PREVENTION OF RETINOPATHY OF PREMATURITY

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OXYGEN-THERAPY IS ASSOCIATED WITH ROP

1951 - Campbell (Australia)

1952 - Crosse & Evans (England)

+ than 20 years

1975 / 1985
Arnall Patz and cols. (USA) demonstrated in prospective and controlled clinical trials the direct relationship between oxygen-therapy and ROP.

OXYGEN-THERAPY IS ASSOCIATED WITH ROP

2012 - It is unclear what range of oxygen saturation is appropriate to minimize ROP without increasing adverse outcomes.

A lower target oxygenation (85 to 89%), as compared with a higher range (91 to 95%) did not decrease the occurrence of severe ROP but resulted in an increase in mortality.


NEOPROM - Australia and New Zealand - BMC Pediatrics 2011

ELGAN Study - USA and Germany - Neonatology 2011

PROP-ROP Canada Protocol - 2011 (SaO2 83 to 89%)
OXYGEN-THERAPY IS ASSOCIATED WITH ROP

American Academy of Pediatrics -
PaO2 from 45 to 80 mmHg (Sola 2005)
GA > 32 weeks SaO2 from 85 to 95%
GA ≤ 32 weeks SaO2 from 85 to 93% (Chow 2003, McGregor 2002, Sola 2005)

At HCPA, to accomplish tighter control of oxygen therapy, strict guidelines are applied. All neonate in critical condition is permanently controlled in his clinical aspects and by the use of pulse oximetry with a recommended saturation pressure between 88 and 94%. All NICU staff is regularly trained on the relationship between hyperoxemia and ROP. This training is helpful because it is possible to control and prevent the occurrence of severe ROP in most cases only by carefully monitoring hyperoxia and avoiding fluctuations.32,33

Fortes Filho et cols. Eye 2009

HCPA 2012 - SaO2 from 88 to 92%; PaO2 from 50 to 70 mmHg
OXYGEN-THERAPY IS ASSOCIATED WITH ROP

INSTRUCTIVE CASE

AP-ROP in an infant with minimal oxygen exposure
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Abstract Retinopathy of prematurity (ROP) is a multifactorial disease affecting the developing retinal vasculature and remains an important cause of blindness in very preterm infants. Rush disease, or aggressive posterior ROP (AP-ROP), progresses rapidly to stage 5 disease without exhibiting the classical course that includes stages 1–3. We describe an infant with minimal exposure to oxygen who developed AP-ROP that led to bilateral retinal detachments and a poor visual outcome, despite following current recommended screening guidelines.

Key words: AP-ROP; retinopathy of prematurity.

• ALTERNATE CYCLES OF HYPEROXIA-HYPOXIA FAVOR ROP PROGRESS
• MAINTAIN STABILITY FROM BIRTH IS THE BEST PRACTICE
• USE OF PULSE OXIMETERS IS THE BEST PRACTICE
• PERIODICAL EDUCACIONAL PROGRAMS WITH NICU’S STAFF
**PATHOGENESIS OF ROP**

**ROP IS A TWO-PHASE DISEASE**

**PHASE 1 OF ROP**
develops from birth to the 30 / 32 weeks PCA

Interruption of the natural vascular growth after premature birth

→ Hypoxic peripheral retina releases VEGF

**PHASE 2 OF ROP**
develops between 32 / 34 weeks PCA

Hypoxia-induced retinopathy

→ Retinal neovascularization and severe retinopathy

PATHOGENESIS OF ROP

PHASE 2 OF ROP IS RELATED TO

1º - VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)
ANGIOGENIC FACTOR REGULATED BY OXYGEN

2º - INSULIN-LIKE GROWTH FACTOR - I (IGF - I)
ANGIOGENIC FACTOR NON-REGULATED BY OXYGEN

Low IGF-I suppresses VEGF-survival: direct correlation with clinical retinopathy of prematurity.
PREVENTION OF ROP

PHASE 1 OF ROP
Prevention by optimizing oxygen-therapy since birth, and strict control over the risk factors

PHASE 2 OF ROP
Prevention by screening and treatment
MAIN RISK FACTORS FOR ROP

- GA
- BW
- USE OF OXYGEN IN MECHANICAL VENTILATION
- POSTNATAL LOW WEIGHT GAIN

GEMELARITY
SGA (<10 percentil)

INTRAVENTRICULAR HEMORRHAGE
SEPSIS •
MENINGITIS
PERSISTENT DUCTUS-ARTERIOSUS

BLOOD TRANSFUSIONS •
SURFACTANT
INDOMETHACIN
ERYTHROPOIETIN •
DOPAMINE
CORTICOSTEROIDS

GENETICS
MATERNAL FACTORS
ANGIOGENIC FACTORS

- Acidic fibroblast growth factor (aFGF)
- Angiogenin
- Angiopoietins
- Basic fibroblast growth factor (bFGF)
- Endothelin
- Erythropoietin
- Fibroblast growth factor-5 (FGF-5)
- Granulocyte-colony stimulating factor (G-CSF)
- Granulocyte-monocyte colony stimulating factor (GM-CSF)
- Growth hormone (GH)
- Hepatocyte growth factor (HGF)
- Insulin
- Insulin-like growth factor-1 (IGF-I)
- Insulin-like growth factor-2 (IGF-2)
- Interleukin-2 (IL-2)
- Interleukin-4 (IL-4)
- Interleukin-6 (IL-6)
- Interleukin-8 (IL-8)
- Kaposi’s fibroblast growth factor (K-FGF)
- Placental growth factor (PlGF)
- Platelet-derived growth factor-B (PDGF-B)
- Pleiotropin
- Substance P
- Transforming growth factor-alpha (TGF-α)
- Transforming growth factor-beta (TGF-β)
- Tumor necrosis factor-alpha (TNF-α)
- Vascular endothelial growth factors (VEGF)

- Factors are necessary to normal retinal development
- Natural angiogenesis stimulators in the whole body
- Factors have neuroprotective effects
GEMELARITY AS A RISK FACTOR

Multiple pregnancies and its relationship with the development of retinopathy of prematurity (ROP)

Background: The influence of multiple gestation on the occurrence of retinopathy of prematurity (ROP) is still not completely understood.

Objectives: To verify the incidence of any stage of ROP and threshold ROP in singletons and in multiple gestation among preterm infants.

Methods: This was an institutional, prospective, and descriptive cohort study, which included preterm newborns with birth weight (BWT) of 1500 g or less and/or gestational age (GA) of

OCURRENCE OF ROP WAS GREATER AMONG TWINS

SGA was not a significant risk factor for ROP

INCIDENCE OF ROP WAS SIMILAR AMONG AGA AND SGA

MATERNAL RISK FACTORS

Maternal Preeclampsia Protects Preterm Infants against Severe Retinopathy of Prematurity

João Borges Fortes Filho, MD, PhD, Marlene C. Costa, RN, Gabriela U. Eckert, MD, Paula G. B. Santos, MD, Rita C. Silveira, MD, PhD, and Renato S. Procianoy, MD, PhD

Objective To study the influence of maternal preeclampsia on the occurrence of retinopathy of prematurity.

Study design A prospective cohort study of 324 preterm neonates with birth weight ≤1500 g and gestational age ≤32 weeks. Multiple maternal and perinatal factors were analyzed for association and confounding by multiple logistic regression analysis.

Results Mean birth weight was 1128 ± 240 g, and mean gestational age 29.7 ± 1.9 weeks. Twenty-four newborns (7.4%) had severe retinopathy of prematurity; 97 had any stage of retinopathy, and 227 had no retinopathy of prematurity. Preeclampsia and complete antenatal steroid treatment course reduced the risk for any stage of retinopathy of prematurity by 60% and 54%, respectively. Preeclampsia reduced the risk for severe retinopathy of prematurity by 80%.

Conclusions Preeclampsia lowered the risk for occurrence of any stage and severe retinopathy of prematurity in very low birth weight infants. (J Pediatr 2011;158:372-6).
RISK FACTORS HAVE A DYNAMIC BEHAVIOR INFLUENCED BY GA MORE THAN BW

VERY IMMATURE BABIES (<28 weeks GA) WILL DEVELOP ROP PER SE

BIGGER BABIES (>32 weeks GA) WILL DEVELOP ROP IF THEY WERE SICK BABIES OR IF THE HAD INADEQUATE NEONATAL INTENSIVE CARE

PEDIATRICS

The influence of gestational age on the dynamic behavior of other risk factors associated with retinopathy of prematurity (ROP)

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Interaction between immaturity, sepsis and oxygen-therapy

ROP
Prevalence of retinopathy of prematurity in Latin America

1.2% - 23.8% Severe ROP

- Lack of quality on perinatal care
- Lack of care with oxygen-therapy
- Lack of ophthalmologic screening and treatment

Abstract: The purpose of this work was to review the studies published over the last 10 years concerning the prevalence of retinopathy of prematurity (ROP) in Latin American countries, to determine if there was an improvement in ROP prevalence rates in that period, and to identify the inclusion criteria for patients at risk of developing ROP in the screening programs. A total of 33 studies from ten countries published between 2000 and 2010 were reviewed. Prevalence of any ROP stage in the regions considered ranged from 6.6% to 82%; ROP severe enough to require treatment ranged from 1.2% to 23.8%. There was no routine screening for ROP, and there was a lack of services for treatment of the disease in many countries. Inclusion criteria for patients in the studies ranged between birth weight \( \leq 1500 \) g and \( \leq 2000 \) g and gestational age \( \leq 32 \) and \( < 37 \) weeks. Use of different inclusion criteria regarding birth weight and gestational age in several Latin American studies hindered comparative analysis of the published data. Highly restrictive selection criteria for ROP screening in relation to birth weight and gestational age should not be used throughout most Latin American countries because of their different social characteristics and variable neonatal care procedures. The studies included in this review failed to provide adequate information to determine if the prevalence of ROP has decreased in Latin America.

Keywords: retinopathy of prematurity, prevalence, incidence, Latin America
PREVALENCE OF ROP AT HCPA 2002/2009

BW $\leq$ 1,500 g and/or GA $\leq$ 32 weeks = 22% ROP / 7% Severe ROP
BW < 1,000 g and/or GA < 28 weeks = 49% ROP / 17% Severe ROP
BW > 1,000 g and < 1,500 g = 18% ROP / 2.3% Severe ROP

Incidence and risk factors for retinopathy of prematurity in very low and in extremely low birth weight infants in a unit-based approach in southern Brazil

Fortes Filho JB, Eckert GU, Procianoy L, Procianoy RS.
SEVERE ROP CAN BE CONTROLLED

- OPTIMIZING OXYGEN-THERAPY ADMINISTRATION SINCE BIRTH
- STRICT MONITORING OXYGEN-THERAPY BY PULSE OXIMETRY
- STRICT CONTROL OVER THE RISK FACTORS
- OPTIMIZING TOTAL PARENTERAL NUTRITION BW < 1,250 g
- OPHTHAMOLOGICAL SCREENING SESSIONS TO DETECT ROP
Severe ROP
BW > 1,500 g or GA > 32 weeks
USA / Europe 1970
HCPA/BRAZIL 2000
Latin-Amercia 2012

Severe ROP
BW < 1,500 g or GA < 32 weeks
USA / Europe 2000
HCPA 2006 and Latin America/Brazil 2012

Severe ROP
BW < 1,000 g or GA < 28 weeks
USA 1990 / 2000
Latin America/Brazil 2010

Severe ROP (Zone I)
BW < 700 g or GA < 26 weeks
USA / Europe 2010
HCPA 2010 - 2020
PREVENTION OF ROP

NEONATOLOGISTS

• Optimizing oxygen-therapy in the NICU
• Control on the risk factors for ROP

NURSING STAFF

• Control the screening program in the NICU
• Direct control on the oxygen-therapy

OPHTHALMOLOGISTS

• Perform the screening to detect and treat ROP
• Periodical educational and motivational programs with NICU’s staff

NATIONAL OR INSTITUTIONAL SUPPORT

• Prevention of ROP must be a bigger project: National or Institutional
• Avoiding preventable blindness or legal demands must be a priority
• It is necessary to provide equipment and conditions in order to prevent blindness for ROP
Muchas gracias!  
Thank you!  
Muito obrigado!