Use of epoetin for anemia in chronic renal failure

Authors' objectives
The primary objective was to assess the outcomes of maintaining target haematocrit (Hct) levels at greater than 36%, compared with maintenance at 33 to 36%, in adult patients with chronic renal failure (CRF). The secondary objectives were to compare the effect on outcomes of: maintaining a target Hct level above 36%, compared with 30 to 36%, in the same population and in other sub-populations of interest; and maintaining Hct target levels of above 30% versus 27 to 30%, and above 33% versus 27 to 33%, in paediatric patients with CRF.

Searching
MEDLINE and EMBASE (both from 1985 to December 1998) and Current Contents (to October 1999) were searched for studies reported in English; the search terms were provided. The reference lists from retrieved articles were checked and experts in the field were contacted.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs), non-randomised controlled trials (CTs) and cross-sectional studies that included at least 10 patients per group and investigated the relationship between outcome and Hct level, statistically controlling for confounding factors, were eligible for inclusion.

Specific interventions included in the review
Studies of recombinant human erythropoietin (epoetin) comparing maintenance of Hct greater than 36% with 33 to 36% or 30 to 36% in adult patients, and maintenance of Hct greater than 30% or greater than 33% with Hct 27 to 30% or 27 to 33%, respectively, in paediatric patients were eligible for inclusion. The included studies investigated Hct maintenance levels of 33 to 36% and 30 to 36%.

Participants included in the review
Studies of adults and children with CRF across the full spectrum of disease severity were eligible for inclusion. Other patients, with or without CRF, with clinical characteristics that might benefit from maintaining Hct above 36% (i.e. coronary heart disease, congestive heart failure, living at high altitude, cerebrovascular disorders, obstructive lung disease and adolescent age) were also eligible for inclusion. Patients with primary haemoglobinopathies were not eligible. The included studies were of adult patients with CRF and adults with cardiovascular disease and cerebrovascular disease.

Outcomes assessed in the review
Studies reporting at least one of the following outcomes were eligible: mortality, quality of life, hospital utilisation, red blood cell transfusions, cardiac outcomes, functional status, adverse effects, and child growth and development or school-related performance. With the exception of child growth and school performance, all of these outcomes were reported by the included studies.

How were decisions on the relevance of primary studies made?
Two reviewers independently selected the studies for inclusion. Any disagreements were reviewed by a third reviewer and by the project group if consensus could not be reached.

Assessment of study quality
Four dimensions of study quality were assessed: use of a double-blind design; missing data for more than 10% of the participants; potential bias in a control group comparison; and the extent to which cross-sectional analyses identified and controlled for confounding influences in the data analysis. Two reviewers independently assessed study quality and resolved any disagreements by consensus.
**Data extraction**
Two reviewers independently extracted the data. Any inconsistencies were resolved by referring to the original paper, or by discussion and consensus if necessary. The extracted data included patient population, study design, anaemia treatment and outcome.

**Methods of synthesis**

How were the studies combined?
The studies were combined in a narrative.

How were differences between studies investigated?
The studies were grouped according to the patient group: adults with CRF, children with CRF and other sub-populations.

**Results of the review**
Five RCTs, 7 non-randomised CTs and 13 cross-sectional studies were included. The number of participants was unclear.

Only the results of RCTs and CTs are summarised. Results from cross-sectional studies were available in the report.

Adults with CRF (5 RCTs, 7 CTs, 11 cross-sectional studies).

No RCTs or CTs that compared the outcomes of maintaining target Hct above 36% with maintenance at 33 to 36% were identified.

Twelve RCTs or CTs (8 had less than 100 patients) compared the outcomes of maintaining the target Hct above 36% with 30 to 36%. For each of the outcomes, there was insufficient evidence to determine whether the former target Hct (>36%) was more beneficial than the latter (30 to 36%).

Children with CRF.

No studies that met the inclusion criteria were identified.

Sub-populations with or without CRF (1 RCT, 2 cross-sectional studies).

The RCT reported evidence on outcomes for haemodialysis patients with cardiovascular disease. There was no statistically significant differences between the two target groups (Hct above 36% versus 30 to 36%) for the primary outcome mortality.

**Authors’ conclusions**
There was no strong or consistent evidence that maintaining the Hct level above 36% is more beneficial for patients with CRF than a Hct target range of 33 to 36%.

**CRD commentary**
The review question was clearly defined. Some relevant electronic databases were searched, but attempts to identify unpublished studies were limited and non-English language studies were excluded. Studies may therefore have been missed. The study selection, data extraction and quality assessment processes were carried out in duplicate, which helps to reduce error and bias. The quality assessment was fairly limited, although the findings were discussed in the context of study quality. Relevant details on the individual studies were given. However, despite being concerned that a fairly substantial number of papers appeared to duplicate patients, the reviewers do not appear to have contacted the relevant authors for further details. The narrative synthesis was appropriate and the studies were grouped suitably. The authors' conclusions follow from the evidence presented.
Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors stated that large well-designed trials are required to assess the outcomes of using epoetin to increase Hct to above 36%, in particular, in adult CRF patients not yet on dialysis and in dialysis patients without overt cardiac disease. The trials should consider differential effects in different groups of CRF patients.

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.