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Guidelines for the management of anaemia in chronic kidney disease

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Anaemia (haemoglobin < 11 g/dl in women and < 12 g/dl in men) is an almost universal complication of chronic kidney disease (CKD), accounting for much of its symptomatology. Deficient renal production of erythropoietin (EPO) is the major cause of anaemia in CKD patients, although iron deficiency is also a significant contributing factor. Patients with diabetes and black patients have a higher incidence of anaemia at each stage of kidney disease. Glomerular filtration rate (GFR) values are calculated from Modification of Diet in Renal Disease (MDRD) and Cockcroft-Gault equations. These form part of urea and electrolyte measurements in most laboratories, the majority of patients with a GFR < 60 ml/min requiring work-up for anaemia. Such anaemia is associated with significant cardiovascular disease and mortality in patients with a reduced GFR.

Treating anaemia early and aggressively will improve the patient's quality of life, and may slow progression of the disease and also reduce cardiovascular risk, while dramatically reducing blood transfusion requirements. The presence of anaemia should be checked at diagnosis and then every 3 - 4 months to ascertain if haemoglobin levels are adequate. When haemoglobin levels fall below 11 g/dl active treatment for anaemia should begin.

Work-up for anaemia

It is important to exclude other causes of anaemia first (blood loss, B₁₂/folate deficiencies, and haemolysis) and

especially to ensure that iron stores are replete. A ferritin level below 100 ng/ml is usually diagnostic of iron deficiency in renal failure, but may be falsely elevated as a result of chronic inflammation or infection. In this situation transferrin saturation is considered the best test and a level < 20% indicates functional iron deficiency. In the pre-dialysis patient iron replacement is best achieved with oral iron supplementation, ensuring that such iron has a high oral bioavailability. Haemoglobin response should be monitored closely as oral iron is poorly absorbed in patients with advanced renal failure and may result in constipation and other GIT disturbances. For these reasons patients' compliance with oral iron is often poor. In this setting intravenous iron may be used, which may be easier if a patient is being treated with haemodialysis. Although very unusual, adverse reactions to intravenous iron do occur and therefore it should be administered by trained personnel in facilities equipped for administering intravenous therapy (such as dialysis units, day wards, or a general practice appropriately equipped).

Treatment of anaemia

The use of recombinant human EPO (rHuEPO) forms the central part of treatment of anaemia in CKD. Two rHuEPO agents are currently available, namely EPO α and β - both are best given subcutaneously at starting doses of 50 -150 IU/kg/week in divided doses. Using pre-filled syringes seems the most practical option. It is essential to monitor the dose response to optimise the patient's overall condition and to practise cost-effective

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medicine. Haemoglobin levels should therefore be monitored regularly, every 1 - 2 weeks in the correction phase and every 4 - 6 weeks in the maintenance phase. Dosages should be adjusted accordingly.

The following fact is important: once patients are iron repleted their EPO usage diminishes and thus becomes even more cost effective. The patient's blood pressure should be monitored during treatment as hypertension may result from EPO therapy. This may be attributed to an increase in peripheral vascular resistance following the relief of hypoxic vasodilatation and an increase in whole-blood viscosity. There seems little reason to improve haemoglobin levels to > 12 - 13 g/dl; in fact, this may be detrimental to the patient with regard to increased cardiovascular risk. Correction of anaemia with EPO is fairly easy to achieve with proven efficacy and safety. In patients who fail to respond to EPO therapy one should consider iron deficiency, underlying infection, anaemia of chronic disease, folate or B₁₂ deficiency, inadequate dialysis dosage, hyperparathyroidism, aluminium toxicity and a primary bone marrow production problem.

Further reading

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