ROP)

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Background: Untreated retinopathy of prematurity (ROP) is one of the most common causes of childhood blindness. In the last years several articles have proposed that therapeutically outcomes after diode laser treatment are superior to cryotherapy. The aim of this study was to determine the anatomical and visual outcomes after transpupillary diode laser coagulation for stage 3+ retinopathy of prematurity.

Patients and methods: The medical records of all premature infants screened at our department were retrospectively reviewed to identify patients with stage 3+ retinopathy of prematurity treated with transpupillary diode laser coagulation. Between January 1996 and May 2006 49 eyes of 26 patients with a median gestational age of 27 weeks (range 24 to 32) underwent diode laser treatment. The median birth weight was 916 g (range 400 to 1800). At follow-up examination best-corrected visual acuity (BCVA), cycloplegic refraction, orthoptic status and anatomic status of the retina were measured. In cases of none-verbal children visual behavior (horizontal and vertical eye movements, face-to-face interaction, and reaction to occlusion) was described.

Results: Follow-up examination was performed in 20 of 26 cases (76.9%). 6 patients were lost for follow-up because of unknown address. In 35 eyes (94.6%) vascular proliferations regressed already after the first laser treatment. A second coagulation was necessary in one child. Thirty-two eyes (86.5%) showed peripheral retinal pigment epithelial scarring with an inconspicuous posterior pole. An 'unfavorable outcome', as described in the Cryo ROP study, could be found in 5 eyes (13.5%) (3 macular ectopia, 1 retinal fold, 1 vitreous haziness). Accurate visual acuity measurements were done in 9 of 20 cases. The mean visual acuity (BCVA) was 0.5 on the right and 0.5 on the left eye. The median spherical equivalent refractive error was - 1.25 D (- 13.0 D to 0 D). Visual behavior was observed in 11 children (55.0%). Normal horizontal and vertical eye movements, face-to-face interaction without objection of occlusion could be found in 8 cases (72.7%). 3 children showed reduced visual behavior and objected occlusion of one eye. Eleven children had strabismus (8 esotropia, 3 exotropia) and additionally 3 of them had a nystagmus.

Conclusions: Favorable anatomical and visual outcomes after transpupillary diode laser coagulation confirm the effectiveness of laser treatment for 3+ retinopathy of prematurity. In our study early treatment led to a total regression of ROP in 94.6%. Only one child underwent second laser treatment. 13 eyes of 9 children (72.2%), with a median age of 26 months at the time of examination, had visual acuity better than 0.4. Strabismus developed mainly in children with myopia of more than - 4.0 D.

LONG-TERM VISUAL OUTCOMES IN EXTREMELY LOW BIRTH WEIGHT CHILDREN

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Purpose: The goal is to analyze the long-term visual outcome of extremely low birth weight (ELBW) children and to determine which factors are most predictive of long-term outcome.

Design: This is a prospective observational longitudinal cohort study of children with birth weight less than 1001g.

Methods: 139 children were recruited. ROP examinations were graded according to the International Classification for ROP. Grating acuity was assessed monocularly with the Teller acuity cards. All children were assessed before 24 months adjusted-age. 123 of the cohort had a grating acuity assessment at over 3 years adjusted-age. Grating acuity results are compared to published normative data. For the children who were capable, assessment of recognition acuity was measured with the Electronic Visual Acuity system.

Visual outcomes were studied by analyzing acuity outcomes at ~36 months of adjusted-age, correlating early acuity testing with final visual outcome and evaluating adverse risk factors for vision.

Results: For this cohort of patients, the mean birth weight was 731g and mean gestational age at birth was 26 weeks. Data are presented for the right eye only and the ages reported are adjusted for prematurity to allow comparison with normative data. Early grating acuity (<6 mos. adjusted-age) was compared to the late grating and recognition acuity (>35 mos. adjusted-age), but in both cases analysis showed no statistically significant association. However the relative risk analysis showed that if the rate of early visual development was slower-than-normal, there was a 5.5 times higher risk of abnormal recognition acuity. Eyes with zone 1 disease were associated with a worse acuity outcome, lower birth weight and gestational age as compared with eyes of infants with zone II/III disease. Eyes of children born at <28 weeks GA had greater risk for abnormal recognition acuity than did those of children born at ≥28 weeks GA. Eyes of children with poorer general health after premature birth had a greater risk of abnormal recognition acuity.

Conclusions: Long-term visual development in ELBW infants is problematic and associated with a high risk of subnormal acuity. Early acuity testing can be useful in identifying children at greatest risk for long-term visual abnormalities, however, some early acuity measurements may be misleading in terms of the visual prognosis. The factor that was most predictive of a poor late outcome was the rate of early visual development, as calculated by the slope of the early acuity measurements. GA at birth of <28 weeks was associated with a higher risk of an abnormal long-term outcome.

SPEECH & HAPTICS BASED 2-D TRAINER FOR ENHANCED SPATIAL PERCEPTION

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This paper aims at developing 2-D cognitive map of a building or a locality to train visually-impaired people to enhance spatial perception thereby assisting them in real navigation. The topographical layout, color-coded identifiers for objects, and haptic feedback correlation with objects is first developed through man-machine interaction. Simulated training allows selection of any combination of starting and target spots. The trainer guides the blind through speech by describing surroundings, guiding directions, and giving early information of a turning, crossings, etc. Additionally, occurrences of various events (e.g. arrival of a junction, arrival of object(s) of interest, etc.) are signaled through haptics using consumer-grade devices.



Posters

THRESHOLD RETINOPATHY OF PREMATURITY IN VILNIUS COUNTY: NINE YEARS EXPERIENCE

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Background: The aim of the study - to present changes of birth weight (BW) and gestational age (GA) among infants who reached threshold ROP and underwent treatment over the period of nine years.

Material and methods: Data was collected prospectively from January 1995 to December 2003. Infants were screened for ROP in Vilnius University children's hospital by the same two ophthalmologists (R.B. and R.S). All infants were outborn. BW and GA had been recorded in all study subjects.

Results: Over the period 1995-2003, 2202 infants were screened for ROP. 320 infants reached threshold (14, 5% of all screened) and underwent treatment. Mean BW of threshold ROP infants dropped from 1558,1grams in 1995 to 1037,3 grams in 2003. Mean GA - from 30.7weeks to 27.2 weeks respectively.

Conclusions:

1. Insufficient experience in neonatal care was the reason for ROP in 'old' and 'heavy' infants.
2. BW and GA of threshold ROP cases are decreasing over the study period.
3. With improvement of neonatal care the incidence of ROP is decreasing but the disease still exists among the most premature infants.

INCIDENCE AND RISK FACTORS FOR DEVELOPMENT OF ROP IN A MATERNAL AND CHILD CENTRE IN INDIA

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Background: ROP is becoming common in developing countries with an improvement in survival of very premature infants. It is likely to emerge as a major problem in India because of improving outcome of 'at-risk' preterm infants.

Methods: We estimated the incidence of ROP among at-risk neonates in a maternal and child care unit in India. Infants with birth-weights of ≤ 1500 g, gestation ≤ 32 weeks and neonates who required supplemental oxygen for ≥ 24 hours were subjected to periodic ophthalmological evaluation for detection of ROP until full retina had vascularized

Results: Fifty four eligible neonates born during Jan 2002 to August 2003 completed the full evaluation. The incidence of ROP was 12% in the cohort and 27% among the very low birth-weight neonates. The incidence of threshold ROP was 4% in the cohort. Risk of developing ROP was inversely related to the gestation and birth-weight. Maternal Anemia, clinical sepsis and blood transfusion were also found to be independent risk factors for development of ROP on step-wise logistic regression analysis. Treatment by Cryotherapy was undertaken in 4 neonates (9 eyes) and led to complete regression of ROP.

Conclusion: The incidence of ROP in our neonates was lower than that reported from other centres. Blood transfusion and clinical sepsis are found to be independent risk factors for ROP.

INCIDENCE OF RETINOPATHY OF PREMATURITY IN EXTREME PREMATURITY AT THE HOSPITAL DE CLINICAS DE PORTO ALEGRE - BRAZIL

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Objectives: To evaluate the incidence of Retinopathy of Prematurity in extremely premature infants (birth weight under 1000 g and gestational age at birth of 30 weeks or less) born at the Centro de Neonatologia do Hospital de Clínicas de Porto Alegre, in southern Brazil, between October 2002 and April 2006, and compare these findings with the incidence of the disease in all very low birth weight infants (with 1500 g or less of birth weight and/or 32 weeks of gestational age at birth or less) in the same institution and period.

Methods: A prospective population-based study performed in all 280 premature infants born with birth weight of 1500 g or less and/or gestational age at birth of 32 weeks or less between October 2002 and April 2006. From this group of patients were considered for the study only those under 1000 g and gestational age at birth of 30 weeks or less. 137 infants fulfilled the criteria for this study and were examined by indirect binocular ophthalmoscopy with the 28 diopters lens after the instillation of Tropicamide 0,5% and Phenylephrine 2,5% drops to dilate the pupils. The mapping of the retina with a lid speculum was first conducted after 6 weeks of extra-uterine life and repeated weekly. To classify the disease was used the International Classification of the Retinopathy of Prematurity (1984/1987).

Results: In this prospective study retinopathy was diagnosed in 69 of the 280 neonates with a incidence rate of 24,64% among very low birth weight prematurity. Considering only the extremely premature infants (59 patients), the incidence was 49,15% (considering all stages). The disease reached stage 1 in 13,56% of the cases (8/59), stage 2 in 22,03% (13/59), stage 3 in 10,17% (6/59) and stages 4 and 5 in 1 patient in each group (1/59 - 1,69%).

Conclusions: The screening program with the ophthalmologic examination at the 6th week of life is an important instrument for the detection of the retinopathy of prematurity and must be done in all very low birth weight infants with 1500 g or less especially in those with gestational age at birth under 32 weeks. This study shows high incidence rates for the disease in neonates under 1000 g of birth weight and gestational age of 30 weeks at birth or less. This group is at the highest risk for retinopathy of prematurity and should be carefully examined and followed during the screening for the disease.

DOES THE SHAPE OF THE DEMARCATION LINE AND THE RIDGE IN COURSE OF ACTIVE STAGE OF RETINOPATHY OF PREMATURITY MATTER CLINICAL?

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Purpose: Retinopathy of prematurity (ROP) is the main reason for blindness in premature babies. So far, there have been no studies on the shape of the demarcation line and ridge in the acute retinopathy of prematurity or its influence on the clinical significance of ROP. In 11.42% of the eyes with acute ROP, irregularities of the demarcation line and ridge called „bays’ were observed. The aim of the study was to facilitate a comparison of the clinical significance of eyes with acute ROP and „bays’ and eyes with ROP but without „bays’.

Methods: One hundred and forty (140) premature babies (280 eyes) with acute ROP were examined. ‘Bays’ were found in the case of 32 eyes (11.42%). Progression to the ROP3c stage in group I (eyes with acute ROP and „bays’) and group II (eyes with ROP without „bays’).

Results: In 87.5% of eyes with „bays’, progression to stage 3c of retinopathy of prematurity was noted. In the group without „bays’, progression to stage 3c was observed only in 33.47% of the cases studied.

Conclusions: The present authors suppose that the presence of „bays’ of the demarcation line and ridge means the worst prognosis during the course of acute retinopathy of prematurity.

RETINOPATHY OF PREMATURITY IN EXTREMELY LOW BIRTH WEIGHT INFANTS: A TOKYO MULTICENTER STUDY

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Background: Retinopathy of prematurity (ROP) increases in Japan, because infants of low birth weight are able to survive in neonatal intensive care units. We investigated how the increase in survival rate in extremely low birth weight (a birth weight of 1,000g or less) infants had affected the incidence of ROP and the frequency of laser treatment.

Methods: We retrospectively reviewed the medical records of 122 surviving premature infants with birth weights less than 1,000g to determine the severity of ROP observed at 16 neonatal intensive care units in Tokyo between April and October 2002. Incidence, age at onset and stages of ROP determined by binocular ophthalmoscopy, and surgical outcomes of laser photocoagulation were analyzed.

Results: The survival rate was 85.6%. The mean gestational age was 26.7 weeks and the mean birth weight was 782.3g. One-hundred-and-five infants (86.1%) developed ROP, at 29-40 (average 32.5) weeks of postmenstrual age (gestational age at birth plus chronological age in weeks, PMA). Fifty infants (41.0 %) received laser treatment, in which the first treatment was performed at 30-43 (average 35.7) weeks of PMA, and retinal detachment developed in six infants (4.9%).

Conclusions: In these extremely low birth weight infants, there was an increase in the survival rate and in the incidence of severe ROP that progressed to the stage that required treatment.

THE CHANGES IN STRUCTURE OF PREMATURE BABIES WITH ROP FOR LAST 10 YEARS

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Retinopathy of prematurity is one of the leading causes of childhood blindness, probably due to an increase in survival rate of extremely small and premature babies in modern neonatal intensive care units. The survival of premature babies with extremely low birth weight is constantly increased.

The **purpose** of our investigation was to compare the morbidity of ROP among premature babies were on treatment in St. Petersburgs Neonatal Intensive Care Unit in 1995 and in 2005 years.

Methods: In 1995 in the Neonatal Center it has been treated 323 premature babies with birth weight less than 2000 g; in 2005 - 447 babies. The growth of premature babies is connected with decreasing of the mortality among children with extremely low birth weight. The mortality of babies with low birth weight has been decreased for the last 10 years in 4 times among babies with birth weight less than 1000 g : 47% in 1995 and 12% in 2005; with birth weight from 1001 g up to 1250 g in 7 times: 41% in 1995 and 6% in 2005; in 6 times with birth weight from 1251 g up to 1500 g: 19% in 1995 and 3% in 2005. With this improved survival we expected increase an incidence of ROP. However, the morbidity of ROP has remained at a former level: in 1995 with birth weight less than 1500 g it has made 46% and 48% in 2005; but the absolute quantity of patients with ROP has increased considerably (in 1995 has been treated 43 babies with birth weight less than 1500 g and 103 babies in similar weight group in 2005).

Results: The comparative analysis of acute stages of disease has shown the essential changes in its structure. So, if in 1995 babies with I stage of the active period have made 64% among all patients with ROP, in 2005 - only 15%. The quantity of patients with severe ROP has essentially increased. The quantity of patients with threshold ROP requiring surgical laser treatment has reached 55% in 2005 and 16% in 1995. We connect increase in quantity of patients with threshold ROP with substantial increase of survival rate of babies with extremely low birth weight as the maximal surgical activity is registered in this group of children. The lasercoagulation has been performed in the hospital since 1995. This method of treatment is constantly improved. Last years for increase of efficiency of treatment we use the stage-by-stage combined method of making the lasercoagulation. The disability because of ROP has not increased, even has a little decreased: 6% of all patients with ROP in 1995 and 4% in 2005.

Conclusion: The mortality of babies with low birth weight has been decreased for the last 10 years in many times. In spite of this fact, the incidence of ROP remained the same but the quantity of patients with severe ROP has essentially increased.

RACIAL VARIATIONS OF THRESHOLD RETINOPATHY OF PREMATURITY IN A MULTICULTURAL CITY

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Background: Retinopathy of prematurity (ROP) is a serious vasoproliferative disorder which primarily occurs in low birth weight (LBW) premature infants. Advances in neonatology have improved survival of LBW infants and therefore increased the number of babies requiring ROP screening and intervention in order to prevent blindness.

The United Kingdom (UK) is a 'vibrant' multicultural nation. It is therefore important to understand whether there are differences in the occurrence of threshold ROP (tROP) among different ethnic groups in order to adjust fund-management in the National Health Service between regions.

Purpose: To evaluate the West Midlands tROP cohort, and detect if differences between Caucasian and non-Caucasian LBW premature infants.

Methods: Prospective consecutive data of tROP presented to and treated by a single paediatric ophthalmologist based in tertiary referral centre, from 1999 to 2006.

All infants were screened under the current guidelines, birth-weight < 1500g and/or < 31 weeks gestation-age, first examination at 42-49 days postnatal-age.

Results: 186 infants (361 eyes) were treated, 88 (47.3%) infants were from outside the operators screening centres. Mean treatment workload was 25 infants/ year.

There were >867 infants screened/ > 2839 eye examinations conducted in the operators screening centres. The mean incidence rate was 32% of detecting any ROP, 65.5% were stage 1-II and 6.65% for tROP.

The mean gestation age (GA) for tROP was 25.7 (23-31) weeks, with the mean birth weight of 800 (300-1900)g. The mean postconceptional-age for tROP was 37.5 (32-47) weeks, with postnatal-age of 11.9 (6- 22) weeks.

Overall, 38 % of infants were non-Caucasian (36% African-Caribbean, 50%Asian, 11% mixed and 2% others); however there were higher proportion of non-Caucasian infants, 64.8% (46% African-Caribbean, 51%Asian and 3% mixed), from the operators screening centres, with urban coverage.

There were no significant differences between the groups in gestation-age (Caucasian 25.8 weeks vs. Non-Caucasian 25.6 weeks), postnatal-age at treatment (Caucasian 12.0 weeks vs. Non-Caucasian 11.7 weeks) and birth-weight (Caucasian 0.82kg vs. Non-Caucasian 0.76kg).

Conclusions: The non-Caucasian ethnic population in U.K. is 8% and 13% of the West Midlands population consists of ethnic minority (1.98% Black, 7.32% Asian, 0.22% mixed), however there were un-expectantly high tROP was found in the non-Caucasian infants, at 38%.

29.7% of Birmingham population consist of non-Caucasian ethnic group, and 64.8% of tROP was found in the non-Caucasian infants in Birmingham. This highlights the ethnic population is more concentrated in the large urban city and there were more tROP in LBW non-Caucasian infants than in LBW Caucasian infants, in this Caucasian dominated cohort population.

The urban-suburban discrepancy of ethnic difference of tROP might be a representation of UK diverse ethnicity. The disparity of tROP could be due to higher proportion of child-bearing age women in the non-Caucasian population, a reflection of their cultural and socio-economic differences.

**EPIDEMIOLOGY, COURSE AND RESULTS OF TREATMENT
OF RETINOPATHY OF PREMATURITY IN THE NEONATOLOGY
DEPARTMENT OF UNIVERSITY OF MEDICAL SCIENCES
IN POZNAN (POLAND)**

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Background: The purpose of this study is to determine epidemiology, course and results of treatment of ROP in the Neonatology Department of University of Medical Sciences in Poznan (Poland).

Method: The study comprised 547 children who were born from 1st October 2004 to 23rd November 2005. The frequency of ROP was evaluated according to the gestational age and the birth weight. Time of making diagnosis, ROP grading and location of changes were statistic analyzed. We estimated ROP treatment by means of diode laser photocoagulation, day of laserotherapy and results of treatment.

Results: ROP was diagnosed in 119 children, 44 of them were qualified for treatment, mean birth weight of treatment children was 1034 ± 284 g and mean gestational age $27,7 \pm 1,9$ weeks. ROP was diagnosed mean in $49,2 \pm 10,1$ day of life, treatment was performed mean in $58,3 \pm 11,5$ day of life. Complete remission was obtained in 95,5% of treated eyes.

Conclusions: It is necessary to create Polish database concerning course of retinopathy of prematurity and direct new recommendations about ROP sreening in Poland.

EPIDEMIOLOGY AND RISK FACTORS FOR RETINOPATHY OF PREMATURITY

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Purpose: To prospectively analyse the incidence of retinopathy of prematurity (ROP) with documenting perinatal clinical characteristics in affected infants, in attempt to describe risk factors for ROP. To evaluate its anatomical and functional consequences for visual development.

Methods: Between March 2002 and April 2004, 161 infants, with a gestational age ≤ 31 weeks and/or a birth weight ≤ 1500 g, were screened according to CRYO-ROP guidelines, using direct ophthalmoscopy with Layden contact lens. Risk factors for ROP were analysed with Student and Fischers tests. Then babies were summoned at 9 months old for strabismus and refractive disorders screening.

Results: ROP developed in 15% of the cases studied, among 1/5 prethreshold or threshold ROP. Gestational age at birth ($p < 0,0001$), low birth weight ($p < 0,0001$), stays length in neonatal intensive care unit ($p < 0,0001$), length of mechanical ventilation ($p < 0,0001$), length of oxygen provided ($p < 0,0001$), blood transfusions ($p < 0,0001$), hyaline membrane disease ($p = 0,0257$) and bronchodysplasia ($p = 0,0012$) were significant risk factors for ROP. Less than 40% of infants came back at 9 months old. Functional results at this period were satisfying : 5% of esotropia, 3% of exotropia, 22% of significant hypermetropia, 5,5 et 3% of myopia and astigmatism and 5,5% of anisometropia. No difference was found between children with or without antecedent of ROP.

Conclusions: Persistence of ROP, with more precocious prematurity and despite best consciousness of risk factors, imposes screening and prolonged following of premature infants, with a cooperation between ophthalmologist, neonatologist and concerned parents.

REFRACTIVE ERROR STATUS IN CASES OF ROP STAGE -2

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Aim: To find out refractive error status in cases of ROP (STAGE-) AT one years of age

Material and methods: 88 patients of ROP (STAGE-2) were included in this study, however 80 patients participated. These patients were initially examined during their neonatal period and were assessed for refractive error status at one year of age. Refraction was done under cycloplegia. These patients were having weight less than 1250gm at the time of birth.

Result: We found that 31.25% were myopic, 48.75% were emetropic and 20 % were hypermetropic.

Conclusion: At one year of age Patients of ROP stage -2 have significant amount of refractive error and myopia is more common than hypermetropia.

EXTREMELY LOW BIRTH WEIGHT INFANT: CASE REPORT

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Background: Retinopathy of prematurity is the main cause of visual impairment in premature infants. The survival of extremely low birth weight infants increased in recent years, due to advances in neonatal care, and it results more infants with very high risk of developing retinopathy of prematurity. Several factors increase the risk of ROP, especially those associated with short gestation and low birth weight, oxygen therapy, mechanical ventilation, and blood transfusion.

Case report: The immature boy was born by Cesarean section on 26th gestational week with 370 grams birth weight. Mechanical ventilation was required for 10 days due to pulmonary hypoplasia and immaturity. On the first day of life surfactant was administered. He required low ventilation settings during the respiratory therapy, and later oxygen therapy until the age of one month. Classical bronchopulmonary dysplasia didn't develop. Blood transfusion was necessary 12 times during his seven months of intensive care therapy. No intracranial pathology developed. He was discharged.

The first ophthalmological examination was performed on 4th chronological week. We didn't find any abnormalities. Follow-up examinations were carried out every week.

On 10th chronological week 4 contiguous clock hours demarcation line was found on right side in Zone II, and 1 clock hour ridge on left side with pre-plus sign. Progression was observed (6 cumulative clock hours ridge and 6 cumulative clock hours demarcation line with pre-plus sign on both sides in Zone II), but this didn't reach the level, which would have indicated treatment.

From 20th chronological week gradual regression was observed.

Discussion: Extremely low birth weight infants are most susceptible to ROP, but threshold level doesn't develop certainly. We hadn't to perform laser therapy because of ROP in our case, for the premature boy. Careful and accurate monitoring and adequate neonatal therapy resulted the regression of retinopathy. The increase of survival rate and improvement of quality of life can be expected with the advances in neonatal care.

INCIDENCE AND RISK FACTORS OF RETINOPATHY OF PREMATURITY REQUIRING TREATMENT IN INFANTS BORN GREATER THAN 30 WEEKS' GESTATION AND WITH A BIRTHWEIGHT GREATER THAN 1250 G

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Aim: To ascertain and compare the clinical risk factors for ROP requiring treatment in infants born less than 30 weeks gestation with a birth weight less than 1250 g (group I) and infants born equal or greater than 30 weeks gestation with a birthweight equal or greater than 1250 g (group II), utilising the Ankara University Neonatal Intensive Care Units' (NICU) data collection from 2000 to 2005.

Methods: This was a retrospective study of all VLBW infants admitted to Ankara University NICU over 6 years, from 2000 to 2005. Preterm infants were examined according to the international guidelines, and retinopathy was graded following the International Classification of ROP. All VLBW infants examined for ROP were included and data were retrieved retrospectively and analysed for obstetric and neonatal risk factors

Results: Out of 259 VLBW infants 33 died prior to examination (%12.7) Of the 226 VLBW infants who fit the screening criteria, threshold ROP was detected and laser photocoagulation was performed in 51 (22.5%) infants. Out of 51 treated infants 24 were in group I with a mean gestational age and birth weight 27.4 ± 1.21 weeks, 1006.25 ± 140.67 g. respectively and 27 were in group II with a mean gestational age and birth weight 31.14 ± 1.29 weeks, 1358.18 ± 253.32 g. respectively.

87.5 % infants vs 44.4% .infants had respiratory distress syndrome ($p < 0.01$), 87.5% vs 51.9% infants need mechanical ventilation ($p < 0.01$), 37.5% infants vs 7.4% infants had bronchopulmonary dysplasia ($p < 0.01$), 62.5% infants vs 66.7% infants had prolonged premature rupture of membranes ($p > 0.05$), 54.2% infants vs 44.2%.infants had early neonatal sepsis ($p > 0.05$), 58.3% infants vs 22.2%.infants had late neonatal sepsis ($p < 0.05$), 25 % infants vs 29.6% infants had patent ductus arteriosus ($p > 0.05$) in group I and II respectively.

Conclusion: In this small study, for infants equal or greater than 30 weeks gestation and with a birthweight equal or greater than 1250 g, the prevalence of ROP requiring surgery was not very low (11.9%).

Among neonatal morbidities prolonged premature rupture of membranes, PDA and early neonatal sepsis could be the factors affecting the development of threshold ROP in this group of patients.

This study does not support the evidence from other studies that screening for ROP could be restricted, at least within our referral network, to infants less than 30 completed weeks and a birthweight less than 1250 g. This study does not support the evidence from other studies that screening for ROP could be restricted, at least within our referral network, to infants less than 30 completed weeks and a birthweight less than 1250 g.

PREVALENCE OF ROP IN INDONESIA: RESULTS FROM SCHOOL FOR THE BLIND STUDIES IN JAVA ISLAND

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Purpose: To estimate the prevalence of Retinopathy of Prematurity (ROP), an avoidable cause of childhood blindness, in Schools for the Blind students representative of rural areas of communities of Java island, Indonesia.

Methods: Four-hundred and seventy-nine of a total of 500 students from 5 Schools for the Blind in Java island, Indonesia, were examined using the standard WHO/PBL eye examination record for blindness and low vision protocol. Data were analyzed for those aged less than 16 years or the onset of visual loss less than 16 years. Data on social demography and medical history factors were collected. ROP was defined when cicatrical retinal detachment or retinal tractional dates from infancy, or a history of prematurity or low birth weight and ocular findings consistent with this diagnosis were identified.

Results: Most of the students (95%) were blind (BL); 4.6% had severe visual impairment (SVI) and 0.4% had visual impairment (VI).

ROP was identified in only 5 of 479 (1.1%) cases. This low prevalence is in accordance with other School for the Blind studies in India (0.5 %) and China (1.9 %), but is in contrast to those in industrialized countries such as Edinburg, UK (18%) and USA (8-19%).

Conclusions: The low incidence of ROP found in our study is most likely the result of the high mortality rate of premature children in the rural areas of Indonesia, as in other developing countries. This finding highlights the need for better interaction between primary and secondary health care and the specialist tertiary centers (and their intensive neonatal care services), to provide high coverage referral access for high risk mothers and/or premature or low birth weight infants. This may help to, first, increase the survival rate of this group of babies, and then, as a next step, to install adequate screening programs by pediatric ophthalmologists and retina specialists to diagnose and treat ROP in due time.

5 YEARS OF RETINOPATHY OF PREMATURITY IN CHILE. RISK FACTORS IN A DEVELOPING COUNTRY

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Background: Chile is geographically a long and narrow country with large distances between the different cities. Is in developing, like others countries in South America. The National Ministry of Health have a large tradition, but the statistics of the extreme prematurity has been a great problem for deficits register. The purpose of this work is to clarify which is the incidence and risk factors of Retinopathy of Prematurity in VLBW newborn in the intensive care units of the public health system maternities of Chile.

Methods: Data were collected on 7376 VLBW infants admitted to 28 neonatal intensive care units between January 2000 and December 2004, without congenital anomalies. All the units worked with an accurate multivariate computational register program, specially designed for this purpose. Descriptive analysis of Retinopathy incidence was made in 4 groups of weight (group1:1500-1250g ; group 2: 1249 -1000 g; group 3: 999- 750 g; and group 4: 749 - 500 g) and for gestational age (23 to 31 weeks). To test and compare occurrence between the groups , RR, and Logistic regression was utilized in the statistical STATA program.

Results: A total of 7376 VLBW, < 32 weeks infants were analyzed with mean weight 1150 gr +300 g. and gestational 29 + 3 sem. (42 infants were eliminated for incomplete data). The incidence of Retinopathy by groups of weight was 11 % in group 1; 22 % in group 2 ; 41 % in group 3 and 50 % in group 4 . A global incidence of Retinopathy in Chile was 22 % in < 1500 g and 24 % in the <32 weeks . 5% of them needed surgical resolution. (20% at 24 weeks and fell to 4% at 28 weeks) . 3% of the babies end with blinding condition (92 babies in 5 years , 62 of them are < of 28 weeks) . In this study the logistic regression model to predict individual risk of ROP for a VLBW newborn in Chile was:

$$Y = 2.37 - \text{weight} \times (0.00067) + \text{ventilatory support days} \times (0.014) - \text{Apgar1} \times (0.048) - \text{gestational age} \times (0.087) + \text{brain ultrasonographic impairment} \times (0.134) + \text{BPD at 36 weeks} \times (0.4351) + \text{Surfactant} \times (0.134)$$

Conclusions: The knowledge that this epidemiologic analysis bring of the Retinopathy of Prematurity in VLBW infant, make possible the design of occurred intervention strategies in Chile. We must to reflect in the opportunity of the surgical resolution in each case to improve the results in our babies with Retinopathy. A local ROP risk model may be a useful tool, that help decisions in neonatal care to prevent the severity of this illness.

APPROACHES TO THE CLASSIFICATION AND DIAGNOSIS OF PLUS DISEASE

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Background: Plus disease is the new driver for the treatment of retinopathy of prematurity (ROP), yet its diagnosis is a crude binary decision - present or absent - which is based on a single photograph published over two decades ago.

Plus disease is a constellation of signs including vascular engorgement and tortuosity at the posterior pole. Yet the normal retinovascular morphological characteristics associated with premature birth and normal development have not been determined.

Here we discuss the diagnosis and categorization of plus disease using two broad approaches: clinical and automated.

Methods: We have trialed the grading system using a panel of paediatric ophthalmologists reading images from a Nidek noncontact narrow field (30°) and RetCam wide field (120 & 130°) images.

Results: CLINICAL DIAGNOSIS A system that grades tortuosity and congestion of both arterioles and venules on a scale - 0 to + + + +.

SEMI-AUTOMATED DIAGNOSIS The two main categories of semi-automated quantification are i) vascular segmentation and ii) scale-space analysis.

Vascular segmentation includes vessel tracking and region growing techniques.

Vessel trackers select a sub-set of pixels and calculate their likelihood of being vascular, and then seed track along the vessels. The Retinal Image multiScale Analysis (RISA) software package involves human input and automated output. The stages of analysis are segmentation, skeletal construction, selection of root vessel and tracking. The system has proved able to distinguish plus disease based on quantification of curvature, diameter and tortuosity. We illustrate this technique on Retcam II images. Region-growing programs calculate a measure of 'vessel-ness' for each pixel and then define a level, for example 1%, at which it is agreed that all selected pixels are vasculature.

The scale-space method uses several filters of different scale placed on the image to delineate the vascular tree. We show examples of scale-space vessel detection with added software to numerically quantify vascular engorgement and tortuosity within the 5 step classification.

Conclusion: Quantifying plus disease will increase the understanding of the vascular changes associated with prematurity and ROP and should lead to more specific guidelines for ROP treatment. Novel imaging techniques and computer based technology are opening up exciting opportunities for the automated diagnosis of plus disease which will facilitate screening.

INCIDENCE OF RETINOPATHY OF PREMATURETY AMONG SINGLETON AND MULTIPLES AT THE HOSPITAL DE CLINICAS DE PORTO ALEGRE - BRAZIL

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Objectives: Low birth weight and gestational age are well known risk factors for the development of retinopathy of prematurity. However, other risk factors such as sepsis, blood transfusion, apnea, intraventricular hemorrhage, mechanical oxygen supplementation and multiple births have been variably implicated. The purposes of this study is to determine differences in incidence of retinopathy of prematurity between multiple-gestation and single-gestation pregnancies and to analyse how this risk factor is implicated with the development of retinopathy.

Methods: This study included prospectively 280 neonates. The clinical outcome was the development of retinopathy of prematurity at any stage. All the newborn of the Institution from October 2002 to April 2006 with birth weight 1500g or lower and/or gestational age at birth less than 32 weeks were included in two groups according singleton and multiple gestations. In each group the incidence rate was determined. Pearson's Qui-Square test was used to compare the two groups. Also the Risk Relative (Incidence Ratio) with 95% confidence interval was calculated. To determine whether the multiple-gestation is related to the development of retinopathy of prematurity independently to another associated factors, Logistic Regression was performed with significance level of 0,05%.

Results: Forty five neonates were included in the Group 1 (multiple-gestations) while 235 were included in the Group 2 (single-birth neonates). The incidence of ROP among patients from multiple-gestation was 31,11% (14/45) and 23,40% (55/235) among the single-birth neonates considering all the ROP stages with Odds Ratio 1,48 (CI 95% = 0,73-2,97) as a independent risk factor. Adjusted for another risk factors for ROP development the Odds Ratio was 1,63 (CI 95% = 0,73-3,63). The general incidence of ROP in both groups was 24,64%.

Conclusions: The incidence of retinopathy of prematurity was higher in the multiple-gestation group, however, the study statistical power showed necessity of a bigger cohort of patients (15,61 x / Power 95%) indicating the necessity of a multicenter clinical trial to validate these results.

RISK FACTORS FOR RETINOPATHY OF PREMATURITY AT THE HOSPITAL DE CLINICAS DE PORTO ALEGRE - BRAZIL

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Objectives: Retinopathy of prematurity is a leading cause of blindness in children. It is a multi factorial disease, occurring most frequently in the smallest and sickest infants. The objectives of this paper is to evaluate, in a prospective study, the significance of the postnatal risk factors in the development of the disease and evaluate if these factors are independent of the two major risk factors, birth weight and gestational age.

Methods: A prospective examination was conducted on 280 premature children born with birth weight of 1500 g or less and/or 32 weeks or less of gestational age at birth, between October 2002 and April 2006. All of the newborns were examined by indirect binocular ophthalmoscopy with the 28 diopters lens after pupil dilatation with association of Tropicamide 0,5% and Phenylephrine 2,5%. The mapping of the retina with a lid speculum was first conducted after six weeks of life and repeated weekly depending on the classification of the retinopathy. To classify the disease was used the International Classification of Retinopathy of Prematurity from 1984/1987. The main risk factors included in this study were: use of mechanic ventilation, intraventricular hemorrhage, sepsis, APGAR index at 5 minutes, indometacin use, low weight gain at 6th week, and blood transfusions.

Results: In this prospective populational-based study, retinopathy of prematurity was diagnosed in 69 of the neonates with a incidence rate of 24,64% (69/280). The disease reached stage ROP 1 in 11,43% of the cases (32/280), stage ROP 2 in 7,86% of the cases (22/280), stage ROP 3 in 4,64% (13/280) and stages ROP 4 and 5 in only 0,36% each (1/280 each). On univariate and multivariate analysis, indometacin use, low weight gain at 6th weeks of life, intraventricular hemorrhage, APGAR index less than 5 at five minutes and mechanic ventilation were considered significantly for the development of the disease.

Conclusions: The incidence rate of 24,64% found in the Hospital de Clinicas de Porto Alegre - Brazil was similar with an others incidence/prevalence papers published in Europe and USA. The ophthalmologic examination at the 6th week of life must be done in all very low birth weight infants with 1500 g or less especially in those with gestational age under 32 weeks. After logistic regression this study confirmed some of the risk factors initially considered. The development of the disease is inversely proportional to weight and gestational age at birth.

LOW WEIGHT GAIN AT 6TH WEEK OF LIFE AS A RISK FACTOR FOR RETINOPATHY OF PREMATURITY

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Introduction: Described at first time over 50 years ago, Retinopathy of Prematurity (ROP) became a leading cause of childhood blindness in developed countries due to the greater survival of preterm infants with very low birth weight or gestational age. The objectives of this study are to evaluate the low weight gain (defined as a gain of weight from birth to the 6th week of life less than half of the birth weight) as a risk factor for the development of ROP, at any stage, in very low birth weight infants born at the Neonatal Intensive Care Unit of the Hospital de Clinicas de Porto Alegre, in southern Brazil, and to determine if the study factor is independently associated with the disease, since ROP is a multifactorial disease.

Methods: A prospective cohort study evaluating the incidence of ROP and the weight gain in the first 6th weeks of life was done. The clinical outcome was the development of ROP at any stage. The main variable was the gain of weight from birth to the 6th week of life less than 50% of the birth weight. All infants born from September 2002 to May 2006 with birth weight \leq 1500 g or gestational age \leq 32 weeks were included. Group 1 comprised infants that gained less than 50% of the birth weight from birth to the 6th week of life, while infants that have achieved the goal of 50% at the same time were enrolled in Group 2. All statistical analysis were done with the Statistical Package for Social Sciences (SPSS, version 13.0) programme. Comparison between variables were done using the chi-square test, and logistic regression was used to evaluate the low weight gain as an independent risk factor for ROP, considering also birth weight, gestational age, use of surfactant, need for blood transfusion and development of sepsis. To classify the disease, the 1984/1987 International Classification of Retinopathy of Prematurity was used.

Results: 115 infants were included in Group 1 and 160 in Group 2. The incidence of ROP in Group 1 was 39.1% and in Group 2 was 15.6%. The comparison between the two groups demonstrated a strong correlation (Chi-square=19.48, $p < 0.0001$), relative risk of 2.50 (CI95%=1.64-3.84) and odds ratio equal to 3.47 (CI95%=1.97-6.12). This represents a high risk for the variable in study participate in the development of ROP. After logistic regression, low weight gain showed high correlation with ROP, independently of another important risk factors. The study statistical power was 98.9%.

Conclusions: The gain of weight from birth to the 6th week of life less than 50% of the birth weight in very low birth weight infants is an important risk factor for ROP development, at any stage. Ophthalmologists and neonatologists should take special attention in the screening of retinopathy of prematurity in this special group of patients.

A PROTEOMIC APPROACH FOR IDENTIFICATION OF BIOMARKERS IN AMNION ASSOCIATED WITH ROP DEVELOPMENT

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Background: During the last 15-20 years a dramatic increase in survival in the most preterm infants has resulted in an increased number of infants with ROP. The third trimester, when these children are born, is a very intensive developmental phase for the fetus, and it is likely that many processes that normally are going on are terminated. Hypoxia is a driving force for proliferative ROP. Experiments using an animal model suggest that the expression levels of vascular endothelial growth factor (VEGF) and insulin-like growth factor 1 (IGF-I) are important for the development of retinal blood vessels. The importance of IGF-I for normal retinal vascularization has been confirmed in patients, where the levels of serum IGF-I were lower in premature children who developed proliferative ROP than in children with no ROP.

The aim of this study was to use a proteomic approach in order to identify additional biomarkers associated with development of ROP.

Method: Surface enhanced laser desorption/ionisation-time of flight mass spectrometry (SELDI-TOF MS) was used for protein profiling of amniotic fluid from women with signs of threatening preterm birth. Amniotic fluid was analysed from 12 cases where the children developed ROP, stadium 2 or higher, and from 13 cases where no signs of ROP were detected. Samples were analysed on weak cation exchange (CM10), strong cation exchange (Q10), hydrophobic (H50) and immobilised metal affinity capture - Cu²⁺ (IMAC -Cu) chip arrays. For the statistical analysis of the results samples were divided into two groups, ROP and non-ROP, depending on the ROP status of the children. The nonparametric Mann-Whitney test was used on normalized peak intensities to calculate single marker statistics for the comparison of ROP versus non-ROP.

Results: Analysis of Q10 and CM10 chip arrays resulted in 4 and 6 differentially expressed proteins with p-value ≤ 0.05 . All but one peak from the Q10 chip array were also present on the CM10 chip array. Three of the differentially expressed protein peaks have previously been associated with intra-amniotic inflammation. One peak with a m/z value of 13,9 kDa was of special interest, since this biomarker has not been studied in relation to intra-amniotic inflammation. The p-value for the 13,9 kDa biomarker was 0.0008 on CM10 arrays and 0.0056 on Q10 arrays, with lower expression in the ROP group of patients. Work is now proceeding in order to establish the identity of the protein representing the 13,9 kDa peak.

Conclusions: Our results suggest that the proteomic approach could be used for identification of biomarkers of potential importance for ROP development.

EVALUATION OF BLOOD FLOW IN THE ARTERIES OF THE EYE IN PREMATURE NEONATES AND IN CHILDREN WITH RETINOPATHY OF PREMATURITY

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Purpose: To estimate blood flow parameters and haemodynamic changes in the orbital vessels in premature children and in various stages of retinopathy of prematurity (ROP).

Material and methods: Color Doppler imaging (CDI) of ophthalmic artery and central retinal artery was performed in 36 preterm infants in particular range of gestational age and 42 premature children with active stages of retinopathy of prematurity. The control group comprised 19 neonates born at term. Maximal systolic velocity (Vmax), end-diastolic velocity (Vmin), resistance index (RI) were assessed for the studied vessels. The picture of the fundus of the eyes was documented using RetCam apparatus.

Results: The analysis of blood flow spectrum in the ophthalmic artery revealed a proportional increase in the value of Vmax and RI for gestational age in children born between 24 and 32 weeks of gestation. The values of Vmax in the central retinal artery were similar in all groups of preterm children and RI decreased proportionally with gestational age.

In threshold retinopathy (presence of plus disease) Vmax in the ophthalmic artery and central retinal artery was statistically significantly lower as compared with prethreshold retinopathy (absence of plus disease). The values of RI were similar in both groups.

Conclusions: The Doppler color ultrasonography is a non-invasive technique which can be useful for the evaluation of haemodynamic parameters in the arteries of the eye in the premature children.

The recorded CDI changes of blood flow in the eye arteries in preterm children with ROP differ, in relation to disease advancement and presence of plus sign.

CORRELATION BETWEEN RESULTS OF CONTINUOUS MONITORING OF HEMOGLOBIN SATURATION DURING THE FIRST MONTH OF LIFE AND THE RISK OF PROLIFERATIVE RETINOPATHY OF PREMATURITY

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Background: The results of experimental studies indicate that the relation between oxygen therapy and the stage of retinopathy of prematurity (ROP) cannot be described by a simple model. Technical progress, new methods of vital signs recording and transmission allow for better, continuous monitoring of the patients status.

Aim: Analysis of correlation between results of continuous monitoring of hemoglobin saturation during the first month of life and the risk of proliferative ROP.

Method: A sample of 70 newborns with mean birthweight equaled to 1087g (range: 600-1500 g) and mean gestational age equaled to 28.4 weeks (range 24-32 wks) were evaluated prospectively. Oxygen hemoglobin saturation (spO₂) was monitored on the continuous basis and recorded in computer database during the first 4 weeks of life. Elimination of noises and artifacts, data compression and computing of derivative values from the data stream were performed with the use of modern mathematical methods based on artificial neuronal networks. Mean spO₂, the percentage of time with spO₂ ≥ 97%, the percentage of time with spO₂ < 85% and standard deviation of recorded spO₂ values reflecting spO₂ fluctuation were calculated. Oxygen therapy periods and oxygen free periods were analyzed separately. The infants were divided into 2 cohorts: A) no ROP or ROP not requiring treatment (n=48), B) ROP requiring laser or cryotherapy (n=22).

Results: Surprisingly, the recorded values of mean spO₂ (94.5-95.3 vs 94.7-94.8%), mean standard deviation of recorded spO₂ during oxygen therapy (3.6-4.6 vs 3.8-4.5%) in the first three weeks of life were similar in both groups. Also, the mean percentage of time with spO₂ ≥ 97% and the mean percentage of time with spO₂ < 85% during first 3 weeks of life did not differ between the groups. Differences were recorded in the 4th week of life. Mean spO₂ (94.9 vs 94.6%) and the mean percentage of time with spO₂ ≥ 97% were similar in both groups, but the mean percentage of time with spO₂ < 85% was two times higher (4,8 vs 2,5%; p=0.01) and mean standard deviation of recorded spO₂ values was also higher (4.9 vs 3.9%; p<0.01) in the ROP group.

One child (birthweight 900g) developed severe ROP although it never received oxygen therapy. Her mean spO₂ during the first month of life was (98.4-99%) and percentage of time with spO₂ ≥ 97% was 78-98%.

The children without proliferative ROP who did not receive oxygen therapy as compared to the children who received oxygen (both with and without retinopathy) had higher mean spO₂ (week 1-4: 97-97.3 vs 94.5-95.3%) and percentage of spO₂ ≥ 97% (54% vs 29%).

Conclusion: At present, when special attention is paid to prevent hyperoxia, hypoxic events seem to be a very important risk factor of ROP. Our data also indicate that high spO₂ values are potentially dangerous only in children who received oxygen support.

IMAGE ANALYSIS OF THE RETINAL BLOOD VESSELS IN RAT MODELS OF ROP

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Background: Accurate diagnosis and optimal management of ROP remain challenges for those involved in the care of premature infants. Retinal Image multiScale Analysis (RISA) has had successful, but limited, application to the study of the retinal vasculature in preterm infants. Herein, we have used RISA in a longitudinal study of the retinal vasculature and the function of the neural retina in two rat models of ROP. Rats exposed to high oxygen during the first weeks after birth develop vascular abnormalities similar to those observed in human ROP. Different oxygen exposures produce distinct patterns of neural dysfunction and vascular abnormalities in the retina.

Method: Digital fundus images and electroretinogram (ERG) records were obtained in one session from rat models of ROP at age 20, 30, and 60 days postnatal. Twenty days is soon after eye opening; 60 day old rats are adults. The images were cropped to the posterior pole, defined as the region circumscribed by the vortex veins and concentric to the optic nerve head. The tortuosity index (TI), integrated curvature (IC), and diameter of the retinal arterioles and venules were calculated using RISA. Function of the neural retina was assessed by ERG. Rod photoreceptor (S, Rmp3) and post-receptor (log \bar{A} , Vmax) response parameters were calculated from the ERG a-wave and b-wave. One rat model was induced by exposing infant rats (aged 7-14 days) to continuous 75% oxygen. The second was induced by exposing newborn rats (aged 0-14 days) to alternating 50/10% oxygen. Room-air reared controls were also studied. Significant changes in each RISA parameter were detected by two factor analysis of variance that compared group (75%, 50/10%, room-air controls) and age (20, 30, 60 days). Linear regression was used to determine the relationship between RISA and ERG parameters.

Results: 175 blood vessels were suitable for the image analysis. At age 20 days, IC of the ROP rats was high; the 75% animals had the highest values. In both 75% and 50/10% animals, IC decreased markedly to approach control values by age 30 days. However, even at age 60 days, IC remained slightly above values observed in controls. TI followed a similar pattern of recovery. Vessel diameters decreased with age in all groups, including the controls. Thus, as in the case of a majority of human infants with ROP, there is substantial resolution of the blood vessel abnormalities in these rat models of ROP. Only IC was significantly related with multiple ERG parameters: rod photoreceptor sensitivity (S), post-receptor sensitivity (log \bar{A}), and post-receptor response amplitude (Vmax).

Conclusions: RISA provides an objective, numeric assessment of the retinal vasculature in these ROP models. Accordingly, it has application in our ongoing animal studies of the interplay of neural and vascular factors. In the clinical realm, RISA promises to refine the diagnosis of ROP and thus contribute to improved management of the preterm infant. Future applications of RISA in telemedicine programs designed to provide diagnostic expertise in ROP may be feasible. Perhaps RISA parameters, especially IC, may prove critical to ROP risk models.

POSTNATAL MORE THAN PRENATAL WEIGHT DEVELOPMENT PREDICTS RETINOPATHY OF PREMATURITY

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Objective: Gestational age (GA) at birth and birth weight have long been described interchangeably as the most significant risk factors for retinopathy of prematurity (ROP). However, other risk factors that emerge after birth must also contribute to ROP. We hypothesized that poor postnatal growth normalized for postmenstrual age and gender as weight standard deviation score (SDS) is associated with ROP

Design: We conducted a prospective longitudinal study measuring weight weekly in 79 premature infants from birth (gestational ages 24 to 32 weeks) until a postmenstrual age of 40 weeks that was then compared to well established norms for post menstrual age to find a weight SDS. Infants were evaluated according to regular ROP screening. Data was compiled so that at each PMA the mean of all weight SDS from infants born at any appropriate GA are combined. This allows us to consider normalized weight data.

Results: The size of the weight standard deviation from the norm at 27 on to 40 weeks PMA was strongly associated with the degree of ROP. The children with the most severe stages of ROP (3 and 3+) had the largest drop in weight SDS (from birth to minimum weight SDS) $p=0.001$, as well as the longest period of weight SDS below -2, independently of GA and WSDS at birth. All premature infants fell in weight SDS after birth independent of GA at birth. This decrease in weight SDS continued until about gestational week 31, independently of ROP stage, then stopped. Interestingly, birth weight in grams correlated significantly with ROP stages ($p<0.0005$). However when birth weight was evaluated taking into account norms for gestational age and gender (weight SDS) there was no correlation between birth weight and ROP indicating that gestational age at birth (degree of prematurity) is the important perinatal risk factor and that normalized weight is important but only with respect to later postnatal changes

Conclusions: Postnatal weight development taking into account post menstrual age and gender norms (weight SDS) after PMA week 27 is strongly associated with the degree of ROP. Weight at birth when norms for postmenstrual age and gender are accounted for is not associated with ROP. These findings stress the importance of postnatal weight, more than intrauterine weight development, in the prediction of ROP.

FLUCTUATION OF ARTERIAL OXYGEN LEVEL AND THE DEVELOPMENT OF THRESHOLD RETINOPATHY OF PREMATUREITY

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Background: This study investigates whether fluctuations in arterial oxygen level (PaO₂) in very early life contribute to the development of threshold retinopathy of prematurity (ROP) in extremely low birth weight (ELBW) infants.

Methods: This case-control study looked at PaO₂ data from the first 12 days of life of 15 ELBW infants. The 5 cases were ELBW infants who developed threshold ROP and these were compared with 10 control infants with no ROP or pre-threshold stages of the disease. The two groups were matched for birth-weight and gestational age.

Results: Statistical comparison of the standard deviations of the datasets showed that ELBW infants who developed threshold ROP experienced greater fluctuations of PaO₂ in very early life ($p < 0.05$).

Conclusions: Increased PaO₂ fluctuation in very early life is an independent risk factor for the development of sight-threatening ROP in ELBW infants. It can be used as an index of value in designing a screening protocol and thereby help to combat the disease.

PRESUMPTIVE OXYGEN INDUCED TOXICITY PRESENTING AS UNUSUAL FORM OF ZONE 1 AGGRESSIVE POSTERIOR RETINOPATHY OF PREMATURITY IN BIGGER PRETERM INFANTS. IS IT SCREENING GUIDELINES OR IS IT OXYGEN MANAGEMENT THAT NEEDS TO BE MODIFIED IN DEVELOPING COUNTRIES?

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Background: Purpose of this study was to compare the incidence of severe zone 1 retinopathy of prematurity (ROP) before and after implementing a different mode of delivery of oxygen in a neonatal intensive care unit (NICU).

Methods: This was a retrospective study. Data of all the babies having zone 1 ROP from two NICUs (A & B) between June 2002 to December 2005 was retrieved from the medical records. Babies in NICU A were given unmonitored 100% oxygen via a plastic funnel which was tied tightly to the infants face fully covering the mouth and nose while in NICU-B it was given in the form of a hood where the oxygen gets dispersed and more diluted. The change in the delivery of oxygen from funnel to hood in NICU A was made in December 2003 after noting the vast difference in the incidence of zone 1 ROP in bigger babies between the two NICUs.

Results: The incidence of APROP in NICU A from June 02 to December 03 was 27% (33/122) while it was 4.5% (2/44) in NICU B. The mean gestational age and birth weights for babies in NICU A were 32 weeks (range 28 to 34 weeks) and 1595 gms (range 850 to 2290 gms). In 2004 the mode of oxygen delivery in NICU A was changed from funnel to hood. After the change, the incidence of APROP dropped to 0%. In 2005 even on hood type of oxygen, 9 cases were seen to develop APROP in NICU A with a mean gestational age and birth weight of 30.4 weeks (range 28 to 35 weeks) and 1524 gms (range 760 to 2080 gms) respectively.

Conclusion: APROP was seen in bigger babies in our series in NICU A. This atypical presentation seemed to have been induced by giving forced oxygen. The fundus findings in these babies was similar to that of oxygen induced retinopathy (OIR) seen in animal models. Our data suggests that unmonitored supplemental oxygen might be playing an important role in producing oxygen induced retinopathy which resembles severe zone 1 ROP in bigger infants in developing countries. Emphasis should be given on proper oxygen management to the pediatricians rather on modifying the screening guidelines in these countries. It is important that both neonatologists and screening ophthalmologist be aware of this unusual presentation of APROP and adjust oxygen supplementation accordingly.

RESULTS OF RETINOPATHY OF PREMATURE TREATMENT WITH DIODE LASER PHOTOCOAGULATION

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The aim of the research is the evaluation of retinopathy of prematurity treatment results with the use of diode laser photocoagulation.

Material: The examined group consisted of 267 patients with the 3rd stage of ROP (525 eyes), 153 boys (302 eyes) and 114 girls (223 eyes). The children were treated with diode laser photocoagulation in Department of Ophthalmology Childrens Memorial Health Institute Warsaw. Patients ranged in birth weight from 490 to 1980 grams (mean 1047, SD=307). Gestational age of the examined patients ranged from 23 to 34 week of pregnancy (mean 27.6, SD= 2,2).

Methods: Laser photocoagulation was carried out on the basis of ophthalmological qualification, according to effective standards. The 3rd stage of active ROP (threshold stage) constituted an indication for treatment. The surgery consisted in laser coagulation of peripheral avascular retina spreading from the ridge with vascular proliferations up to ora serrata. The results of treatment were evaluated on the basis of criteria set by multicentered CRYO-ROP Cooperative Group.

Results: As a result of laser photocoagulation of originally avascular retina, total regress of disease with leaving proper posterior pole of retina was obtained in 432 eyes (82,3%); ectopia of macula occurred in 53 eyes(10,1%); partial retinal detachment excluding macula occurred in 1 eye (0,2%). These three groups - 486 eyes - were qualified according to above mentioned criteria as good results of treatment, constituting 92,6%. Bad results were observed in 39 eyes constituting 7.4%: falciform retinal fold including macula occurred in 8 eyes (1,5%); partial detachment including macula occurred in 8 eyes (1,5%); total retinal detachment was observed in 23 eyes (4,4%).

The following side effects were observed: in two patients (4 eyes - 0.8%) uveitis occurred. As a results of this complication, the occurrence of postinflammatory synechia was observed in 3 eyes (0.6%).

In three patients (4 eyes- 0.8%) cataract was observed. Cataract in one patient underwent further complication in the form of glaucoma (0.2%).

In 21 patients (29 eyes- 5.5%) preretinal hemorrhages were observed.

Conclusions: The effectiveness of ROP treatment with laser photocoagulation is high with rare side effects.

NEONATOLOGISTS AND THE MANAGEMENT OF RETINOPATHY OF PREMATURITY (ROP)

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Background: To determine the depth of knowledge of neonatologists regarding retinopathy of prematurity and its incidence, diagnosis, and management in a neonatal intensive care unit (NICU) setting.

Methods: A multiple-choice on-line questionnaire was sent to all 4136 Board-certified neonatologists in the United States to determine their depth of knowledge regarding retinopathy of prematurity.

Results: Will be available

Conclusions: Pending

ENDOPHTHALMITIS IN THE NEWBORN

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Background: To determine the incidence, etiology, and associated risk factors for the development of endophthalmitis in the newborn over a 4-year period in a neonatal intensive care unit.

Methods: A comprehensive retrospective review was performed on the charts of all newborn patients in the neonatal intensive care unit at Jackson Memorial Hospital/Bascom Palmer Eye Institute who underwent ophthalmic examinations from March, 2002 to March, 2006. Clinical variables recorded from the patients charts included: diagnosis of endophthalmitis, causative pathogen, type of treatment, and any associated risk factors, including prolonged ventilatory support, indwelling catheters, systemic bacterial or fungal infection, and premature birth status.

Results: The diagnosis of endophthalmitis was made in 4 out of 3459 patients (0.12%). Blood and/or urine cultures were positive for *Candida Albicans* in 3 of the 4 patients and *Pseudomonas Aeruginosa* in 1 patient. Pars plana vitrectomy with vitreous cultures (positive in 2 patients) and injection of intravitreal amphotericin B was performed in all 3 patients who were culture-positive for *Candida*. Pars plana lensectomy was performed at the time of vitrectomy in 2 patients. The remaining patient underwent a vitreous tap which was positive for *Pseudomonas* and was given an intravitreal injection of vancomycin and amikacin. The patient subsequently developed a corneal perforation requiring evisceration of the eye. Three of the 4 patients were born premature (gestational age, 26-27 weeks, birth weight, 825-1000 g). The full-term newborn was diagnosed with myotonic dystrophy by DNA analysis. All newborns had indwelling catheters and required prolonged ventilatory support.

Conclusions: Endophthalmitis is rare in newborns. Indwelling catheters and the need for prolonged ventilatory support appear to be significant risk factors. Fungal or bacterial septicemia should raise the suspicion of ocular involvement. Neonatologists should be aware of these risk factors as prompt referral and treatment will result in the best visual and anatomic outcomes.

RESULTS OF A SCREENING PROGRAM FOR RETINOPATHY OF PREMATURITY FROM OCTOBER 2002 TO APRIL 2006 AT THE HOSPITAL DE CLINICAS DE PORTO ALEGRE - BRAZIL

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Objective: To describe the results of a screening program for retinopathy of prematurity implanted at the Hospital de Clinicas de Porto Alegre - Brazil, since October of 2002.

Methods: Were included all the premature infants under 1500 g of birth weight and/or under 32 weeks of gestational age at birth who survived until the 6th week of life in the period between October 2002 to April 2006. The ophthalmological examination was initiated after the 6th week of life and repeated accordingly the criteria defined for the Brazil after the 1st Workshop ROP realized in Rio de Janeiro 2002, organized by the Sociedade Brasileira de Oftalmologia Pediatrica and sponsored by Conselho Brasileiro de Oftalmologia and Sociedade Brasileira de Pediatria.

Results: Were included 280 neonates in this study. The incidence of retinopathy of prematurity was 24,64%. The disease reached stage ROP 1 in 11,43% (32/280), stage ROP 2 in 7,43% (22/280), stage of ROP 3 in 4,64% (13/280), stage of ROP 4 in 0,36% (1/280) and stage of ROP 5 also in 0,36% with only one neonate affected. The blindness was prevented in 14 prematures by the use of diode laser photocoagulation. A total of 2127 ophthalmologic examinations were needed for this purpose.

Conclusions: The Brazilian screening for retinopathy of prematurity implanted in this institution since 2002, after the 1st Workshop ROP, was effective in detect all the cases of ROP stage 3 threshold disease needing laser treatment and prevented the blindness in 14 neonates in this period. The widespread of the screening criteria could prevent one of the leading causes of childhood blindness.

ASSESSMENT OF VISUAL FUNCTION IN ROP BABIES WITH AND WITHOUT BRAIN DAMAGE

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Purpose: To compare the visual status between a group of non brain damage ROP children (group A) and a group of brain damage ROP children (group B).

Methods: Group A (54 children) and Group B (51 children) participated in this study. Their gestational age was less than 32 weeks and their birth weight was less than 1500 gr. All children (in both groups) had a brain MRI at the age of 18 months and ophthalmological evaluation (cycloplegic refraction, best corrected visual resolution / visual acuity, strabismus, index K) at the age of 18 months and 30 months since birth, using the VFA-K test. None of the children had any eye surgical intervention

Results: In Group A the brain MRI was normal, while in group B the brain MRI showed mild periventricular leukomalacia (PVLmild) in 9 children, moderate PVL in 22 children, severe PVL in 9 children, cortical atrophy in one child, parenchymal cerebral atrophy in two children and mixture cerebral atrophy (cortical and parenchymal) atrophy in 8 children. In group A the majority of children appeared with insignificant refractive error ($x < 0.50$ D) (85.15%), while in group B only the 37.25% of children appeared with insignificant refractive error (in both assessments). In first assessment of visual resolution (VR), in group A 94.44% of children appeared with BCVR > 1.75 cpd, while in group B only 56.86% appeared with BCVR > 1.75 cpd. In the second assessment of visual acuity (VA), in group A 96.26% appeared with BCVA $> 6/18$, while in group B 56.86% appeared with BCVA $> 6/18$. In strabismus assessment at the age of 10 months, in group A 85.18% of children were orthophoric, while in group B 58.82% of children were orthophoric. Finally, the assessment of index K at the age of 30 months showed that in group A 77.77% of children appeared with score within or very close to normal range, while in group B only 29.41% of children scored within the normal range for their age.

Conclusion: The visual function of brain damaged ROP children is significantly impaired than a group of non brain damaged ROP children.

DOES OBSERVER BIAS CONTRIBUTE TO VARIATIONS IN THE RATE OF RETINOPATHY OF PREMATUREITY BETWEEN CENTRES?

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Background. Two large observational studies give the proportions of very preterm infants with retinopathy of prematurity (ROP) who have stage 1, 2, and 3 disease. The CRYO-ROP study included infants of <1251 g birthweight (BW) cared for in collaborating centres in the United States#. There was an exhaustive process of 'certification' of ophthalmologists who contributed to the study and agreement on the criteria for reporting examination findings. Acute ROP occurred in 65.8% of infants. Amongst 4099 infants with ROP, the highest stage was 1 in 38.7%, stage 2 in 33.3% and stage 3 or more in 28.0% (the ratio of stage 1 : 2 : 3 being 1.4 : 1.2 : 1).

More recently the ETROP study screened 6998 infants of <1251 g BW throughout the United States*. As with the earlier CRYO-ROP study, ophthalmologists had to complete a certification process. Acute ROP was observed in 68% of screened infants. For 2320 infants with ROP, who were followed further, the highest stage was stage 1 in 29%, stage 2 in 35.4%, and stage 3 in 35.6% (the ratio being 0.8 : 1 : 1).

Methods. We have reported on all infants of <29 weeks gestation in the ANZNN, which comprises all 29 NICUs in both countries, who were screened for ROP and survived to 36 weeks post-menstrual age. Our focus has been on antenatal and perinatal risk factors for acute ROP\$, and on between centre variations in the incidence of severe, stage 3 or 4 ROP**. The ANZNN database records the highest stage of ROP reached in either eye. In this report we focus on the proportions of infants with ROP who were reported to have stage 1, 2 or 3 disease. Our aim has been to indirectly assess the contribution to between centre variability from assessment bias.

Results. All NICUs in the ANZNN were surveyed on their clinical practice with respect to screening for ROP. All examining ophthalmologists followed recommended guidelines and reported findings using the ICROP classification##. Amongst 2105 infants born in 1998-1999 ROP occurred in 42%. The highest stage was stage 1 in 34%, stage 2 in 44%, and stage 3 in 23% (the ratio being 1.5 : 1.9 : 1). There was considerable variation in this ratio amongst hospitals, from 8.5 : 3.0 : 1 to 0 : 3.8 : 1. Any ROP varied from 8% to 66%. Amongst infants with ROP, stage 1 varied from 0% to 66%; stage 2 from 18% to 79%; and stage 3 from 0% to 43%. Treatment varied from 15% of stage 3 cases to 120% (i.e. some infants without stage 3 disease were treated), with a mean of 57%.

Conclusion. Ascertainment bias may make a significant contribution to the variation in the incidence of ROP that is observed between centres. It may be important in future studies for all examining ophthalmologists to have study-specific accreditation through means of a certification process.

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A SYSTEMATIC REVIEW OF UK SCREENING CRITERIA FOR RETINOPATHY OF PREMATURITY

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Background: UK guidelines for the screening and treatment of ROP were last revised in 1995. Since then there have been advances in the methodology of guideline development and a significant amount of new research into ROP. In 2005 the Royal College of Paediatrics and Child Health, the Royal College of Ophthalmologists and the British Association of Perinatal Medicine initiated a collaborative project to revise the UK guidelines. This paper reports the methods and results of a systematic review of the research evidence to inform the UK birthweight and gestational age (GA) screening criteria against a background of concerns that the 1995 criteria (birthweight ≤ 1500 g, and/or GA of ≤ 31 weeks) lead to too many babies being screened.

Method: A multi-disciplinary guideline development group (GDG) defined clinical questions in relation to which UK babies are at risk of developing sight-threatening ROP (defined as ICROP stage 3, prethreshold or threshold disease). These questions were used to inform a comprehensive literature search using Medline (1974-2005) and EMBASE (1966-2005). Abstracts of papers identified were independently reviewed by two assessors against predefined inclusion criteria, including ensuring the study reported primary data on babies screened using the 1984 ICROP classification, the study population was representative of the UK population, and included infants which met the 1995 screening criteria. Only studies conducted within the top 30 countries of the UN human development index were included to ensure that the neonatal care in the study centre was comparable to the UK.

The search identified 337 papers, 80 of which were selected on abstracts. The full papers were translated where required and read to confirm that they met the inclusion criteria, leaving 42 papers. These were critically appraised by trained members of the GDG to ensure that studies were of a high methodological quality, that data reported were representative of UK infants at risk of ROP and that ophthalmic definitions had been consistently applied.

Results: After appraisal 23 cohort studies were considered to be of sufficient quality to inform the review. These papers reported 10,481 screened babies, of which 643 (6.1%) developing sight-threatening ROP. Study data were analysed and displayed graphically to establish where the birthweight and GA criteria should lie to ensure that no babies with sight-threatening ROP would be missed. This exercise established that criteria set at ≤ 1500 g and/or ≤ 31 weeks GA would have captured all babies reported in the included studies. These criteria were then validated against unpublished data on an additional 175 babies who developed sight-threatening ROP submitted by members of the GDG.

Conclusions: On the basis of this review the GDG agreed that the 2006 UK ROP guidelines will recommend that all infants with a birthweight ≤ 1500 g and/or a GA of ≤ 31 weeks should be included into the UK ROP screening programme. The evidence from published literature, validated by personal practice data, suggests that setting birthweight or GA criteria below these levels would result in some babies with sight-threatening ROP not being screened.

SERUM IGF-I CONCENTRATION IN PRETERM INFANTS MAY PREDICT AN INCREASED RISK OF ROP

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Background: Low levels of serum insulin-like growth factor I (IGF-I) in preterm infants seems to prevent normal retinal vascular growth and precipitate the appearance of retinopathy of prematurity (ROP).

Method: a prospective, longitudinal study measuring serum IGF-I concentrations in 60 premature infants (33 boys) from birth (postmenstrual ages: 25-33 weeks) until discharge from the hospital. Children with congenital anomalies were excluded. All infants were in a neonatal intensive care unit and samples were not taken exclusively for the study, but when the infant needed any other blood evaluation.

Results: Mean gestational age was 29.15 ± 1.87 weeks (80% less than 30 weeks). Mean birth weight was 1087.08 ± 197.62 g. Thirteen infants developed ROP (5 stage 1, 5 stage 2, 2 stage 3, 1 stage 4). The diagnoses were done from 31 to 101 days of postnatal life. IGF-I concentrations were evaluated for every week of postnatal life in infants with and without ROP. IGF-I concentrations consistently increased during postnatal life in the group without ROP (median of 7.5, 10, 13.5, 16 and 19 $\mu\text{g/L}$ at weeks 1, 2, 3, 4 and after 4, respectively), whereas the respective values in children with ROP were 8, 13.5, 10, 8 and 13 $\mu\text{g/L}$, respectively). As a consequence, as a group, children with ROP presented lower levels of IGF-I at 4 weeks of postnatal life (median 8.0, range 2.0 to 14 $\mu\text{g/L}$) compared with children without ROP (median 16.0, range 3.0 to 38 $\mu\text{g/L}$), $P < 0.01$. The same tendency was observed after 28 days of postnatal life. In a multiple stepwise regression analysis, duration of O₂ therapy, weight at birth and IGF-I concentration could explain 43% of the occurrence of ROP at 4 weeks of postnatal life. The risk to develop ROP was 2.7 times higher if IGF-I concentration was $\leq 13 \mu\text{g/L}$ at 4 weeks of life.

Conclusion: Our data reinforce the observation that low levels of serum IGF-I in preterm infants predict an increased risk of ROP. Longitudinal measurements of IGF-I might identify infants at risk.

RETINOPATHY OF PREMATURITY SCREENING - A 9 YEAR RETROSPECTIVE STUDY IN HOSPITAL FERNANDO FONSECA, PORTUGAL

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Background: The authors performed a retrospective review of all premature infants admitted to Hospital Fernando Fonseca NICU and eligible for ROP screening, throughout a 9-year period dating from 1 October 1997 to 31 May 2006.

Methods: Serial eye examinations were conducted in 416 infants born weighing less 1501g and with gestational age inferior to 32 weeks and they were classified according to the International Classification of ROP (ICROP).

Results: The incidence of any ROP was 39% among all infants and we verified a 8,4% incidence of threshold or high-risk prethreshold ROP wich implied laser treatments in 67 eyes. Of the treated eyes, 57 (85%) had a favourable outcome.

Conclusions: ROP remains a common important cause of blindness among prematures and an effective screening program is crucial to identify the relatively few preterm infants who require treatment for ROP and decrease the risk of vision-threatening complications.

IT-BASED METHODS FOR ROP SCREENING

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Background: A frequent and severe complication in neonatologic intensive care is Retinopathia of the premature (ROP). In almost half of the cases ROP leads to total blindness if not treated sufficiently. Today there are neither feasible devices nor efficient methods for systematic screening and comprehensive documentation of ROP.

Methods: As a part of development of a telemedical screening platform for newborn, we created a module for ROP documentation. An additional digital camera system was used to examine prematures retina.

Results: Especially for ROP screening we developed an electronic patient record that was implemented in the internet based platform for newborn screening. A simple graphical tool generates a diagrammatic representation of retinal findings.

In addition we build a prototype camera system using standard components which guarantees mobile application even in confined spaces. Furthermore our system provides a cost-efficient solution.

Conclusions: A central storage of all findings in combination with a mobile examination and reliable progression tracking is essential for systematic screening and consequently improves early detection of ROP.

THE MODEL OF SCREENING AND TREATMENT OF ROP IN SERBIA

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Background: In my country, in Serbia, the success in saving Low Birth Weight infants is not followed by awareness in preventing Retinopathy of Prematurity in many centres. Consultation with ophthalmologists is usually done after the baby had Stage V ROP. All neonates at risk of ROP need an examination by an ophthalmologist. All babies who need the treatment have to be referred on a time basis to a hospital with indirect laser.

Methods: In Novi Sad the program of screening for ROP is performed since 1991 by one ophthalmologist. Cryo was performed for active threshold disease, and diode laser therapy is performed since 1998. The treatment is performed at Eye Clinic in topical anesthesia.

In last 3 years the screening is performed in other centres, and the children are sent for treatment in only this one, where diode laser unite is available.

Results: In last 3 years 167 premature babies with active disease of ROP had laser treatment of peripheral retina. More babies, 141/167 were from other centres other than Novi Sad. Screening and treatment is performed by only one ophtalmologist. Fortunately, last month we received a donation, the second laser. This laser is situated in Belgrade.

Conclusions: There is no doubt that the occurrence of blindness and visual impairment due to ROP may be reduced by a successful program to screen at risk premature infants, backed up by effective measures to treat threshold disease, but the implementation of the screening and treatment is problematical.

THE SCREENING OF THE RETINOPATHY OF PREMATURE IN THE OPHTHALMOLOGICAL CLINIC FROM CLUJ-NAPOCA

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Background: this study aims to present the preliminary results after the screening of the retinopathy of prematurity (ROP) in the Ophthalmological Clinic from Cluj-Napoca.

Method: all the babies that were born under 32 weeks of postconceptional age, were included in the screening for ROP. The first examination took place at 4-6 weeks after birth. The follow-up examinations were carried out approximately 2 weeks after every examination that reveals no ROP. In infants in whom ROP was discovered, the frequency of examinations was increased, depending on the severity of the disease. Examination continued until the retina was adequately vascularized in zone III or the ROP has resolved.

Results: during january 2005 - may 2006, 95 prematurely new-born babies have been examined by indirect ophthalmoscopy, in the Ophthalmological Clinic from Cluj-Napoca. The postconceptional age ranged from 28 to 32 weeks, the birth weight varied between 800 - 2000 grams. 93 infants did not develop ROP requiring laser therapy. In 2 cases, indirect laser photocoagulation has been performed for threshold ROP.

Conclusion: the screening for ROP as previously presented, allowed us to intervene in reasonable time to stop the progression of ROP.

TREATMENT OF THE RETINOPATHY OF PREMATUREITY WITH TRANSPUPILLARY DIODE LASER PHOTOCOAGULATION IN VERY LOW BIRTH WEIGHT INFANTS AT THE HOSPITAL DE CLINICAS DE PORTO ALEGRE - BRAZIL

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Objectives: To present the results of all patients receiving diode laser treatment for retinopathy of prematurity at a single institution Hospital de Clínicas de Porto Alegre - Brazil.

Methods: A prospective study included all the 280 prematures born with birth weight of 1500 g or less and/or 32 weeks or less of gestational age at birth screened for retinopathy of prematurity between October 2002 to April 2006. Their medical charts were reviewed and baseline birth weight, gestational age, classification of retinopathy at the moment of treatment, severity of the disease, number of laser spots and necessity of re-treatments were all the data recorded. All neonates were initially examined at the 6th week of life under binocular indirect ophthalmoscopy with a lid speculum and a 28 diopters lens, after the instillation of Tropicamide 0,5% and Phenylephrine 2,5% drops to dilate the pupils. To classify the disease was used the International Classification of Retinopathy of Prematurity (1984/1987).

Results: In this prospective study, retinopathy was diagnosed in 69 of the neonates with an incidence rate of 24,64% (69/280). The stage of ROP 3 threshold disease was reached in only 4,64 % (13/280). All of the threshold diseases were in Zone II, none in Zone I. The mean birth weight of the treated group was 964,29 g and the mean gestational age was 28,79 weeks. Transpupillary diode laser was used in all of the 13 patients. Both eyes were treated in the same time, under general anesthesia in surgical room. Confluent laser spots, around 800 in each eye, were used for all children without any complications of the laser treatment. Four of the 13 patients needed a second laser treatment in both eyes four weeks latter the initial treatment. One patient of the re-treated group needed scleral buckling with an equatorial silicon band after progression for stage ROP 4.

Conclusions: The ophthalmologic examination at the 6th is an important instrument for the detection of ROP and must be done in all very low birth weight infants with 1500 g or less especially in those with gestational age under 32 weeks at birth. The anatomical outcome was good in all neonates treated in spite of the 30% laser re-treatment in this study. Some reasons for this high re-treatment level in Zone II threshold disease could be explained by the number of laser spots under 800 in all patients.

RESULTS OF TREATMENT OF ACTIVE STAGE OF RETINOPATHY OF PREMATURITY WITH DIODE LASER PHOTOCOAGULATION IN LOCAL ANAESTHESIA

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Purpose: Operation of diode laser photocoagulation of primary avascular retina in the course of active stage of retinopathy of prematurity are usually make on general anaesthesia. Some premature babies in haevy general condition can not be enter to general anaesthesia in spite of possibilities of complication which may be if danger of their life. The aim of the study is the estimate of results of photocoagulation of retina in this premature babies with using retrobulbar anaesthesia and local conjunctival anaesthesia with presence of anaesthesiologist with monitoruing of basic circulatory and respiratory parametres.

Material: In years 2002-2004 the diode laser photocoagulation of primary avascular retina was performed in 60 babies (116 eyes) with retrobulbar anaesthesia (group 1) and in 15 babies (28 eyes) in local conjuncival anaesthesia (group 2) using diode laser of 800nm lenght of wave. All eyes qualified to treatment had a picture of the threshold retinopathy.

To indirect estimate of comfort of patients in time of photocoagulation it was counted an average heart rate and average respiratory rate and increases of these parameters in both groups in 3 stages of inrtervention: before intervention, just after compulsory standstill of neonate and about 10 minutes after beginning of intervention.

Results: All premature babies were examined in 14-th day, 1.5 month, 3-rd and 6-th month of life. Regression was stated in 114 eyes of babies from group 1 and in all 28 eyes of babies from group 2.

Conclusions: The diode laser photocoagulation of primary avascular retina in the course of active stage of retinopathy of premturity made with local anaesthesia despite of considerable technical difficulties is a full value method of curing this illness and lets to avoid a lot of general complication connected with general anaesthesia.

ROP 1 ZONE : CLINICAL FEATURE AND LASER TREATMENT

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Background: Advances in neonatology have increased the survival rate of low birthweight infants.

It has changed the ROPs classic features.

The ROP 1 zone is different from the traditional type: it doesn't present the typical classification but there are new ophthalmoscopic findings defined 'flat' by American Authors.

These pictures have changed the ophthalmologist management about timing of screening.

Method: We present the timing of screening, timing and modality of treatment of ROP 1 zone. The laser therapy is elective in ROP 1 zone.

Conclusions: The Authors report their experience on laser treatment.

SAFETY AND EFFICACY OF LOCAL ANAESTHESIA FOR LASER TREATMENT OF ROP

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Introduction: A UK survey performed by our group has shown a wide variation in the anaesthetic techniques employed in the treatment of threshold ROP, with general anaesthesia being the most frequently used modality. Having developed local anaesthetic as our preferred method it was our aim to determine that it was effective and safe.

Methods: We audited our results using subtenons anaesthesia with oral sedation (chloral hydrate) on 20 eyes of 11 patients undergoing laser treatment (14 sessions or treatment episodes) between November 2002 and August 2005. Cardio-respiratory indices in the peri-operative period (between 1 day prelaser and up to 4 days postoperatively) were compared with the standard published in the literature.

Results: 1 eye out of 20 (5%) progressed to stage 4b ROP despite maximal laser applied in two sessions. The peri-operative cardio respiratory stability index was calculated from the apnoea score and bradycardia index recorded over the first 4 post treatment days. The score was 1.2, which was comparable to the standard published for general anaesthesia (1.25). Major cardio respiratory distress necessitating intervention occurred on 2 occasions (2/20 ie 10%) and was better than the standard published. There were no life threatening events necessitating interruption or postponement of laser treatment and no adverse effects from the local anaesthetic.

Conclusions: The use of subtenons anaesthetic combined with oral sedation is safe and effective and offers many practical advantages over the use of general anaesthesia.

OUTCOME OF ZONE 1 RETINOPATHY OF PREMATURITY

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Purpose: To analyse the clinical characteristics and structural outcome of zone 1 Retinopathy of Prematurity (ROP) and compare it to the results of treatment in cases with Conventional ROP.

Methods: Preterm infants between 2000 and 2005 were screened for ROP. Cases with Conventional ROP were classified according to the International Classification of Retinopathy of Prematurity (ICROP) cases with zone 1 disease were treated according to the The Early Treatment for Retinopathy of Prematurity Study (ETROP)

Results: Of the 85 eyes that had treatable ROP, 16 (18.8%) had zone 1 ROP. The mean gestational age and birth weight was higher in Conventional disease compared to Zone 1 ROP. (28.3 weeks (range 23-35weeks) and 1135 gms (range 440-1650gms) vs 26.9 weeks (range 24-30 weeks) 914 gms (range 595-1200)). The mean gestational age at laser was 35.4 weeks (range 31-39weeks) in zone 1 ROP and 37.5 weeks (range 31-41 weeks) in the other group. The average number of laser spots applied was 2002.5 (range 1100 -2683) for zone 1 disease and 1076.4 for conventional disease. Six eyes (37.5%) required retreatment of missed areas that had persistent plus disease (enlarged posterior veins and tortuous arterioles) in zone 1 disease group. The structural outcome was favorable in 93.8 % and

98.6 % of the zone 1 and conventional groups, respectively ($P = .343$).

Conclusion: Zone 1 ROP had an atypical morphology which was difficult to classify according to ICROP classification and a poor anatomical and visual prognosis. Earlier treatment of zone 1 disease according to ETROP study improve the visual outcome.

EARLY LENS-SPARING VITRECTOMY FOR AGGRESSIVE POSTERIOR RETINOPATHY OF PREMATURITY

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Background: stage 3 aggressive posterior retinopathy of prematurity (APROP) can result in poor vision if untreated. Aim of the study is to value the anatomic results and complications of lens-sparing vitrectomy (LSV) for stage 3 APROP.

Methods: A retrospective, noncomparative, consecutive case series of 12 eyes (8 patients born at gestational age 23-25 weeks) with stage 3 APROP. All eyes failed to respond to retinal laser photocoagulation, showing signs of progression of the disease. All eyes underwent LSV, intraoperative additional laser photocoagulation and internal tamponade, before retinal detachment appearance.

Results: All eyes underwent LSV, intraoperative additional laser photocoagulation. Eight eyes were tamponaded with air, 4 with balanced salt solution. At the end of follow up (10 months, range: 6-18), retina was completely attached in all eyes, with no more signs of progression. We did not observe any intraoperative or postoperative complication.

Conclusions: Our study could suggest that surgical treatment of stage 3 APROP could be effective and safe to avoid the progression of the disease in those eyes refractory to laser photocoagulation.

TREATMENT OUTCOMES OF RETINOPATHY OF PREMATURITY AT A TERTIERY LEVEL HOSPITAL IN TURKEY

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Purpose: To report the treatment outcomes of retinopathy of prematurity (ROP) in a tertiary level hospital in Ankara, Turkey.

Methods: Data from the medical records of neonates with a gestational age ≤ 34 weeks and who were examined for ROP between March 1999 and September 2005 were analyzed for the treatment outcomes of ROP.

Results: The frequency of ROP was 37.1% for any stage and 7.2% for severe ROP (stage 3 or greater). Nineteen (16.1%) neonates with severe ROP needed treatment. Mean age at threshold disease was (mean) 35.8 ± 1.8 weeks of gestational age (GA; range, 33 to 39 weeks). Photocoagulation or cryotherapy (3 neonates) was performed between 33 and 40 weeks of GA. Among 38 eyes of 19 treated neonates, 30 eyes of 15 neonates (78.9%) regressed and 8 eyes of 4 neonates (21.1%) progressed to an advanced stage in spite of photocoagulation or cryotherapy. The rate of treatment was 32.4% (12/37) for extremely low birth weight neonates (<1000 g), 20.8% (16/77) for the neonates <1250 g, and 12.9% (18 /140) for the neonates <1500 g ($p=0.017$).

Conclusion: Immaturity is a significant factor for the development of threshold disease in preterm infants. Although photocoagulation or cryotherapy seems to be effective for the treatment of ROP, undesirable results of threshold disease are still problems for the visual outcomes of preterm infants.

A SAFE ANAESTHETIC TECHNIQUE FOR ADMINISTRATION OF DIODE LASER PHOTOCOAGULATION FOR RETINOPATHY OF PREMATURITY (ROP)

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Introduction: Anaesthesia can have numerous complications in premature infants. Compared with cryotherapy, the diode laser photocoagulation is better tolerated but it is necessary an adequate stillness of the patient for a correct retinal spot focus. Since 1999 we are using an anaesthetic technique: sedation with inhaled anaesthetic agents without traqueal intubation associated with topical anaesthesia. We analyzed the results of this technique.

Material and Methods: We have treated 72 consecutive patients with ROP using sedation with inhaled anaesthetic agents associated with topical anaesthesia without traqueal intubation. We have recorded: patient data (gestational age, birth weight, postconcepcional age at treatment and systemic pathology associated) and treatment data (duration of treatment, complications intra-and postoperatively).

Results: Intraoperative complications occurred in 12 patients (16,6%). Complications were autolimited in 9/12 cases. Only 3/12 cases (4%) needed traqueal intubation. Postoperative complications occurred in 4 cases (5,55%). There was not statistical relationship between intraoperative complications and mean gestational age, mean birth weight, presence of apnea of prematurity, III-IV intraventricular hemorrhage or patent ductus arteriosus. There was statistical relationship between postoperative complications and III-IV intraventricular hemorrhage.

Conclusion: Anaesthesia using inhaled agents without traqueal intubation associated with topical anaesthesia is a safe technique for administration of diode laser photocoagulation for ROP, with low rate of complications and achieves optimal conditions for surgeon to apply treatment.

RETINOPATHY OF PREMATURITY. CONSEQUENCES AND CONTROVERSIES OF ETROP

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Purpose. To notice the clinical impact of the revised indications for the early treatment of Retinopathy of Prematurity defined in ETROP (Early Treatment for Retinopathy of Prematurity Study) and to analyse the recent modifications of ICROP (International Classification of Retinopathy of Prematurity).

Setting. Department of Ophthalmology and Department of Paediatrics of Hospital Fernando Fonseca - Lisbon

Methods. Based on ten years on screening and treatment of premature infants of our hospital we describe the impact on our clinical routine, of the results of ETROP and revised indications for the treatment of ROP. Also we rise some doubts and controversies about the new clinical algorithm, the time of first observation and the treatment of ROP Zone I.

Results. The results of ETROP were anxiously waited, because they tried to answer the real expectation of saving more eyes from this preventable and avoidable cause of blindness. It was a very nicely designed study supported by a risk analysis model RM-ROP2, which help us calculate the risk that a child has to develop severe ROP and poor functional and structural outcome, offering to those with high risk an early treatment. However we have some doubts concerning the timing of first observation, the definition of 'plus' disease, the treatment of eyes with ROP2+ in zonell and the treatment of ROP Zone I.

Conclusions. The results of the early Treatment for ROP provides us more information to treat better our premature infants, however clinical judgement is necessary to incorporate these guidelines on our clinical management and also, we are looking forward new treatments as the anti-VEGF(Avastin) for the worst forms of ROP.

INTRAVITREAL BEVACIZUMAB (AVASTIN) ADDED TO CONVENTIONAL THERAPY FOR THRESHOLD ROP

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Objective: To study the effects of adding intravitreal bevacizumab (Avastin) to conventional LASER treatment on regression of retinal neovascularization in threshold ROP.

Materials and method: Intravitreal injection of bevacizumab (1.25mg) in one eye of each of three newborns with threshold ROP was performed in addition to laser treatment. The other eye of each patient was treated with laser alone. Changes in retinal neovascularization, its regression and unfavorable anatomical outcome were assessed on fundus photographs by Retcam and frequent funduscopy. ERG was performed four months after injection.

Results: ROP regressed in both eyes at the same time. There were no differences in normal retinal vascularization. We had no adverse effects due to injection including cataract, endophthalmitis or vitreous hemorrhage. We didnt observe any differences in ERG between two eyes.

Conclusion: Intravitreal injection of bevacizumab seems to have no adverse effect in newborns with threshold ROP. It is recommended to perform more studies in order to assess its effect.

CLINICAL SIGNIFICANCE OF TUNICA VASCULOSA LENTIS IN THE OUTCOME OF THRESHOLD RETINOPATHY OF PREMATURITY

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Background: Many intraocular vessels are transitory and disappear by birth. In this report we analyse the importance of the tunica vasculosa lentis TVL in treatment outcome of threshold ROP.

Material and methods: The study was performed at the Vilnius university children's hospital (VUCH) between July 1, 1997 and May 1, 2006. All consecutive and otherwise unselected infants who reached threshold ROP and underwent treatment were included into the study cohort, comprising 261 babies. Tunica vasculosa lentis of various grades (1-4) was found bilaterally in 94 infants (188 eyes). This group was labelled TVL (+) group. The rest of investigated infants (167) formed the TVL (-) group.

Results: Cryo or laser/cryotherapy was applied on 518 eyes (261 infants) with threshold ROP. Treatment was applied once in 449 eyes. 160/187 eyes of the TVL (+) group and 289/331 eyes of the TVL (-) group underwent one treatment session. Treatment was carried out twice in 27 eyes with TVL and in 38 eyes without TVL. 4 eyes were treated three times, all from the TVL (-) group.

Tunica vasculosa lentis disappeared in 151 eyes after the first session of therapy. Treatment was successful in all these eyes.

Total number of failures - 30 eyes: 19/187 eyes (10 children) in the TVL (+) group and 11/331 eyes (8 children) in the TVL (-) group. All failed eyes belonged to Zone I disease.

Conclusions: Eyes with persistent tunica vasculosa lentis at threshold - have a greater risk for unfavourable outcome after therapy for threshold ROP.

Cryotherapy can be used safely in eyes with tunica vasculosa lentis.

Dissolution of tunica vasculosa lentis after treatment of threshold ROP was directly proportional to favourable fundus outcome.

REFRACTIVE OUTCOME AFTER MODIFIED TREATMENT FOR ROP

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Purpose: To examine the level of refractive errors if former prematures who underwent modified treatment modalities: cryotherapy for Zone II ROP, and laser-cryotherapy for Zone I ROP (aggressive posterior ROP).

Methods: Retrospective analysis of 79 consecutive cases (154 eyes) examined at the private office since 1996 till 2006 was performed. For all examined children treatment of threshold ROP was performed by the same two ophthalmologist (RB & RS). Two experienced pediatric ophthalmologists (LSh & ED) performed cycloplegic retinoscopy at the chronologic age between one to two years. Zone I threshold ROP was present in 42 eyes (22 children), Zone II threshold ROP was treated in 112 eyes (57 children).

Results: The average spherical equivalent refraction of all treated eyes was -0.56 ± 3.99 dptr (range from -16.5 to +6.5D, median +0.63 dptr, mode +1.0D dptr). Mean BW of all infant was 1173.5 ± 312.7 grams and mean GA was 28.3 ± 2.0 weeks.

Among Zone II threshold ROP infants, who received modified cryotherapy (treatment on the ridge and anterior to the ridge) the average spherical equivalent refraction was $+0.01 \pm 3.43$ dptr (median and mode +1.0D). Among Z-I threshold ROP infants who underwent modified laser –cryotherapy on both sides of the ridge, the average spherical equivalent refraction was -2.1 ± 4.9 dptr (median: -1.5 dptr, mode: +1.5 dptr). The difference of mean refraction was statistically significant between Zone II and Zone I ROP infants (F test: $F=0.49$, $p=0.002$). No statistically significant difference was found between mean BW of Zone II and Zone I ROP infants (1197,4 grams vs1093,3grams respectively). Mean GA of those infants (28.5 weeks vs 28.0 weeks) also did not differ statistically.

64.3% of Zone II ROP eyes had refractive error from -1.0 to +3.0 dptr and 69.1% of Zone I ROP eyes had refractive error from -2.0 to +2.0 dptr.

Conclusions: Our modified cryotherapy for Zone II threshold ROP resulted in emmetropic refraction. Among Z-I ROP infants the shift to myopic refraction was more evident.

We suppose that shift to myopia is related more to the zone of the disease.

REGRESSED ASPECTS OF NATURAL EVOLUTION OF THE RETINOPATHY OF PREMATURITY

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Objectives: The retinopathy of prematurity is a vascular proliferative disease of the retina affecting very low birth weight and extreme prematures which cause important visual impairment or even blindness in its natural evolution without treatment. This work aims to show the retinal cicatricial aspects on fundoscopic examinations in a group of visual handicapped patients aged 7 to 17 years. All patients were prematurely born survivors.

Methods: Retrospective analysis of the medical records and cases presentation of five patients of the Hospital de Clinicas de Porto Alegre - Brazil in the period between 2003 and 2006 after the implantation of the Prevention Program for Blindness by Retinopathy of Prematurity in this institution. None of the patients had previous knowledge of its condition of survivor visually affected of the extreme prematurity.

Comments: The retinopathy of prematurity is always a progressive disease. If not diagnosed and treated during the after-birth period it will cause important visual sequels or irreversible blindness as in the cases of the patients here related. Patients in the stage of ROP 3 threshold disease not treated by laser in the neonatal period will evolve to formation of vitreous-retinal traction and tractional detachment of retina affecting the noble structures of the posterior pole of the eye. These patients could reach visual acuity of 20/100 or less. Prematures reaching stage of ROP 4, without laser treatment, in the after-birth period will develop greater complications and visual acuity around hand movements or only light perception. The routine fundoscopic examination in the neonatal intensive care unity of all prematures in the group of risk is the only way to control the disease in those with possibility to develop the final and irreversible complications of retinopathy of prematurity. The objective of the treatment in the perinatal period is the prevention of retinal detachment and the future low vision in these patients.

INCIDENCE OF REFRACTIVE ERRORS, STRABISMUS AND RETINAL CHANGES AT SIX MONTHS OF AGE AMONG INFANTS SCREENED FOR RETINOPATHY OF PREMATURITY IN THE HOSPITAL DE CLINICAS DE PORTO ALEGRE - BRAZIL

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Objectives: To evaluate the six month outcome of patients screened for Retinopathy of Prematurity (ROP) at Hospital de Clinicas de Porto Alegre - Brazil .

Methods: It was performed a follow up study including all prematures screened for retinopathy of prematurity in the Hospital de Clinicas de Porto Alegre - Brazil between October 2002 and April 2006. All of them with less than 1500 g of birth weight or less than 32 weeks of gestational age at birth and that presented for the follow up appointment regularly until the 6 months of corrected age. All the patients were examined by the same group of ophthalmologists. The indirect ophthalmoscopy with a 28 diopters lens and lid speculum was first conducted at 6 weeks of life and repeated weekly or more depending on the classification of the disease accordingly to the International Classification of Retinopathy of Prematurity (1984/1987). All patients were examined at 6 months of corrected age for presumed visual acuity, exam of the eye motility and alignment, cycloplegic refraction, indirect ophthalmoscopy and retinal mapping. The retinoscopy and the fundus examination were performed 30 minutes after the instillation of 2 drops of Cyclopentolate 1%, Phenylephrine 2.5% and Tropicamide 0.5%.

Results: 67 patients (134 eyes) were studied. Twenty five patients (37,31%) developed retinopathy of prematurity at any stage, and seven needed laser treatment for ROP stage 3 threshold disease. The mean gestational age for the ROP group was 29.47 weeks (range 25-36 weeks), compared to 31,9 weeks (range 27-34 weeks) for the non ROP group. At 6 months of corrected age, patients who developed ROP were significantly more myopic (9 patients, 36%) than those who didn't (2 patients, 4.7%). Otherwise, non ROP patients were significantly more hyperopic (37 patients, 88%) than the ROP group (16 patients, 64%). Astigmatism presented in 20 (80%) of the ROP patients and in 25 (59.5%) of the non-ROP infants. Among the patients who underwent laser therapy, 57,14% developed myopia. On the other hand, only 27,7% of patients on ROP group without laser therapy developed myopia. Strabismus was detected in 3 patients on ROP group and 2 on non-ROP group. Retinal changes were diagnosed just in the ROP group. Fundus abnormalities included macular changes in one patient, zone 1 retinal scars also in one patient, peripheral retinal scars in 6 patients and pale optic disc in one patient.

Conclusions: This study suggests a higher risk for myopia (especially on ROP group that was submitted to retinal photocoagulation) and retinal changes among patients that developed ROP. The results are in agreement with other studies published in the literature.

RETINAL DETACHMENT AS A LATE COMPLICATION OF RETINOPATHY OF PREMATURITY - CASE REPORT

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Problem: Retinal detachment (RD) is a less frequent late complication of retinopathy of praematurity (ROP) than myopia, amblyopia, anisometropia, strabismus and glaucoma.

Patient and method: A fourteen-year-old formerly preterm patient was operated on the left eye with rhegmatogenous retinal detachment as a late complication of ROP. A preventive laser photocoagulation was applied in the right eye because of peripheral tear.

Results: RD was successfully treated with pars plana vitrectomy. After the operation the visual acuity improved from 5/8 to 5/6. During the 15-month follow-up-period the retina remained attached.

Conclusion: ROP is a life-long disease with possible late complications. Serious visual deterioration caused by retinal detachment could be prevented in most of the cases during the accurate and long-term follow-up. The patient must be well informed about the early signs of this potential complication.

VISUAL FUNCTIONS IN PREMATURE CHILDREN IN SCHOOLAGE

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Objective: Evaluation of vision in premature children with birth weight bellow 1500 g in schoolage.

Methods: We have evaluated 37 premature born children with birth weight bellow 1500 g (700-1500 g) in age 8 years. These children were born between 24 and 35 weeks gestation. We evaluated visual acuity, refraction, contrast sensitivity, color vision, strabismus and results after strabismus surgery. We search connection between visual deficits and gestation age, birth weight and other disorders. We compare these results with a group of full-term infants.

Results: Pathological refraction was found in 49% of the premature infants, strabismus was found in 19% of the premature infants. Contrast sensitivity was significant poorer in the group of the premature infants.

Conclusions: Low birthweight children have deficit in both visual acuity and contrast sensitivity, increased incidence of strabismus and increased number of refractive errors. A significant assotiation between 'ophthalmic morbidity' and neurology disorders such as muscular paresis and hydrocephalus was noted.

THE LONG TERM OPHTHALMIC OUTCOME IN SINGLETONS AND TWINS

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Background: Although the long term ophthalmic outcome in low birth weight has been studied, there is a lack of data on the impact that sharing a similar intra-uterine environment and genetics, as occurs in twins, may have on outcome. The aims of this analysis are to determine whether twins have a similar outcome and how this compares to a matched comparison group of singletons.

Methods: This cohort of children comes from a population based study of ROP in the 1980s where all children with a birth weight ≤ 1701 g were recruited. Within this cohort there were 62 pairs of twins (n=124) and of those 62 pairs 35 (n=70) were assessed at 10 yrs. To enable comparison with singletons a 'comparison group' was created (n=102, 51 pairs). These children were matched to each other in terms of birth weight (± 30 g), whether they were small for gestational age, their ethnicity and the maternal smoking habits. A subset of this group n=48 (24 pairs) were matched specifically to the twin population with 15 of the pairs having long term ophthalmic measures. Uniocular visual acuity was measured with a logMAR chart, contrast sensitivity with the Pelli Robson chart, strabismus by the cover test and refraction with the Retinomax K-plus.

Results: ROP was present in 56.7% of the twins cohort who were more likely to behave similarly with respect to acute phase ROP with 43.3% both having no ROP while 28.3% both had ROP (chi square p=0.001). In the comparison group ROP was present in 73.5% but there was no statistically significant relationship between the pairs of singletons (chi square p=0.3). There was no relationship between the twin siblings in terms of the presence of strabismus (Fishers, p=0.1) with a similar finding in the comparison group (chi square p=0.2). However there was a statistically significant relationship between the twins with respect to the presence or absence of myopia (≤ -0.0 D) where 80% had the same outcome as their twin, (Fishers p=0.015) whereas for the singletons only 66.7% had the same outcome as the matched singleton, (chi square p=0.9). Analysis of the subgroups compared directly the difference in right eye acuity between the twins and the matched comparison group. The results showed no similarity between the pairs (paired t-test p=0.5). The same finding occurred when the contrast sensitivity and mean spherical equivalent were analysed (paired t-test, p>0.1 in both cases).

Conclusions: This analysis shows that twins are more likely to have a similar outcome to each other in terms of acute phase ROP and myopia so suggests that similar genetics and intra-uterine environment do impact on the outcome. However, in the small subgroup analysis where there is no statistically significant relationship it suggests that other neonatal factors have a greater impact on those factors.

ANATOMICAL AND FUNCTIONAL OUTCOME AFTER EARLY CRYOTHERAPY IN ROP

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Purpose: To present the anatomical outcome and the visual progress in ROP babies in whom early cryotherapy was performed.

Methods: In thirty eight ROP babies (76 eyes) cryotherapy was performed according to ET study guidelines. The babies were followed for 2 and half years after cryotherapy. Total and partial retinal detachment as well as dragging of the macula after cryotherapy, were considered as unfavorable anatomical outcomes. The best corrected visual resolution (BCVR) and visual acuity (BCVA) (where possible) was evaluated in all babies twenty four months after the cryotherapy performed, using Leas grating cards and Kay pictures test.

Results: From the 38 babies, the majority of them appeared with gestational age less than 28 weeks and birth weight less than 1250 gr. Fourteen babies presented with ROP in zone 1 and the rest in zone 2. After early cryotherapy 37 babies (74 eyes) appeared with favorable anatomical outcome and only one baby appeared with subtotal retinal detachment to both eyes. Two children appeared with BCVR less than 0.43cpd and one child with BCVA equal to 6/60. Three children appeared with $0.43\text{cpd} < \text{BCVR} < 1.75\text{cpd}$ and two children with $6/60 < \text{BCVA} < 6/18$. Finally, thirteen children appeared with $\text{BCVR} > 1.75\text{cpd}$ and seventeen children with $\text{BCVA} > 6/18$.

Conclusion: Early cryotherapy treating ROP babies leads to an impressive increase of favourable anatomical outcome. It leads also to good functional visual results.

THE VFA-K TEST IN VISUAL ASSESSMENT OF ROP BABIES

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Purpose: To present the results of testing the visual function (globally) of ROP babies, using the new VFA-Kozeis test.

Methods: 155 ROP babies, who did not undergo cryotherapy or photocoagulation, were visually evaluated by VFA-K test at the age of 24 months since birth. This test assesses 10 visual subfunctions as: visual attention, visual resolution and / or far visual acuity (according to the age), near visual acuity, contrast sensitivity, colour perception, peripheral vision, binocular cooperation, saccades, smooth pursuits movements and eye- hand coordination. Each subfunction is scored separately, leading to a total score (Index K). In this study, the visual resolution, far visual acuity, colour perception, contrast sensitivity, peripheral vision, refractive status (cycloplegic refraction) and index K are reported.

Results: Most of children who participated in this study appeared with gestational age of less than 32 weeks and birth weight of less than 1500 gr. The vast majority of them (86.45%) appeared with an insignificant refractive error ($x < 0.50$ D). 58.70% of the children appeared with best corrected visual resolution (BCVR) > 1.75 cpd, also 34.83% of the children appeared with best corrected visual acuity (BCVA) $> 6/18$. All the children appeared with normal colour perception and contrast sensitivity. The functional peripheral vision was also normal to the vast majority of the children. Finally, 66.45% of the children appeared with index K within or very close to normal score for their age group, while the rest appeared with reduced index K.

Conclusion: The VFA-K test is an easy to perform visual test, having the ability to evaluate and follow the progress of visual function of ROP children in a global way.

LONG TERM MACULAR CHANGES REPORTED WITH OCT IN FORMERLY PRETERM CHILDREN

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Aim: To report macular anatomic abnormalities in formerly preterm children.

Patients and methods: A prospective study on 29 eyes of 15 patients (mean age 103 years at the time of testing, gestation time < 32 weeks): Group I. Best corrected visual acuity BCVA (LogMAR values of Snellen chart), refractive errors (automatic refractometry) and axial bulbus length (UH biometry) were investigated. Macular anatomic abnormalities were imaged with digital fundus photography and optical coherence tomography (OCT3). For quantitative comparison the total macular volume (TMV) were measured with OCT. All the results were compared to those of age-matched normal control volunteers: Group II.

Statistics: Mann-Whitney-U Test and Spearman Rank Order Correlations Analysis

Results: There was no difference between the two groups in refractive errors. Mean BCVA was 0,155230,28 logMAR in Group I and 0 logMAR in Group II. Mean total macular volume was 6,62520,8 mm³ in premature eyes and 7,12190,38 mm³ in the control group (p=0,03). In Group I, the lower was the TMV the weaker was the BCVA (correlation coefficient=0,61067). In this group no correlations were found between TMV and refractive errors or bulbus axial length, respectively.

Conclusion: The macular volume was significantly lower in formerly preterm children compared to fullterm children. Visual acuity correlated with the macular volume significantly in formerly preterm children.

OCCURRENCE OF RETINOPATHY OF PREMATURE IN A LEVEL 3 UNIVERSITY HOSPITAL NEONATAL UNIT IN EAST LONDON: A CASE SERIES

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Background: In the United Kingdom, The Royal College of Ophthalmologists and College of Paediatricians joint guidelines on the screening of premature infants for the development of retinopathy of prematurity (ROP), currently recommend that all infants born at 32 weeks gestation or less and/or weighing 1500g or less are screened. Neonatal units in the UK are sub-grouped into three levels viz: 1, 2 or 3. A level 3 unit provides the highest level of intensive care of the pre-term infant. Very premature infants born in level 1 or 2 unit facility, if necessary, are transferred to the nearest available level 3 unit for intensive care.

ROP occurrence is higher in the smallest and most premature infants, particularly if there are additional risk factors such as patent ductus arteriosus, respiratory distress syndrome or necrotizing enterocolitis. These infants are most likely to be found in level 3 units. The present study presents data of ROP screening from a single level 3 unit in the Moorfields Eye Hospital catchment area.

Methods: Retrospectively, case notes of all infants admitted to the 31 cot, level three unit at Homerton Hospital, London for ROP screening were reviewed over the three year period, January 2003 to December 2005.

Results: A total of 330 infants were identified to meet the screening criteria and 251 were screened. Of those not screened, 28 infants died prior to starting or during ROP screening, a mortality rate of 8.5%, and 52 infants were transferred to other units before starting screening. Retinopathy of prematurity was seen in 76 of the 251 screened (30.3%). By gestational age, ROP was detected in; 24 out of 40 (60%) that were born at 23-24 weeks gestation; 36 out of 71 (51%) born at 25-26 weeks; 12 out of 71 (17%) born at 27-28 weeks and 3 out of 74 (4%) born at 29-30 weeks. None of the 59 born at 31 weeks or more developed ROP. 1 infant out of 15, in whom the gestational age was undocumented, developed ROP.

A total of 27 infants reached threshold disease and received laser, 11% of those screened. No infants required re-treatment and no infants progressed to stage 4 or 5 ROP. No infant born weighing \geq 1000g or with a gestational age of \geq 30 weeks required treatment for ROP.

Conclusions: Adherence to screening guidelines in our hospital has allowed early detection and treatment of those with ROP. Increasing survival rates for the most premature means there will continue to be a group with high risk for this disease.

RESULTS OF CRYOTHERAPY AND LASER PHOTOCOAGULATION FOR THE TREATMENT OF RETINOPATHY OF PREMATURITY

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Aim: To analyse the results of cryo and laser therapy for acute ROP.

Materials and methods. In the period from 1994 to 1999 transscleral cryotherapy was performed in 170 babies (320 eyes). In the period from 1999 to 2006 140 patients (250 eyes) were treated by transpupillary diode and argon laser photocoagulation. 86 babies (172 eyes) with ROP zone 1 and 'plus-disease' had the combination of transscleral cryo or diode coagulation for the anterior avascular retina with transpupillary diode or argon laser photocoagulation for posterior avascular retina.

The treatment was performed in babies with threshold ROP zone 1 or 2. Cryo and laser treated eyes had comparable stages and extension of ROP.

Results. Cryotherapy was effective in 71% of eyes. Only 12,5% eyes with 'plus-disease' and 57% ROP zone 1 demonstrated favourable anatomical outcomes. In the results of transpupillary laser photocoagulation 85% of eyes had favourable structural outcomes. But, transpupillary laser photocoagulation is more difficult to apply anteriorly, especially in the presence of a small pupil or unclear media, or vitreous haze.

Combined treatment allowed to achieve favourable outcomes in 88% of ROP zone 1 and in 75% with 'plus-disease'.

Conclusions. Laser ablation appeared to be more effective as cryotherapy for treatment for threshold ROP. The best results were achieved with combined therapy, which significantly decrease the risk of unfavourable outcomes in cases with 'plus-disease' and ROP zone 1.

THE LATE VISUAL FIELDS, ELECTRORETINOGRAMS AND PERIPHERAL RETINAL CHANGES IN PATIENTS WITH CICATRICAL ROP

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Aim: to study the late peripheral retinal changes, visual fields and electroretinograms (ERG) in patients with ROP.

Materials and methods: 25 patients (45 eyes) with ROP 1-3 stages in age 8 - 16 years underwent a Humphrey 120 full- field screening test and a full field flash ERG. The retinal examinations included indirect ophthalmoscopy, wide angle fundus camera (RetCam 120), and fluorescein angiography. 8 infants (16 eyes) were treated by cryotherapy an acute stage of ROP.

Results. The dragging of disk and central retinal vessels were detected in 13 eyes. The abnormal and incomplete vascularisations of the peripheral retina - in 12 of 25 eyes in patients without cryo. Pigmented chorioretinal atrophic scars, retinal thinings were at 10 eyes without cryo and in all cases with cryo. Only 6 eyes had no any peripheral changes of retina. Fluorescein angiography revealed avascular zones, anastomoses and arcades of vessels, and another pathology of vascularisation of the peripheral retina.

Peripheral visual field constrictions and defects of visual field were detected at 28 from 45 eyes (60%). There was circumferential constriction of the visual fields at 6 eyes with cryo and 4 eyes without cryo. In two eyes with cryo the visual field constricted to a small central island.

Normal ERG was registered only in 22% eyes with 1-2 stages of ROP. Full-fields flash ERG was reduced at 78% eyes with ROP 1-3 stages.

Conclusions. Incomplete and abnormal vascularisation, atrophic scars, pigmental changes of the peripheral retina were found in ROP patients. There was correlation between the peripheral retinal changes and visual fields defects and ERG reduction.

NO MORE BLIND CHILDREN, DETECTION AND OPPORTUNE TREATMENT OF THE RETINOPATIA OF PREMATURITY. HOSPITAL CIVIL DE GUADALAJARA. JALISCO, MEXICO.

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Antecedents: According to the INEGI statistics and geography mexican institute 4.600 blind children younger than 14 years exist in Jalisco, of which 2.852 (62%) have their origin in the perinatal period. The Retinopathy of Prematurity (ROP) is the main cause of blindness between premature new borns, particularly in urban regions of the developing countries. In 2004 in the Hospital Civil Fray Antonio Alcalde, in the external consultation of Ophtalmology 16 non treatad ROP-blinded children from the metropolitan area and the interior of the State asked for medical assistance.

The strategy of detection and treatment of ROP in the neonatal intensive care was evaluated, in this evaluation relatively few cases were found, treated some of them in delayed due to the lack of information-coordination between the services of ophthalmology-neonatology.

Main actions: The intervention 2005 was based on clinical training directed to nonophtalmologists of the Civil Hospitals of Guadalajara, information with which the medical workers in charge of the premature patients participated in the identification of cases and pursuit. Patients that were identified with ROP in both Hospital Units which required laser treatment were treated in the Fray Antonio Alcalde Unit.

Objectives: To diminish the number of blind by ROP.

1.1 Avoid the ROP- blindness through the training for the prevention

1.2 Diagnosis and opportune treatment of ROP in premature with weight at birth <1.501 grams and gestacional age <35.1 weeks, from the Jalisco not health-insured population.

1.3 To enable to nonophtalmologists for the detection of population at risk and diagnosis of ROP.

Results:

1. Training of the nonophtalmologist medical workers for the detection of patients at risk of ROP-blindness.

2. Optimization of human and technological resources in both hospital units.

3. 100% of the ROP-risk population at the Guadalajara Civil Hospital were covered.

4. Detection and successful treatment of 39 patients in risk of blindness by ROP.

5. Increase of the 2004 productivity in a 78%

Obstacles: Ignorance of ROP by health workers. 1.5 km Distance between both hospital units. Deficit of equipment for detection and treatment. Limited economic resources.