Guideline on the Management of the Fetus and Neonate with a Potential Bleeding Disorder

NHS Lothian

Title:			
Date effective from:	09/04/2024	**Review date:**	09/04/2027
Approved by:			
Approval Date:	Click here to enter a date.		
Author/s:			
Executive Lead:	Dr Corinne Love		
Target Audience:	Neonatologists, Obstetricians, Paediatric Haematologists, Midwives		
Supersedes:			
Keywords (min. 5):	Bleeding, Treatment, Haemophilia, Vitamin K, Vaccination, Prophylaxis		

Guideline on the Management of the Fetus and Neonate with a Potential Bleeding Disorder

NHS Lothian

Version Control

Date	Author	Version/Page	Reason for change

Guideline on the Management of the Fetus and Neonate with a Potential Bleeding Disorder

NHS Lothian

Contents

1.0 Purpose

To provide guidance for the management of the fetus and neonate with a potential bleeding disorder.

2.0 Scope

To be used by all trained staff (nursing, medica, midwifery and pharmacy) as part of the management of fetuses and neonateswho have a potential bleeding disorder, who are patients of RHCYP/RIE Edinburgh. This may be at RHCYP, St John's Hospital or the Haemophilia unit RIE.

3.0 Definitions

FII: Factor II, FV: Factor V, FVII: Factor VII, FVIII: Factor VIII, FIX: Factor IX, FX: Factor X, FXI, Factor XI, FXIII: Factor XIII, VWD: Von Willebrand Disease, vWF:Ag: Von Willebrand Antigen, vWF:RiCof: Von Willebrand Ristocetin Co-Factor Assay, ICH: Intracranial Haemorrhage.

4.0 Roles and responsibilities

Author: Dr Matthew Howard-Jones (Consultant Paediatric Haematology).

Reviewers: Dr Susan Baird (Consultant Paediatric Haematology), Dr Rosina Shujaat (Consultant Paediatric Haematologist), Dr Andrew Page (Consultant Haematologist).

5.0 Introduction

The delivery and care of a neonate with a potential bleeding disorder can be challenging and frightening for both obstetric, midwifery and neonatal staff. This guideline is intended to provide clear and practical advice to all involved staff in the care of these patients. Dosing guidance is in the relevant treatment guidelines as replication of factor dosing has been avoided.

6.0 Main Content

Management of the fetus at risk of haemophilia during pregnancy and at delivery

General antenatal management

- The antenatal care of known or potential carriers of haemophilia should be undertaken by obstetric units in association with a haemophilia centre.

- Written management plans should be readily available on the patient electronic record (EPR).
- These plans should reflect input from the multidisciplinary team and include the haemostatic management of the mother and baby.

Genetic screening and fetal sexing

- Fetal sexing should be undertaken either by maternal blood sampling at around 10 weeks gestation or by US scan at between 18 and 20 weeks.
- Third trimester amniocentesis may be considered where confirmation of an affected male fetus will influence management at delivery.

Management of delivery

- Mode of delivery should be informed by both obstetric and haemostatic factors; haemophilia carrier status itself is not a contraindication to vaginal delivery.
- The option of elective caesarean section to reduce the risk of neonatal intracranial haemorrhage (ICH) may be considered on an individual basis, considering knowledge of the fetal haemophilia status and potential maternal morbidity.
- Ventouse extraction, rotational and mid-cavity forceps are associated with an increased risk of bleeding and should be avoided.
- Invasive monitoring procedures, such as placement of intrapartum scalp electrodes and fetal scalp blood sampling, should be avoided.
- Decisions regarding the management of labour should always involve a consultant and have had input from the obstetric haematology team.

Diagnosis of haemophilia/von Willebrand disease/other rare coagulation disorders/severe platelet disorders in the newborn infant

- A cord blood sample should be sent for relevant factor assays (FVIII or FIX), where the neonate is male and may have haemophilia A or B.
    - FVIII: Citrated sample (green-top) to the RIE laboratory.
    - FIX: Citrated sample (green-top) to the RIE laboratory.
- If the mother has history of any other clotting factor deficiency then this should be ordered on the cord blood.
- A cord blood sample should be sent for relevant factor assays (vWF:Ag, vWF:RiCof), where the neonate has a parent with moderate/severe VWD (e.g., Type II VWD, Type III VWD or Type I VWD with baseline VWF RiCof <20%).
    - vWF:Ag, vWF:RiCof: Citrated sample (green-top) to the RIE laboratory.
- A cord blood sample should be sent for relevant factor assays (intrinsic factors, common pathway/extrinsic factors, FXIII, alpha-1 antiplasmin, flow cytometry for

glycoproteins), where the neonate may have inherited a bleeding disorder that has been defined as moderate or severe or has excessive bleeding or bruising at time of delivery.
    - Fibrinogen: Citrated sample (green-top) to the RIE laboratory.
    - Intrinsic factors (FVIII, FIX, FXI): Citrated sample (green-top) to the RIE laboratory.
    - Common Pathway /Extrinsic Factors (FII, FV, FX): Citrated sample (green-top) to the RIE laboratory.
    - FXIII: Citrated sample (green-top) to the RIE laboratory.
    - Alpha-1 Antiplasmin: Citrated sample (green-top) to the RIE laboratory.
    - Flow Cytometry for Platelet Glycoproteins: Citrated sample (green-top) to the RIE laboratory to be couriered immediately or next morning to Gartnavel Hospital, Glasgow.
- These samples should be discussed with haematology; it is important that the cord sample is not contaminated with maternal blood. There may be a need for repeat which should be undertaken from venous sample carried out with care by experienced staff.
- Note: female neonates who are or may be carriers of haemophilia do not require cord blood sampling as they rarely have low factor levels.
    - This may be changed if there is a history of low level carriership.
- The diagnosis of haemophilia should be established using uncontaminated cord blood as soon as possible following delivery.
- Results should be interpreted using age/gestation-adjusted normal ranges.
- Appropriate assays should be carried out on the cord sample regardless of the coagulation screen if a bleeding disorder is suspected.

Management of the newborn infant with haemophilia

Vitamin K Administration

- Intramuscular vitamin K should be withheld until haemophilia is excluded. Oral vitamin K should be given if there is a delay in diagnosis or if haemophilia is confirmed.
- If the level of factor is >10% then the baby can have intramuscular vitamin K (based on the intramuscular vaccination advice from the COVID 19 vaccine). It does not matter if they have already had the oral vitamin K.
- Intramuscular vitamin K can be administered to patients with type 1 and 2 VWD unless there is a history of a low vWF:RiCof <0.2iu/ml (<20%), in which case oral vitamin K should be given until the vWF:RiCoF is known. If the infant is considered at risk of type 3 VWD they must have oral vitamin K administered.

- The diagnosis of a severe platelet disorder (Glanzmann Thrombaesthenia or Bernard-Soulier Syndrome) will be dependent on the platelet glycoprotein flow cytometry. This is usually available after a few days. The patient should have oral vitamin K.
    - If the diagnosis is confirmed on flow cytometry then oral vitamin K administration should continue.
    - If the diagnosis is disproved then intramuscular vitamin K can be offered irrespective of previous oral vitamin K doses.
- For families who do not wish the intramuscular route then the full oral course must be offered.
- All doses given and the route must be documented clearly in the EPR.

Management of bleeding

- Recombinant factor VIII or IX concentrate is the treatment of choice for Haemophilia A or B and should be immediately available. The dosing can be found in.
    - 'Guideline on the Treatment of Bleeds in Children and Young People with Haemophilia A and B Treated with FVIII'.
- For other deficiencies there should be a detailed plan on dosing, and doses can be found in.
    - 'Guideline on the Management of Von Willebrand Disease in Children and Young People'.
    - 'Guideline on the Treatment of Bleeds and Prophylaxis in Children and Young People with Rare Coagulation Disorders'.
    - 'Guideline on the Management of Inherited Platelet Disorders in Children and Young People'.
- Any factor replacement must be at the maximal dose or to 100% correction.
- Replacement therapy during the neonatal period should be monitored as neonates may require higher doses to achieve desired factor levels and may demonstrate a shortened factor half-life.
- Virally inactivated fresh frozen plasma 15-25ml/kg may be given if treatment is urgently required before the diagnosis of haemophilia has been confirmed.
- Desmopressin should not be given to a neonate as treatment for haemophilia.
- Heel stab sampling or careful venepuncture for other neonatal screening procedures should not be omitted and should be carried out with care by experienced staff.

Early detection and prevention of intra-cranial and extra-cranial bleeding

- Where there is a strong clinical suspicion of ICH (or other bleeding), factor concentrate should be given immediately and not withheld pending definitive imaging studies.
- If ICH is suspected they should have a cranial USS as soon as possible.

- Symptoms and signs of IVH in neonates.
    - Pauses in breathing (apnoea).
    - Slow heart rate (bradycardia).
    - Pale or blue colouring (cyanosis).
    - Weak suck.
    - High-pitched cry.
    - Seizures.
    - Lethargy, stupor, or coma.
    - Swelling or bulging of the soft fontanelles.
    - Anaemia.
    - Decreased reflexes.
    - Decreased muscle tone.
    - Abnormal eye movement.

Radiological assessment of intracranial bleeding

- Cranial US should be undertaken prior to discharge in all neonates with severe or moderate haemophilia.
- If ICH is suspected they should have a cranial USS as soon as possible.
- Due to the low sensitivity of US for the detection of subdural bleeding, cranial MRI or CT scan should be undertaken in symptomatic neonates even if an US is normal.

Prophylactic treatment of neonates with factor concentrates.

- Following confirmation of diagnosis, short term prophylactic replacement therapy should be given in neonates at increased risk of bleeding.
    - Traumatic delivery, including ventouse or forceps extraction.
    - Prolonged 2nd stage of labour.
    - Preterm delivery (<34 weeks).
    - Unexplained neurological signs.

Information on diagnosis and follow-up

- Parents of an affected neonate should be informed of the diagnosis and presenting features of significant bleeding prior to discharge from hospital by the paediatric haematology team. This will be a face to face visit and the mother and child must not be discharged until this has happened.
- Written information will be provided.
- This will include.
    - An information sheet for parents with a newly diagnosed baby.
    - Appropriate haemophilia society information which will be supplied/printed by the team.

    - Contact advice which will also be in written form.
- Early follow up by haemophilia clinician should be arranged prior to discharge.
- This will consist of.
    - An appointment on the day care unit within 2 weeks for severe/moderate disorders. This for families to be introduced to day care and to know where to come.
        - At this visit appointments for subcutaneous vaccinations will be arranged.
    - A clinic appointment at 6 weeks. The details of this will be provided before discharge.
    - All possible or obligate haemophilia carriers will be reviewed at 6-12 months, or earlier if bleeding symptoms or other concerns. No day care review is needed.
    - All other neonates who were tested at birth and found to have reduced factor levels, but not severe/moderate deficiency will be reviewed at 1-2 months, or earlier if bleeding symptoms. No day care review is needed.
    - All other neonates with possible mild bleeding disorder (e.g. Type 1 VWD), but levels not yet measured will be reviewed at 6-12 months. No day care review is needed.
- Childhood vaccinations
    - All children in whom a severe/moderate bleeding disorder is diagnosed at or shortly after birth should have their routine vaccinations by subcutaneous injection.
    - These will be delivered via the day care unit.
- Infants with possible mild vWD or possible carriers (i.e. those who are due to be assessed at clinic at 6-12 months of age) usually have their vaccinations as normal, although this will be reviewed in symptomatic neonates or carriers with particularly low levels.

7.0 Associated materials

Guideline on the Treatment of Bleeds in Children and Young People with Haemophilia A and B Treated with FVIII.

Guideline on the Management of Von Willebrand Disease in Children and Young People.

Guideline on the Treatment of Bleeds and Prophylaxis in Children and Young People with Rare Coagulation Disorders.

Guideline on the Management of Inherited Platelet Disorders in Children and Young People.

Factor Prescription Chart RHCYP

8.0 Evidence base

Moorehead PC, Chan AKC, Lemyre B, Winikoff R, Scott H, Hawes SA, Shroff M, Thomas A, Price VE. A Practical Guide to the Management of the Fetus and Newborn With Hemophilia. Clin Appl Thromb Hemost. 2018 Dec;24(9_suppl):29S-41S.

Chalmers, E., Williams, M., Brennand, J., Liesner, R., Collins, P., Richards, M. and (2011), Guideline on the management of haemophilia in the fetus and neonate[†]. British Journal of Haematology, 154: 208-215.

9.0 Stakeholder consultation

Haemophilia Multi-Disciplinary Team.

10.0 Monitoring and review

3-yearly Review.