The ROYAL COLLEGE of OPHTHALMOLOGISTS

Clinical Guidelines

Treating Retinopathy of Prematurity in the UK

Date of Evidence Search: 20 August 2021
Date of Publication: March 2022
Date of Review: March 2025

Executive Summary

Retinopathy of prematurity (ROP) is a potentially blinding condition affecting low gestation and very low birth weight infants. Worldwide it is a major cause of preventable blindness. Screening for ROP is undertaken to identify ROP that requires treatment.

This evidence-based guideline for the treatment of ROP was developed by a guideline development group (GDG) of The Royal College of Ophthalmologists (RCOphth), the UK special interest group of ROP screeners and treaters (ROP-SIG) and the charity Bliss. The guideline was produced according to RCOphth standards for guideline development.

The guideline provides evidence-based recommendations and good practice points. Recommendations are graded A-D using SIGN grading hierarchy, according to the strength of the evidence underpinning them. The good practice points (GPP) are a consensus of the GDG. All recommendations and GPPs are given in the Executive Summary. The full guideline should be consulted for the evidence base behind the recommendations.

The guideline has been produced for use within the UK and supersedes the guideline published in 2008. It will not be applicable in countries where more mature infants are at risk of sight threatening ROP.

The guideline will be updated within five years of its publication date.

Clinical appendices A-E give clinical advice on the management of neonatal endophthalmitis, practical advice on referral for vitreoretinal surgery, a suggested referral form for use by screeners when referring to treaters, a Parent / Carer information leaflet and suggested approaches to ROP clinical management coordination. Methodology appendices F-J give the Scope of the guideline, the Guideline Methodology used, the Search strategy and Selection criteria used, Evidence tables and Conflict of Interest statements.

All documents are available on the websites of RCOphth and RCPCH.

The following recommendations and GPPs, with their evidence levels have been made:

What are the indications for treatment of ROP?

Evidence Grade A

Treat infants in whom a screening examination has detected:

- Zone I any stage ROP with plus disease
- Zone I stage 3 ROP without plus disease
- Zone II stage 2 or 3 with plus disease
- A-ROP

Plus disease should be present in at least two quadrants. Vessel changes should be assessed within Zone I. GPP: Zone II stage 2 with Plus ROP, is borderline for treatment and close watching is an acceptable alternative approach.

Closely monitor infants (weekly review and if concerned discuss with the network treating ophthalmologist) in whom a screening examination has detected:

- Zone I stage 1 or 2 without plus disease
- Zone II stage 3 without plus disease

How urgently should treatment for ROP be given?

Evidence Grade B

Infants with A-ROP or zone I stage 3 with plus ROP should be treated as soon as possible and within 48 hours. Infants with zone I stage 1 or 2 ROP with plus disease, zone I stage 3 ROP without plus disease, or zone II stage 2 or 3 with plus disease should be treated within 48-72 hours.

What information should be provided to parents of infants with ROP?

GPP

The treating ophthalmologist should have a consent discussion with the parents/carers of an infant requiring treatment for ROP and should gain informed explicit consent prior to the procedure taking place.

Treating discharged infants

GPP

Infants who require treatment for ROP after discharge from hospital should be admitted to a suitable neonatal or paediatric unit with facilities and experience of caring for infants after neonatal surgery.

How should ROP be treated?

Evidence Grade A

Zone I and Posterior Zone II

Treatment-requiring A-ROP and ROP in zone I should be treated with an intravitreous injection of an anti-VEGF agent. Anti-VEGF agents must NOT be administered if there are any signs of periocular infection.

In the view of the GDG, posterior Zone II (2 disc diameters anterior to the junction of Zone I and Zone II) or any "notch" of ROP that encroaches backwards into Zone I, may behave in a similar way to Zone I and may be treated accordingly.

Zone II (except posterior zone II)

Treatment-requiring ROP in zone II should be treated with transpupillary laser, to produce near-confluent ablation of the entire avascular retina.

Anti-VEGF treatment results in fewer eyes with high myopia, but requires more intensive follow up and carries a higher rate of retreatment. Anti-VEGF agents must NOT be administered if there are any signs of periocular infection.

When should infants treated for ROP be reviewed and what are the indications for retreatment of ROP?

Post-treatment review is important to detect and treat adverse events, monitor disease regression, detect disease reactivation and determine if retreatment is necessary.

Laser

The first examination should take place 5-9 days after treatment and should initially continue weekly to assess for signs of regression or for any signs that re-treatment may be required. From 7-14 days start to consider re-treatment with laser if disease regression is inadequate and untreated retinal areas are identified. Rescue treatment with an anti-VEGF agent should be considered from 14 days if disease regression is inadequate and laser treatment has been optimal.

Anti-VEGF

The first examinations should take place 1-2 days and 5-7 days after treatment to detect adverse effects of treatment. Following partial or complete disease regression, regular examinations should be maintained to detect disease reactivation: weekly for 4 weeks, 2 weekly for a further 12 weeks and then 4-weekly for at least a further 8 weeks (total of 24 weeks) and up to 32 weeks in eyes treated for A-ROP with bevacizumab).

Disease reactivation in the form of plus disease and / or extraretinal new vessels should be treated with transpupillary laser, to produce near-confluent ablation of the entire avascular retina.

Anti-VEGF agents may be used for retreatment but require more intensive follow up and carry a higher rate of further disease reactivation, requiring further retreatment. Anti-VEGF agents differ. The above follow up schedule was used in the RAINBOW trial of ranibizumab. Longer follow up may be needed following bevacizumab (follow up to 65 weeks PMA has been recommended).

GPP

EUA following anti-VEGF

Following initial Anti-VEGF treatment consider EUA / Examination under sedation with possible transpupillary laser to produce near-confluent ablation of the entire avascular retina IF the retina has not fully vascularised (or this is uncertain) AND:

- Regular follow-up is becoming unsustainable for social and / or geographic reasons.
- The growing child's limited cooperation precludes adequate examination of the peripheral retina.
- There is uncertainty about the presence of signs of disease reactivation.

OR:

- During longer term follow-up a significant area of Persistent Avascular Retina is seen or suspected.

What are the indications for vitreo-retinal surgery?

Evidence Grade B

As soon as any significant peripheral retinal traction is detected, the case should be discussed with a specialist paediatric VR surgery centre, with a view to possible transfer for early vitreoretinal surgery.

What skills and training are required for those who treat ROP?

Evidence Grade C

Any ophthalmologist undertaking treatment or making treatment decisions must be skilled in examining premature retinae to identify the type of ROP and which treatment modality is most appropriate for the patient. Ophthalmologists in treating centres should have experience in undertaking both laser and anti-VEGF injection in preterm infants so they can offer the most appropriate treatment for each patient. Some local ophthalmologists may be competent in anti-VEGF injections but will refer for laser therapy. When this expertise is not available within the local unit, formal network arrangements must be in place with good communications for prompt transfer to the treating centre.

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NICE has accredited the process used by The Royal College of Ophthalmologists to develop content used in Treating ROP in the UK. Accreditation is valid for 5 years from 31 July 2020. More information on accreditation can be viewed at www.nice.org.uk/accreditation.Accreditation evaluates only the processes used to develop content and excludes recommendations displayed by decision support systems in specific clinical settings as these are dependent on technical algorithms which are outside of the scope of NICE accreditation. Accreditation can be used to inform compliance with ISB 0129 – Clinical Safety Risk Management System – Manufacture of Health Software (DSCN 14/2009) and ISB 0160 – Clinical Safety Risk Management System – Deployment and Use of Health Software (DSCN 18/2009), but cannot be used in isolation to release any product for clinical use.

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