Nursing Practice Guidelines: Care of the Patient with Sickle Cell Disease and Iron Overload

Introduction

The International Association of Sickle Cell Nurses and Physician Assistants has developed this guideline with the intention of promoting interaction among disciplines to ensure consistency of practice for patients with sickle cell disease and iron overload. This nursing practice guideline is not intended to limit or dictate practice for iron overload therapy.

Transfusion therapy is often used to treat complications of sickle cell disease (see *Nursing Practice Guideline for Care of the Patient with Sickle Cell Disease Receiving Transfusion Therapy*). Patients who receive recurrent or chronic red blood cell transfusions will eventually accumulate excess iron because the human body has no mechanism to eliminate iron from the body. One unit of packed red blood cells (PRBC) contains approximately 200-250 mg of iron; chronically transfused patients have an iron excess of approximately 0.4 to 0.5 mg/kg/day (1 gram/month). With repeated transfusions, iron accumulates and signs of iron overload may be apparent after 10-20 transfusions.

Although iron is an essential nutrient that is critically important for oxygen transport, and iron deficiency remains the number one nutritional deficiency worldwide, excess iron deposits as insoluble hemosiderin in vital organs. Without a means to eliminate this deposition, iron overload ultimately leads to increased oxidative stress, tissue damage and end organ failure, particularly of the liver, heart and endocrine organs.

Thus, there is a need for methods in which to quantify iron accumulation and treat iron overload in a safe, accurate/effective and readily available way.

Assessment

Effective management of iron overload begins with frequent assessment of iron burden. Ideally, this should be a quantitative method of iron measurement which is safe, effective, and provides a high level of accuracy.

Typically treatment for iron overload is felt to be needed when one or all of the following parameters are met:

- cumulative blood transfusions equal or surpass 120-200 mL PRBC's/kg of body weight/year (approximately 1-2 years after starting chronic transfusions)
- liver iron content (LIC) by biopsy, superconducting quantum interference device (SQUID) or Magnetic Resonance Imaging (MRI) is elevated above 7mg/g dry weight
- liver/cardiac MRI or SQUID is not available and persistently elevated ferritin levels of 1000-1500 are present in the steady state

Lab testing:

- Serum ferritin
  - Advantages:
    - easy to perform on a frequent basis
    - at present there is no other serum marker which is a better indicator of body iron stores
  - Disadvantages:
    - results may be influenced by infection/inflammation, vitamin stores and liver disease.

Radiology testing:

- Magnetic Resonance Imaging (MRI-with specialized software)
  - Advantage:
    - validated with good correlation to liver biopsy in some diseases
  - Disadvantage:
    - has not yet been validated in sickle cell disease
    - may not be readily available
- Superconducting Quantum Interference Device (SQUID)
  - Advantage:
    - direct assessment based on magnetic susceptibility of iron
  - Disadvantage
    - not readily available
- Ferriscan™
  - Advantage:
    - diagnostic test service uses existing MRI machines which have been configured to provide suitable scans of the liver
  - Disadvantage
    - images are analyzed at a centralized image analysis center (Australia) to quantify iron loading using proprietary software
    - additional cost to the standard MRI scanning fee
- Computed Tomography (CT)
  - Not recommended
- Liver Biopsy:
  - Advantages:
    - liver is the major site of iron storage, and accounts for about 70% of total body iron stores
    - considered to be the best predictor of body iron stores
  - Disadvantages:
    - risk for bleeding and infection
    - uneven distribution of iron secondary to fibrosis in cirrhotic livers

Intervention

Iron overload can be effectively managed with the *consistent* use of an iron chelating agent. Currently available products include oral, subcutaneous and intravenous medications. These medications are capable of selectively binding intracellular and plasma iron to varying degrees and facilitating iron excretion in either the urine or feces. Each medication to be reviewed has different binding affinity to iron, optimal dosing schedule and common toxicities.

- Chelation Agents:
    - Oral
        - Defirosirox (Exjade)
            - rapidly absorbed
            - usual dose is 20-40mg/kg/day; once daily dosing; mixed in water, orange juice or apple juice and taken on empty stomach
            - fecal excretion
            - toxicities include nausea, diarrhea, skin rash, renal or liver toxicities
            - licensed in the US and distributed through assigned specialty pharmacies
            - requires scheduled monitoring for specific toxicities
                - monitor complete blood count (CBC), reticulocyte count, ferritin,
                - renal and liver function monthly
        - Deferiprone (L1)
            - rapidly absorbed-short plasma half-life
            - usual dose is 75mg/kg/day orally and divided in three doses;
            - urinary excretion
            - may be effective when used in combination with other chelating agents
            - toxicities include neutropenia, agranulocytosis, arthropathy, transaminitis
                - monitor CBC with differential monthly; monitor ferritin, renal and liver function quarterly
            - licensed in Europe; compassionate use in US
    - Subcutaneous or intravenous
        - Deferoxamine (desferol)
            - usual dose is 25-50mg/kg infused subcutaneously over 8 to 12 hours, 5 to 7 days/ weekly or intravenously over 24 hours
            - urinary, fecal excretion
            - toxicities include local injection site reactions, hearing loss or tinnitus, vision changes (cataracts, night blindness, visual field changes, blurred vision), growth retardation, osteopenia/osteoporosis, infection
            - requires scheduled monitoring for specific toxicities
                - monitor for changes in hearing, night blindness or blurred vision, local reactions, growth parameters
                - routine vision and hearing testing
            - intravenous administration requires internal or external catheter

- indicated for severe iron overload with symptoms/complications such as decreased cardiac function, decreased ejection fraction or increasing cardiac iron as measured by T2*
- routine cardiac monitoring (echocardiogram, holter monitoring, T2*/MRI if available)

- Phlebotomy:

(see *Nursing Practice Guideline for Care of the Patient with Sickle Cell Disease Receiving Transfusion Therapy*)

- A safe, effective, inexpensive and well tolerated means to remove excess iron
- Follow institutional guidelines; monthly schedule
  - In general, remove 5-10 ml/kg of venous blood at 5-10ml/ minute increments; needs large bore (20 gauge catheter) intravenous access; following phlebotomy infuse an equal volume of normal saline solution over 30 minutes
- Preferred method for iron overload associated with hemochromatosis
- Excellent alternative to chelation therapy in patients with transfusional iron overload if transfusions can be discontinued.

- Exchange Transfusion:

(see *Nursing Practice Guideline for Care of the Patient with Sickle Cell Disease Receiving Transfusion Therapy*)

- Method of choice when available to achieve a negative iron balance in those patients who require chronic transfusion.

Management

Management

- Recommend follow up in Comprehensive Sickle Cell Center
- Carefully monitor volume of red blood cells transfused to assess rate of iron accumulation
- Obtain serum ferritin every two to three months; monthly as previously noted for oral chelation surveillance
- Obtain liver iron content by liver biopsy, SQUID if available or MRI if available at the initiation of chelation, and then every one to two years
- At initiation of chronic transfusion, patients and family members should receive education about iron overload and the future need for chelation therapy

Treatment

- Automated exchange transfusion when available and feasible
- Initiate chelation therapy
  - After one to two years of transfusion therapy &/or
  - Cumulative blood transfusions ≤ 200 ml of packed red blood cells/kg of body weight &/or
  - Liver iron content ≥ 7mg/gm dry weight &/or
  - When liver biopsy/SQUID is not an option and ferritin levels persistently exceed 1000 ng/ml.

Education

- As noted, all patients and family members should receive education about iron overload and the future need for chelation therapy at the initiation of chronic transfusion. This education should continue and be built on at each subsequent visit.
- Compliance with prescribed therapy should be evaluated at each visit; recommendations should be reviewed and strategies to aid with compliance should be enlisted.
- Every attempt should be made to accommodate chelation therapy within the patient and families existing lifestyle.

References

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