ပြည်ထောင်စုမြန်မာနိုင်ငံ၊ အထူးဒေသ(၁) ကျန်းမာရေးဌာန

缅甸联邦第一特区卫生部

The Union of Myanmar, SR(1) Department of Health

Thalassaemia

Standard Operating Procedure (SOP)

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HAEMATOLOGY

Thalassaemia

Clinical Diagnostic Features

- Pallor which is long standing and gradually progressive
- Lethargy and failure to thrive from chronic anaemia
- Jaundice which is usually mild and intermittent
- Thalassaemic face
- Hepatosplenomegaly
- Have family history of thalassaemia

Investigations

For all new patients

- Complete blood count (CBC)-Hypochromic microcytic anaemia
- Increased retic count
- Haemoglobin electrophoresis
  - Typical finding: HbA decreased or absent, HBF increased, HBA, variable
  - In addition, parents and siblings should be screened
- Serum ferritin-Increased
- Infection screen-HIV, Hepatitis B & C, VDRL screen (Before first transfusion)
- Every three months, bilirubin, AST (SGOT), ALT (SGPT), and alkaline phosphatase should be measured via a blood test, If ALT is elevated, it should be repeated in two weeks

Treatment

Blood transfusion

- The mainstay of care for child with thalassaemia major and many with intermedia
- Purpose of transfusion
  - To improve anaemia
  - To suppress ineffective erythropoiesis0
  - To prevent skeletal, and neurological complications
- Decision to start transfusions is based on Signs of increased cardiac effort (Tachycardia, sweating, poor feeding)
  - Poor growth
  - Bone changes
  - Massive splenomegaly
  - Inability to maintain daily routine activities as going to school

- Evidence of organ dysfunction

Assessing the need for routine transfusions

- Start regular transfusions when initial haemoglobin level <6 g/dL
- Haemoglobin level<7 g/dL may require regular transfusions in the presence of growth impairment, marked skeletal changes or extramedullary haematopoiesis
- If symptom of anemia is not severe and hemoglobin level s7 g/dL, with hold transfusions and monitor hemoglobin level weekly
- If hemoglobin drops <7 g/dL on two occasions regular transfusions should becommenced

Transfusion administration and monitoring

- Type of blood product
  - Packed red blood cells
- Should be assessed for haemolytic reactions if any adverse event is noted during transfusion
- Patients who develop allergic reactions should be given washed packed red blood cell
- **Target haemoglobin and frequency of transfusions**
  - To maintain the haemoglobin level between 9 and 10 g/dL, give packed cell 10-15 ml/kg
  - Duration for transfusion should be 5 mL/kg per hour
  - Post-transfusion haemoglobin should not exceed 14 g/dL
- Transfusion interval- Three to four weeks for thalassemia major patients depending on Hb percent
- In patients with severe anaemia (haemoglobin less than 5 g/dL) or cardiac compromise, the rate of transfusion should be reduced to 2 mL/kg/hour
- Avoid fluid overload with furosemide (1 mg/kg)
- If cardiac insufficiency is present, higher pre-transfusion haemoglobin levels (10 to 12 g/dL) should be maintained with smaller volume transfusions given every one to two weeks
- Patient's weight, pre-transfusion hemoglobin and volume of transfusion should be recorded at each visit

Splenectomy

Indications of splenetomy in thalassaemia major

- Very huge splenomegaly causing discomfort
- Transfusion requirement increases to 1.5 times normal or more than 250 ml/kg/ year of packed red cells or more than 400 ml/kg/year of whole blood
- Evidence of hypersplenism

Note

- Give pneumococcal and HIB vaccinations 4-6 weeks prior to splenectomy
- Meningococcal vaccine required in endemic areas

- Penicillin prophylaxis (125 mg twice daily for <5 year and 250 mg twice daily for >5year) for life after splenectomy and be instructed to seek urgent medical attention for a fever over 101°F
- Low dose aspirin (75 mg daily) if thrombocytosis >800,000/mm after splenectomy
- Before splenectomy, if platelet count is reduced- Give PRP and prednisolone 2 mg/kg, dayx4 days

Iron overload and chelation Therapy

- Iron overload is the major cause of morbidity for thalassaemia patients
- Even non transfused patients develop iron overload secondary to increased intestinal absorption of dietary iron.

Goals of iron chelation therapy

- Binding of toxic non-transferrin bound iron in the plasma
- The removal of iron from the body.

Initiation of chelation

- lit is important to delay the start of chelation until the patient is significantly iron loaded
- The decision points are based on total amount of blood transfused and ferritin levels
- Chelation should be started when patient becomes significant iron loaded
- Usually when the child is >2 years old and when the serum ferritin reaches1000 ng/ml.
- This usually occurs after 10-20 unit blood transfusions

Desferrioxamine (Desferral)

- Dosage and route
  - Average daily dose is 20-60 mg/kg/day by subcutaneous continuous infusion using a portable pump over 8-10 hours daily, 5-7 nights a week
  - Aim to maintain serum ferritin level below 1000 ng/ml
  - Vitamin C augments iron excretion with Deferral

Deferiprone/L1 (Kelfer/Ferriprox)

- Can be given orally as an alternative if iron chelation is ineffective or inadequate despite optimal Desferral use,or if Desferral® use is contraindicated. (However, there is no formal evaluation in children <10 years of age)
- Deferiprone is given 75-100 mg/kg/day in 3 divided doses
- Can also be used in combination with Desferral®, using a lower dose of 50mg/kg/day.

Side effects:
Small risk of reversible agranulocytosis, arthritis or gastrointestinal disturbance

Weekly full blood counts are advised. Stop if neutropenic (<1,500/mm³)
Zinc deficiency may occur particularly with deferiprone and require supplementation.
Deferasirox (Exjade) is recently approved for use in transfusional iron overload inpatients 2 years or older, The advantage is giving once daily in oral form. The dose is20-30 mg/kg/day in liquid dispersible tablet. There is a small risk of transient skin rash GI disturbance and a reversible rise in serum creatinine below upper limit of norma (ULN) in some patients, Monthly monitoring of renal function is required.

Regular Screening

Every 3-6 months

- Evaluate growth and development
- Serum ferritin
- Liver function test

Every year or more frequent if indicated

- Evaluate growth and development
- Endocrine assessment- RBS, T4/TSH, Ca, PO, (If Ca low - Check PTH and vitamin D)
- Pubertal and sexual development from 10 years onwards
- Tanner stage of breast and genitalia
- Infection screen (6 monthly)- Hepatitis B and C, HIV, VDRL Calculate transfusion indices (Volume of pure red blood cell transfused/median weight)
- Evaluate iron balance
- Bone-Osteoporosis and skeletal abnormalities

Cardiac dysfunction

Cardiac assessment at variable intervals and especially after 10 years of age

- Yearly ECG and echocardiography

Infection

- Remains a major cause of death
- Treating serious infections will prevent unnecessary mortality.
- Prompt treatment with broad spectrum antibiotics should start before the results
- Blood cultures are indicated as there is an increased risk of Yersinia enterocolitica infection

Dental evaluation

- The teeth can be significantly affected in patients with thalassemia
- Addition to regular annual dental care, thalassemia patients should be evaluated by a dentist to determine if bony changes requiring orthodontic treatments have developed

Nutrition

- Adequate dietary intake of calcium, vitamin D, folate, trace minerals (copperzinc, and selenium) antioxidant vitamins (E and C)
- Multivitamin supplementation without iron
  Note: Vitamin C should be used only with Chelation treatment (Vitamin C increased iron absorption)
- Folate supplementation- 1-5 mg/day
- Avoiding iron- Fortified cereals and excessive consumption of red meat

Vaccinations

- Optimal immunization is critical for all patients with thalassaemia, especially transfused patients and splenectomized patients
- Prior to splenectomy-should receive meningococcal conjugate vaccine andshould be up to date for Hib, Pnuemococcal boosters should be considered every five to ten years