Editorial

Retinopathy of Prematurity and Pakistan; an Epidemic Coming

Retinopathy of prematurity (ROP) is responsible for blindness in an estimated 50,000 children in the world each year. In middle income countries 15 – 35% of childhood blindness is due to ROP[1,2]. In the USA between 1999 – 2012, 13 – 14% of childhood blindness was attributed to ROP[3]. Studies have shown that this can amount to a financial burden of $69-117 million a year. These estimates do not include loss of potential life long earnings, especially in the developing countries where services to train individuals with blindness are lacking. Although gestational age is the most important risk factor in the development of ROP, there are other factors that have been implicated, such as oxygen therapy.

In developed countries, the 1940s-1950s saw the first epidemic of ROP due to inadequately monitored oxygen therapy[4-6]. With changes in clinical practice, and controlled oxygen administration, this epidemic was brought under control. In USA, the proportion of blindness due to retrolental fibroplasia dropped from 50% in 1950 to 4% by 1965[7]. However, the decrease in oxygen therapy resulted in an increase in neonatal deaths, due to respiratory compromise[8]. Increased survival rates of extremely premature (gestational age < 29 weeks) and very low birth weight infants (750-999g) gave rise to the second epidemic of ROP in the late 1970s and 1980s[9-11]. Data from the developing countries is very limited. Gilbert et al, speculate that infant mortality rates (IMR) may negatively correlate with the risk of ROP related blindness. With improvement in neonatal care, more preterm infants are surviving worldwide; in high income countries, with IMR of < 9 per 1000 live births, the risk of ROP related blindness is low, due to good screening and treatment facilities. In countries with high IMR (>60 per 1000 live births) not many preterm babies survive, due to lack of basic health care facilities and proper neonatal intensive care, so ROP is not a significant problem. However, middle income countries in Latin America, Eastern Europe, India, China and other countries in Asia, with IMR of 9 – 60 per 1000 live births, represent the population at the highest risk of ROP blindness since 1990s. This has been described as the third epidemic of ROP; although neonatal care has improved, good screening and treatment facilities are inadequate in these regions[1,2]. Babies are being exposed to risk factors which, to a large extent, have been addressed in high income countries e.g., oxygen exposure.

Screening for the disease is a key component of the treatment of ROP. Specific 'standard' criteria, based on gestational age of less than 32 weeks and birth weight of less than 1500 gms, is being used in the United States. Results show, that 66% of infants < 1,250g and 82% of infants < 1,000g developed ROP, while 9% became eligible for treatment[1-12]. However, these screening criteria may not be applicable to middle and low income countries, where more mature and heavier babies have been shown to develop ROP[13-20]. Gilbert et al highlighted (Table 1) that 13% of infants would have been missed if the 'standard' screening criteria had been applied in such countries[2].

Table 1:

	Developed N = 262	Poor / Mod Developed N = 1091
Ave GA	< 26 weeks	26.3 - 33.5
GA > 32 wk / BW > 1501 g	0.4% (1)	13% (142)
GA > 37 wk	0	0.5% (5)
GA > 34 wk / BW > 1751 g	0	3.6% (39)

Multiple trials involving infants with ROP have highlighted the importance of timely treatment to reduce the risk of blindness[21-22]. The latest trial ETROP (Early Treatment for ROP) has shown that laser retinopexy within 48 hours for type 1 ROP (definition) was associated with a decrease (19.8% to 14.3%) in unfavorable visual outcomes[23]. Therefore screening protocols are being followed in NICUs to identify infants needing treatment. Oxygen regulation trials, such as STOP – ROP, SUPPORT and BOOST – II, have been conducted to observe ophthalmic outcomes with

supplemental oxygen[13-15] and the results reveal that ROP is best controlled by avoidance of fluctuations and by strict maintenance of SpO_2 between 85% - 92% in theses babies[24,25].

ROP IN PAKISTAN

Neonatal care services have expanded and more premature babies are now surviving. Infant mortality rate (IMR) in Pakistan dropped to 61.3 per 1000 live births in 2012 from 82.5 per live births in 2000, thus Pakistan is now at the threshold for an epidemic of blindness due to ROP[26].

There are only 2 published studies on ROP, both from Aga Khan University Hospital, with a very well equipped tertiary care NICU. In 2008, a retrospective analysis of 68 premature infants with birth weight < 1500 gm and gestational age < 32 weeks, had reported an incidence of 32.4% of any stage of ROP, with 20.6% with severe ROP[27]. A later studied conducted prospectively at the same institute with a broader screening criterion i.e., birth weight ≤ 2000g and gestational age ≤ 35 weeks – any stage of ROP, showed that no ROP was seen in the 66/301 infants who weighed > 1500g at birth and/or were born at > 32 weeks of gestation. Using the standard screening criteria, there was an improvement with only 11.5% developing ROP, while stage 3 ROP requiring treatment were 8.1% of the cases as compared 20.6%, in the earlier study[28]. These levels are now comparable to ROP outcomes in high income countries.

There is still a severe lack of awareness of the disease, appropriate screening criteria, consequences of delayed or no treatment as well as a lack of expertise for the management of such babies[29]. In 2010 a descriptive study conducted at 10 centers with highest delivery rates in Karachi showed that only 2 centers had a screening protocol for ROP in place, but which was not being followed. Only 2 out of the 15 pediatricians who were interviewed were aware that ROP can cause blindness[30].

FUTURE RECOMMENDATIONS

There is an urgent need for creation of appropriate screening and oxygen protocols, training of ophthalmologist to screen the infants, creation of close liaison between the NICU, ophthalmologist and parents, education for all care givers on the importance of ROP, to protect premature infants in Pakistan from permanent blindness.

We propose the creation of a Pakistan Retinopathy of Prematurity Educational and Research Alliance (PROPERA). Initially, a few hospitals in 2 to 3 major cities should be involved. An ROP coordinator and an ophthalmologist for screening should be designated. An initial screening criteria and an Oxygen protocol should be followed at these sites. Data should be collected and transmitted to a central collection center weekly. Subsequently, the network should be expanded, by adding other centers, and additional cities. An annual ROP conference should be organized to include all health care individuals involved with management of infants at risk of ROP. Collected ROP data should be presented, deficiencies identified, creation of appropriate screening guidelines and formulation of a plan for the next year agreed upon.

Individuals with experience and interest in ROP will be vital for the success of this endeavor to save the sight of our next generation.

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