



Obstetric strategies to reduce blindness from retinopathy of prematurity in infants born preterm

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TITLE PAGE

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Obstetric strategies to reduce blindness from retinopathy of prematurity in infants born preterm

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Running title: Preventing blindness from retinopathy of prematurity

Disclosure Interests

None of the authors has any relevant financial disclosures

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Retinopathy of prematurity

Retinopathy of prematurity (ROP) is a potentially blinding condition of preterm infants who have received neonatal care.¹ The blindness is usually bilateral and irreversible. The first epidemic of blindness from ROP (then called retrolental fibroplasia) occurred in the USA and Western Europe in the 1940s/1950s as neonatal intensive care became established. The epidemic came to an end after it was realized that 100% supplemental oxygen is highly toxic to immature retinal blood vessels. Blindness from ROP is now largely controlled in highly resourced countries where neonatal care is generally of high quality, and preterm infants are screened for ROP and treated if necessary. However, a further epidemic of ROP blindness is now occurring in middle income countries and in urban settings of low income countries as services for preterm infants expand, but where neonatal care is suboptimal and coverage of ROP screening and treatment is low.² A recent meta-analysis estimated that 32,300 preterm infants become blind or visually impaired from ROP every year, with the highest incidence in South East Asia.³

In ROP the developing retinal blood vessels initially stop growing and then proliferate abnormally. There is an international classification for ROP, the natural history is well described and the pathogenesis has been elucidated.¹ The initial stages (Stages 1 and 2) often regress spontaneously, but if more advanced disease develops (Stage 3), particularly if there are signs of active proliferation (plus disease), there is a high risk of progression to blinding retinal detachment (Stage 5). The purpose of screening, which should start within a few weeks of life, is to identify and treat vision-threatening ROP (VT-ROP). The gold standard treatment is laser photocoagulation of the peripheral, avascular retina, which must be delivered within 48-72 hours. Intraocular injection of anti-vascular endothelial growth factors holds promise, but the short and long-term ocular and systemic safety of these agents is not known.

The risk of VT-ROP is inversely related to the degree of prematurity and smaller size at each gestation, and can affect $\geq 10\%$ of infants with birthweights $< 1500\text{g}$ in resource poor settings⁴ Although a direct link between chorioamnionitis and ROP has not been proven, there is good evidence that perinatal inflammation, associated with factors such as severe pre-eclampsia and chorioamnionitis, play a role.¹ Other risk factors during the first few weeks of life include hyperoxia or fluctuating hypo-hyperoxia as a result of exposure to poorly regulated supplemental oxygen, sepsis, red blood cell transfusion and poor weight gain.

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5 can play a critical role. Although there are currently no obstetric interventions which directly
6 reduce ROP, there are aspects of care likely to have an impact. These include strategies to
7 reduce the risk of preterm birth (PTB), appropriate management in pregnancy, and when
8 mothers present with threatened or established preterm labour, during labour of mothers
9 threatening preterm delivery, and the care of preterm babies at birth.

15 **Prevention of preterm birth**

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18 Despite global efforts to reduce PTB, rates are increasing in most countries where data are
19 available, with 1 in 10 babies born prematurely in 2010.⁵ Increasing rates of multiple pregnancies
20 and medically-indicated PTBs are the main reasons for the increase.⁶ Babies born extremely
21 preterm and at very low birthweight have the highest risk of lifelong disability, including ROP.⁵

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26 The causes of PTB are varied and multi-factorial. Risk factors include multiple pregnancy,
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35 birth spacing can reduce the risk of PTB and improve perinatal outcomes.⁵ Thus provision of
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31 **Summary**

32 Preventing preterm birth and its complications, including blindness from ROP, requires a multi-
33 disciplinary approach before and during pregnancy and immediately after PTB. Meticulous care,
34 team work and the engagement of mothers are required, underpinned by policies, regulatory
35 frameworks and protocols. Obstetricians, gynecologists and midwives can play an very-important
36 role in reducing blindness from ROP which can lead to developmental delay and promoting
37 child development and preventing the emotional, economic and social costs to affected children
38 and their families.¹⁵
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