



Guidelines for ROP Screening and Treatment in Latin American Countries

Childhood Blindness subcommittee, LA IAPB

Sponsored by:
Christoffel Blindenmission
International Centre for Eye Health
London School Hygiene and Tropical Medicine



Guidelines for ROP screening and treatment in Latin American Countries

Specific aims of this report

- 1) background on prevalence of blindness from ROP**
- 2) screening criteria, methods, and timing**
- 3) treatment**
- 4) follow-up of premature babies**
- 5) current capacity (infrastructure, human resources, and equipment)**
- 6) current recommendations**

Background

VISION2020 is a global initiative of the International Agency for the Prevention of Blindness, whose mission is the elimination of avoidable blindness by the year 2020. This will require the co-ordinated effort of all stake holders, and ongoing commitment from Ministries of Health. The key elements of VISION2020 are a) strategies for the control of the major blinding eye diseases (cataract, trachoma, onchocerciasis, blindness in children, refractive errors, and low vision), b) infrastructure development and supplying and maintaining equipment, c) human resource development, and d) community participation. Blindness from ROP is recognised as a priority for control in Latin America, Eastern Europe, and urban areas of Asia.

Globally there are estimated to be 60,000 children who are blind from ROP – Latin America being the region with the largest number (25,000). In addition, blindness due to ROP is likely to increase in India and China (home to 1/3 of the worlds population) as their economies improve, and neonatal intensive care services expand.

Criteria for ROP screening programmes.

In industrialized countries, the population of premature babies at risk of threshold ROP has changed over time, and nowadays severe ROP almost exclusively affects extremely premature babies (i.e. those with birth weights (BW) <1,000 gms). In these countries screening is only undertaken on babies with BWs <1,500 gms, and gestational age (GA) criteria are <32, <31, or <29 weeks. More mature babies are only examined at the discretion of the neonatologist. However, data from middle and low income countries suggest that babies with “first epidemic” characteristics are also developing severe ROP. The implications of this are that larger, more mature babies need to be included in screening programmes, to ensure that no baby needing treatment is missed. Criteria adopted in Latin American countries vary (e.g. <1,900 gms in Ecuador; <2,000gms in Peru), and given the fact that GA data are often unreliable, BW criteria tend to be relied on more than GA. The important message is that screening criteria developed for use in neonatal intensive care units in the USA or Western Europe do not apply in countries where resources for support neonatal care scarce. Ideally screening criteria should be based on data obtained by careful monitoring of data from screening programmes.

Indications for treatment of sight-threatening ROP

Based on results from the cryotherapy for ROP randomized clinical trial initiated in 1986 (CRYO-ROP), ablation of the peripheral avascular retina using laser photocoagulation and/or cryotherapy when sight-threatening ROP develops was shown to decrease the incidence of blinding disease by more than 43% compared to eyes that go untreated. A recent report from this study when the children were 15 years old, showed that despite the advantage of improved retinal outcomes, almost half of the treated eyes (44%) had visual acuity of 6/60 or worse.

In late 2003, the multicentre early treatment trial (ET-ROP) conducted in the US documented that treatment at moderately severe acute phase ROP resulted in a significant benefit to eyes that were randomly allocated to early laser treatment (i.e. treatment when “high risk” prethreshold disease was present) compared to delayed treatment (i.e. treatment was only given if threshold disease developed and the eyes that regressed without treatment were simply observed). The outcomes were assessed at 9 months: i.e. visual acuity, structural findings, and complications during treatment. The findings of the trial were that babies treated earlier had better functional and structural outcomes than babies treated at threshold, but there were higher rates of ocular and systemic side effects in the group treated earlier. As a result of this trial the following are recommended:

Treatment for babies with Type 1 pre-threshold ROP:

- Zone 1, any ROP with plus disease
- Zone 1, Stage 3 ROP +/- plus
- Zone 2, Stages 2 or 3 with plus disease

Increased frequency of follow up of babies with Type 2 pre-threshold ROP:

- Zone 1, Stages 1 or 2 without plus
- Zone 2, Stage 3 without plus

The implications of this trial for ROP programs are that more babies will need to be treated; their eyes will be treated when the babies are at an earlier postmenstrual age, and systemic complications such as apnea, bradycardia and reintubation are more likely, and more frequent follow up will be required for babies with Type 2 pre-threshold ROP.

In general, ROP requiring treatment occurs around 36-38 weeks postconceptional age, a time when many of the babies are nearing discharge. It is essential to detect and treat retinopathy of this severity within two to three days or blindness may result. Thus, any screening program undertaken must detect and provide treatment for these babies in a timely manner.

Need for follow up of premature babies.

Parents need to know about the possibility of blindness from ROP and the need for follow-up, particularly once their baby has been discharged from the neonatal intensive or intermediate care unit. The baby will need to return after treatment, and long term follow up may be required to detect and manage late complications such as refractive errors, amblyopia, and strabismus. Premature babies may have visual impairment from ROP as well as from lesions of the higher visual pathways (optic nerve, visual cortex, and higher association areas).

Current capacity (infrastructure, human resources, and equipment)

- 1) Situation analysis: Some countries, but not all, have a clear idea of the extent of their current screening programs, and the degree to which the need is currently being met. An analysis should be undertaken in each country to provide information on the number of units in the country, and the provider for those units; the number and survival rate of preterm babies at risk by birth weight group, the extent to which the current screening program, if any, is meeting this need, and the current status of ophthalmologists adequately trained for ROP screening and treatment. This information is essential for planning.
- 2) Increasing coverage: There are many challenges to increasing coverage of ROP programs. Lack of financial reimbursement for time spent by ophthalmologists on the program is a major factor. In addition, partnerships with in-country governmental agencies must be developed. Countries in Latin America with well established programs can assist those countries where programs have only just started.
- 3) Developing guidelines: Regional guidelines need to be developed by neonatologists and ophthalmologists, under the auspices of the IAPB, PAHO, PAAO and SIBEN, which can be used (after modification, if required) not only for program implementation, but also for advocacy and to mobilise resources.
- 4) Awareness and advocacy: Parents, governmental agencies and health care providers must be advised of the seriousness of the ROP issue in Latin America. This can be achieved through publications, public service announcements and other means. Extensive educational material is available in several countries and it should be more widely dispersed.

The curriculae of nurses, pediatricians, obstetricians and neonatologists must include information about their role in primary prevention of blindness from ROP. These responsibilities include:

- a. Developing minimal acceptable standards for oxygen monitoring
- b. Information given to parents by neonatologists with respect to ROP
- c. Identifying and recording of babies needing examination (who and how)
- d. Care during examinations in intensive and intermediate care
- e. Ensuring discharged and treated babies attend follow-up
- f. Care during laser/cryo treatment
- g. Follow-up of premature babies by pediatricians

h. Data to be collected for monitoring and evaluating programs

The curriculae of medical students, residents and general ophthalmologists must include basic information about ROP including recognition of the disorder and its treatment. In particular, ophthalmologists who serve as screeners and/or treaters must be familiar with the disease process and screening and treatment of ROP. The responsibilities of screeners/treaters include:

- a. Providing information for parents
- b. Developing screening criteria in collaboration with neonatologists
- c. Determining frequency of examinations, and ensuring adequate follow-up
- d. Indications and consent for treatment
- e. Method of treatment and follow up after treatment
- f. Referral to low vision services for children with visual impairment from ROP

- 5) Evaluation of current programs: Each country must determine the minimal information needed to monitor current programs in terms of adequacy of coverage and quality. A standard reporting form and database used region wide will facilitate this process. Such a database or website would serve as a mechanism for sharing ideas across borders and discussing problems and their possible solutions.
- 6) Low vision care for premature babies. Currently there are inadequate low vision services for children who have the potential to benefit in Latin America. Parents are key to the success of visual rehabilitation of children and need to be included as a key component, and other professionals (e.g. teachers) also need to be involved. Many premature infants who have visual impairment have associated multiple other disabilities (sensory, motor and cognitive developmental delays) which compound their developmental delay.

Current recommendations:

1) Data collection for establishing current status and monitoring progress:

- a. For each country:
 - Number of newborns < 2000 g birth weight
 - Rate of premature babies surviving with < 2000 g birth weight
 - Number of Neonatal Intensive and Intermediate Care Units
 - Number of Units with ROP screening
 - Number of Units that provide treatment for ROP
 - Number of premature babies screened
 - Number of premature babies treated
 - Birth weight and gestational age of babies treated
- b. For each unit:
 - Date of birth
 - Sex
 - Birth weight
 - Gestational age
 - Days on oxygen and ventilation
 - Date of first eye examination
 - Date of last eye examination
 - Stage of ROP
 - Treatment given (laser, cryo, VR surgery), and outcome of treatment
 - Subsequent ophthalmologic checkups: at 6 and 12 months
 - If patient dropped out of program

2) Neonatal care:

Minimal acceptable standards for monitoring of oxygen:

- Personnel trained in procedure of administration of oxygen.
- Adequate equipment must be available (e.g. pulse oximeter) to monitor all babies receiving supplemental oxygen
- Adequate blenders and heater humidifiers must be available

- Maintain oxygen saturation between 88% and 92% and monitor arterial oxygen between 70 and 80 mm Hg

3) Training of ophthalmologists for screening and treatment

Training for a general ophthalmologist who already knows how to perform indirect ophthalmoscopy should take place at least twice a week for 3 – 6 months, examining at least 100 cases with an experienced screener. The ophthalmologist treating ROP should have observed at least 10-15 treatments and should begin to provide treatment under expert supervision.

4) Information for parents of at-risk babies:

The following information should be provided to all parents of babies at risk of ROP:

- A description of the maturing process of the retina
- Risks to the maturing retina from prematurity, illnesses and therapies.
- Possibility of preventing blindness with timely diagnosis and treatment, and what this will entail
- Treatment, even when administered in a timely and appropriately manner, not always successful
- Importance of timely examinations, even if baby is discharged from NICU.

5) Screening criteria suggested:

The following criteria are suggested:

- Birth weight: $\leq 1,750$ g and/or gestational age ≤ 32 weeks.
- Birth weight $>1,750$ g at the discretion of the neonatologist

However, as the risk of ROP in any NICUs is related to case mix as well as neonatal outcomes and levels of care, NICUs may want to set their own criteria. This should be done on the basis of longitudinal studies of at least one year in which details of the BW, GA and eye findings of consecutive babies are recorded.

It is the responsibility of the neonatologist to identify those babies who should be examined, to keep a diary for determining when the first examinations are needed, and to notify the ophthalmologist of the need for ROP screening examinations in a timely manner.

6) Timing and frequency of screening examinations:

When a reliable estimate of gestational age is not available, the first examination should be 4-6 weeks after birth.

For babies with a reliable estimated gestational age of at least 28 weeks, examinations should begin at 4-6 weeks after birth. As neonatal care improves and increasingly premature babies survive, these guidelines may need to be modified (see below).

Gestational age	Timing of first examination	Post-gestational age
≥ 28 weeks	4-6 weeks	32-34 weeks
27	4	31 weeks
26	5	31 weeks
25	6	31 weeks
24	7	31 weeks
23	8	31 weeks

Subsequent examinations:

- If the retina is immature and there is no ROP, the next examination should be at 2 - 3 weeks
- If there is ROP in zone 3, the next examination should be at 2 weeks
- If there is ROP zone 1 or 2 the next examination should be at 1 week, or at 3-4 days depending on the stage of disease and the appearance of the posterior pole vessels
- Examinations should continue until the retina is fully vascularized (within 1 disc diameter of the ora serrata) or the ROP has regressed

It is the responsibility of the ophthalmologist to decide when the next examination should be, to inform the neonatologist caring for the baby if the child is an inpatient or the mother/parents if the child is an outpatient, and to document the date for the next visit.

If, in the opinion of the neonatologist, the infant is too unstable to undergo the eye examination at the interval suggested by the ophthalmologist, the reason for the delay should be documented in the infant's chart.

7) Procedure of the eye examination:

Before scheduling an ROP screening examination, the neonatologist should check that the baby on the NICU is stable enough to be examined. A neonatologist must be available during screening in case a baby develops cardiovascular or respiratory problems.

Pupil Dilatation: Cyclopentolate 0.5 % combined with phenylephrine 2.5% or Tropicamide 0.5%. All mydriatic eyedrops should be instilled at least 30 minutes or 1 hour prior to examination.

Retinal examination: Indirect ophthalmoscopy with a 28 or 30 D lens is recommended, after fully dilating the pupils. Instillation of topical anesthetic is strongly recommended if a lid speculum is being used. The examination should be performed by an ophthalmologist experienced in diagnosis of ROP. The examiner should first examine the posterior pole, to look for signs of vascular dilation and/or tortuosity (pre-plus or plus disease), examine first the nasal retina and then the temporal retina to determine the zone of vascularization and stage of retinopathy if present.

8) Location of examination:

If the baby is still on the NICU, the baby should be examined in the NICU at the appropriate postnatal age, regardless of whether the baby is in an incubator / being ventilated. Avoid unnecessary transport of the baby as this may increase morbidity of the examination.

After discharge the baby should be followed up as an outpatient either at the NICU or in the ophthalmologist's office.

9) Ensuring follow-up of babies at risk:

The NICU should collect detailed addresses and telephone numbers (including those of parents and other relatives) for each baby so they can be easily contacted for follow up examinations.

Every effort should be made to ensure timely follow up. This might include telephoning, or by requesting personnel health assistant, or social workers to contact the family

10) Treatment indications:

Written, informed consent should be obtained from the parents / guardian using an information sheet that is easy to understand.

Treatment is indicated for Type 1 pre -threshold disease (ET-ROP definition) within 48 hours and includes:

Zone 1 any stage

Zone 2 Stage 2 + plus

Zone 2 Stage 3

The current recommended method of treatment is 360-degree ablation of the peripheral avascular retina, treating anterior to any ROP, using an indirect laser and/or cryotherapy.

The patient should be prepared and monitored during the entire procedure by the neonatal nurse, neonatologist and/or anesthesiologist. The procedure should be done in an operating room or appropriate care sector. The choice of sedation, analgesic or general anesthetic will depend on the possibilities of each service. Post-treatment recovery should be done in the neonatal intensive care unit. Postoperative ocular medications might include steroid/antibiotic combinations for a week to 10 days.

Treatment of ROP:

Treatment for Type 1 ROP consists of ablation of the avascular retina anterior to the region of the active disease to arrest the progression of ROP. The ridge and extravascular fibroproliferation at the junction between the avascular and vascularized retina should be avoided.

Both cryo and laser treatment may be painful procedures, thus, both should be performed under either sedation or full anesthesia, ensuring a good analgesia. The stress caused by pain should be

avoided as systemic complications may ensue. When an anesthetist is not available, an experienced neonatologist should give support. If the treatment is not being performed at the neonatal unit, facilities for artificial ventilation, resuscitation equipment and intravenous line must be available.

Mydriasis should be achieved prior to cryotherapy or laser.

A. Cryotherapy technique:

- 1) A retina probe or modified probe maybe used.
- 2) Indent the eye without pressure, excess of pressure is to be avoided.
- 3) The end point for adequate treatment using cryotherapy is a sudden whitening of the retina.. Cryo-applications should be 1 spot apart from each other as they tend to expand.
- 4) The cryo-probe should be withdrawn from the eye at periodic intervals to ensure perfusion of the retina and the disc.
- 5) Treatment of both eyes generally takes between 45-90 minutes.

Potential complications:

Systemic: Apnea, bradycardia, oxygen desaturation are common. These complications can occur during the first 3 days after treatment and require mechanical ventilation.

Eye: Subconjunctival haematoma, swollen of the eyelids, conjunctival laceration, vitreous haemorrhage.

B) Laser Photo-coagulation:

- Diode Laser (used extensively).
1. Laser Indirect delivery system.
 2. 200-500 milliwatts, and 0.2-0.5 seconds.

The avascular retina should be treated with a distance between laser spots of no more than half of spot

Complications:

As a direct result of Laser photocoagulation cataract may develop in 1-2%.

Treatment of very posterior ROP is generally easier with laser photocoagulation.

2. Postoperative care:

- 1) Post operative medication includes ointment or drops twice daily for 3-5 days. Cycloplegia is optional.
- 2) The fundus should be re-examined 5-7 days following treatment. If plus disease is still present, then the periphery must be examined to determine whether or not there are significant untreated areas. If there are, then more treatment should be applied.

After treatment the baby should be re-examined at 1 week. Untreated areas should be looked for, as well as signs of regression / progression of ROP and/or of plus disease. Careful observation for progression to retinal detachment is needed in the postoperative weeks.

The peripheral retina should be retreated with laser or cryotherapy if there are signs of progression. In general, retreatment of skip areas is needed only if there is progression.

Eyes with partial retinal detachments (stage IVa and stage IVb): Vitreoretinal surgery may be indicated for Stage IVa or b, but the decision to operate, and the nature of the surgical intervention, needs to be based on a careful assessment of the eye, and of the child, by an experienced vitreoretinal surgeon, in collaboration with the anaesthetist, and paediatrician. There are no internationally agreed guidelines concerning the timing of treatment, nor evidence from clinical trials as to which are the optimum interventions.

Stage V: Complex vitreoretinal surgery is not recommended at present, as the functional results are generally extremely poor even in anatomically successful results.

References:

- 1.- ICROP Committee: International classification of retinopathy of prematurity. ARCH OPHTHALMOL. 102:1130-1134, 1984.
- 2.- ICROP Committee for classification of late stages of ROP: An international classification of retinopathy of prematurity: II The Classification of Retinal Detachment. ARCH OPHTHALMOL. 105:906-912, 1987.
- 3.- An International Committee for the Classification of Retinopathy of Prematurity. The International Classification of Retinopathy of Prematurity- Revisited. ARCH OPHTHALMOL 123:991-9, 2005.
- 4.- Gilbert C, Fielder A, Gordillo L, Quinn G, Semiglia R, Visintin P, Zin A on behalf of the International NO-ROP Group. Characteristics of infants with severe retinopathy of prematurity in countries with low, moderate and high levels of development: Implications for screening programs. PEDIATRICS 115:e518-e525, 2005.
- 5.- Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter Trial of Cryotherapy for Retinopathy of Prematurity: One year outcome - Structure and Function. ARCH OPHTHALMOL 108:1408-1416, 1990.
- 6.- Cryotherapy for Retinopathy of Prematurity Cooperative Group. Multicenter Trial of Cryotherapy for Retinopathy of Prematurity: Fifteen-year Outcomes following Threshold Retinopathy of Prematurity: Final Results from the Multicenter Trial of Cryotherapy. ARCH OPHTHALMOL 123:311-8, 2005.
- 7.- Early Treatment for Retinopathy of Prematurity Cooperative Group. Revised Indications for treatment of retinopathy of prematurity. ARCH OPHTHALMOL 121:1684-96, 2003.
- 8.- Regional workshop on retinopathy of prematurity, November 14-16th 2005, Lima, Peru. May be located at <http://www.lav2020.org>

=====

DRA. ANDREA ZIN
IAPB-LA
Subcomité Ceguera Infantil - ROP
Coordinador Lengua Portuguesa
andreazin@hotmail.com

DR. MARCO A. DE LA FUENTE TORRES
IAPB-LA
Subcomité Ceguera Infantil - ROP
Coordinador Lengua Española
marcodelafuente@hotmail.com

DRA. CLARE GILBERT
IAPB - Visión 2020
International Centre for Eye Health
London School Hygiene and Tropical Medicine

GRAHAM E. QUINN, MD, MSCE
The Children's Hospital of Philadelphia
Philadelphia, USA