Iron Overload from Chronic blood Transfusion

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15th Oct 2016
Moncton patient education day
What is the role of Iron.

Iron metabolism.

Why iron overload is a bad thing.

How can we remove extra iron.

Current recommendation for treatment of iron overload.

What does Iron do?

- Oxygen transport
  1- Hemoglobin RBC.
  2- Myoglobin (muscle cells)

About 70% of the body’s iron is in these proteins.
Iron Shortage

- Iron Deficiency:
  - Blood loss,
  - Low intake.
  - Malabsorption.

About 1000 mg of iron is stored as ferritin. Intestinal absorption of iron increases in response to deficiency.
Iron Overload

- Iron is exerted by shedding off intestinal cells.
- There is no renal excretion of iron.

Iron Overload

Easy to diagnose and treat -- if you think of it.

diabetes
gray skin
joint pain
dilated cardiomyopathy
heart rhythm disturbances

Primary iron overload:
The duodenum absorbs iron too well. Genetic.

High Fe/TIBC ratio

Elevated liver enzymes
cirrhosis
addisonism

Gross

Microscopic

Prussian Blue stain

Treat it BEFORE
cirrhosis develops!
Blood transfusion

- Normal daily iron flux is 1-2 mg.
- Patients who receive transfusion, each unite of blood contains 200-250 mg.
Iron balance

- Normally not much iron enters or leaves body.
- The body can’t increase its excretion of iron.
- Blood transfusions contain much iron so patients who need frequent transfusions will build up excess iron.
Diagram showing iron metabolism:

- Red blood cells: 1800 mg/day
- Bone marrow: 300 mg
- Liver: 1000 mg
- Other cells and tissues: 400 mg

Iron loss: 1-2 mg/day

Iron absorption in the duodenum: 1-2 mg/day

Iron is transported as iron(III) transferrin (Fe(III)Tf).
When does iron become a problem?

- Normally 2.5-3 grams of iron in the body.
- Tissue damage when total body iron is 7-15 grams. After 30-50 Unites of red blood cells.
Iron Overload

Organs that may be affected by iron overload:

- Pituitary gland
- Thyroid and parathyroid gland
- Adrenal gland
- Heart and circulation
- Liver
- Pancreas
- Testis
- Man
- Woman
- Ovary
Course of Hereditary Hemochromatosis

- Genetic mutation
- Asymptomatic
- Non-specific symptoms
- Signs of organ damage
- Bronze diabetes
- Early death

Body Iron Content in Grams vs. Age
How do we diagnose iron Overload?

- History.
- Serum ferritin level.
- Liver Biopsy.
- Magnetic resonance imaging MRI.
Serum Ferritin Level

- Easy.
- Inexpensive.
- Can be misleading in cases of liver function abnormalities, or inflammation.
Liver Biopsy

- Specific.
- Invasive, and potentially risky.
- Not often needed for patients with chronic transfusions.
Magnetic Resonance Imaging
Iron Overload

- Iron overload caused by transfusions causes malfunction of the liver, heart, and endocrine organs.
- Problems may begin after 30 units of red blood cells.
- Serum Ferritin helps to estimate iron levels.
- MRI.
How can we treat?

- Iron Chelation = pumping out iron.
What is Chelation Therapy?

Chelator + Metal → Toxic

Metal + chelator → Non-Toxic

Outside The Body
What are the available agents?

- Dferoxamine (Desferal)
- Deferasirox (ICL670, EXJADE)
- Alternative: Deferiprone (L1)
Challenges of Deferoxamine

- Subcutaneous/Intravenous route of administration
  - Expensive.
  - Cumbersome.
  - Uncomfortable.

Rapid metabolism (30 min half life) necessitates prolonged infusion (12-15 hours)

Complications due to iron overload still occur due to poor compliance with therapy.
Deferoxamine infusion
Overall survival in patients with myelodysplastic syndromes (MDS) according to receipt of ICT in a subgroup analysis.

Heather A. Leitch, and Linda M. Vickars Hematology
2009;2009:664-672
Overall survival of transfusion-dependent patients with myelodysplastic syndrome (MDS) according to ferritin level.

RA/RARS/5q–
(HR = 1.42, p < 0.001)

RCMD/RCMD-RS
(HR = 1.33, p = 0.07)

Heather A. Leitch, and Linda M. Vickars Hematology
2009;2009:664-672

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Common Side Effects of Deferoxamine

- Local reactions
  - Erythema (localized redness)
  - Induration (localized swelling)
  - Pruritus (itchiness)

Ophthalmologic

- Reduced visual acuity
- Impaired color vision
- Night blindness.

- Increased by presence of diabetes.

Hearing loss, Zinc Deficiency.
Iron Chelation and deferroxamine

- Chelation works by attaching a drug to iron, which allows the body to excrete it.

- Deferoxamine is inconvenient and uncomfortable but works.
Deferasirox; Exjade

- Oral, dispersible tablet.
- Taken once daily.
- Highly specific for iron.
- Chelated iron excreted mainly in faces.
- Less than 10% excreted in urine.
Exjade is Generally Tolerable

- The most common adverse events were mild and transient:
  - Nausea (10%)
  - Vomiting (9%)
  - Abdominal pain (14%)
  - Diarrhea (12%)
  - Skin rash (8%)

Rarely required discontinuation of drug.

There are reports of Kidney failure, worsening blood counts.
Exjade is Available.

- Approved in 2006 for chronic iron overload in patients with transfusion dependent anemias aged 6 years old and older.

- Chronic iron overload is patients with transfusion-dependent anemias aged 2-5 years old who can’t be adequately treated with deferoxamine.
Exjades works

Canadian Guidelines;

- **Why:** to prevent end-organ complications of iron overload and extend lifespan.

- **Whom:** transfusion-dependent patients with expected survival >1 year or BMT candidates.

- **When:** ferritin >1000, TfSat>0.5.

- **How:** DSX 20 mg/kg/day or DFO 50 mg/kg/day 5/7; target ferritin <1000.

Iron Overload in Myelodysplastic Syndrome: A consensus Guideline. 2008
Summary

- Iron overload is an inevitable consequence of Chronic RBC transfusion.
- Iron toxicity affects the function of the liver, heart, and endocrine organs.
- Chelation therapy should be offered to iron overloaded patients with life expectancy > 1 year.
- Desferal and Exjade are both effective.
Thanks, Questions?