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Research Article

Evaluation for Retinopathy of Prematurity for High Risk Premature Infants

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Abstract

Retinopathy of prematurity (ROP) is a disorder of the developing retinal blood vessels in preterm infants of low birth weight, and is a leading cause of childhood blindness, especially in the developing world. With timely screening and intervention, even babies at high risk for developing visual problems can be adequately treated and their vision saved. Evaluation of these fragile babies requires an experienced team, good communication, and excellent record keeping.

SCREENING

Current screening guidelines set forth by the American Academy of Ophthalmology (AAO) and American Academy of Pediatrics (AAP) [1], aim to ascertain the presence of ROP as early as possible, to allow for prompt intervention at a nascent stage of disease, thus preventing the progression to blindness. All infants with birth weight (BW) ≤ 1500 g or a gestational age (GA) of 30 weeks or less (as defined by the attending neonatologist) and selected infants with a BW between 1500 and 2000 g or a GA of >30 weeks who are believed by their attending pediatrician or neonatologist to be at risk for ROP (such as infants with hypotension requiring inotropic support, infants who received oxygen supplementation for more than a few days, or infants who received oxygen without saturation monitoring) should be screened for ROP. Timing of the initial exam is based on post-menstrual age (PMA) and is beyond the scope of this article; in brief, it should be planned for 31 weeks PMA or 4 weeks postnatal age, whichever is later.

Follow-up examinations should be recommended by the examining ophthalmologist on the basis of retinal findings at that time.

EXAMINATION METHOD AND TECHNIQUES

Screening examination should be performed after both pupils are pharmacologically dilated, using binocular indirect ophthalmoscopy, with a lid speculum and scleral depressor. The eye drops used to dilate the pupils can be absorbed systemically, and can cause tachycardia, flushing, or hypertension. For this reason, a lower concentration of medication is used, typically 1% phenylephrine and 0.3% cyclopentolate. A combination drop offers ease of administration. In the neonatal intensive care unit (NICU), it is often noted that babies will develop bradycardia after eye drop administration. This is likely due to the oculocardiac reflex stimulated by placing pressure on the globe. Minimization of direct pressure, with careful manual eyelid retraction during drop administration, will avoid this complication.

Screening examination should occur with good communication with the NICU team.

Advance notice of the timing of the examinations allows staff to place eye drops at least 1 hour in advance, so the babies are well dilated when the team arrives. A NICU nurse should be designated to assist whenever possible, particularly for babies who are on ventilators. At a minimum, the examining team should "check in" with the neonatology team to ensure that the baby is stable to be examined.

Proper positioning of the infant allows the examiner to gently rotate the head from side to side to see to the far edges of the retinal vasculature. Scleral depression is required in most cases, especially for slightly older babies whose vasculature has progressed towards the periphery of the retina. Heart and respiratory rate should be monitored during and after the examination.

Examinations should be performed by an ophthalmologist who has sufficient knowledge and experience to accurately identify the location and sequential retinal changes of ROP. The recently published International Classification of Retinopathy of Prematurity, 3rd edition (ICROP3) defines the stages and location of disease, which are used to determine severity and when treatment is indicated [2]. This is a 2021 revision of the original classification, first published in 1984. The ICROP should be used to identify, diagram, and record these retinal findings at the time of examination.

Using Photo imaging for Screening

In recent literature [3], it has been suggested that a carefully organized program of remotely interpreted wide-angle fundus camera ROP screening may initially be used in place of binocular indirect ophthalmoscope examinations up to the point at which treatment of ROP is believed to be indicated; at this point, indirect ophthalmoscopy is required. Captured images and their interpretations should be incorporated into the permanent medical record. It is also recommended that indirect ophthalmoscopy be performed at least once by a qualified ophthalmologist before treatment or termination of acute-phase screening of ROP for infants at risk for ROP.

Remote ophthalmologist interpreters must provide timely clinical input on the timing of follow-up imaging sessions and ophthalmoscopic examinations using appropriate methodology. These findings must be communicated in a manner that is compliant with rules of the Health Insurance Portability and Accountability Act (HIPAA) and other federal and state legal requirements.

COMMUNICATION

Communication with parents by members of the care team is important, as is documentation of those communications. Parents should be aware of ROP examinations and should be informed if their child has ROP, with subsequent updates on ROP progression, and should be aware of the possibility of blindness if they do not adhere to the examination schedule after discharge. The possible consequences of serious ROP should be discussed at the time that a significant risk of poor visual outcome develops. Documentation of such conversations with parents in the nurse or physician notes is highly recommended, as is the use of standardized parental educational materials. Parents may be asked to sign a pre-discharge form indicating that they have been informed about the findings and have been given a follow up appointment. Missed follow up can lead to failure of timely diagnosis and treatment in the outpatient setting, and has been associated with adverse outcomes. To mitigate this risk, the Ophthalmic Mutual Insurance Company (OMIC) has a "TOOLKIT" [4], that recommends all of the steps to ensure careful tracking and communication between the inpatient team and the outpatient ophthalmologist. Many NICUs will not permit discharge or transfer of babies with high risk ROP, at least without physician-to-physician communication regarding a timely plan of care for follow up.

PREPARATION OF INFANTS FOR EXAMINATION

Separate sterile instruments or instruments cleaned in accord with the anti-infective protocol for metal instruments for each NICU should be used to examine each infant to avoid possible cross-contamination by infectious agents.

SIDE EFFECTS AND MEDICAL RISKS OF EXAMINATION

Effort should be made to minimize the discomfort and systemic effect of this examination. Pupillary dilation should be adequate for examination of fundi, but care should be taken in using multiple drops if the pupil fails to dilate because poor pupillary dilation can occur in advanced ROP, and administering multiple doses of dilating drops can adversely affect the cardiorespiratory and gastrointestinal status of the infant.

During the exam, a member of the team should monitor the infant's vital signs, being on the lookout for evidence of bradycardia in particular, at which point the examiner should pause the examination and remove the instruments until the infant returns to baseline.

NURSING INVOLVEMENT BEFORE AND AT BEDSIDE, AFTERCARE

Nursing assistance is important in helping to position infants during and after the examination, and to maintain a close watch on the infant's vital signs.

Mild swelling of the eyelids and the occasional subconjunctival hemorrhage may be observed after; parents should be reassured that these findings are not harmful and will resolve quickly.

TREATMENT

Decisions about when and how to treat infants with ROP is beyond the scope of this article. The two mainstays of treatment, ablative laser therapy and intravitreal injections of anti-vascular endothelial growth factor (VEGF) medication, each offers distinct advantages and disadvantages, and are crucial modalities in the appropriate setting, depending on the location and severity of disease. Cryotherapy is no longer commonly used, and pars plana vitrectomy is a treatment option of last resort, and will not be addressed here.

PREPARATION

Infants must be appropriately sedated and/or anesthetized to allow for the treatment; the duration of treatment is significantly longer for laser relative to injection, and needs to be adequately accounted for by the neonatology team when deciding on anesthesia modalities and options. Some treating physicians prefer to perform laser ablations in the operating room under general anesthesia; however, it is more common that these are done at the bedside or in an NICU treatment room. Blackout shades and proper laser eye protection for assistants are required. Sucrose 24% administered orally may also be administered for pain relief. Good swaddling and head positioning will aid in the facility of the procedure.

ABLATIVE LASER THERAPY

The pupils should be dilated; a speculum and scleral depressor are required; sterile irrigation solution should be available as well to allow for corneal lubrication and adequate view.

A laser indirect ophthalmoscope (810 nanometer infrared wavelength) is used to apply ablative therapy to the peripheral avascular retina. Laser settings can vary based on uptake and media clarity. Some surgeons prefer to use an argon laser which has less scleral penetration and therefore is less painful for the infant. The entire 360 degrees of avascular peripheral retina should be targeted. Burns are placed in a semi-confluent pattern, ½ to 1 burn width apart, which can require upwards of 3000 laser spots in each eye, and take 1-2 hours to administer. If the infant

is unable to be anesthetized for that duration, then treatment can be broken into multiple sessions, if needed.

RISKS AND COMPLICATIONS

Acutely, the eyelids and conjunctiva may have edema, erythema, and subconjunctival hemorrhage. Topical ointment (steroid and antibiotic combination) can be applied by the NICU team twice daily to minimize inflammation.

Vitreous hemorrhage may occur which can worsen the underlying retinopathy and make visualization of response to laser difficult. If there are untreated or undertreated areas, repeat laser administration may be required.

Long term, ablative laser therapy weakens the sclera and can lead to eye elongation, myopic progression and peripheral visual field loss. Rarely, errant laser shots might hit the lens of the eye causing a cataract; this possibility is more likely if there is a tunica vasculosa lentis (fetal blood vessels) still present on the lens, which absorbs laser energy.

INTRAVITREAL INJECTION

Intravitreal bevacizumab is the most widely used agent in the treatment of ROP. There are currently several studies aiming to ascertain the optimal dose required for injection, as well as whether specific anti-VEGF agents are more effective [5]. Currently, the most widely utilized dose is 0.625 mg, which is half the adult dose. It is important that the volume be limited (0.025 ml) so that excess is not injected into the eye, which can increase the eye pressure and lead to vascular perfusion problems. Because of the tiny volume, a special syringe and needle are utilized, prefilled and diluted by the pharmacy.

RISKS AND COMPLICATIONS

The risk profile of intravitreal injections is well established from its prevalent use in the adult population, and includes serious risks, such endophthalmitis and damage to intraocular structures, and more benign risks, like subconjunctival hemorrhage.

In the infant population, special consideration needs to be given to the potential neurodevelopmental risks associated with anti-VEGF use; to date, the literature is indeterminate on the long term sequelae. Obtaining a detailed informed consent is essential, because there remain unanswered questions involving dosage, timing, safety, and visual and systemic outcomes.

Additionally, infants treated with anti-VEGF rather than ablative laser needed to be closely followed for a longer duration, as late reactivation of ROP is a known phenomenon that can require re-treatment.

FOLLOW-UP

Follow-up is recommended in 3 to 7 days after laser photocoagulation or anti-VEGF injection to ensure that there is no need for additional laser treatment in areas where ablative treatment was not complete, or for additional anti-VEGF injections.

SUMMARY

ROP is a potentially blinding condition, but with proper screening and timely intervention, infants can have optimal outcomes. Care must be taken to minimize the risks involved in examining and treating infants, and close communication with the NICU team and family are of utmost importance.

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