Review

Screening program for retinopathy of prematurity in Spain


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Objective: To prepare a retinopathy of prematurity (ROP) screening program as agreed by most of Spanish ophthalmologists dedicated to this topic.

Materials and methods: A draft of the protocol was produced taking into account the experience of the participants and current publications. This draft was corrected by all the

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Introduction

Retinopathy of prematurity (ROP) is a retinal vasculopathy which appears in premature babies and is able to produce blindness in a small but significant percentage of cases.

Retinal neovascularization begins in the sixteenth week of fetal development and is completed between week 36 and 40. ROP development will depend on intrinsic factors of the disease (degree of prematurity, prenatal ischemic factors, etc.) as well as on iatrogenic factors (oxygen therapy).

Since the “Multicenter Cryotherapy Study for ROP” (1988)\(^1\) and the “Randomized Clinical Trial for Early Treatment of ROP” (2003)\(^2\) confirmed the efficacy of treatment for severe ROP forms, infants at risk of developing the disease require a retinal assessment at the appropriate time in order to detect the disease at an early stage and provide adequate treatment.

Accordingly, the authors propose this screening guide for ROP in order to execute all the procedures in a regulated time frame and manner.

Objective

To identify premature infants who may require treatment for ROP as well to establish short and long-term follow-up.

Recommendations

Neonatologists in charge of premature infants should inform the parents, at least verbally and if possible in writing, of the newborn’s inclusion in the ROP screening program and about the assessments that will be performed.

Every hospital that attends premature infants should establish written protocols of the screening program, agreed by neonatologists and ophthalmologists. This program should be reviewed regularly.

The responsibilities and participants of the screening and follow-up program for infants at risk of ROP must be clearly defined in the ophthalmology as well as the Neonatology Units, both at the medical level as well as the auxiliary medical level (supervisors, nurses, clinic staff, etc.).

Identification of patients: subjects at risk

Criteria for inclusion

Considering the most accepted inclusion criteria\(^3\)\(^{-10}\) it is recommended to include:

- NB with WB ≤ 1.500 g or GA < 32 weeks. The GA would be determined by the neonatologist and ophthalmologist on the basis of the last menstruation date (LMD) and on the early fetal echography. If this is not available, the GA shall be
established by means of the \( P_D \) of the Lejarraga–Fustiñana table (overestimating in patients with retarded intrauterine growth but not underestimated, reducing the risk of a first delayed ocular assessment).\(^8\)

- NB con GA ≥ 32 weeks and WB between 1.501 and 2.000 g provision of oxygen for a period > 72 h or with unstable clinical course as assessed by the neonatologist. The main risk factors are considered to be extended assisted ventilation, apnea, neonatal acidosis, demise of twin, intraventricular III–IV hemorrhage, persistence of ductus, sepsis, necrotizing enterocolitis, intercurrent surgical interventions and poor postnatal weight gain.\(^10,11\)

Even though some individual studies suggested reducing GA and WB,\(^12\) the above criteria are most widely accepted in the medical literature reviews on the topic. However, each hospital can modify the criteria according to the characteristics of its population, although this must always be done on a scientific basis demonstrating that the modifications would not involve loss of patients.

**Calendar of action**

It is recommendable to utilize the post-menstrual of post-conception age (PME) as it correlates better than postnatal age with the onset of severe ROP.

**Time of first assessment**

It is recommended to focus exploration of premature infants in the course of a single day. In this manner, the neonatology unit will be ready to receive the ophthalmologist that will carry out the assessment and will have organized the tasks for the adequate preparation of the infants to be assessed. In turn, the ophthalmologist must have enough time to carry out an adequate assessment of these patients.

The indication of the first assessment will be determined by the neonatologist of the unit in joint consultation with the ophthalmology section of the hospital in charge of premature infants, with sufficient time for inclusion in weekly evaluations.

The recommended calendar, which follows the most widely agreed standards\(^3-10\) is shown in Table 1.

**Follow-up**

The date of follow-up evaluations will be set by the ophthalmologist who, after the first assessment and each follow-up evaluation will annotate in the patient clinical record as well as the registration sheet the time and date of the following evaluation.

A member of the neonatology unit as well as in the ophthalmology unit should be designated to list on a weekly basis the patients that will be evaluated according to the indications made by the ophthalmologist. Said designated members must check their data in order to avoid delays or mistakes in evaluation appointments.

<table>
<thead>
<tr>
<th>GA (weeks)</th>
<th>Age of initial evaluation (weeks)</th>
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<tr>
<td></td>
<td>Post-menstrual</td>
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<tr>
<td>22(^a)</td>
<td>30–31</td>
</tr>
<tr>
<td>23(^a)</td>
<td>30–31</td>
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<tr>
<td>24(^a)</td>
<td>30–31</td>
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<td>25(^a)</td>
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<td>35–36</td>
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<td>32</td>
<td>36–37</td>
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</tbody>
</table>

\(^a\) In these cases it is only a recommendation because, even though ROP does not usually appear before week 30 of postmenstrual age, some authors have found rush forms at week 3 of life even though these did not require treatment up to week 6.\(^13\) In these cases the first evaluation could be performed earlier, above all in prematures with low weight for gestational age.\(^14\) All the clinical aspects that may combine to suspect early onset of the disease should be taken into account in order to establish the time of the first evaluation (for example, the development of ROP is rare when infants are intubated and is more frequent when supplementary \( O_2 \) is withdrawn). In addition, it is not clear if under 25 weeks the physiopathological mechanisms of the disease are the same.

It is recommended to:

1. Perform an evaluation at weekly or shorter intervals in case of:
   - Zone I stage 1 or 2.
   - Zone II stage 3.
   - Any disease in the presence of plus signs.
2. Perform an evaluation every one or 2 weeks in case of:
   - Zone I stop (no ROP) (one week if oro-tracheal intubation [OTI] is not used or is withdrawn, 2 weeks the patient remains with OTI).
   - Zone II stage 2.
   - Regression to zone I.
3. Perform an evaluation every 2 weeks in case of:
   - Zone II stage 1.
   - Regression in zone II.
4. Perform an evaluation every 2 or 3 weeks in case of:
   - Zone II stop (no ROP).
   - Zone III stage 2 or 3.
   - Regression in zone III.

**End of hospital evaluations**

Ocular fundus evaluations can be suspended when the following conditions are met:

- Complete retinal neovascularization in 360°.
- Post-menstrual age > 45 weeks and absence of pre-threshold disease.
- Post-menstrual age > 36 weeks with vascularization in zone III without previous ROP signs with at least 2 ocular fundus evaluations.
ROP regression with non-reactivation certainty (although patients with post-menstrual age > 43 weeks generally stabilize, if ROP has existed relapses can occur associated to surgical interventions, general anesthesia for evaluations or deterioration of overall condition, e.g. due to sepsis).

Hospital release

If the general condition of the patient allows hospital release without completing ophthalmological evaluations, the ophthalmologist must annotate in the clinical record of the patients the date of the following evaluation. In turn, the neonatologist must indicate in the release report the last evaluation of the patient and the date of the following one.

It is recommended that for children who have been released from hospital and require additional evaluations, these should be carried out ensuring the welfare of the patient and in rooms equipped with all available means for adequate attention because the overall instability of these infants and the stress involved in mydriatic treatments as well as the evaluation itself can give rise to side effects.

If the patient is transferred to another hospital, the ophthalmologist must annotate in the clinical record of the patient the recommended date for the following evaluation. In turn, the neonatologist must make sure that the other hospital is adequately equipped for performing follow-up evaluations and possible treatment for the patient, indicating in the release report the performed evaluations, the clinical and ophthalmological condition of the patient and the recommended date for the following evaluation.

Long-term evaluations

High incidence of ophthalmological involvement of prematures and particularly of those with ROP history is demonstrated.14-17 Accordingly, it is recommended to maintain long-term follow-up.

It is recommended to follow up prematures with WB < 1500 g. The first evaluation should be carried out between 9 and 12 months. The remaining evaluations will depend on the results of the assessments or the patient development. Every hospital should establish a calendar of evaluations indicating the place where these shall be carried out.

Study methodology

The evaluations must be made by ophthalmologists with sufficient knowledge and experience to ensure the identification and location of retinal changes in ROP. At least 2 experienced ophthalmologists should be available for assessing prematures in each hospital in order to cover vacation periods and other events such as days on leave because delays of 3-4 weeks in reaching a diagnostic could have severe consequences.

It is recommended that the ophthalmologist should have a file with the data of patients included in the program. This file should include at least the following data:

- Personal and family information.
- Date of birth.

- Gestational age and weight at birth.
- Evaluation date with the appropriate clinical data.
- Date of the following evaluations.

Said file can also include the following data:

- Events during gestation (preeclampsia, eclampsia, chorioamnionitis, etc.).
- Oxygen therapy exposure time.
- Intercurrent diseases (sepsis, HIV, enterocolitis, persistence of ductus, etc.).

Evaluations must be carried out with indirect ophthalmoscopy and previous pupil dilatation at the neonatology unit where the patient is admitted.

Pupil dilatation with midriatics must adhere to a guideline applying the minimum efficient dosage to avoid side effects.18-20 It is best to associate parasympathetic blockers (1% tropicamide [Colircusi tropicamida] or 0.5 or 1% cyclopentolate [Colircusi ciclopérgico] al 0.5 or 1%) with sympathomimetics (2.5 or 1% phenylephrine [Colircusi Fenilefrina]) The guidelines for midriasis may be established at each hospital on the basis of studies that have demonstrated efficacy and safety. The neonatology unit should be in charge of training auxiliary staff for adequate administration of midriatics (adequate palpebral opening, lachrymal point compression after administration, removing drug remains to avoid accidental ingestion, etc.). It should be the responsibility of the nurse in charge of the premature to provide adequate midriasis when the ocular fundus is being assessed.

Blepharostats should be pediatric and sterile for each infant. It is essential to wash hands between evaluations to avoid contagion of hospital infections. The neonatology service shall establish the necessary isolation guidelines in each case (use of gloves, gowns, etc.).

The welfare of the infant must be ensured during the evaluation, endeavoring to avoid side effects as much as possible.21,22 The nurse in charge of the premature should assist in obtaining the adequate position of the infant and take the necessary measures to avoid loss of temperature. In turn, the neonatologist should establish necessary analgesia and monitoring measures. Anesthetic eye drops should be used (oxybuprocaine) before beginning the evaluation as well as fixing the blepharostat if applicable.

Ocular fundus exploration should begin at the posterior pole without scleral indentation to avoid changes in the plus if any, and subsequently the peripheral retina should be explored utilizing scleral indentation only if necessary.

The ophthalmologist must annotate the results of the exploration in the clinical record of the patient and in the registration sheet. If ROP signs appear, the area, stage extension and presence of plus signs must be registered following the international ROP classification.23

Although at present ocular fundus digital photography does not substitute ophthalmoscopic exploration,24 digital photographs should be taken as a standard procedure utilizing currently available retinographs in order to avoid controversies about the ophthalmological situation of the patient. From the legal protection viewpoint, it is recommendable to have a pre-treatment digital photography of the ocular fundus of
patients who require treatment and when the patient is to be transferred to another hospital.

**Conflict of interests**

No conflict of interests has been declared by the authors.

**REFERENCES**