Epoetin (Recombinant Human Erythropoietin)
A Review of its Pharmacodynamic and Pharmacokinetic Properties and Therapeutic Potential in Anaemia and the Stimulation of Erythropoiesis

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Summary

Epoetin (recombinant human erythropoietin) is a sialoglycoprotein hormone that appears to be immunologically and biologically equivalent to the endogenous compound, enhancing erythropoiesis dose-proportionally. The therapeutic efficacy of epoetin in the treatment of anaemia associated with chronic renal failure has been established, with almost all patients responding with increases in haematocrit and haemoglobin levels, and improvements in quality of life. Some patients demonstrate relative epoetin resistance and require a higher dosage to achieve target haemoglobin and haematocrit levels.

Maintenance of an adequate iron supply is essential and iron supplementation is recommended if serum ferritin is below 100 to 150 μg/L or transferrin saturation is less than 20%. The incidence of serious adverse effects may be reduced by maintaining a moderate rate of increase in the haematocrit with close monitoring of blood pressure and dialysis efficacy. Individual titration of epoetin dosage is recommended, with increases made in small increments to achieve haematocrit and haemoglobin levels of 30 to 33% and 10 to 12 g/dl, respectively, although the optimal haematocrit for each patient should be individually determined. Some patients will also require a modest increase in heparin dosage because of a possible increase in clotting tendency. Hypertension is the most common adverse effect in patients with chronic renal failure, occurring partially as a result of increasing blood viscosity and peripheral vascular resistance with the correction of anaemia.

Maintenance epoetin therapy has been given for more than 2 years without a decrease in responsiveness and does not appear to adversely affect the outcome of renal transplantation.

Thus, epoetin represents a significant therapeutic advance in the treatment of anaemia associated with chronic renal failure and should be considered a first option for these patients. Its potential value in the treatment of anaemia associated with other disorders and in facilitating autologous blood donation remains to be fully determined.

Pharmacodynamic Studies

Epoetin (recombinant human erythropoietin) stimulates proliferation and differentiation of committed erythroid progenitors dose-proportionally, with increases in reticulocyte count followed by rises in haematocrit and haemoglobin levels. In chronic haemodialysis patients red cell mass also increases but cell lifespan may remain considerably reduced. Tissue iron stores are mobilised during epoetin therapy, and iron supplementation to maintain erythropoiesis is recommended when serum ferritin is < 100 to 150 μg/L and/or transferrin saturation is < 20%; therapy has also been associated with modest increases in platelet and monocyte counts in some studies although these remain within normal limits. A reduction in bleeding times and improved platelet function have been