Abstract

Evaluation of a Diagnostic Diagram for Monitoring of rHuEPO Therapy in Patients with Anemia of Chronic Disease

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The hypochromic red cell is a direct indicator of functional iron deficiency (FID) in contrast to biochemical markers that only measure iron storage or iron supply for erythropoiesis. An effective real-time marker for the identification of FID is the haemoglobin content of reticulocytes measured as CHr or Ret_{He}. Most recently, Thomas and Thomas, using both indices and sTfR/log ferritin (sTfR-F index) have developed diagnostic plots which proved useful in identifying FID, both in iron-replete and iron- depleted states. The plots, which are distributed into four quadrants, were generated as follows: A cut off value of CHr (Ret_{He}) < 28 pg as determined in patients with a normal, complete blood cell count indicated FID. The sTfR-F index cut offs in these states, selected from ROC analyses of patients with iron deficiency anaemia (IDA), anaemia of chronic disease (ACD) and the combined state of ID/ACD were 3.2 in patients without and 2.0 in patients with APR (C-reactive protein >5 mg/l) using the sTfR assay from Roche Diagnostics and 1.5 and 0.8 using the sTfR assay from Dade Behring.

Significant haematological benefits have occurred for patients with ACD since the introduction of rHuEPO. The response of the ACD to rHuEPO is dose related and cannot always be predicted because it depends on the balance between stimulation of erythropoiesis and an inadequate iron supply causing FID. Identification of a significant erythropoietic response may take months, because effectiveness of each sequential raise in rHuEPO dosage is evaluated by monitoring increase in hemo- globin 4 to 5 weeks after increase of rHuEPO dosage. Thus, it is important to identify laboratory tests that change in real time in response to an increase of rHuEPO dosage and are able to predict a pending erythroid response at a given rHuEPO dose. The enhanced erythropoiesis induced by rHuEPO administration is closely tied to iron demand, because there is concurrent requirement for an adequate iron supply for new red cell production.

The scope of the present study was to evaluate the diagnostic diagram to predict response to rHuEPO and to monitor the balance between stimulation of erythropoiesis and iron supply. Twenty-eight surgical intensive care patients with anaemia (Hb <11 g/dl) were treated with rHuEPO at a dose of 5,000 IU subcutaneously twice per week. Stimulation of erythropoiesis was measured by an increase of the sTfR-F index and a CHr or Ret-H_e > 28 pg in 22 patients. No significant increase of sTfR-F index indicating no response of erythropoiesis to rHuEPO was observed in 6 patients. A decrease in CHr or Ret-H_e < 28 pg demonstrating FID developed in 4 patients after the first rHuEPO dose within 2 weeks. A sTfR-F index > 3.2 (Roche sTfR assay) or 1.5 (Dade Behring assay) indicating high stimulation of erythropoiesis in relation to iron supply was seen in a patient with a ferritin concentration of 13 µg/L before rHuEPO therapy.