BANGLADESH J CHILD HEALTH 2006; VOL 30 (1/2/3) : 25-28

Retinopathy of Prematurity - Are We Prepared to Face the Third Epidemic?

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Introduction

Retinopathy of prematurity (ROP) is a disease in which retinal blood vessels of very sick premature infants fail to grow and develop normally, sometimes resulting in visual impairment and blindness[1]. The proportion of blindness as a result of ROP varies greatly among countries[2,3] being influenced both by levels of neonatal care (in terms of availability, access, and neonatal outcomes) and by the availability of effective screening and treatment programs[4]. Though ROP has been thought to be a cause of blindness in developed countries it has emerged as a problem in developing countries as well, along with the increased survival of younger and smaller infants[5]. Based on various screening guidelines, the incidence of ROP worldwide is reported to be 10-65.8%[6].

Risk factors and Pathophysiology

Since the link between supplemental oxygen and ROP was established[7], there has been intensive research into the role of oxygen in the pathogenesis of this condition. ROP begins to develop between 32 and 34 weeks after conception, regardless of gestational age at delivery[8], and has two distinct phases. During the acute first phase, the normal vasculogenesis of the retina is disturbed by the relative hyperoxia of the extrauterine environment. This causes vaso-obliteration and non-vascularisation of some areas of the anterior retina[9]. The subsequent hypoxia causes a second chronic phase, characterized by the proliferation of vascular and glial cells, arteriovenous shunt formation, occasionally leading to involution or permanent cicatrical changes and visual impairment[10-12].

Other than low birth weight, low gestational age, and supplemental oxygen therapy following delivery[13-15] several recent studies have suggested a multifactorial basis for ROP development. These risk factors include apnoea treated by bag and musk ventilation, sepsis, prolonged parenteral nutrition, repeated blood transfusion, hypoxaemia, hypercarbia and hypocarbia[16]. Ventilator hours, xanthine administration, maternal bleeding and multiple birth were significant risk factors of ROP[17]. Several indirect evidence suggest the role of a genetic component in the pathogenesis of ROP[18]. The incidence of ROP is more frequent in white infants than in black infants and in male infants than in female infants[18].

Diagnosis[19]

Following pupillary dilation using mydriatics, the retina is examined using indirect ophthalmoscope. An expert opthalmologist can perform the examination without difficulty.The peripheral portions of the retina are pushed into view using scleral depresion. Examination of the retina of a premature infant is performed to determine how far the retinal blood vessels have grown (the zone), and whether or not the vessels are growing flat along the wall of the eye (the stage).

Zones of retinopathy : The zones are centered on the optic nerve (Fig.-1)

- Zone I is the posterior zone of the retina, defined as the circle with a radius extending from the optic nerve to double the distance to the macula.
- Zone II is an annulus with the inner border defined by zone I and the outer border difined by the radius defined as the distance from the optic nerve to the nasal ora serrata.
- Zone III is the residual temporal crescent of the retina.

The Stages of retinopathy describe the ophthal-moscopic findings at the junction between the vascularized and avascular ratina.

- Stage 1 is a faint demarction line.
- Stage 2 is an elevated ridge.
- Stage 3 is extraretinal fibrovascular tissue.
- Stage 4 is sub-total retinal detachment.
- Stage 5 is total retinal detachment.

Plus disease is the dilation and tortuosity of the posterior retinal blood vessels.

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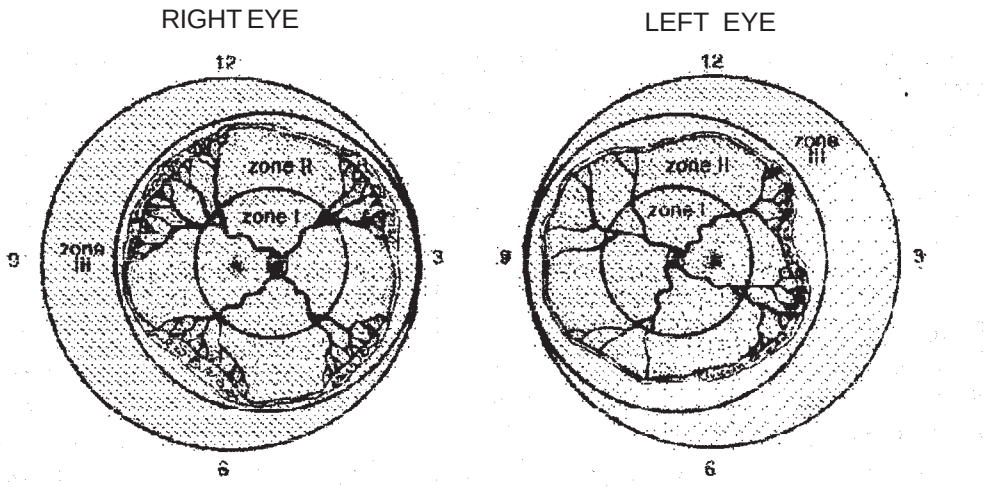

Fig.-1 : *Zones of ROP*

Retinal examination is generally recommended for patients bron at 30-34 weeks gestation, with birthweight 1500 grams or less, or at the discretion of the treating neonatoligist. The initial examination is usually performed at 4-6 weeks of life, and then repeat every 1-3 weeks until vascularization is complete (or until disease progression mandates treatment). Persence of at least stage 3 disease with plus disease in zones I or zone II or zone III is the indication for treatment.

Treatment

Early identification is the most important prerequisite for an effective treatment. Commonest and proven treatments for ROP are laser therapy or cryotherapy[20]. Laser therapy "burns away" the periphery of the retina, which has no normal blood vessels. With cryotherapy, physicians use an instrument that generates freezing temperatures to briefly touch spots on the surface of the eye that overlie the periphery of the retina. Both laser treatment and cryotherapy destroy the peripheral areas of the retina, slowing or reversing the abnormal growth of blood vessels. Scleral buckling surgery and/ or vitrectomy is usually performed for stages 4 and 5[20].

First and Second epidemic of ROP

In developed countries, ROP has been recognised by two notable epidemics over the past 60 years[18]. Severe ROP (initially termed "retrolental fibroplasia" or RLF) was first described during an epidemic of the disease in the 1940s[21]. In 1951, Campbell suggested that the toxic effects of uncontrolled supplemental oxygen to newborns were responsible for the epidemic[21]. This epidemic ceased following controlled oxygen administration.

During the late 1970s and 1980s, reports emerged of a second epidemic of ROP similar in size to the first despite the careful monitoring of oxygen delivery to neonates since the 1950s[22]. It was concluded that this epidemic was due to increased survival rates of very low birth weight premature infants weighing 750-999 g and not to new iatrogenic factors. Survival rates for premature infants less than 27 weeks' gestation continued to improve in the 1990s and, while some studies showed greater occurrence of more severe ROP[23].

Incidence is increasing in developing countries- the third epidemic

A current concern is that a third epidemic of ROP is emerging[22]. In Sri Lanka and in Lithuania reports of ROP have only recently been documented[2,24]. In Thailand and the Philippines, ROP is not reported in rural areas but causes 15% of visual loss in the cities where better medical facilities are available[25]. It is predicted that as the survival of increasingly premature infants improves in developing countries, the overall numbers of children with ROP will increase[2]. In our country neonatal intensive care services are being progressively improved in large cities. So, more infants are likely to develop ROP[26]. Sporadic opthalmogical examination for ROP revealed a good number of cases (unpublished data).

What can we do to Prevent the 3rd epidemic?

The first and foremost necessity is to increase the awareness among pediatrician, neonatologists as well as opthalmologists. Neonatologists play a central role in ensuring the timely identification of ROP. Unit-specific criteria with respect to birth weight and gestational age for examination for ROP should be established for each NICU by consultation and agreement between neonatology and ophthalmology services[19]. Neonatologists are responsible for ensuring that infants at risk for ROP and receive timely examinations. Neonatologists should (1) ensure the availability of any needed follow-up eye care after transfer or discharge, (2) discuss the need for these services with the next pediatrician or the family, and (3) arrange the follow-up eye care before transfer or discharge[14]. With this in mind, it might seem that ROP screening and detection would be simple. But the present situation is far away from this asumption. To begin, advanced ROP can occur in a distribution of time extending from as early as 31 weeks' gestational age to as late as many weeks after the expected due date (40 weeks). The infants need a long term follow up. The parents who recovered the nightmare of a long hospital stay refuse to come back to the hospital. Again, the infants are discharged back to home; not to any pediatrician. Even if the infant seek medical attention, are visited by physician who are less familiar with ROP or with the infant's ROP status. After some children are discharged, even with careful follow-up instructions, they fail to attend outpatient visits. Since prematurity is often a condition of lower socioeconomic status, the afflicted may have more difficulty gaining access to necessary health care.

Even when infants remain in a tertiary care facility during their ROP-vulnerable period, there are important obstacles to timely management of the disease. One of these obstacles is the timing and frequency of ROP examinations. The other is availability of ophthalmologist and logistic support. These problems should also be solved.

Conclusion

Although ROP has been recognized as an important cause of blindness in developed countries for many years, it is now becoming more frequently in developing countries[2]. The World Health Organization's Vision 2020 programme[5] targets ROP as an "avoidable disease" requiring early detection and treatment to prevent blindness and the inherent costs to the individual and the community. As a lower cost option for developing countries screening only infants under 1200 g may be more cost effective[27]. Current treatment options are expensive and can have potentially serious complications[20]; thus prevention is still the best strategy available at present to avoid blindness caused by ROP. However, in the short term, improved awareness on the part of pediatrician as well as opthalmologists, implementation of a screening protocol and treatment programs at Government level are likely to be most effective measure in reducing blindness caused by ROP in developing countries.

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