



Polish Ophthalmological Society revised guidelines for the management of retinopathy of prematurity*

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ABSTRACT

According to the consensus of Polish neonatologists and the Pediatric Ophthalmology Section of Polish Ophthalmological Society, screening for retinopathy of prematurity (ROP) should be performed in children born ≤ 33 weeks of gestational age with birth weight ≤ 1800 g and in premature infants born over 33 weeks and weighing over 1800 g with respiratory failure, low weight gain and other pathologies connected with prematurity qualified by the neonatologist due to the general condition and high risk of ROP. The recommended time of the first examination is in the 4th week of chronological age. Subsequent examinations should be performed at the intervals depending on the retinal vascularization in periods of one to three weeks. If a child is discharged from the hospital before a complete retinal vascularization, parents/guardians must be informed of the need for timely follow-up check-up ophthalmic visits.

In the treatment of ROP, laser photocoagulation of the avascular retina or intravitreal anti-VEGF injections (bevacizumab, ranibi-

zumab, aflibercept) are used. Diode or argon laser therapy remains the method of choice for ROP treatment. Current global guidelines do not specify strict indications for the use of anti-VEGF therapy. Available observations suggest its effectiveness in the treatment of aggressive posterior ROP (APROP). Anti-VEGF therapy can be used in patients in whom photocoagulation is difficult or impossible, e.g. when corneal, lens or vitreous haze occurs, or when pupil dilatation is not possible.

Treatment should be performed no later than 72 hours after diagnosis. If retinal detachment occurs despite treatment, it is recommended to perform a vitrectomy in selected cases. Treatment is necessary for ROP type 1, defined as: 1. Any stage of ROP in zone I with plus disease, 2. Stage 3 ROP without plus disease in zone I, 3. Stage 2 or 3 with plus disease in zone II. Treatment for both eyes should be considered when ROP type 1 is present in only one eye.

KEY WORDS: retinopathy of prematurity, screening, laser photocoagulation, anti-VEGF therapy, current Polish guidelines.

INTRODUCTION

Retinopathy of prematurity (ROP) is a retinal disease resulting from uncontrolled vascular proliferation, developing in the eyes with incomplete retinal vascularization. ROP remains an important cause of significant visual impairment and blindness

in children. The study published in 2010 indicated the estimated number of children blind because of ROP in the world at 20,000, and the number of children with visual impairment at 12,300 [1]. In the last decade, the survival rate of extremely immature premature babies has increased, resulting in higher incidence of ROP [2].

*Guidelines of scientific societies and associations (including the Polish Ophthalmological Society) do not constitute binding laws and do not determine the only correct procedures; they are only an opinion of a group of experts from a given field. The opinion reflects the current state of knowledge based on available scientific research results.

The guidelines do not exempt healthcare workers from personal liability with regard to making the correct decisions for individual patients.

Personal responsibility for the used therapeutic methods rests with all individuals who practise medicine. It should be based on thorough knowledge and practical skills, while observing necessary safety measures with regard to oneself and the patient.

Readers of this paper are obliged to make themselves familiar with current information on the presented treatments and pharmacotherapies with special attention paid to manufacturers' information on doses, time, and administration as well as side effects of the used drugs.

The publishers and editors of the paper shall not be responsible for any damages that could in any way be connected to the contents of this paper.

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In premature newborns, areas of non-vascularized (avascular) retina are the more extensive the more immature the child is [3]. Besides retinopathy, amblyopia, strabismus and refractive defects occur more commonly in premature babies, compared to the population of children born on time.

RECOMMENDATIONS REGARDING EXAMINATION OF PREMATURE BABIES

The examination should be carried out by an ophthalmologist experienced in the diagnosis of ROP, who knows the international classification of ROP [4]. Pupil dilatation is required before the examination. 2-3 instillations of eyes with 2.5% phenylephrine and 0.5% tropicamidum are recommended an hour before the examination. Since both administration of drops and activities associated with the examination may cause general symptoms, in particular bradycardia and arrhythmia – it is advisable to monitor the child's condition during the examination. Administering local anesthetic drops (proxymetacaine, Alcaine) is recommended immediately before the examination. The examination is performed following placement of a speculum, using an intermediate speculum and a 20 and 28 D magnifying glass, using an indenter or a squint retractor to visualize changes in the peripheral retina. Tools have to be sterile. When retinopathy is confirmed, fundus lesions should be described in accordance with the current international ROP classification, stating the stage, state of retinal vessels and retinal zone in which lesions occur. When the diagnosed ROP is eligible for treatment, photographic documentation (RetCam, Icon) is recommended.

According to the consensus of Polish Neonatologists and the Pediatric Ophthalmology Section, screening for retinopathy of prematurity should cover children born ≤ 33 weeks of gestational age with birth weight ≤ 1800 g, and premature infants born over the age of 33 weeks and weighing over 1800 g with cardiovascular respiratory failure, low weight gain and other pathologies associated with prematurity, qualified by the neonatologist considering the child's general condition and high risk of ROP. The first examination should be performed in the 4th week of chronological age. According to the recommendations of the American Academy of Pediatrics (AAP) and other global guidelines, the date of the first ophthalmological examination depends on the maturity of a newborn [5].

Subsequent examinations should be carried out at intervals of one to three weeks, depending on retinal vascularization.

Weekly checks are recommended in case of:

- immature vascularization in the zone I, with no ROP,
- immature retina on the border of the zone I and II,
- stage 1 or 2 in the zone I,
- stage 3 in the zone II,
- suspicion of aggressive posterior ROP.

Checks every 1-2 weeks are recommended in case of:

- immature vascularization in the central zone II,
- stage 2 ROP in the zone II,
- regression of ROP in the zone I.

Checks every two weeks are recommended in case of:

- stage 1 ROP in the zone II,
- immature vascularization in the zone II, with no ROP,
- regression of ROP in the zone II.

Checks every 2-3 weeks are recommended in case of:

- stage 1 or 2 ROP in the zone III,
- regression of ROP in the zone III.

If a child is discharged from hospital before the end of complete retinal vascularization, parents/guardians have to be informed of the need to report to their follow-up appointments in a timely manner.

The decision to end periodical examinations may be made in case of children who:

- did not have type 1 ROP (or retinopathy requiring treatment) or deterioration of ROP stage after completion of 45 PMA (some authors recommend 50 PMA),
- have retinal vascularization reaching the zone III,
- had never have ROP in the zone I or II,
- present regression of ROP and show no presence of abnormal vascular tissue posing a risk of reactivation in the zone II or III.

TREATMENT OF RETINOPATHY OF PREMATURE

Therapeutic methods

The treatment involves laser photocoagulation of the avascular retina or intravitreal administration of anti-VEGF preparations (bevacizumab, ranibizumab, aflibercept). Diode or argon laser therapy remains the method of choice for ROP treatment.

Anti-VEGF therapy can be used as monotherapy or as in combination with laser. From August 2019, Ranibizumab obtained the marketing authorization, and other anti-VEGF preparations are used off label based on the consent of the Bioethics Committee and parents. In anti-VEGF therapy, despite its wide use in the world, knowledge on the choice of the drug to be used, dose and distant general adverse effects is insufficient. Also, detection of late reactivation of ROP in cases of anti-VEGF monotherapy poses a major diagnostic problem. The advantage of anti-VEGF therapy is that it is a technically simpler, shorter procedure (possibility of administering the drug without general anesthesia), there is the probability of developing a normal retinal vascularization, and a lower myopia compared to laser therapy.

The current global guidelines do not specify strict indications for the use of anti-VEGF therapy. Available observations suggest efficacy of the treatment in aggressive posterior ROP (APROP).

Anti-VEGF therapy can be used in patients in whom photocoagulation is difficult or impossible, e.g. when haze of the cornea, lens or vitreous body occurs, and when pupil dilatation is not feasible.

Vitreotomy involves resection of the vitreous body and fibrous membranes, causing elimination of retinal pull. Removal of the lens is necessary in selected cases.

Indications

Treatment is necessary in case of type 1 ROP, that is: 1. Any stage of ROP in the zone I with plus disease, 2. Stage 3 ROP with no disease in the zone I, 3. Stage 2 or 3 with plus disease in the zone II.

Treatment should be considered if type 1 ROP had developed in one eye and the other eye does not meet the criteria for the diagnosis of type 1 ROP. Sometimes in such cases it is better to qualify both eyes for treatment.

Treatment should be started no later than 72 hours after the diagnosis. In the event of posterior aggressive ROP

(APROP), treatment should be initiated as soon as possible. If retinal detachment occurs despite treatment, it is advisable to perform vitrectomy in selected cases of stage 4A, 4B and 5A. Outcomes of surgical treatment of stage 5B are usually non-satisfactory [6].

DISCLOSURE

The authors declare no conflict of interest.

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