

HAEMOPHILIA

Definition

A group of blood disorders in which there is a defect in the clotting mechanism. Of X-linked recessive inheritance, but in 30% there is no family history as it is a spontaneous new mutation. The most common haemophilias are:

- Haemophilia A – Deficiency of factor VIII (85% cases)
- Haemophilia B – Deficiency of factor IX (15% cases)

Clinical Manifestation

- bleeding in the neonatal period is unusual.
- usually present with easy bruising when crawling and walking (9-12 months age)
- haemarthrosis is characteristic of haemophilia. Large joints are usually affected (knee, ankle, elbow); swollen, painful joints are common.
- epistaxis, gum bleeding, haematuria also occur
- life-threatening intracranial haemorrhages can be life threatening
- bleeding may also occur spontaneously or after trauma or operation.

Diagnostic Investigations

- full blood count
- coagulation screen: PT, APTT (*in haemophilia: the APTT is prolonged, PT normal*)
- specific factor assay: FVIII level (low in Haemophilia A)
- specific factor assay: FIX level (low in Haemophilia B)

Table 6. Classification of haemophilia and clinical presentation

Factor level	Classification	Clinical presentation
< 1 %	severe	spontaneous bleeding, risk of intracranial haemorrhage
1-5 %	moderate	bleeding may only occur with trauma or after surgery
5-25 %	mild	

Further Investigations

- Hepatitis B surface antigen, anti HBS antibody
- Hepatitis C antibody
- HIV serology
- Diagnosis of carrier status for genetic counseling.
 - mother of a newly diagnosed son with haemophilia
 - female siblings of boys with haemophilia
 - daughter of a man with haemophilia

Once a child is diagnosed to have haemophilia, check the viral status at diagnosis and then yearly. This is because treatment carries the risk of acquiring viruses. All haemophiliacs should be immunized against Hepatitis B.

Treatment

- treatment consists of replacing the missing factor:
- Factor VIII concentrates for haemophilia A; Factor IX concentrates in Haemophilia B.
- avoid Fresh frozen plasma and cryoprecipitate as high risk for viral transmission.
- the dose of factor replacement depends on the type and severity of bleed (refer Table 7)

Table 7. Suggested replacement doses of factor VIII and XI concentrate

Type of bleed	Factor VIII dose	Factor XI dose
Haemarthrosis	20 U/kg	40 U/kg
Soft tissue or muscle bleeds	30-40 U /kg	60-80 U/kg
Intracranial haemorrhage or surgery	50 U/kg	120 U/kg

- alternative formula for calculating dose:
 - units of Factor VIII: (% rise required) x (weight in kg) x 0.5
 - units of Factor IX: (% rise required) x (weight in kg) x 1.4
- the percentage of factor aimed for depends on the type of bleed.
 - for haemarthroses, 30-40 % is adequate.
 - for soft tissue or muscle bleed aim for 40- 50 % level.
(there is potential to track and cause compression/compartment syndrome)
 - for intracranial bleeds or patients going for surgery, aim for 100%.
- factor VIII is given every 8 – 12 hours. Factor IX is given every 12 – 24 hours.
- duration of treatment depends on type of bleed:
 - haemarthroses 2-3 days
 - soft tissue bleeds 4-5 days
 - intracranial bleeds or surgery 7-10 days.

Supportive Treatment

Analgesia

There is rapid pain relief in haemarthroses once missing factor concentrate is infused. If analgesia is required, avoid intramuscular injections. Also do not use aspirin or the non-steroidal anti-inflammatory drugs (NSAIDS) as risk of bleeding.

Dental care

Good dental hygiene is important as dental caries are a regular source of bleeding. Dental clearance with factor replacement will be required in severe cases.

Immunisations

These are important and must be given: in this case intramuscular injections are allowed: use the smallest gauge needle to minimise trauma. If a baby has had a haematoma after immunization, give the next injection under factor cover.

Complications

Joint destruction

Recurrent haemarthroses into the same joint will destroy the joint causing osteoarthritis and deformity. This can be prevented by prompt and adequate factor replacement.

Acquisition of viruses

Hepatitis B, C or HIV: immunisation and regular screening is recommended.

Inhibitors

In 15-25% cases of haemophilia A, patients may develop antibodies to the missing factors. This is suspected when factor replacement does not result in clinical improvement. If a patient is suspected to have inhibitors, the case should be discussed with a haematologist.

SPECIFIC GUIDELINES FOR MANAGEMENT

Intracranial haemorrhage (ICH)

- give factor replacement before suspected bleed is confirmed by CT scan
- aim to increase Factor VIII:C level to 100%
- for haemophilia B, aim for 80 % if monoclonal factor IX is used, or 50 % if prothrombin complex concentrate (PCC)
- urgent CT scan:
 - if scan confirms ICH : maintain factor level > 50% , give factor concentrates 6-8 hourly for at least 3-5 days depending on the clinical response, then reduce dose to maintain at 30%, initially 12 hourly and then daily up to a total of 10 -14 days replacement therapy
 - if CT scan show no evidence of ICH, admit 1 day for observation
- lab investigations:
 - full coagulation profile – PT,PTT
 - pre-treatment factor assay level and inhibitor level before starting treatment and to repeat after 3 days of treatment to ensure adequate levels have been achieved and no inhibitor has developed
 - post treatment factor assay level (½ hour after infusion) to ensure required factor level is achieved (if the level is not achieved , consider development of inhibitors) and should be repeated after 3 – 5 days
- follow up CT scan after 2 weeks

Surgery

- pre-op investigations
 - full coagulation profile – PT, PTT
 - pre-factor assay level and inhibitor level
 - blood grouping, full antibody screening and full cross matching if required
- calculate dose
 - ½ hour before operation, infuse patient with appropriate factors.
 - preferable level :
 - 80-100% for factor VIII
 - 70% for monoclonal factor IX
 - 50% if prothrombin complex concentrate (PCC) used
- check post transfusion specific factor level ½ hour later if necessary or after surgery to ensure correct factor level is achieved
- clotting factor level should be maintained above 50% during the operation and 24 hours after surgery.
- repeat pre factor assay and check inhibitor level on day 3 to ensure adequate level and no inhibitors have developed
 - day 3 till day 7 – maintain at 50%
 - day 8 till day 14 – reduce the dose gradually
- replacement therapy is recommended post operatively for at least 10 -14 days
- replacement therapy should be given as long as there is bleeding plus another 5 –10 days after the bleeding stops, until the wound heals

Iliopsoas bleed

Investigations

- abdominal ultrasound to assess the size of haemorrhage
- full coagulation profile, pre-factor specific assay and inhibitor screen
- full blood picture
- renal function test

Management

- complete bed rest
- give factor replacement early - aim for level > 50% for haemophilia A & B
- maintain level > 50% with factor concentrates given 8 hourly for haemophilia A and 12 hourly for haemophilia B for at least 3-5 days. Reduce dose accordingly.
- a minimum of 10 – 14 days replacement therapy is recommended
- physiotherapy – when pain subsides
- repeat abdominal ultrasound 1 week later to assess progress

Haematuria

Management

- bed rest
- drink plenty of water (1 ½ maintenance).
- monitor for first 24 hours: UFEME & Urine C&S
- if bleeding persists for > 24 hours, start factor concentrate infusion.
- perform KUB & Ultrasound of the kidneys

DO NOT give anti-fibrinolytic drugs (tranexamic acid) because this may cause formation of clots in the tubules which may not recanalize.

Haemarthroses (Joint haemorrhages)

- episodic replacement therapy is the main stay of treatment
- most spontaneous haemarthroses respond to a single infusion of factor concentrate. Aim for a level of 30 % to 40%.
- if swelling or spasm is present, treatment to level of 50% is required and infusion may have to be repeated at 12-24 hours interval, until pain subsides
- minor haemarthroses may not require immobilization
- elastic bandage or slings and ice may help in pain relief
- in severe haemarthroses:
 - rest, splint in position of comfort, give analgesics if required
 - factor replacement
 - joint rehabilitation to be started as soon as possible

HAEMOPHILIA SOCIETY

All haemophiliacs should be registered with the Haemophilia Society, and have a medic-alert bracelet/chain which identifies them as haemophiliacs. They usually carry a book in which the diagnosis, classification of severity, types of bleeds and admissions can be recorded.

Address: The Haemophilia Society of Malaysia
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