Which EPO dose per week?

Sir,

Weiss et al. [1] have reported that once weekly erythropoietin (EPO) is as effective as more frequent dosing intervals in haemodialysis (HD) patients receiving treatment for the anaemia of end-stage renal failure. In view of their findings we switched all of our stable HD patients to once a week erythropoietin (EPO) providing that they were receiving less than 10 000 U subcutaneously/week. A total of 36 otherwise unselected patients were then followed monthly by routine monitoring as part of our on-going audit process. Patients were using both EPO α and β.

Mean haemoglobin (Hb) decreased from 12.1 ± 1.1 to a nadir of 11.0 ± 1.6 g/dl at 16 weeks (paired t-test, P = 0.002). The Hb achieved by > 85% of patients fell from 11 to 9.5 g/dl, a value below the standard set by the UK Renal Association. Mean weekly EPO dose increased from 97 ± 59 to 107 ± 46 U/kg/week (P = 0.04) equating to an increase in weekly EPO cost from £46 to 51. As a result of these audit results, patients were converted back to two or three times per week regimes. At a further 16 weeks Hb had increased to 12.1 ± 1.3 g/dl and the Hb achieved by 85% of patients was 10.5 g/dl. The EPO dose reached a plateau and had started to decrease but remained higher than baseline at 102 ± 60 U/kg/week. Serum ferritin and C-reactive protein remained stable during the audit period.

We conclude that converting the evidence base from a carefully conducted study to an unselected patient population must be approached with caution. A rigorous audit process is necessary to ensure that there is no detriment to achieved outcomes. In our experience, EPO once a week is less efficient and less cost effective than more frequent dosing schedules. We suggest that this approach cannot be recommended in everyday practice.

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Reply

Sir,

On behalf of the Swedish Study Group, I would like to thank Jones and colleagues for their comments. As the authors point out, our trial involved a selected population: adult patients receiving regular haemodialysis treatment and subcutaneous (s.c.) epoetin beta two or three times weekly, with a stable haemoglobin level and adequate iron status, and a delivered Kt/V > 1.0 [1]. Therefore, the inclusion criteria were not restrictive enough to produce a patient population that was completely unrepresentative of the normal Swedish haemodialysis population seen in the clinic setting.

In our study, the epoetin beta dose and haemoglobin level remained stable during the 24-week study, with no statistically significant differences between the groups in change from week 0 to 24. Also, a subgroup analysis was conducted of all patients who were initially receiving epoetin beta injections three times weekly. They had a mean dose of approximately 10 000 IU/week and converted to once weekly treatment [2]. Both epoetin beta dose and haemoglobin levels remained stable in this subgroup for the duration of the study. These results are supported by those of another multicentre, randomized study [3], which showed that once weekly and three times weekly s.c. epoetin beta administrations are clinically and statistically equivalent. This was demonstrated by rigorous and validated statistical means, and showed stable haematoctit levels and epoetin beta dose requirements in 173 haemodialysis patients. Moreover, a previous study of haemodialysis patients suggested similar efficacy and tolerability at the same cumulative dose between once weekly and more frequent s.c. epoetin administrations [4]. In regard to the difference between the efficacy observed by Jones and colleagues and that observed in the epoetin beta trials (our study an the study reported by Locatelli et al. [3]), we can only provide suggestions as to the reasons for such a discrepancy. Jones et al. mentioned that both epoetin alfa and epoetin beta were used. Several reports indicated differences in the pharmacological properties of the two compounds [5,6]. These differences concerned pharmacokinetic and pharmacodynamic parameters [5], as well as their glycosylation and isoform composition [6]. This prompted some investigators to suggest that there might be a need for separate international standards for these two types of epoetin [6].

In summary, we are unable to provide a clear explanation for the lack of efficacy observed by Jones and colleagues. We can only emphasise the positive results observed in two large-scale studies [1,3], which showed that once weekly epoetin beta is an effective regimen in stable haemodialysis patients. These results are of significance, given the potential advantages associated with the ability to administer epoetin beta treatment once weekly, in terms of patient and clinic time and resources.

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