Current and future challenges in anaemia management

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The introduction of recombinant human erythropoietin (rhEPO; epoetin) nearly 20 years ago revolutionized the management of renal anaemia. The correction of anaemia with epoetin is associated with improvements in the quality of life of patients with chronic kidney disease (CKD), and reductions in morbidity and mortality. In this supplement, the authors present an overview of pertinent issues in renal anaemia management that were tackled during two satellite symposia held on June 9 and 10, 2003 at the World Congress of Nephrology in Berlin, Germany: ‘Current and future challenges in anaemia management’ and ‘Who wants to defeat anaemia? An interactive insight into anaemia management today’.

All recombinant human proteins can potentially induce an immune response, especially when administered repeatedly over prolonged periods. A multitude of factors, including structural properties, storage and handling, contaminants and impurities, administration and formulation, may affect immunogenicity. In recent years, a peak was noted in the number of cases of pure red cell aplasia (PRCA) associated primarily with one particular epoetin-α product available outside of the USA, Eprex®/Erypo®. As a result, regulatory authorities in Europe restricted the administration of this product to the intravenous (i.v.) route. Currently there is no evidence for an increasing trend in antibody-mediated PRCA for this or other epoetin formulations.

The optimal route of epoetin administration has been explored in numerous studies. Current European Best Practice Guidelines and K/DOQI Guidelines on renal anaemia management recommend subcutaneous (s.c.) administration as the preferred route for epoetin in CKD patients not on dialysis, in haemodialysis, peritoneal dialysis and transplanted patients, when not contraindicated. These recommendations take into account the efficacy, frequency of dosing, cost and convenience of epoetin treatment, alongside the safety and tolerability of specific products. Target haemoglobin (Hb) levels can be maintained with much lower doses of epoetin when administered by the s.c. route. Clearly, therefore, s.c. administration of epoetin is associated with economic advantages in terms of direct drug cost and may also provide cost benefits by relieving the burden on health care services. In the case of epoetin-β, s.c. administration allows for reduced dosing frequencies at once weekly and even once every 2 week intervals during the maintenance phase of treatment in stable peritoneal dialysis patients, without compromising safety or efficacy. Reduced dosing frequency and the availability of a pen device, specifically designed for the self-administration of s.c. epoetin-β, should increase patients’ readiness to self-administer treatment and should facilitate the early initiation of anaemia treatment in patients with CKD not yet requiring dialysis.

Anaemia contributes to the progression of cardiovascular disease. Detrimental effects begin at an early stage of CKD, well before kidney function deteriorates to the point when dialysis is required. Indeed, low Hb is an independent risk factor for left ventricular (LV) growth in CKD patients not needing dialysis, as well as in patients receiving dialysis, and in those who have undergone renal transplantation. Data suggest that management of anaemia can significantly reduce the cardiovascular risks associated with CKD; early correction of anaemia may be especially important in improving patient outcomes. The ability of epoetin to reverse changes in LV geometry may be limited in patients with advanced renal and cardiac disease. In this regard, the ongoing Cardiovascular risk Reduction by Early Anaemia Treatment with Epoetin β (CREATE) study, which is investigating the benefits of early, complete anaemia correction with epoetin-β on cardiovascular events in patients with CKD not receiving renal replacement therapy, will provide important information.

The risk of developing cardiovascular disease is even higher in patients with CKD who also have diabetes. Diabetes is now the most common primary diagnosis associated with end-stage renal disease (ESRD), and a
recent German study has shown that early referral of patients with diabetes to the renal unit is associated with better prognosis. Interestingly, anaemia is more severe and is seen earlier in patients with diabetic nephropathy than in patients with non-diabetic renal disease; thus, early epoetin treatment is anticipated to be of benefit. To date, however, only small-scale investigations of early intervention in patients with diabetic nephropathy have been completed. Two ongoing, large-scale studies of anaemia correction in patients with diabetes, Anaemia CORrection in Diabetes (ACORD) and Individualized Risk-profiling and intervention In DIabEtes Mellitus (IRIDIEM), will provide additional information on the benefits of early intervention with epoetin-β in patients with diabetic kidney disease.

The United States Renal Database System estimates that the prevalence of ESRD will reach >650,000 by the year 2010—approximately double that seen in 2000. These figures are largely a consequence of the increasing number of individuals with diabetes in the USA, but illustrate clearly the need for appropriate management strategies in renal anaemia, particularly in early CKD, where effective treatment might prevent further disease progression and development of serious cardiac effects.

Optimal anaemia management requires a patient-centred approach that takes into account not only starting and target Hb levels, but also patient characteristics and preferences, concomitant medications and co-morbidity status. Numerous studies have shown that anaemia therapy based on the use of epoetin-β has a well-established safety and efficacy profile, together with >12 years proven clinical experience (over a million patient-years given by either the s.c. or i.v. route). As our knowledge of renal anaemia therapy and its associated benefits expands, the need to adapt epoetin treatment according to individual patient needs and circumstances is becoming increasingly apparent.

Conflict of interest statement. None declared.