Risk Factors and Postnatal Low Weight Gain as predictors for Retinopathy of Prematurity

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PROROP: PREVENTION OF ROP RESEARCH GROUP
ROP IS RELATED TO OXYGEN-THERAPY

1951 - Campbell (Australia)

1952 - Crosse and Evans (England)

1975 / 1985
Arnall Patz et al. (USA) clearly showed the direct relationship between use of oxygen and the onset of ROP in controlled studies.

+ 20 years
MAIN RISK FACTORS FOR ROP

- BW
- GA
- USE OF OXYGEN-THERAPY IN MECHANICAL VENTILATION

MULTIPLE GESTATION
SGA (<10 PERCENTILE)
LIGHT IN THE NICUs

SEPSIS
INTRAVENTRICULAR HEMORRHAGE
MENINGITIS
PERSISTENT DUCTUS-ARTERIOSUS

BLOOD TRANSFUSIONS
USE OF SURFACTANT
USE OF INDOMETHACIN
USE OF ERYTHROPOIETIN
USE OF DOPAMINE
USE OF STEROIDS

GENETICS

MATERNAL RISK FACTORS
RISK FACTORS HAVE A DYNAMIC BEHAVIOR INFLUENCED BY GA MORE THAN BW

MORE IMMATURE BABIES < 28 WEEKS DEVELOP ROP BY IMMATURITY PER SE
BIGGER BABIES > 1,500 g DEVELOP ROP IF SYSTEMIC ILLNESS OCCURS OR LOW QUALITY IN NEONATAL CARE

Graefes’s Arch Clin Exp Ophthalmol 2010

Interaction between immaturity, sepsis and oxygen-therapy → ROP
HOW TO IDENTIFY THE BABIES IN RISK TO SEVERE ROP?

• SCREENING TO DETECT ROP
• RISK FACTORS FOR ROP
SCREENING TO DETECT ROP

INCLUSION CRITERIA: BW / GA

• Repeated ophthalmological examinations during several weeks until 42\textsuperscript{nd} PCA

↑ INCREASING WORKLOAD

↑ STRESS AND PHYSICAL DEBILITATION

Zin A, Moreira ME, Bunce C, Darlow BA, Gilbert CE. Retinopathy of prematurity in 7 neonatal units in Rio de Janeiro: screening criteria and workload implications.

ROP OCCURS SOME WEEKS AFTER BIRTH

PREDICTION OF SEVERE ROP ➔ VERY IMPORTANT

BW
GA

SERUM LEVELS OF IGF – I
SCORES OF ILLNESS SEVERITY: CRIB, SNAP, SNAPPE II
POSTNATAL LOW WEIGHT GAIN
BIOLOGICAL MARKERS

PCA 30 | PCA 32 | PCA 34 | PCA 38 | Risk for Threshold ROP

Phase 1 | Phase 2 | 4 weeks | 6 weeks | PCA for laser treatment ➔ 38 weeks

Peripheral retinal vascularization completed by PCA 42nd

GA 28
SCORES OF ILLNESS SEVERITY WERE NOT GOOD PREDICTORS FOR ROP

SNAPPE-II values at admission were significantly higher among ROP patients, but after adjustments by logistic regression and ROC curve, this score did not enhance the assessment of risk for ROP.
POSTNATAL LOW WEIGHT GAIN

2000 - Wallace, 111 patients → ROP if < 50% BW by the 6th week of life

2003 - Allegaert, 31 pacientes → ROP in IUGR (< 25% percentile)

2006 - Hellström et al. developed the algorithm WINROP based in 79 patients  GA < 32

IGF - I serum levels
Longitudinal weight gain measurements

Longitudinal Postnatal Weight and Insulin-like Growth Factor I Measurements in the Prediction of Retinopathy of Prematurity

Chatarina Löfqvist, PhD; Eva Andersson, PhD; Jon Sigurdsson, MD; Eva Engström, MD, PhD; Anna-Lena Härd, MD, PhD; Aimon Niklasson, MD, PhD; Lois E. H. Smith, MD, PhD; Ann Hellström, MD, PhD

Archives Ophthalmol 2006
POSTNATAL LOW WEIGHT GAIN IS A BETTER PREDICTOR FOR SEVERE ROP THAN BW OR GA

Graefes Arch Clin Exp Ophthalmol
DOI 10.1007/s00417-008-1012-3

PEDIATRICS

Weight gain measured at 6 weeks after birth as a predictor for severe retinopathy of prematurity: study with 317 very low birth weight preterm babies

Joao Borges Fortes Filho · Pedro P. Bonomo · Mauricio Maia · Renato S. Procianoy

Graefes’s Arch Clin Exp Ophthalmol 2009

Low weight gain by 6th week of life in an important and independent risk factor for severe ROP and is capable to predict the development of severe ROP in most patients needing treatment.

| PN ≤ 1.000 g | OR 4,708 | IC: 1,890 - 11,726 | P < 0,001 |
| PN > 1.000 g | OR 3,102 | IC: 1,556 - 6,184 | P < 0,001 |
POSTNATAL LOW WEIGHT GAIN

2009 - Hellström et al. presented the WINROP without use of IGF-I

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2010 - Hellström, Fortes Filho et al. Validated WINROP using only weekly measurements of weight gain
ROPScore  IN ORDER TO PREDICT SEVERE ROP

Prospective study including 417 VLBW

| BW (birth weight) in grams | 1000 | Use the birth weight in grams |
| GA (gestational age) in weeks | 28 | Use the gestational age in weeks |
| BLOOD TRANSFUSION (up to 6th week of life) | 1 | Use 0 for none or 1 for yes if the baby underwent any blood transfusion |
| OXYGEN IN MECHANICAL VENTILATION (up to 6th week of life) | 1 | Use 0 for none or 1 for yes if the baby underwent oxygen-therapy |
| WEIGHT AT COMPLETED 6 WEEKS OF LIFE | 1400 | Use the weight in grams measured at completed the 6th week of life |
| PROPORTIONAL WEIGHT GAIN | 0.40 | Automatic Calculation / Do not fill in |
| ROPScore | 16.9 | Automatic Calculation / Do not fill in |

Higher the ROPScore = Higher the risk for developing ROP

Cuttoff point for any stage ROP = 11 and for severe ROP = 14.5

NPV (Negative predictive values) = 93% of not developing any stage of ROP and 99% of not developing severe ROP

NPV = probability of a patient with ROPScore below 11 of not developing any stage ROP
NPV = probability of a patient with ROPScore below 14.5 of not developing severe ROP

ROPScore = 24.985-0.004*C2-0.264*C3-1.222*C7+2.148*C4+2.248*C5
ROC Curves for ROPScore

AUC 0.77 (P<0.001; CI95%: 0.72-0.82)  AUC 0.87 (P<0.001; CI95%: 0.81-0.93)

ROPScore curves are superior to BW and GA curves alone

(study submitted to Eye)
PINT-ROP MODEL to predict severe ROP

2011 - Binenbaum G, Quinn G et al. → PINT-ROP uses BW, GA and daily weight measurements

A Clinical Prediction Model to Stratify Retinopathy of Prematurity Risk Using Postnatal Weight Gain
Gil Binenbaum, Gui-shuang Ying, Graham E. Quinn, Stephan Dreiseitl, Karen Karp, Robin S. Roberts, Haresh Kirpalani and the Premature Infants in Need of Transfusion Study Group
Pediatrics published online Feb 14, 2011;
DOI: 10.1542/peds.2010-2240

N = 367
BW < 1,000 g
Severe ROP = 67 (19%)
99% Sensibility
BIOLOGICAL MARKERS TO DETECT ROP

2009 - Vitreous cytokine levels 19 patients with ROP stage 4. VEGF has highest correlation with vascular activity in ROP eyes than all other cytokines.


2010 – Cytokine plasmatic levels remained significantly high across ROP groups, suggesting that SIRS may be involved in the pathogenesis of ROP. (SIRS = Systemic Inflammatory Response Syndrome)

CYTOKINES AND BDNF AS BIOLOGICAL MARKERS

2011 - Fortes Filho e cols. → Use of cytokines to detect ROP

Retina
Assessment of the Contribution of Cytokine Plasma Levels to Detect Retinopathy of Prematurity in Very Low Birth Weight Infants
Rita C. Silveira, João B. Fortes Filho, Renato S. Procianoy

N = 74 VLBW
IL-6 >357 pg/ml
IL-8 >216 pg/ml
TNF-α >245 pg/ml
IOVS 2011

2011 - Hellström e cols. → Use of cytokines and BDNF

Original Paper
Proliferative Retinopathy Is Associated with Impaired Increase in BDNF and RANTES Expression Levels after Preterm Birth
Gunnar Hellgren, Keirnan Willett, Eva Engstrom, Poul Thorsen, David M. Hougaard, Bo Jacobsson, Ann Hellstrom, Chatarina Lofqvist

BDNF ↓ severe ROP
N = 33 (GA 23 - 30 weeks)
Neonatology 2011
www.prorop.com
Provides plenty of information about ROP and enables exchange of scientific information

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