Iron in haemoglobinopathies and rare anaemias

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Abstract

Iron overload in haemoglobinopathies and rare anaemias may develop from increased iron absorption secondary to hepcidin suppression, and/or from repeated blood transfusions. While the accumulation of body iron load from blood transfusion is inevitable and predictable from the variable rates of transfusion in the different conditions, there are some important differences in the distribution of iron overload and its consequences between these. Transfusion-dependent thalassaemia (TDT) is the best described condition in which transfusional overload occurs. Initially iron loads into macrophages, subsequently hepatocytes, and then the endocrine system including the anterior pituitary and finally the myocardium. The propensity to extrahepatic iron spread increases with rapid transfusion and with inadequate chelation therapy but there is considerable interpatient and interpopulation variability in this tendency. The conduits through which iron is delivered to tissues is through non transferrin iron species (NTBI) which are taken into liver, endocrine tissues and myocardium through L-type calcium channels and possibly through other channels. Recent work by the MSCIO group¹ suggests that levels of NTBI are determined by three mechanisms: i) increasing with iron overload; ii) increasing with ineffective erythropoiesis; iii) and decreasing when level of transferrin iron utilisation is high. In TDT all three mechanisms increase NTBI levels because transferrin iron utilisation is suppressed by hypertransfusion. It is hypothesized that the transfusion regimen and target mean Hb may have a key impact on NTBI levels because high transfusion

regimes may suppress the 'sink' effect of the erythron though decreased clearance of transferrin iron. In sickle cell disease (SCD) without blood transfusion the anaemia results mainly from haemolysis rather than from ineffective erythropoiesis.² Thus there is a tendency to iron depletion because of urinary iron loss from intrascular haemolysis outweighs any increased iron absorption from hepcidin suppression. These effects result in a low transferrin saturation and NTBI levels and a low tendency from extrahepatic iron distribution. In rare anaemias that result from low production of red cells such as Diamond Blackfan Anaemia (DBA) there is little or no clearance of transferrin iron by the erythron. This leads to high NTBI and a high tendency to extrahepatic iron distribution in DBA. These differences potentially impact on strategies for monitoring and treatment of iron overload in these different conditions.

References

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