CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF RETINOPATHY OF PREMATURITY

— SUMMARIZED VERSION —

2017
DEVELOPER GROUP

A multidisciplinary team was created to develop evidence-based recommendations for the adaptation of clinical practice guidelines for retinopathy of prematurity (ROP), based on the highest methodological standards. These guidelines were developed with methodological and topic-related support from the Clinical Research Institute of the National University of Colombia, the Cochrane STI Group, and the Ibero-American arm of the Guidelines International Network (GIN).

COORDINATORS

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PERSON IN CHARGE OF SEARCHES


PEER REVIEWERS


EXPERT PANEL DEVELOPED DURING THE II LATIN AMERICAN SUMMIT ON PREMATURITY, BOGOTÁ 2016

<table>
<thead>
<tr>
<th>NAME</th>
<th>COUNTRY</th>
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<tbody>
<tr>
<td>Diana Faríña</td>
<td>Argentina</td>
<td>Neonatology</td>
<td>Ministry of Health of the Nation</td>
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<tr>
<td>Patricia Fernández</td>
<td>Argentina</td>
<td>Neonatology</td>
<td>Ministry of Health of the Nation</td>
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<tr>
<td>Alejandro Colmenares</td>
<td>Colombia</td>
<td>Neonatology</td>
<td>Central Military Hospital</td>
</tr>
<tr>
<td>Clara Esperanza Galvis</td>
<td>Colombia</td>
<td>Neonatology</td>
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<tr>
<td>Jose María Solano</td>
<td>Colombia</td>
<td>Neonatology</td>
<td>Colombian Association of Neonatology</td>
</tr>
<tr>
<td>Enrique Udaeta</td>
<td>México</td>
<td>Neonatology</td>
<td>Children’s Hospital of Mexico and Mexican Association of Pediatrics</td>
</tr>
</tbody>
</table>
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*HCPA, Porto Alegre Central Hospital; UFRGS, Federal University of Rio Grande do Sul; UNIFESP, Federal University of São Paulo.
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**PRESENTATION**

The Pan American Health Organization (PAHO) is pleased to provide the health community in the Region with a series of recommendations for the prevention, diagnosis, treatment, and rehabilitation of newborns who are affected or at risk of being affected by retinopathy of prematurity (ROP). This disease affects children who are premature or low birthweight or have recognized conditions of vulnerability, greatly threatening their future visual health and leading to substantial consequences.

This document is the result of a rigorous collaborative effort between PAHO, the National University of Colombia, the Cochrane Sexually Transmitted Infections (STI) Group, and a group of experts from Latin America and the United Kingdom made up of neonatologists, perinatologists, pediatricians, newborn critical care specialists, ophthalmologists, pediatric ophthalmologists, epidemiologists, and experts in literature searches and critical reviews. The recommendations presented here were prepared by adapting and updating existing regional documents and drafting evidence profiles that contain necessary, sufficient information to respond to questions developed by consensus between PAHO and the Guide’s Developer Group.

Although these guidelines do not contain cost-effectiveness considerations, they are innovative because they incorporate the implementation strategy that PAHO suggested and developed for this type of documents. The goal is to contribute efficiently to the development of public policies related to the visual health of premature infants in the Region of the Americas and the Caribbean. Thus, this document presents an implementation matrix for each group of recommendations, which integrates the quality of the information, the expectations of professional groups involved in patient care, and a balance between the expected benefits and the acceptability of the recommendations for each area.

The guidelines were constructed according to the methodology suggested in the World Health Organization (WHO) Handbook for Guideline Development and have been evaluated by peer reviewers using the AGREE II tool to confirm their quality. We hope that the recommendations presented here are useful for all of the professionals, institutions, authorities, and health agencies committed to the well-being of newborns in conditions of vulnerability and that they help to improve these newborns’ visual health and psychoemotional development.
SCOPE AND USERS

These clinical practice guidelines provide evidence-informed recommendations for the prevention, diagnosis, treatment, and follow-up of retinopathy of prematurity, with respect for the local or regional area and health system where these recommendations will be implemented.

The recommendations are directed to all pediatric ophthalmologists, neonatologists, retina specialists, pediatricians, nurses, and professionals who work in neonatal units, with the goal of preventing and managing retinopathy of prematurity. They also apply to general practitioners who refer newborn children with suspected or confirmed diagnosis of ROP to specialists. They can also be used by decision-makers and governmental entities to facilitate the implementation process.

This document does not include premature care recommendations not associated with ROP. For the general care of premature children, each country should implement its corresponding evidence-informed programs, policies, and national guidelines.

RATIONALE

ROP is one of the principal pathologies responsible for preventable blindness in children (Marroquín G, 2006). Therefore, all at-risk premature children should receive neonatal screening for ROP to prevent disease progression that can lead to visual disability or blindness (A.A.O., 2013; Holmstrom, 1993).

The vast majority of ROP cases occur in premature children with a birthweight of less than 1,500 grams or a gestational age of less than 32 weeks (Palmer et al., 1991). Advances in the field of perinatology and especially in neonatology have increased the survival of very low weight premature babies, in turn producing an increase in ROP. Unusual cases of ROP can occur in babies of higher weight or more advanced gestational age at birth who receive oxygen or present other risk factors (Lomuto et al., 2010).

In general, in high-income countries, ROP affects children with a birthweight of less than 1,000 grams or a very low gestational age. Cases in children who weigh 1,250 grams or more are rare and unusual cases or missed opportunities for adequate treatment are uncommon (Lomuto et al., 2010). Even so, ROP is the most frequent cause of child blindness in high-income countries. In the United States, 14,000 to 16,500 premature children who weigh less than 1,250 grams are born every year; of these, approximately 9,000 to 10,500 develop some degree of ROP, 100 to 1,500 require treatment, and 400 to 600 will have an unfavorable visual outcome (Blanco Teijeiro, 2006).

In low- and middle-income countries, these statistics vary greatly across and within countries. ROP can affect up to 34% of premature children with a birthweight of less than 1,500 grams; of these, 6% to 27% will require treatment (Lomuto et al., 2010). A systematic review identified the ROP population prevalence rates in Latin America: Argentina, 26.2% of all premature children (2010); Bolivia, 14.3% (2002); Brazil, 9.3% (2010); Chile, 12.3% (2004); Cuba, 5.1% (2010); Guatemala, 13.0% (2010); Nicaragua, 23.8% (2004); and Peru, 19.1% (2007) (Zimmermann-Paiz & Quiroga-Reyes, 2011). Mexico reported a prevalence of 9.4% in 2011 (Grupo ROP Argentina, 2016,) and Colombia reported 3.2% in 2016 (Ministry of Health and Social Protection, 2016).

The WHO Vision 2020 program took these factors into account and included management of ROP in its priority policies to improve visual health and reduce the prevalence of preventable blindness (WHO, 2007). Interventions to reduce ROP-associated blindness include the creation of ROP diagnosis and treatment programs, reduction of the access barriers for specialized visual health services, training of professionals in indirect ophthalmoscopy to diagnose ROP in preterm newborns, and timely surgical treatment of newborns with ROP (WHO, 2007).

These considerations demonstrate the need for guidelines for the prevention, diagnosis, and treatment of retinopathy of prematurity in Latin America.

OBJECTIVES AND POPULATION

These clinical practice guidelines were developed with the following objectives:

1. Diagnose retinopathy of prematurity (ROP) early and prevent ROP risk factors in preterm newborns during their stay in the neonatal care unit.
2. Present the strategies available for the diagnosis, treatment, and follow-up of newborns with retinopathy of prematurity in Latin America.

The target population is made up of:

- Premature newborns with a gestational age of less than 32 weeks and/or a birthweight of less than 1,500 grams.
- Premature newborns with gestational ages from 33 through 36 weeks, of any birthweight, who required oxygen or presented other risk factors for retinopathy of prematurity at some time between birth and hospital discharge.
DECLARATION OF CONFLICT OF INTERESTS

All Developer Group and expert panel members and all individuals who participated in the expert collaboration and external review signed a conflict of interest form. The Guide general coordinators reviewed all participant forms and curriculum vitae to identify any conflicts that may affect value judgments and recommendations. Everyone involved declared that they have no conflicts of interest related to the formulation of recommendations, are not involved as investigators in ongoing clinical trials on the topic, and have not received donations or benefits from interest groups. Several members of the Developer Group participated in the systematic reviews developed for the National Visual Health Program of Colombia 2016-2022. Generally, no conflict that could bias the guide’s recommendations was identified.

CLINICAL SETTING

The current guide aims to support clinical and surgical medical personnel who provide care for premature children.

The guide is directed to the Latin American population that is covered by the health system, with respect for the local or regional area.

LEVEL OF EVIDENCE AND STRENGTH OF RECOMMENDATIONS

The current guide used the GRADE system (Grading of Recommendations Assessment, Development and Evaluation) to grade the levels of evidence and strength of recommendations (Guyatt et al., 2011).

LEVEL OF EVIDENCE

<table>
<thead>
<tr>
<th>GRADE</th>
<th>JUDGMENT</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>HIGH</td>
<td>New studies are very unlikely to change the confidence in the estimate of effect.</td>
</tr>
<tr>
<td>B</td>
<td>MODERATE</td>
<td>New studies are likely to have a significant impact on the confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>C</td>
<td>LOW</td>
<td>New studies are very likely to have a significant impact on the confidence in the estimate of effect and are likely to change the effect.</td>
</tr>
<tr>
<td>D</td>
<td>VERY LOW</td>
<td>Any estimate of effect is very uncertain.</td>
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</tbody>
</table>

STRENGTH OF RECOMMENDATIONS

<table>
<thead>
<tr>
<th>STRENGTH OF THE RECOMMENDATION</th>
<th>MEANING</th>
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<tbody>
<tr>
<td>STRONG FOR</td>
<td>The desirable effects clearly outweigh the undesirable effects. RECOMMEND IMPLEMENTATION</td>
</tr>
<tr>
<td>WEAK FOR</td>
<td>The desirable effects probably outweigh the undesirable effects. SUGGEST IMPLEMENTATION</td>
</tr>
<tr>
<td>WEAK AGAINST</td>
<td>The undesirable effects probably outweigh the desirable effects. SUGGEST NO IMPLEMENTATION</td>
</tr>
<tr>
<td>STRONG AGAINST</td>
<td>The undesirable effects clearly outweigh the desirable effects. RECOMMEND NO IMPLEMENTATION</td>
</tr>
<tr>
<td>GOOD PRACTICE POINT</td>
<td>Recommended practice, based on the clinical experience of the guide’s developer group, which supports the recommendations.</td>
</tr>
</tbody>
</table>
SUMMARY OF THE RECOMMENDATIONS

The methodology followed international methodological standards. Details and evidence to support the recommendations can be found in the long version of these clinical practice guidelines (CPG).

METHODOLOGY

The present CPG was developed following WHO guideline preparation standards (OMS, 2014), the adaptation methodology of agencies such as the National Institutes of Health (NIH) and the National Institute for Health and Care Excellence (NICE), and the experience of the Clinical Research Institute at the National University of Colombia. The multidisciplinary developer group was made up of topic experts, epidemiologists, methodologists, and users. Two CPGs were identified as candidates for adaptation given their methodological quality, objectives, use of the GRADE approach, and publication date. First, the evidence selection process was validated and updated using electronic databases (PubMed, EMBASE, Cochrane) and a manual search starting from the CPG search date through October 2016. Then, the synthesis and evidence profiles were created using the GRADE approach. Cost considerations were not included since the guide is directed to different Latin American contexts. The recommendations were adjusted with experts from the Region's countries during an expert panel at the II Summit for the Day of the Premature Child in Bogotá in 2016. The guidelines were evaluated by topic and methodological pairs. All panel participants and the developer group signed conflict of interest forms, which were analyzed by the coordinators.

Evidence summaries, evidence profiles, and methodological details are in the long version of this document, which can be found in http://iris.paho.org/xmlui/bitstream/handle/123456789/34948/9789275320020_spa.pdf?sequence=5&isAllowed=y

RECOMMENDATIONS

Recommendations marked with * have been selected as key recommendations for the implementation process.

<table>
<thead>
<tr>
<th>NO.</th>
<th>SUMMARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The use of enteric feeding with breast milk and colostrum is recommended for premature newborns due to their protective impact on the incidence of ROP. Quality of the evidence: very low ⊕⊕⊕</td>
</tr>
<tr>
<td>2</td>
<td>The administration of oral lactoferrin is suggested due to its effect on reducing ROP incidence in countries where it is available. Quality of the evidence: very low ⊕⊕⊕</td>
</tr>
<tr>
<td>3</td>
<td>The creation of an alarm system for ROP risk in neonatal care units is suggested, to evaluate gestational age, weight gain and birthweight for the purpose of determining ROP risk. Quality of the evidence: very low ⊕⊕⊕</td>
</tr>
<tr>
<td>4</td>
<td>Supplementation of premature newborns with vitamin A, vitamin E, or inositol is suggested due to their effect on reducing ROP. Quality of the evidence: very low ⊕⊕⊕</td>
</tr>
<tr>
<td>5</td>
<td>The use of erythropoietin is not recommended since it increases the incidence of serious ROP. Quality of the evidence: low ⊕⊕Ο</td>
</tr>
<tr>
<td>6</td>
<td>In premature newborns in the delivery room, initiation of resuscitation with positive pressure ventilation with low oxygen levels (between 21% and 30%) and constant monitoring of oxygen saturation are recommended. * Quality of the evidence: low ⊕⊕Ο</td>
</tr>
<tr>
<td>7</td>
<td>In delivery rooms, maintenance of the following ranges of saturation in preterm newborns at risk of developing ROP is recommended: 3 minutes: 70-75% 5 minutes: 80-85% 10 minutes: 85-95% Quality of the evidence: low ⊕⊕Ο</td>
</tr>
</tbody>
</table>
Strong for

<table>
<thead>
<tr>
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<th>SUMMARY</th>
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<tr>
<td>Strong for 8</td>
<td></td>
<td>Adjustment of the oxygen levels (increase or reduce) every 90 seconds is recommended, using the expected parameters at 3, 5 and 10 minutes as a reference. Quality of the evidence: low ⊕⊕⊕</td>
</tr>
<tr>
<td>Weak for 9</td>
<td></td>
<td>Permanent monitoring of oxygen saturation with a pulse oximeter is suggested, to maintain oxygen saturation between 89% and 94%. Place the minimum saturation alarm at 88% and the maximum saturation alarm at 95% for all premature newborns receiving oxygen. Quality of the evidence: moderate ⊕⊕⊕</td>
</tr>
<tr>
<td>Good practice point</td>
<td></td>
<td>Compressed air-oxygen blenders and environmental oximeters for the periodic control of FiO2 are suggested for all neonatal care units, especially when there are disagreements between the mixture indicated and the saturation achieved.</td>
</tr>
<tr>
<td>Good practice point</td>
<td></td>
<td>Bronchial hygiene through the endotracheal tube should be applied using a closed aspiration system. Observation: this is carried out so that the child receives a constant concentration of oxygen. To avoid episodes of hypoxia or hyperoxia, consider other strategies (increase in PIM and RR), instead of “preoxygenating” the child by increasing the FiO2.</td>
</tr>
<tr>
<td>Good practice point</td>
<td></td>
<td>Flowmeters, both low flow (1 to 3 liters/minute) and mass flow (15 liters/minute), are suggested. When nasal cannulas are used, low flow flowmeters should be used. When a cephalic chamber is used, the flow should be from 8 to 10 liters/minute, with a minimum of 5 liters for smaller patients. When the CPAP system is used, use of a lower flow to reach the desired PEEP is recommended.</td>
</tr>
</tbody>
</table>

ROP, retinopathy of prematurity; FiO2, fraction of inspired oxygen; PIM, maximal inspiratory pressure; RR, respiratory rate; CPAP, continuous positive airway pressure; PEEP, positive end-expiratory pressure.QUESTION 2. WHAT ARE THE USEFULNESS AND CONDITIONS OF SCREENING FOR RETINOPATHY OF PREMATURITY IN PREMATURE NEWBORNS?

Strong for 10

<table>
<thead>
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<th>Recommendation</th>
<th>NO.</th>
<th>SUMMARY</th>
</tr>
</thead>
<tbody>
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<td>Strong for 10</td>
<td></td>
<td>When screening for ROP, it is recommended to use gestational age and birthweight, regardless of extrauterine growth restriction – and not only weight gain during the first weeks of life. Quality of the evidence: very low ⊕⊕⊕⊕</td>
</tr>
<tr>
<td>Strong for 11</td>
<td></td>
<td>Screening for ROP is recommended for every newborn with a birthweight of &lt; 2,000 g and/or a GA of 36 weeks or less of any birthweight, who presents at least one of the situations identified as risk factors for ROP.* Quality of the evidence: very low ⊕⊕⊕⊕</td>
</tr>
</tbody>
</table>

The first examination for ROP screening is recommended according to the following scheme for gestational age and timing of first ROP screening. In all cases, newborns at risk of ROP should have at least one ROP screen before being discharged from the neonatal unit. (Recommendation through expert consensus)

<table>
<thead>
<tr>
<th>Gestational age (weeks)</th>
<th>Timing of first ROP screening</th>
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<tbody>
<tr>
<td></td>
<td>Postnatal weeks</td>
</tr>
<tr>
<td>22</td>
<td>8</td>
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<td>23</td>
<td>7</td>
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<td>32</td>
<td>4</td>
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<tr>
<td>33</td>
<td>4</td>
</tr>
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</table>

Quality of the evidence: very low ⊕⊕⊕⊕
Follow-up to ROP screening should be carried out according to the following scheme:

<table>
<thead>
<tr>
<th>STAGE</th>
<th>ZONE I</th>
<th>ZONE II</th>
<th>ZONE III</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>INMATURE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>STAGE I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>STAGE II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>STAGE III</td>
<td></td>
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</tr>
<tr>
<td>V</td>
<td>STAGE I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VI</td>
<td>STAGE II</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VII</td>
<td>STAGE III</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**STAGE I**
- Type 2 exam in 3 or 4 days
- Type 1 treatment within 48 hours

**STAGE II**
- Exam in one week

**STAGE III**
- Exam in two weeks

**STAGE IV**
- Exam in one week

**STAGE V**
- Exam in one week

**STAGE VI**
- Exam in two weeks

**STAGE VII**
- Exam in two weeks

Source: From Zero to Always Program (Colombia, 2016).

**Quality of the evidence:** very low ⊕⊕⊕⊕
(Recommendation through expert consensus)

**Strong for**

13

It is important to properly record each ophthalmological examination result, detailing the zone, stage and extent in terms of “clock hours” of any type of ROP and the presence of preplus or plus disease.

**Quality of the evidence:** very low ⊕⊕⊕⊕

**Good practice point**

14

Suspension of ophthalmological examinations in newborns without ROP is recommended when retinal vascularization has extended to zone III and not before week 37.

**Quality of the evidence:** very low ⊕⊕⊕⊕

**Strong for**

15

In the presence of ROP, discontinuation of active disease screening is suggested when any of the following characteristics are present in at least two successive examinations:
- Lack of progression in disease severity.
- Complete regression of retinopathy.
- Partial resolution that progresses to complete resolution.
- Color change in the ridge from salmon pink to white.
- Transgression of vessels through the demarcation line.
- Start of the process of replacement of active ROP injuries by scar tissue.
- 45 weeks of age.

**Quality of the evidence:** very low ⊕⊕⊕⊕

**Weak for**

16

Once screening for potentially treatable ROP is finalized, ophthalmic examinations can be continued when the ophthalmologist considers that the identification of significant ophthalmic sequelae that would be amenable to treatment is likely.

**Good practice point**

17

Before screening for ROP, instilling a dose of one drop of a combination solution of phenylephrine 2.5% with tropicamide 0.5% in each eye is recommended to dilate the newborn’s pupil. Instill one drop in two or three doses, with 15 minutes interval between each application.*

Observation: each country can adapt the concentration according to drug availability and dosage, with an epinephrine concentration no higher than 2.5%.

**Quality of the evidence:** low ⊕⊕

**Strong for**

18

Use of the lowest possible quantity and dosage of mydriatic drops to dilate the pupils is recommended, with monitoring of the newborn’s heart and respiratory rates and blood pressure during the process.

**Quality of the evidence:** low ⊕⊕⊕⊕

**Good practice point**

Any pupil-dilating drops should be applied at least one hour before the examination.

**Quality of the evidence:** low ⊕⊕⊕⊕

**Strong for**

19

The use of anesthetic drops prior to the ophthalmological examination is recommended (e.g., proparacaine hydrochloride 0.5%, one to two drops, 30 to 60 seconds beforehand) if an eyelid separator (speculum) or scleral buckle will be used.

**Quality of the evidence:** low ⊕⊕⊕⊕
### Strong for

19. The use of techniques to reduce stress and pain during the newborn ophthalmological examination for ROP screening is recommended, such as: administration of a sucrose solution, support on the care giver lap, wrapping up the baby with a sheet, and/or the use of a pacifier.  
Quality of the evidence: low ⊕⊕ΟΟΟ

20. The duration of the ophthalmological examination for ROP screening should be as short as possible and precautions needed to promptly, efficiently resolve any risk situation that may emerge, such as effects on the newborn’s BP, RR or respiratory function, should be taken.  

21. The use of digital image acquisition systems is suggested when there are no ophthalmologists trained in diagnosing this pathology. These systems make it possible to transfer the images to trained specialists at specialized diagnostic centers.  
Quality of the evidence: very low ⊕ΟΟΟΟ

22. It is recommended that pediatric ophthalmologists or retina specialists carry out screening in neonatal care units.  
Quality of the evidence: very low ⊕ΟΟΟΟ

23. Use of a sterile eyelid speculum and scleral buckle is suggested to visualize the outlying regions of the retina.  
Quality of the evidence: very low ⊕ΟΟΟΟ

24. Treatment of ROP is recommended for any of the following situations:
- Zone I: any stage of ROP with plus disease.
- Zone I, stage 3, WITHOUT plus disease.
- Zone II, stage 2, WITH plus disease.
- Zone III, stage 3, WITH plus disease.  
Quality of the evidence: very low ⊕ΟΟΟΟ

25. Initiation of treatment within the first 48 hours of diagnosis is recommended for children with aggressive posterior ROP. In other cases, initiation of treatment within 72 hours of diagnosis is suggested.  
Quality of the evidence: very low ⊕ΟΟΟΟ

26. Therapy with a transpupillary diode laser is recommended as the first line of treatment for newborns with ROP.  
Quality of the evidence: low ⊕⊕ΟΟ

### Good practice point

- During the screening procedure, monitor blood pressure, heart rate and oxygen saturation levels since they can decline during the exam.  
Quality of the evidence: very low ⊕ΟΟΟΟ

- It is suggested that the attending ophthalmologist explain the need for treatment to parents and obtain their informed consent before carrying out the procedure.  

- For children who require treatment after being discharged from their hospitalization, readmittance to a neonatal (or in its absence, a pediatric) intensive care unit is suggested.  

- Therapy with general anesthesia can be implemented in an operating room, although this takes longer and requires an anesthesiologist with experience in pediatrics, as well as monitoring by a neonatologist or pediatrician and a skilled nurse.

BP: blood pressure; HR: heart rate; ROP: retinopathy of prematurity.

### QUESTION 4. WHAT ARE THE TREATMENT INDICATIONS FOR NEWBORNS DIAGNOSED WITH RETINOPATHY OF PREMATURENESS?

<table>
<thead>
<tr>
<th>RECOMMENDATION</th>
<th>NO.</th>
<th>SUMMARY</th>
</tr>
</thead>
</table>
| Strong for 24  |     | Treatment of ROP is recommended for any of the following situations:  
- Zone I: any stage of ROP with plus disease.  
- Zone I, stage 3, WITHOUT plus disease.  
- Zone II, stage 2, WITH plus disease.  
- Zone III, stage 3, WITH plus disease.  
Quality of the evidence: very low ⊕ΟΟΟΟ |
| Strong for 25  |     | Initiation of treatment within the first 48 hours of diagnosis is recommended for children with aggressive posterior ROP. In other cases, initiation of treatment within 72 hours of diagnosis is suggested.  
Quality of the evidence: very low ⊕ΟΟΟΟ |
| Good practice point | √ | It is suggested that the attending ophthalmologist explain the need for treatment to parents and obtain their informed consent before carrying out the procedure. |
| Good practice point | √ | For children who require treatment after being discharged from their hospitalization, readmittance to a neonatal (or in its absence, a pediatric) intensive care unit is suggested. |
| Strong for 26  |     | Therapy with a transpupillary diode laser is recommended as the first line of treatment for newborns with ROP.  
Quality of the evidence: low ⊕⊕ΟΟ |
| Good practice point | √ | Treatment in the neonatal unit with sedation and analgesia is suggested for newborns with ROP.  
Treatment with general anesthesia can be implemented in an operating room, although this takes longer and requires an anesthesiologist with experience in pediatrics, as well as monitoring by a neonatologist or pediatrician and a skilled nurse. |
<table>
<thead>
<tr>
<th>RECOMMENDATION</th>
<th>NO.</th>
<th>SUMMARY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weak for</td>
<td>27</td>
<td>It is suggested that topical anesthesia not be used as the sole source of analgesia when treating ROP.</td>
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<tr>
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<td>It is suggested that the use of anti-vascular endothelial growth factor (anti-VEGF) antagonist drugs is suggested when first-rate surgical treatment is not available and in the following cases:</td>
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<td>- Failure with laser treatment.</td>
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<tr>
<td></td>
<td></td>
<td>- When it is not possible to carry out laser treatment because the child has a critical condition for tolerating treatment or visualization of the retina to carry out laser or cryotherapy treatment is not possible.</td>
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<tr>
<td></td>
<td></td>
<td>- In newborns with aggressive posterior ROP</td>
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<tr>
<td></td>
<td></td>
<td>- In newborns with ROP type 1 in zone I.</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Quality of the evidence: very low ⊕ΟΟΟ</strong></td>
</tr>
<tr>
<td>Good practice point</td>
<td>√</td>
<td>The treatment-associated benefits and risks and the lack of evidence of long-term efficacy and effects should be explained to parents and their signed informed consent should be obtained. Furthermore, their commitment to continue with post-treatment follow-up should be confirmed.</td>
</tr>
<tr>
<td>Weak for</td>
<td>28</td>
<td>At discharge, a plan is suggested for all newborns with an ROP diagnosis, whether they are treated or untreated. The plan should include periodic ophthalmology, neonatology, or pediatric follow-ups and a premature newborn follow-up appointment for as long as the physician considers these follow-ups to be pertinent, according to clinical criteria.</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Quality of the evidence: very low ⊕ΟΟΟ</strong></td>
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<td></td>
<td>(Recommendation through expert consensus)</td>
</tr>
<tr>
<td>Strong for</td>
<td>29</td>
<td>A postoperative check-up during the first week (4 to 8 days) is recommended for every newborn that receives treatment, to evaluate complications or the need for retreatment or complementary treatments and as long as clinical criteria indicate that check-ups are pertinent.</td>
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<td></td>
<td><strong>Quality of the evidence: very low ⊕ΟΟΟ</strong></td>
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<td></td>
<td></td>
<td>(Recommendation through expert consensus)</td>
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<tr>
<td>Good practice point</td>
<td>√</td>
<td>A pediatric ophthalmologist or retina specialist should continue with follow-up until retinal vascularization is confirmed. Follow-up should take place at 3, 6 and 12 months and then annually for all premature children.</td>
</tr>
<tr>
<td>Weak for</td>
<td>29</td>
<td>Referral of newborns who present any degree of ROP for early visual stimulation is suggested as early as possible, during the first months of life and even during hospitalization in the neonatal care unit.</td>
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<td></td>
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<td><strong>Quality of the evidence: very low ⊕ΟΟΟ</strong></td>
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<td></td>
<td>(Recommendation through expert consensus)</td>
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<tr>
<td>Strong for</td>
<td>30</td>
<td>The incorporation of blind or visually impaired children into formal education is recommended as early as possible. Education can be regular, special, or integrated, based on the characteristics of the child's disability and family and the educational options in his or her community.</td>
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<td></td>
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<td><strong>Quality of the evidence: very low ⊕ΟΟΟ</strong></td>
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<tr>
<td></td>
<td></td>
<td>(Recommendation through expert consensus)</td>
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</tbody>
</table>

**ROP**, retinopathy of prematurity.


