Retinopathy of prematurity - an update on screening and management

Retinopatia de prematuritate - actualizare de screening și management

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Abstract

Retinopathy of prematurity is a proliferative disorder of the developing retinal blood vessels in premature infants. It is the most common complication of prematurity, especially in extremely preterm infants. The neonatologist's role in preventing is important, because retinopathy of prematurity is the second leading cause of childhood blindness in the world. The strongest predictors for retinopathy of prematurity are lower gestational age and birth weight. Prolonged administration of oxygen, IUGR, and duration of assisted ventilation are also associated with retinopathy of prematurity.
Keywords: *retinopathy of prematurity, ROP screening, premature infants*

Rezumat

Retinopatia de prematuritate este o tulburare proliferativă a dezvoltării vaselor sangvine retiniene la nou-născuții prematuri. Este una din cele mai frecvente complicații ale prematurității, în special la prematurii foarte mici. Rolul neonatologului în depistarea precoce este important, deoarece retinopatia de prematuritate este a doua cauză de orbire la copii în lume. Cei mai puternici predictori ai retinopatiei de prematuritate sunt vârsta gestațională mică și greutatea mică la naștere. Administrarea îndelungată de oxigen, întârzierea în creșterea intrauterină, durata ventilației asistate sunt de asemenea asociate cu retinopatia de prematuritate.
Cuvinte-cheie: *retinopatie de prematuritate, screening retinopatie de prematuritate, nou-născuți prematuri*

Introduction

Retinopaty of prematurity (ROP) is an eye disease that affects the blood vessels and neurons of the incompletely developed retina in infants born preterm. Abnormal vascular shunting and neurovascularization may occur as the retina reacts to subsecquent hipoxia. Infants born prematurely have incompletely vascularized retinas.

Premature baby with ROP are known to develop early and late visual sequelae. The incidence of ROP is increasing in India, between 38% and 51.9%, in low birth weight infants[7]; in USA also, it affects each year 14.000 to 16.000 preterm infants[9].

Pathophysiology

In the normally developing retina, there are no retinal vessels until about 16 weeks of gestation.

Retinal vascularization begins at the optic nerve at 16 weeks of gestational age (GA) and is completed by 40 weeks GA.

Preterm infants have incompletely vascularized retinas. ROP is a biphasic disease consisting of an initial phase of vessel growth cessation and loss followed by a second phase of vessel proliferation.

■ **Phase 1** appears from birth to aproximately 30-32 weeks of postmenstrual age (PMA); concentrations of insulin, like growth factor (IGF 1), are low and suppresses vascular endothelial growth factor (VEGF).

■ **Phase 2** starts at 32-34 weeks PMA. Insult and high oxygen exposure released by the hypoxic retina, VEGH are increase and appears retinal neovascularization.

Risk factors

The most significant risk factor of ROP is extreme prematurity. Birth characteristics and postnatal risk factors may also lead to the development of ROP. Younger GA and low birth weight, white race, and multiple birth increase the risk of severe ROP.

Postnatal risk factors include excessive or fluctuating oxygen levels (oxygen monitoring is an important part of the care of preterm infants), respiratory distress, hypercapnia and hypocapnia, exchange transfusion and anemia, sepsis and intrauterine infections, hyperglicemia, prolonged parenteral nutrition, lactic acidosis, low IGF 1 levels, low omega-3 fatty acids, and low energy delivery.

For every 10 kcal/kg/day increase in energy intake, there was an associated 24% decrease in severe ROP[12]. Total energy was indirectly associated with the risk of ROP.

The effect of this nutritional parameters was evident in the first four postnatal weeks[1].

Classification of ROP

ROP stages - there are 5 stages:

- **Stage 1:** flat demarcation line.
- **Stage 2:** ridge (demarcation line with height and width).
- **Stage 3:** ridge with extraretinal neurovascularization that extends into the vitreous.
- **Stage 4:**
  substage 4A - extrafoveal retinal detachment.
  substage 4B - fovea involving retinal detachment.
- **Stage 5:** complete retinal detachement.

Diagnosis

ROP screening

The time of the first examination should be based on menstrual age rather than postnatal age.

1. neonate born at 26 weeks of gestation;
2. neonate born at 29 weeks of gestation with a birth weight of 1000 g;
3. neonate born at 36 weeks of gestation with a birth weight of 1499 g.
4. neonate born with a birth weight <1500 g or GA<30 weeks.

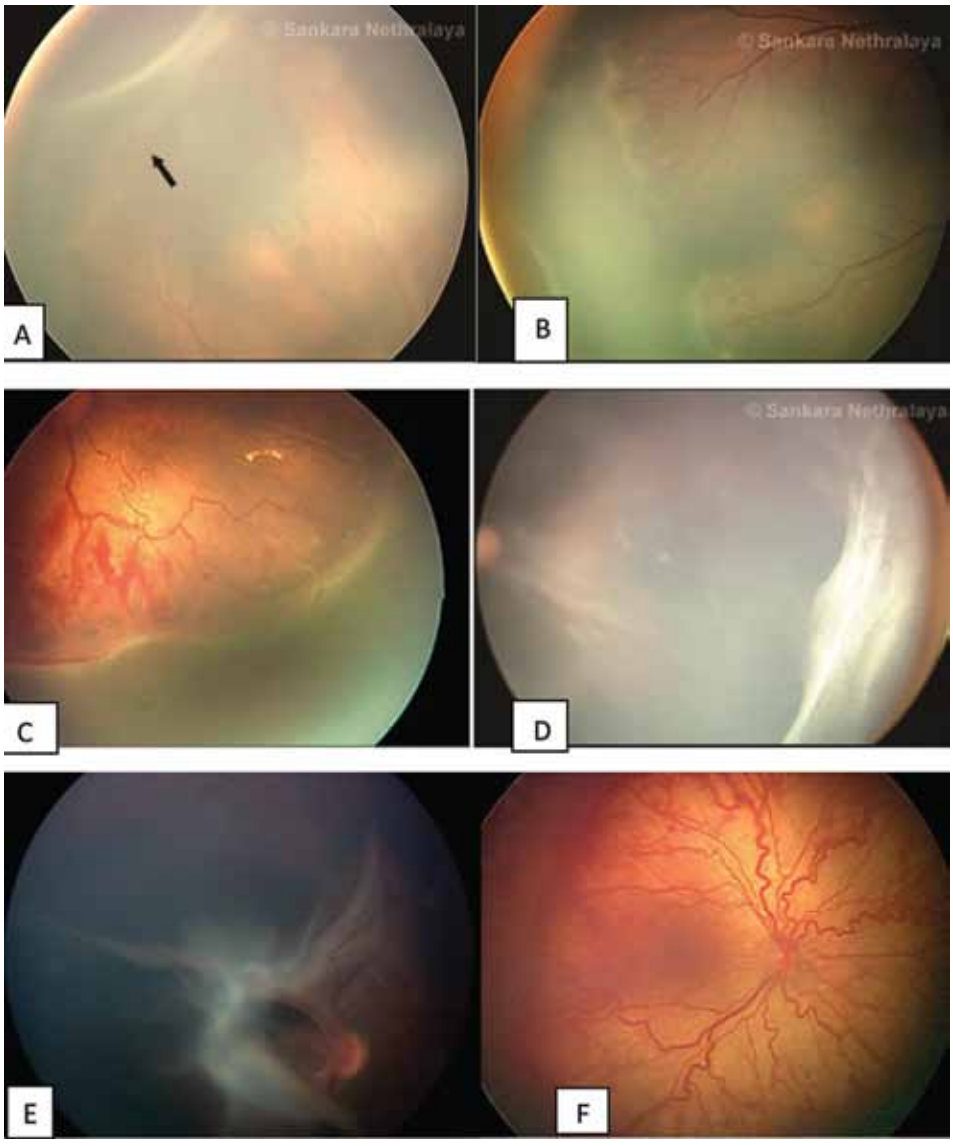

Figure 1. (A) Stage 1: Demarcation line. (B) Stage 2: Ridge. (C) Stage 3: Ridge with extraretinal fibrovascular proliferation. (D) Stage 4A: extrafoveal retinal detachment. (E) Stage 4B: fovea involving retinal detachment. (F) Plus disease with dilated and tortuous retinal vessels. Reproduced with permission from Committee for the Classification of Retinopathy of Prematurity. An international classification of retinopaty of prematurity[2]

5. neonate born with birth weight between 1500 g and 2000 g or GA>30 weeks who had an unstable clinical course and are belived to be at risk for severe ROP[3,10].

Screening guidelines - Indian scenario[4]

- birth weight <1700 g;
- gestational age at birth <34-35 weeks;
- exposed to oxygen >30 days;
- infants born at <28 weeks and weighting <1200 g are particulary at high risk of developing severe form of ROP;
- other factors: respiratory distress syndrome, sepsis, multiple blood transfusions, multiple births (twins/triplets), intraventricular hemorrhage. In these cases, screening should be considered even for babies >37 weeks of gestation or >1700 g birth weight[9].

The moment for the initial ophtalmologic examination to screen for ROP is based on postmenstrual age for preterm infants of lower gestational age, taking a longer time to develop significant ROP (Table 1).

Guidelines on timing for ROP screening

In infants with specific retinal findings, with significant disease, after this initial screening examinations, it is required a careful follow-up[3].

ROP follow-up

ROP follow-up examinations:

1 week or less follow-up for:

- Zone I or border of zones I and II, immature vascularization.
- Zone I, stage 1 or 2 ROP.
- Zone II, stage 3 ROP.
- Presence or suspected presence of aggressive posterior ROP.

1 to 2 weeks follow-up for:

- Posterior zone II, immature vascularization.
- Zone I, regressing ROP.
- Zone 2, stage 2 ROP.

2 weeks follow-up for:

- Zone II, immature vascularization.
- Zone II, regressing ROP.
- Zone II, stage 1 ROP.

2 to 3 weeks follow-up for:

- Zone III, stage 1 or 2 ROP.
- Zone III, regressing ROP.

ROP screening continues until:

- Full retinal vascularization.
- Zone III retinal vascularization without previous zone I or II ROP.
- Regression of ROP.
- 50 weeks postmenstrual age with no prethreshold or worse ROP present.

The treatment of ROP

Retinal ablation is the standard treatment of ROP. The laser photo coagulation effectiveness is well established[6]. The least severe ROP for which intervention should be considered is type 1 ROP. Ideally, therapy should be performed within 72 hours after the diagnosis of treatable disease based on ophtalmologist recommendation[8]. The structural and functional benefits of treatment have been maintained through the 15-year follow-up report. Because no preventive medical treatment has been confirmed for ROP yet, only interventions made during phase 1 of ROP may lessen the disease[11].

Table 1 American Academy of Pediatrics Section on Ophtalmology, American Academy of Ophtalmology, American Association for Pediatric Ophtalmology and Strabismus. Screening examination of premature infants for ROP. Pediatrics 2013;131: 191[5]

Gestational age at birth (weeks)	Chronologic age at first examination (weeks)
23	8
24	7
25	6
26	5
27-30	4
30 with birth weight <1500 g or risk factors	4
31	4
32	4

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1. Teh AL et al. Genome Res 2014;24(7):1064–1074. **2.** Aproximativ 25% din sănătatea copilului pe parcursul vieții este determinate exclusiv de genetica si pana la 75% poate fi influentata de interactiunea stilului de viata matern cu genele fatului. Stilul de viata include: nutriția, greutatea normală a mamei și copilului, evitarea stresului și fumatului. **3.** Ca supliment la o alimentație echilibrată și un stil de viață sănătos. **4.** Aportul suplimentar de acid folic crește rezervele materne de folați. Un nivel scăzut al folaților materni reprezintă un factor de risc important pentru apariția defectelor de tub neural (DTN). De aceea se recomanda un aport suplimentar zilnic de 400 µg cu 1-3 luni înainte de concepție. În afara de nivelul de folați materni, există și factori ereditari care determină creșterea riscului de apariție a DTN. **5.** Aportul matern suplimentar de DHA contribuie la dezvoltarea normal a creierului și ochilor fatului și copilului alimentat la sân. Efectul benefic este obținut cu un aport zilnic de 200 mg DHA, suplimentar față de doza zilnică recomandată pentru adulți de 250 mg acizi grași omega – 3 (DHA și EPA). **6.** IMS Data, MAT 12/2014, Europa.

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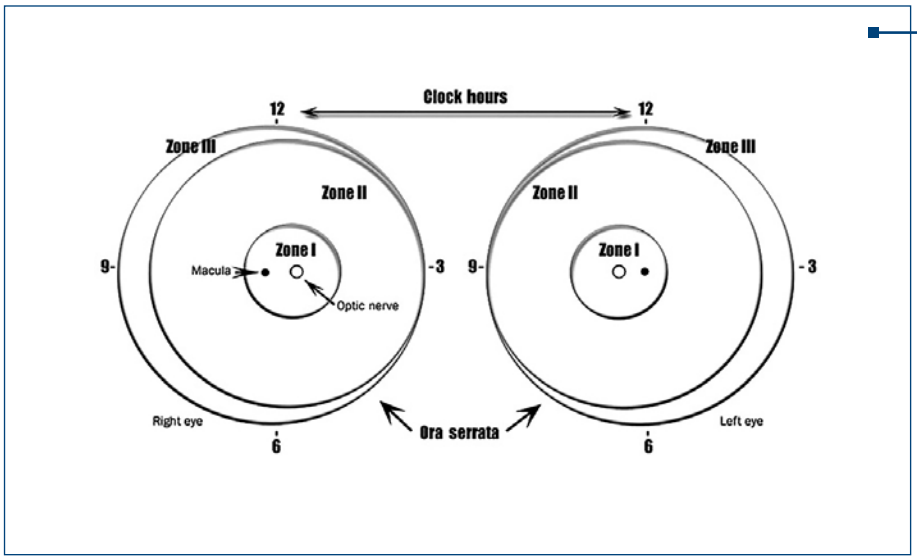

Figure 2. American Academy of Pediatrics, Section of Ophthalmology, and American Academy of Ophthalmology, American Association for Pediatric Ophthalmology and Strabismus. Screening examination of premature infants for ROP. Pediatrics. 2013; 131:191[5]

Conclusions

The neonatologist must know the groups of infants who should be screened for ROP. The risk of severe ROP was highest in newborns <28 weeks GA or birth weight <1000 g at birth. The neonatologist must recognize those preterm infants who have been treated with oxygen, because they require a first retinal examination at 4-6 weeks of age, in order to identify those who develop ROP[1].

For the prevention of ROP, it is important to know the causes, to use the oxygen terapy cautiously and to make an early diagnosis of ROP. ■

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