Recent Update in Retinopathy of Prematurity

Dr. ANUSHRI AGRAWAL*, Dr. ROHIT SHAHI**
Dr. M.K. Upadhyaya***, Dr. KAMYA SHARMA****, Prof. Dr. SHRIKANT*****

INTRODUCTION

Retinopathy of prematurity (ROP) is a vaso-proliferative disorder of developing retina. It occurs principally in premature children but not exclusively. ROP was first described as "retrolental fibroplasia" in 1942. Prematurity continues to be the single most important risk factor for ROP.

The pathogenesis of ROP is still not fully understood but involves an intricate interplay between retinal blood vessels, oxygen, angiogenic and growth factors, of which vascular endothelial growth factor (VEGF) is most important.

Clinical picture of ROP is very similar to other vasoproliferative disorder of retina but having two major differences:

1) Proliferating elements are developing mesenchyme and

2) Progression is very fast i.e. more aggressive form.

ROP is described in two phases.

The first phase begins after preterm birth secondary to the hyperoxicextrauterine environment and involves suppression of VEGF, vaso-obliteration with cessation of retinal blood vessel growth and endothelial apoptosis.

The second phase is proliferative and involves neovascularisation of retinal vasculature by vasoactive factors such as VEGF, produced secondary to hypoxic and avascular retina of phase 1. The second phase begins around 32 weeks postmenstrual age but can have a wide range of onset.

EPIDEMIOLOGY

ROP is one of the more severe consequences of preterm birth and a major cause of childhood blindness and visual impairment in the developing and developed world.

The disease is more common in infants of less than 31 weeks gestation with infants of lesser gestation at higher risk and severity of ROP.

A Korean study reported a 20.7% incidence and reported that a GA of 28 weeks or less and a birth weight of 1000 g or less were the most significant risk factors.

In infants with a birth weight of <1500 g, the reported incidence of ROP ranges from 20% to 50% in different populations.

Mortality :

Long term outcomes for serious disease include several visual impairment and blindness. In addition myopia, amblyopia and strabismus may occur.

*Resident Aravind Eye Hospital Pondicherry
**Resident IMS B.H.U
***Associate Professor, Narayana Medical College, Sasaram.
****Senior Resident IMS B.H.U
*****Prof and Head ,Vitreo-Retina & LASER Unit
Jointly Department of Ophthalmology, Institute of Medical Sciences, B.H.U., Varanasi , INDIA

Race :

Some reports indicate a decreased incidence of progression to threshold disease in black infants.

Sex :

Although some reports indicate a male predilection, the CRYO-ROP study revealed no differences based on sex.

Age :

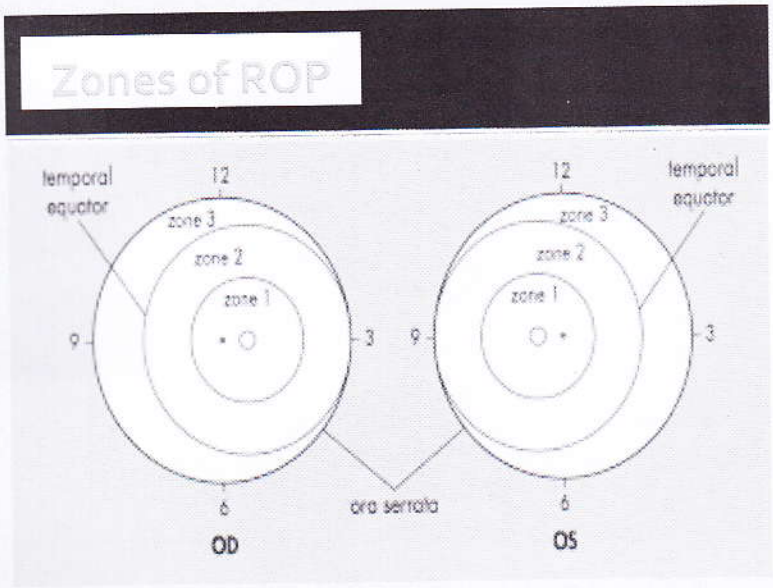
Retinopathy of prematurity is a disease of the immature retina, and the occurrence of ROP is inversely related to gestation age.

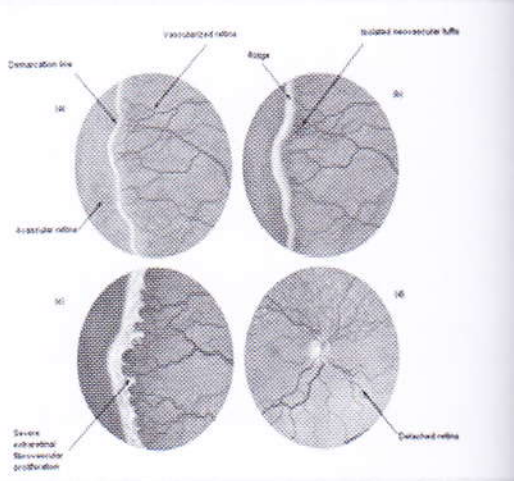
GLOBAL INFORMATION

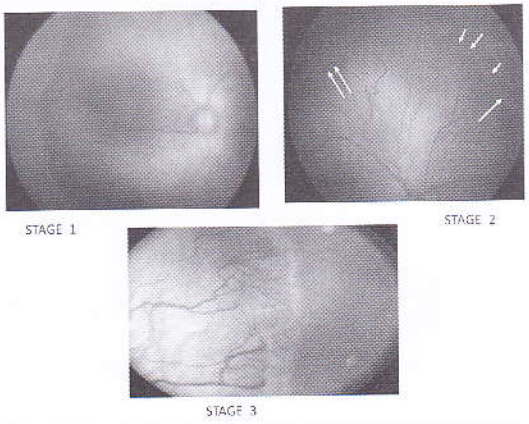
- Retinopathy of prematurity (ROP) is a leading cause of preventable childhood blindness in middle-income countries (Gilbert, 2008).
- ROP occurs primarily in infants of low birth weight and low gestational age at birth.
- Most studies report ROP incidences that are about 60% for babies less than 1500 g (Zin and Gole, 2013).
- The worldwide prevalence of blindness due to ROP is approximately 50,000.
- One of the greatest challenges in less-developed countries is having adequate screening done by ophthalmologists trained to diagnose ROP with indirect ophthalmoscopy.
- Telemedicine with the use of digital imaging and fundus photography may also be a potential strategy for ROP screening in regions where there are few trained ophthalmologists who can manage ROP.

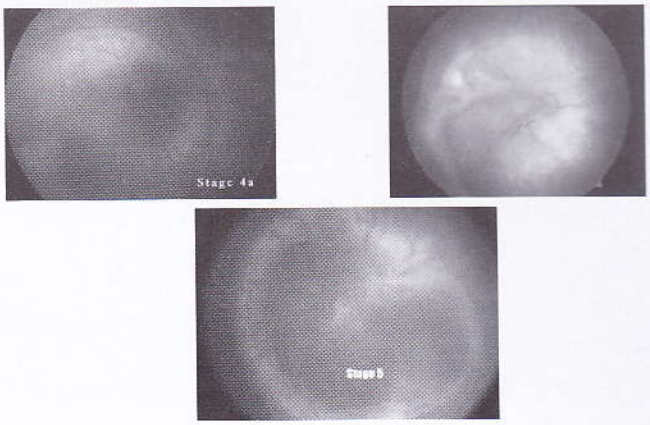
REGIONAL INFORMATION (INDIA)

- The incidence of ROP is increasing in India because of improved neonatal survival rate.
- Out of 26 million annual live births in India, approximately 2 million are <2000g in weight and are at risk of developing ROP.
- The incidence of ROP is between 38 and 51.9 % in low birth weight infants.









SCREENING FOR ROP

Which children are to be screened for ROP ?

1) Less than 1500 g birth weight.

2) Less than or equal to 32 weeks of gestational age.

3) exposed to oxygen for than 30 days.

When should the screening be done ?

32 weeks of post conceptional age (PCA) or 4-5 weeks after birth

Whichever is earlier but usually no need to examine the child in first 2 weeks after birth.

How to perform the screening examination for ROP

Before embarking upon the screening exam for ROP one has to keep in mind that the children to be screened are premature infants and thus susceptible to a particular set of problems.

PLACE : The ideal place for the screening is a temperature controlled room, since premature neonates are susceptible to hypothermia.

Preparation of the child : The Pupils are dilated with a mixture of phenylephrine 2.5% & tropicamide 0.5% instilled 3 times at 10 min. interval about one hour before the screening.

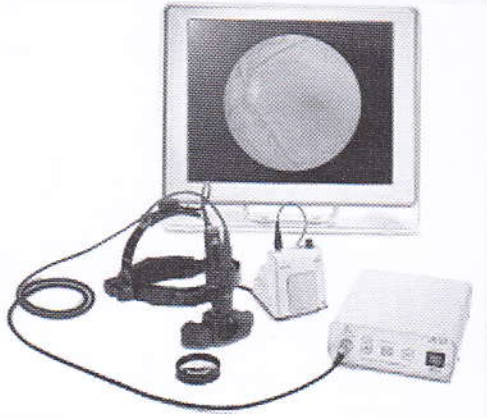
Alternatively a combination of 0.2% cyclopentolate& 2.5% phenylephrine may be instilled twice at 5 min. interval.

RetCam 3

- It is a wide angle pediatric retinal imaging system useful for screening ROP.
- It is non stressful way to screen premature babies & easier to perform.
- It can be use in undilated pupils.
- Images can be magnified

VIDEO INDIRECT OPHTHALMOSCOPE

It is also called poor man's Ret Cam 3. It is done using 20D & 28 D(preferably 28 D) lens under sedation. It also gives a good stereoscopic view both to examiner and viewer, inexpensive, light weight, portable and enable proper documentation in screening ROP.



When should we treat ROP?

The classical criteria for treating ROP is given by the CRYO ROP study.

- Stage 3 with Plus disease in zone 1 or 2
- 5 contiguous / 8 interrupted clock hours of stage 3.

We now perform cryo/ laser if -

- 3+ ROP in 3 contiguous / 5 cumulative clock hours in zone 2.
- Any stage of ROP with Plus disease in Zone 1.
- The child is re-examined after treatment at 72 hours & any skip area are retreated.
- Once ROP of stage 3 + severity is detected, the treatment should be initiated within 72 hours of detection in order that the treatment is effective.

Surgery in ROP

- In the absence of any other form of treatment in advanced stages of ROP if remains as a last hope in salvaging a small island of vision.
- The indication of surgery begins with stage IVB, when there is peripheral retinal detachment due to traction by proliferating vascularized tissue.
- In stage IVB, a scleral buckling often is necessary in the form of a silicon band.
- Moreover the buckle needs a removal at a later date so as to prevent strangulation of sclera& eye as a whole.
- Therefore the second surgery needs to be planned and performed.
- Stage V is an advanced stage where surgery is not only difficult but results are unpredictable.
- The surgery primarily involves removal of lens, separating and dissecting out retinal adhesions and flattening the retinal folds as much as possible.
- Lens sparing is also a point which is often discussed.
- In view of poor outcome of surgery in severe ROP case, it is emphasized that the cases at risk should be identified early and preventive measures in the form of follow up.

- Lens sparing is also a point which is often discussed.
- In view of poor outcome of surgery in severe ROP case, it is emphasized that the cases at risk should be identified early and preventive measures in the form of follow up.
- Lens sparing is also a point which is often discussed.
- In view of poor outcome of surgery in severe ROP case, it is emphasized that the cases at risk should be identified early and preventive measures in the form of follow up.

Insulin like growth factor (IGF) in ROP

- It is a polypeptide hormone critical to normal vascular development.
- IGF acts indirectly as a premissive factor by allowing maximal VEGF stimulation of vessel growth.
- Lack of IGF in preterm infants prevents normal retinal vascular growth allowing pathological neovascularization.
- IGF measurement will give a rough idea about development of ROP.
- Serum IGF-1 level is directly related to the gestational age of the infants.
- Lower the serum IGF-1 level the more the chance of developing severe ROP.
- IGF-1 level correlates for development of retinopathy of prematurity (ROP) in serum of premature

infants.

- 73% of infant developed Stage 1 ROP and the rest develop Stage 2.
- Zone III involvement never progress beyond Stage 1, and Zone II beyond Stage 2.
- Severity of ROP could not be related to the level of IGF-1.
- All cases develop ROP of Stage 1 and Stage 2 irrespective of serum IGF-1.
- The study was presented in EU RETINA nice france and published in journal 'ANNALS OF OPHTHALMOLOGY'

CLINICAL TRIALS IN ROP

- Multicenter trial of cryo-therapy for retinopathy of prematurity CRYO-ROP
- Light reduction in ROP study (LIGHT- ROP)
- Supplement therapeutic oxygen to prevent PTh(prethreshold) ROP (ROP)
- High oxygen percentage retinopathy of prematurity (HOPE-ROP)
- Vitamin E trial
- Early treatment for retinopathy of prematurity(ETROP)
- Beat ROP(Bevacizumab in the treatment of ROP)

REFERENCE

1. Goble RR, Jones HS, Fielder AR. Are we screening too many babies for retinopathy of prematurity? Eye. 1997;11:509–14.
2. American Academy of Pediatrics. Screening examination of premature infants for retinopathy of prematurity. Pediatrics. 2001;108:809–11.
3. Wright K, Anderson ME, Walker E, Lorch V. Should fewer premature infants be screened for retinopathy of prematurity in the managed care era? Pediatrics. 1998;102:31.
4. Andruscavage L, Weissgold DJ. Screening for retinopathy of prematurity. Br J Ophthalmol. 2002;86:1127–30.
5. Yanovitch TL, Siatkowski RM, McCaffree MA, Corff KE. Retinopathy of prematurity in infants with birth weight ≥ 1250 grams-Incidence, severity and screening guideline cost-analysis. J AAPOS. 2006;10:128–34.
6. Royal College of Ophthalmologists and British Association of Perinatal Medicine. 1995. Retinopathy of prematurity: Guidelines for screening and treatment The report of a joint working party.
7. Gopal L, Sharma T, Ramchandran S, Shanmugasundaram R, Asha V. Retinopathy of prematurity. A study. Indian J Ophthalmol. 1995;43:50–61.
8. Bagdoniene R, Surtautiene R. Threshold retinopathy of prematurity in Lithuania. In: Reibaldi A, Di Petro M, Scuderi A, Malerba E, editors. Progress in Retinopathy of Prematurity. Amsterdam/NewYork: Kugler Publications; 1997. pp. 31–6.
09. Shah PK, Narendran V, Kalpana N, Gilbert C. Severe retinopathy of prematurity in big babies in India: history repeating itself? Indian J Pediatr. 2009;76:801–804.
10. An international classification of retinopathy of prematurity. The Committee for the Classification of Retinopathy of Prematurity. Arch Ophthalmol. 1984;102:1130–1134.
11. International Committee for the Classification of Retinopathy of Prematurity. The International Classification of Retinopathy of Prematurity revisited. Arch Ophthalmol. 2005;123:991–999.
12. Gilbert C. Retinopathy of prematurity: a global perspective of the epidemics, population of babies at risk and implications for control. Early Hum Dev. 2008;84:77–82.
13. Wilson CM, Ells AL, Fielder AR. The challenge of screening for retinopathy of prematurity. ClinPerinatol. 2013;40:241–259.
14. Shrikant , Usha, Bhatia, Kamson Anthony, Gaurav Seth: Pattern of retinopathy and its correlation with insulin-like growth factor-1 (IGF-1).Ann Ophthalmology;41(3-4):170-3 20214050.