Iron overload and chronic blood transfusion

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Blood transfusions and iron chelation have changed the natural course of both thalassemia major (TM) and sickle cell disease (SCD) in industrialized countries. In TM, the institution of a transfusion program is required at a very early age in order to avoid the effects of anemia and the deformity of facial features. In SCD, transfusions transfusions may be needed occasionally for several acute complications or regularly for some chronic complications. Unfortunately, transfusions come with a downside: iron overload. Excessive iron accumulates in several organs and is responsible for organ injury.

The organs mainly affected by iron overload are: the liver (fibrosis, cirrhosis, liver failure, hepatocellular carcinoma); the heart (heart failure, arrhythmias); the pancreas (diabetes); endocrine glands (hypogonadism, hypothyroidism, hypoparathyroidism, short stature).
Interestingly, organ damage is different in TM and SCD. Cardiac and endocrine dysfunctions are more common in TM mainly because of the longer duration of chronic transfusion.

Therefore, monitoring of iron overload is important. Iron overload may be estimated by calculating the iron transfused since one blood bag contains 200mg of iron. Serum ferritin, although very variable, is also used to predict iron overload. Finally, liver and cardiac iron concentration can be quantified thanks to MRI with the convenience of being noninvasive.

To prevent complications related to iron overload, iron must be neutralized. Treatment should begin when cumulative transfusions of red blood cells exceed 120cc/kg, when serum ferritin is consistently greater than 1000 mcg/L or when liver iron concentration goes beyond 7 mg/g dry weight. Nowadays, three iron chelators are available: Deferoxamine (Desferal®), Deferasirox (Exjade®) and Deferiprone (Ferriprox®). Each of them has its pros and cons. Deferoxamine (DFO) has been available for over 50 years. The subcutaneous therapy is a major issue in patient's compliance. Rare case reports of audiometric and retinal toxicity have been described in overchelated patients. Deferasirox (DFX) seems to be as effective as DFO in reducing liver iron and has the advantage of being given once daily in tablet form. Moderate gastrointestinal side effects are common. Mild decreases in renal function have been observed and may therefore raise some safety issues in patients with renal disease. Lastly, Deferiprone (DFP) is usually given 3 times daily as a tablet. DFP has been shown to remove cardiac iron more efficiently than DFO. Although rare, agranulocytosis is its most serious side effect; weekly blood count monitoring is recommended. In patients with severe iron overload, combination therapy may be required in order to rapidly clear iron overload and reverse organ dysfunction.