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**GSTFT Clinical Practice Guideline**

**Paediatric Thalassaemia Guidelines**

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## **Thalassaemia Disorders**

The thalassaemia are genetic disorders of haemoglobin production. Most are inherited in an autosomal recessive pattern and in the case of  $\beta$  thalassaemia major are due to mutations of the  $\beta$  globin gene causing reduced or absent production of  $\beta$  globin and as a result, Hb A. This results in globin chain imbalance and subsequent ineffective erythropoiesis, anaemia and bone marrow expansion.

Most of the patients seen at the Royal London Hospital can be classed as having  $\beta$  thalassaemia major or  $\beta$  thalassaemia intermedia. Patients with  $\beta$  thalassaemia major need regular transfusions from infancy to maintain normal growth and development. Those with thalassaemia intermedia (usually Hb E /  $\beta$  thalassaemia) may only require transfusion for specific indications. Untreated anaemia results in cardiac failure.

Other than transfusion therapy, standard treatment also consists of iron chelation therapy usually started a year after regular transfusions have begun. Good compliance with this treatment is necessary to prevent iron induced toxicity to the heart, liver and endocrine organs.

Diagnosis of  $\beta$  thalassaemia is often made in the neonatal period following identification of 'at risk' pregnancies and by the neonatal screening programme. However not all cases of thalassaemia intermedia will be identified this way. Older children with thalassaemia may also present following migration of families to the UK from high prevalence regions.

### **Management of the Newly Diagnosed Child**

All infants identified by the neonatal screening programme should have an initial home visit organized by a specialist nurse counsellor. Referral to the local centre and review should be planned within 2 weeks of the diagnosis.

Following careful history and examination, particularly to monitor growth and development, the diagnosis should be confirmed as below:

#### **1. Routine Baseline Investigations:**

- FBC and blood film
- Haemoglobin analysis by HPLC
- Genetic analysis for  $\beta$  globin mutations
- A thalassaemia genotype and Xmn status
- G+S and red cell phenotype
- G6PD screen

In older children presenting with an uncomplicated thalassaemia, and those scheduled to start transfusion therapy viral hepatitis screen, serum ferritin and LFTs should also be added.

#### **2. Additional Investigations:**

Other tests may be indicated based on presentation eg acutely presenting untreated patients

- Bone profile (Ca, phosphate)
- Glucose

- TFTs
- ECG
- USS abdomen
- CXR
- Echocardiogram , Septic screen

All children with  $\beta$  thalassaemia major require initial monthly review with monitoring of growth, development, presence of organomegaly, head circumference and FBC. More frequent monitoring may be required for those with increased transfusion requirement.

Appropriate written information should be made available and details of community support networks explained. Hand held patient information records should be encouraged.

Family members should be offered screening.

For patients previously treated outside of the UK enquiry should into age/mode of diagnosis, transfusion history, chelation history, and history of complications. A careful evaluation for complications should be carried out.

### **Transfusion Policy**

- Most patients will attend Paediatric Phlebotomy on Ocean floor for pre-transfusion sampling (FBC, G+S, U+Es, LFTs)
- This will be requested by the Day Case Unit-bleep 0821
- This should be done to minimize absence from school but no later than 1700
- ‘All-in-one’ transfusions are prearranged with the haematology team and are for exceptional circumstances only
- Patients should arrive on Arctic day Case Unit, according agreed time
- Patients will be admitted to the available ward by the allocated nurse, weight and observations recorded and reviewed by the junior doctor covering the day unit
- The transfusion prescription will be organized by the junior doctor according to the transfusion algorithm below
- Prompt cannulation will be organized by the paed SHO or CNS
- Patients arriving later than 12pm (regular transfusion) and 11am for ‘all in one’ will be rescheduled
- Evening transfusion sessions end at 8pm or patient is transferred to Mountain ward
- An accurate electronic transfusion record will be recorded for each patient with documentation of transfusion date and volume

### **Decision to Start Transfusions**

This is a clinical decision based on

- Evidence of severe anaemia (usually  $<7\text{g/dL}$ )
- Failure to thrive
- Thalassaemic bone deformity

Infants will be monitored for signs and symptoms indicating need for transfusion. The aim is to initiate transfusion to prevent the complications of anaemia and bone marrow expansion. Attention should be paid to:

- Worsening fatigue
- Poor feeding and impaired growth
- Developmental delay or regression
- Worsening splenomegaly
- Facial bone expansion

Factors contributing to anaemia should be investigated

- Iron deficiency
- G6PD deficiency
- Intercurrent infection

### **Transfusion Algorithm**

Aim to maintain pre transfusion Hb 9.5-10g/dL. Transfusions are given 3-4 weekly.

***Hb <9g/dl, transfuse 20ml/kg and bring back 1 week earlier***

***Hb 9-9.5g/dl, transfuse 20ml/kg***

***Hb 9.5-10.5g/dl, transfuse 15ml/kg***

***Hb 10.5-11.5g/dl transfuse 10ml/kg***

***Hb >11.5 No transfusion- come back in 1 week***

**Prior to commencing transfusion programme potential complications of transfusion must be discussed and documented.**

- 1. Transfusional iron overload.**
- 2. Transfusion transmitted infection – aim for Hepatitis B /C + HIV screen prior to starting.**
- 3. Transfusion reactions.**
- 4. Ensure hepatitis B vaccination status satisfactory**

### **Annual Investigations**

Annual virology (hepatitis B,C, HIV) should be organised for all patients on regular a transfusion programme in January. Vaccination for hepatitis B should be organised prior to the first transfusion and booster doses administered as necessary following annual monitoring of anti HBs titre.

## Iron Chelation

Please see chelation policy for chelation options, monitoring for iron overload and monitoring chelation therapy.

### Management of Complications

#### Endocrine Complications

Endocrine complications predominantly due to iron overload are not uncommon. Delayed puberty and hypogonadism are most commonly seen. Endocrine failure is difficult to reverse but can be prevented with iron chelation therapy and should be screened for and actively managed.

#### **Monitoring:**

- Biannual growth monitoring (sitting and standing height / weight)
- Annual assessment of pubertal development from age 10
- Random glucose 3-6monthly
- Glucose tolerance test from puberty or age 10 if family history
- Bone profile 3-6monthly from age 12
- Annual TFTs from age 12
- Consider 25 OH Vit D / PTH if deranged bone profile
- Dexa Scan from age 10

All complications should be discussed and jointly managed with a paediatric endocrinologist.

Declining height velocity should be investigated; Desferrioxamine toxicity and growth hormone deficiency should be considered.

Delayed puberty should be investigated, hormone replacement therapy should be considered.

**Exercise and adequate consumption of diet rich in Vitamin D / calcium should be encouraged.**

#### Liver Complications

**Liver disease is common. This is due to iron loading, biliary disease, viral hepatitis and potential drug toxicity.**

Clinical presentation includes acute and chronic hepatitis, obstructive jaundice, cholangitis, portal hypertension, hepatic failure and hepatocellular carcinoma.

#### Monitoring:

- Monthly LFTs
- R2/T2\* MRI monitoring for iron loading

**All complications should be discussed and jointly managed with a paediatric hepatologist.**

Liver biopsy may be needed for unexplained changes to liver function.

Hepatitis C should be actively treated.

USS should be considered to screen for gallstones if obstructive picture.

### Cardiac Complications

Cardiac complications are less commonly seen in children.

Monitoring:

- Cardiac T2\* MRI monitoring should be organized from age 8-Refer Royal Brompton-Prof Pennel
- Assessment by Paediatric cardiologist should be scheduled from age 10

### Acute Decompensation and Sepsis

There is increased risk of sepsis and subsequent increased mortality particularly in splenectomised patients. Risk factors include:

- Previous splenectomy
- Use of central venous catheters
- Iron chelation therapy
- Transfusion transmitted infection

Fever should be investigated and treated promptly.

Splenectomised patients with fever should be admitted for IV administration of broad spectrum Antibiotics (piperacillin/tazobactam/amikacin) .

For central venous catheter associated sepsis vancomycin / teicoplanin should be considered.

Chelation therapy should be interrupted during acute illness due to sepsis.

Yersinia infection should be considered in patients presenting with fever and abdominal pain and treated with ciprofloxacin.

All patients presenting with fever on chelation therapy with deferiprone and deferasirox should have an urgent FBC organized to exclude neutropenia / agranulocytosis.

Other presenting complications include:

- Dysrhythmias, heart failure
- Acute hepatitis (consider viral, chelation associated )
- Endocrinopathy (tetany due to hypoparathyroidism, hyper/hypoglycaemia)

Urgent specialist haematology input is necessary with input from paediatric specialists when managing these complications.

Authorship

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