Retinopathy of Prematurity: Screening and Treatment

University Hospitals of Leicester NHS Trust

Trust ref C12/2009

Contents

1. Introduction and Who Guideline applies to

This guideline is aimed at all Health care professionals involved in the care of infants within the Neonatal Service.

Key Points:

- Untreated severe Retinopathy of Prematurity (ROP) is associated with a significant risk of blindness.
- Appropriate screening can detect babies who require treatment with laser therapy or Avastin (bevacizumab) intra-vitreal injection therapy (IVT)
- Guidelines for screening and treatment of ROP have been produced by the Royal College of Ophthalmologists, RCPCH and BAPM.

Related UHL documents

- **ROP Information for Parents**

ROP-screening-information-parents-carers-2024.pdf

- Pain and Distress in the Neonate UHL Neonatal Guideline **C13/2010**

Background

The paediatric ophthalmology team attends the neonatal unit every Tuesday and covers both LGH and LRI. During this time, they will carry out eye screening on the premature infants that meet the UK Guidelines criteria.

Occasionally babies will require more extensive examination. Babies that require treatment will be treated within 48 hours of identification and preferably on the same day if possible. During eye screening, the ROP specialist nurses will be available to assist. If laser surgery is required, an allocated ANNP will be available to take of the care of the baby during treatment.

2. Screening & Treatment

2.1 Which Infants to screen

Screening is indicated for infants born at less than 31 weeks gestation (up to 30+6) ***or*** less than 1501g birthweight.

2.2 Timing of the initial ROP screen

Gestational Age at birth	Timing of First Screen
< 31+0 (30+6) weeks (i.e. up to 30 weeks and 6 days)	31+0 and 31+6 weeks postmenstrual (corrected) age or 4 weeks postnatal age whichever comes later
>/= 31+0 weeks but with birthweight < 1501g	36 weeks postmenstrual age or 4 completed weeks postnatal age whichever is sooner

	Timing of first ROP screen	
Gestational age (weeks)	**Postnatal Weeks**	**Postmenstrual weeks**
22	9	31
23	8	31
24	7	31
25	6	31
26	5	31
27	4	31
28	4	32
29	4	33
30	4	34
31 (BW <1501g)	4	35
32 (BW <1501g)	4	36
33 (BW <1501g)	3	36
34 (BW <1501g)	2	36
35 (BW <1501g)	1	36

2.3 ROP Screening Procedure

All babies undergoing eye examination need to have their pupils dilated. Drops need to be instilled at least one hour before examination is due to take place.

The following drops are to be used for routine eye examinations: For eye examination only:

G.Cyclomidril (combined eye drop preparation of cyclopentolate 0.2% + phenylepherine 1%)	Instill 1-2 drops in each eye at 60 minutes before the ophthalmology ward round.
Proxymetacaine 0.5% anaesthetic drops (instilled by examiner prior to using lid speculum)	

Equipment

The equipment used for the ROP screening:

1) Cook's paediatric ocular speculum and Schocket scleral depressor/indenter.
2) A wire blue ocular speculum for use with RetCam® (wide angle retinal imaging camera).
3) Lens (28 dioptre).
4) Binocular indirect Ophthalmoscope (BIO).
5) RetCam® (only available at LRI)

Prior to the examination the baby will be given 24% sucrose (Algopedol) for pain relief. During the examination, the ROP specialist nurse will ensure that all babies are monitored and will indicate if the screening needs to be stopped because of concerns.

2.4 LASER Treatment

Once laser treatment has been identified as being necessary, it is the allocated ANNP who takes on the responsibility for preparation of the baby. There is a laser checklist that is kept in the eye treatment room that is used pre, during and post laser treatment.

Indication for treatment of sight threatening ROP (Type 1):

- Zone I any ROP with plus disease.
- Zone I stage 3 without plus disease
- Zone II stage 2 or stage 3 with plus disease
- Threshold (5 continuous or 8 non-continuous clock hours of Stage 3 with or without plus disease)
- AP-ROP (aggressive posterior ROP)

Timing of treatment:

- Babies with aggressive posterior ROP (as defined by ICROP revisited) should be treated as soon as possible and within 24 hours.
- Other Type 1 ROP should ideally be treated within 24 - 48 hours and no longer than 72 hours.

Follow up, Treatment and Re-treatment:

- ROP treatment is provided by the ophthalmologist using indirect diode laser and 28 Dioptre (28D) lens with indentation and speculum. Laser is applied to the avascular retina (anterior to the demarcation) and sometimes posterior to the demarcation depending on severity.
- Treatment with near-confluent laser burn spacing should be administered to the entire avascular retina. Sixty to ninety minutes is allocated for the treatment of each eye.
- Infants should be followed up at weekly intervals following laser treatment for up to 4-6 weeks depending on progress. Follow up guidelines following IVT are below.
- Re-treatment should be performed if there is a failure to regress after 2 weeks from initial treatment, or there has been progression.

PREPARATION AND PROCEDURE FOR LASER

Pre-procedure

- Ensure consent has been obtained prior to preparation.
- The laser room should be checked - equipment in working order, including resuscitation equipment, and omnibed available.
- Ensure that baby is nil by mouth at least for 4 hours and if NG tube is place aspirate prior to operation. In emergency time line to be decided on individual basis.
- Pre-laser eye drops should be prescribed and 1-2 drops of each given in both eyes every 10 minutes starting 1 hour before treatment starts:

DICLOFENAC 0.1%
PHENYLEPHRINE 2.5%
CYCLOPENTOLATE 0.5%

- Ensure baby is cannulated.
- All babies requiring laser will need to be electively intubated prior to the procedure. This should be done in a controlled environment in the ITU room with pre-prescribed intubation drugs to ensure maximum safety of the baby.
- Morphine and atracurium and maintenance fluids should be prescribed and ready to start post intubation.
- A chest x-ray will be ordered to check tube position (unless baby already intubated prior to treatment).
- The baby will be transferred into the laser room with Ambu bag ventilation.
- Ensure baby has a name band prior to moving into laser room.

During Procedure

- Blood gases should be carried out prior to the laser therapy, and then at 2 hours and post-laser therapy.
- Observations should be carried out prior to treatment and every 15 minutes throughout the procedure.
- During treatment the persons present must have completed the e-learning laser package. All staff must wear protective goggles at all times. Ensure the door is locked and the DO NOT ENTER sign is displayed.
- It is the responsibility of the laser surgeon to ensure laser safety for attending staff and staff are requested to comply with instructions regarding use of goggles.
- In case of emergency if neonatal team is called, the laser should be turned off prior to the team entering the room.

Post-procedure

- After treatment is completed, Atracurium and morphine will be discontinued, and baby will be transferred back to ITU.
- A full handover should be given to the medical and nursing staff.
- Post laser eye drops to be prescribed: **DEXAMETHASONE 0.1% BD CYCLOPENTOLATE 0.5% BD for 5 days**
- The green eye sheet should be filled in and filed in the baby's notes.
- The laser checklist should be photocopied, with 1 copy filed in the notes and 1 copy stored in the laser room.
- The equipment and room should be cleared and cleaned.

2.5 Intra-vitreal therapy (IVT)

AVASTIN® (bevacizumab) Intra-vitreal therapy (IVT)

Indications for Avastin IVT to be discussed and offered to parents:

- Any ZONE 1 disease ('Plus' disease with any stage ROP, Stage 3 without Plus in Zone 1), any progressing ROP stage without plus (see international guidelines).
- Consider for posterior aggressive zone 2 disease

IVT using anti-vascular endothelial growth factors (VEGF)) such as Avastin® has been advocated in certain aggressive ROP clinical scenarios where the outcome from treatment has been reported as being better to that of laser treatment.

- The use of anti–VEGF for ROP is on a named patient basis only. **Parents must be made aware that laser treatment may still be required following IVT** either due to recurrence of ROP within 2-4 weeks following IVT, or at 40-42 weeks PMA to reduce the risk of recurrence in the future.
- Following discussion about treatment options with the Parents, informed consent should be taken by an Ophthalmologist.

PREPARATION FOR AVASTIN TREATMENT:

Pre-procedure

- Communicate plan with ITU consultant, registrar and nurse in charge.
- Ensure consent has been obtained for treatment and parents are informed that it is "off label" use of the medication.
- Administer eye drops to both eyes every 10 minutes 1 hour before treatment:

  DICLOFENAC 0.1%
  PHENYLEPHRINE 2.5%
  CYCLOPENTOLATE 0.5%
- For *ventilated* babies, ensure that baby is sedated with morphine and settled. If required, Atracurium may be considered.
- For babies who are *self-ventilating*, chloral hydrate should be administered 30 minutes prior to the procedure (as per Neonatal drug dose formulary)
- Safely transfer baby into laser room. If baby is ventilated use an ambu bag for transfer.

During Procedure

- Baby should be fully monitored during procedure including ECG leads.
- Use the same documentation as with laser. Document base line observations prior to the treatment and a full set of observations post procedure. A copy should be filed in the notes and a copy in the eye treatment room.
- All treatment is carried out in the laser room in a sterile environment.

Avastin injection:

Intra-vitreal injection will be performed by a trained ophthalmologist.

Preparation for administration of Avastin IVT: equipment:

Trolley 1 Open gown and gloves

Trolley 2 Use sterile drape
Open all other equipment onto trolley
Add approx. 20ml 5 % iodine and 20ml 0.9 % sodium chloride into pot Draw up 2ml iodine mix into syringe

Procedure:

Prepare baby

1. Apply 0.5 %. proxymetacaine
2. Clean with iodine mixture or other cleaning solution that may be applied to the eye
3. Drape
4. Insert speculum

Prepare bevacizumab (Avastin)

1. Put Yellow 30G short needle onto the syringe
2. Push out excess medicine ensuring no bubbles or dead space

Giving Avastin

1. Measure and mark 1mm from limbus
2. Hold needle vertically over mark
3. Insert needle vertically HALF DEPTH of the needle
4. Assistant to plunge syringe gently while surgeon to maintain position of needle.
5. Remove needle from the eye (swift vertical movement)
6. Assistant to apply cotton bud dipped in iodine
7. Apply more Iodine to the eye using prepared syringe
8. Apply G. Chloramphenicol 0.5% to the eye

For the second eye patient needs to have **separate sterile equipment including syringe with Avastin.** Surgeon and assistant **will rescrub for second eye.**

Post procedure by Ophthalmology team:

1. Check central artery pulsation
2. G. chloramphenicol 0.5% TDS 7 days

3. Red reflex check – day 1 and day 3 post procedure
4. Dilated fundoscopy day 2 post procedures
5. Document operation details (**note batch number of Avastin**)
6. Avastin syringe and needles to be disposed of in purple – lidded yellow bins.

Post-procedure

- After treatment transfer baby back to ITU for continued care.
- Ensure a full hand over is given to the ITU registrar and nursing staff.

3. Fluorescein Angiography on the UHL Neonatal Units

3.1 Aims

To provide information on the process of Fundus Fluorescein Angiography on the UHL Neonatal Units

3.2 What is Fluorescein Angiography?

Infants under 1000 grams (extremely low birthweight) and under 27 weeks gestational age are at greater risk of Type 1 ROP, that requires treatment.

Fundus Fluorescein Angiography (FFA) is a diagnostic test used to visualise retinal blood vessels. Fluorescein, an orange dye, is injected intravenously. This dye highlights the retinal blood vessels which can then be photographed. The test itself takes about 6 minutes to perform as part of the ROP screening round. The dye may cause temporary skin discolouration following the procedure. It is eliminated via kidneys and the urine may appear fluorescent for 24-36 hrs.

FFA is a safe method of investigation which can provide additional information about the developing retinal blood vessels in high risk infants. This is necessary in order to decide the best time to offer treatment particularly in Stage 2 ROP with Pre-Plus disease and in cases of Zone 1 disease.

Useful links:

Checklist for outpatients undergoing FFA When reaction to FFA is suspected Information for parents

3.3 Who will need FFA?

Babies with birth weight up to and including 800 gms and babies that the ophthalmologists deem high risk for ROP will be offered FFA. **Serial FFA over a number of weeks may be performed during the time the baby attends for ROP screening.**

3.4 Procedure

1. Ophthalmologist will obtain written consent for FFA.

2. Neonatal team will be informed at least a day before the test to ensure that the baby has a functioning cannula. If a baby is attending as an outpatient, the neonatal team should be informed 1 week in advance to ensure that a doctor will be available to insert cannula for the outpatients.

3. 0.08mls/kg of fluorescein sodium 10% injection (comes as 500mg in 5 ml) is administered IV as a bolus followed by 1ml of 0.9% sodium chloride flush.

4. The baby is to be monitored during the procedure and up to 1 hour after the procedure in the laser room. This will be the responsibility of the ANNP looking after the baby, or the ROP specialist nurses for those attending as outpatients. (A further checklist is provided for attending outpatients requiring FFA.)

5. Resuscitation equipment and oxygen should be available during this procedure. When the outpatients are undergoing FFA, the arrest trolley should be in the room

6. A named doctor from special care, Consultant and the charge nurse should be made aware when an outpatient is to undergo FFA.

7. It will be the responsibility of the ROP specialist nurses/ANNP to remain with the outpatient baby until 1 hr after the procedure.

3.5 Potential Side effects of FFA

Common: temporary discolouration of skin
Uncommon: urticaria, injection site extravasation and redness
Very Rare: vomiting, shock, respiratory distress, cardiac arrest and seizures.

3.6 Checklist for outpatients undergoing FFA

1. ANNP to put IV cannula on baby's arrival. Consider the use of topical anaesthetic cream and other non pharmalogical method such as swaddling or sucrose solution.

2. Consent to be obtained prior to procedure. A leaflet on what to expect post FFA should be provided.

3. Resuscitation trolley and drugs available in room.

4. Nurse in charge and medical staff in special care aware that this procedure is going to be undertaken and are available if necessary.

5. Fluorescein to be prescribed by Ophthalmologist.

6. Heart rate, respiration, saturation and temperature should be taken just prior to Fluorescein administration, 30 minutes post-procedure and one hour post-procedure. These observations should all be charted in baby's notes.

3.7 ADVERSE REACTION TO FFA

A reaction to FFA may be recognised by clinical signs such as apnoea, desaturation, bradycardia, cyanosis/pallor, clamminess.

When a reaction to FFA is suspected

- **Stop procedure.**
- **Pull the emergency button** – *for additional medical team and nursing support.*
- **Provide oxygen as required**
- **Start resuscitation** - *as per NLS guideline/ UHL Neonatal Resuscitation guideline*

3.8 Information for Parents

Your baby is to undergo Fundus Fluorescein Angiography or FFA with your consent.

FFA is an investigation that will provide insight on the progression and severity of ROP in your baby's eyes.

A small amount of Fluorescein (a water-based orange dye) will be injected through a drip into a vein and will allow the Ophthalmologist to take detailed photographs of the small delicate developing blood vessels in the retina (located at the back of the eye).

The test is not painful and takes approximately 6 mins to perform during the routine eye screening that your baby will undergo. Because the dye is orange in colour it may result in a *temporary* orange discolouration of skin and urine.

It can take up to 24-36 hours for all the dye to leave the body. Like any medicines that your baby receives on the neonatal unit, there can be a small risk of a reaction to the dye, resulting in problems with breathing or heart rate. However, this risk is very low and generally the test is tolerated well by babies.

The test is used by many neonatal units around the world in eye screening for premature babies if their risk of developing ROP is high.

However, if you are worried about any unusual symptoms your baby is showing after the test, please inform a doctor.

The eye specialist will record the photographs of the dye test and will discuss any serious abnormalities and the recommended treatment for your baby.

4. Education and Training

None

5. Monitoring & Audit

Auditable standards:	All the babies meeting the criteria will be screened at least fortnightly. All eligible infants will have their first screen according to the Royal College guidelines. All infants will be followed up at least until they are 38 weeks corrected.
Results reported to:	NNU Governance team
Action plan to be signed off by:	Ophthalmology team and Neonatal Team
Person responsible for completion of action plan:	Ms S Anwar and Mr S Tyradellis

Monitoring	
Process for monitoring:	Retrospective badger review
How often will monitoring take place:	Yearly
Population:	Babies ≤ 1500g and /or ≤30+6
Person responsible for monitoring:	ROP Screening team
Auditable standards:	All the babies meeting the criteria will be screened at least fortnightly. All eligible infants will have their first screen according to the Royal College guidelines. All infants will be followed up at least until they are 38 weeks corrected.
Results reported to:	NNU Governance team
Action plan to be signed off by:	Ophthalmology team and Neonatal Team
Person responsible for completion of action plan:	Ms S Anwar and Mr S Tyradellis

6. References

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7. Key Words

Laser therapy, Avastin (Bevacizumab), Intra-vitreal injection therapy (IVT), Ophthalmologists, Fundus Fluorescein Angiography

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details			
Guideline Lead (Name and Title) Kelly Gamble - ANNP Himadree Thanki, - Clinical Staff Sam Brown			**Executive Lead** Chief Medical Officer
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
1995	**1**	Initial Guideline (GW)	
Jul 2009	**2**		Guideline review
Nov 2015	**3**	Neonatal Guidelines meeting Neonatal Governance Meeting	
April 2016			Editorial changes (guidelines lead – REM)
Nov 2018	**4**	Neonatal Governance Meetings	Guideline review
July 2020	**5**	Neonatal Guidelines meeting Neonatal Governance Meeting	

Sept & Oct 2021	**6**	Neonatal Guidelines meeting Neonatal Governance Meeting	Updated equipment list used for ROP screening Laser Treatment: Added to indications Altered timing of treatment. Treatment & retreatment amended Pre-procedure added if NG tube is in place aspirate prior to operation. Added In case of emergency if neonatal team is called, the laser should be turned off prior to the team entering the room. IVT: Indications added - any progressing ROP stage without plus (see international guidelines).Consider for posterior aggressive zone 2 disease Solution %/concentration added for Iodine, sodium chloride &Proxymetacaine Disposal of Avastin syringe - specified purple lidded sharps FFA Changed gestation from 32 weeks to 27 weeks in regards to Infants at greater risk of Type 1 ROP, that require treatment
December 2024	**7**	Neonatal Guidelines meeting Neonatal Governance Meeting	**Timing of ROP screen updated to;** < 31+0 (30+6) weeks (i.e. up to 30 weeks and 6 days) - 31+0 and 31+6 weeks postmenstrual (corrected) age or 4 weeks postnatal age whichever comes later. >/= 31+0 weeks but with birthweight < 1501g - 36 weeks postmenstrual age or 4 completed weeks postnatal age whichever is sooner. **Timing of first ROP screen amended pre gestation 22weeks to 35 weeks**