Does epoetin alfa improve health-related quality of life in chronically ill patients with anemia: summary of trials of cancer, HIV/AIDS, and chronic kidney disease

Kimel M, Leidy NK, Mannix S, Dixon J

CRD summary
The authors concluded that epoetin α treatment of anaemia in various conditions had a statistically and clinically significant impact on health-related quality of life, particularly fatigue. In light of the possibility of error and bias in the review process, and the unclear quality of the included studies, the authors’ conclusions should be treated with caution.

Authors’ objectives
To evaluate the impact of epoetin alpha (epoetin α) on haemoglobin levels and health-related quality of life across a variety of populations with underlying causes of anaemia.

Searching
MEDLINE and EMBASE were searched from January 1993 to September 2005 for articles published in English. Search terms were reported. References of identified articles were handsearched.

Study selection
Studies of epoetin α used as treatment for anaemia, with varying underlying causes, that measured haemoglobin levels and health-related quality of life, were eligible for inclusion. Studies of patients with kidney disease undergoing dialysis were excluded from the review. Studies that did not provide quantitative data for the measurement of health-related quality of life were also excluded from the review. Study designs eligible for inclusion were restricted to randomised controlled trials (RCT) for studies that evaluated health-related quality of life in cancer patients. All clinical trials were eligible for inclusion for patients with other underlying conditions.

The included studies evaluated epoetin α in doses that ranged from 4,000 units subcutaneously every day (QD) to 60,000 units subcutaneously every week, in patients with various types of cancer, human immunodeficiency virus (HIV)/ acquired immunodeficiency syndrome (AIDS) or in the pre-dialysis stage of chronic kidney disease. The duration of treatment ranged from eight to 52 weeks. In controlled trials, epoetin α was compared to placebo or standard care. A variety of disease specific and generic standardised scales were used to measure health related quality of life in the included studies; the most commonly used were the Functional Assessment of Cancer Therapy, the Linear Analogue Scale Assessment, and subscales derived from the Medical Outcomes Study. Other outcomes reported in the included studies were haemoglobin levels, percentage of patients requiring a transfusion, and work capacity.

The authors did not state how the studies were selected for the review, or how many reviewers performed the study selection.

Assessment of study quality
The authors did not state that they assessed validity.

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Methods of synthesis
The results were combined in a narrative synthesis.

Results of the review
Eighteen studies were included for the review (n=5,421 patients); seven double blind RCTs (n=1,472), seven open-label RCTs (n=1270) and four open-labelled non-randomised trials (n=2,679).
Cancer (nine RCTs, n=1,949 patients): Epoetin α was associated with statistically significant improvements in haemoglobin levels compared with controls in four out of eight trials (p<0.001); significantly fewer patients who received epoetin α needed a transfusion compared with controls (p<0.02). Treatment with epoetin α did not result in significantly different survival rates between the groups in two of the three trials that measured this. Fatigue, as measured by Functional Assessment of Cancer Therapy scale, was significantly improved in patients treated with epoetin α compared to controls (p=0.02 to p<0.0001) in four out of eight trials. Three out of five trials found significant improvements on the Functional Assessment of Cancer Therapy anaemia subscale in patients treated with epoetin α compared with controls (p=0.01 to p<0.0001). Four out of seven trials found significant improvements in energy, ability to perform daily activities, and overall health-related quality of life, as measured by the Linear Analogue Scale Assessment, in patients receiving epoetin α compared with controls at follow-up (p =0.02 to p<0.0007).

HIV/AIDS (six studies, n=1,715 patients): Patients receiving epoetin α showed a significant increase in haemoglobin levels at 16 weeks of follow-up compared with baseline levels (mean change in haemoglobin 2.9g/dL and 2.5g/dL; two studies; p<0.0001). Within-group analyses demonstrated significant improvements in patients receiving epoetin α at follow-up on all domains of the Medical Outcomes Study-HIV subscale (p<0.05 to p<0.0001) in two studies. One study found significant within-group improvements in energy and health distress (p<0.05), but not in physical or role function at follow-up in patients receiving epoetin α. Two out of the three studies using the Linear Analogue Scale Assessment found significant improvements in energy, daily activities, and overall health-related quality of life at follow-up compared with baseline levels in patients with HIV/AIDS receiving epoetin α. One RCT found no significant difference between epoetin α and standard care on health-related quality of life as measured by the Medical Outcomes Study physical outcomes subscale and the medical outcomes subscale.

Pre-dialysis chronic kidney disease (three studies, n=1,757): Pre-dialysis chronic kidney disease patients with anaemia showed significant improvements in haemoglobin when receiving epoetin α compared with controls: mean change in haemoglobin 4.7g/dL versus -1.0g/dL in two studies (p<0.0001) and percentage of patients with greater than 6% increase in haemoglobin 57% to 90% versus 10% in one study (p<0.05). One RCT reported significantly improved energy (change in Medical Outcomes Study score 5.8 versus -3.0; p=0.036) and physical function (change in Medical Outcomes Study score 7.8 versus -4.8; p=0.006) in pre-dialysis chronic kidney disease patients receiving epoetin α compared with controls. There were no other significant differences on a range of other health-related quality of life scales used in this trial. One RCT found a significantly improved work capacity in patients treated with epoetin α compared with controls (p<0.05). One within-group study found significant improvements at 16 weeks compared with baseline on all Linear Analogue Scale Assessment scales (p<0.0001) and kidney disease questionnaire domains (p<0.0001).

Authors’ conclusions
Epoetin α treatment of anaemia in various conditions had a statistically and clinically significant impact on health-related quality of life, particularly fatigue.

CRD commentary
Inclusion criteria were well-defined for intervention and participants, and broadly defined for study designs and outcomes. Two databases were searched, but studies were restricted to English language, which may have introduced language bias. A search for unpublished material did not appear to have been carried out, so publication bias may have been introduced. There was insufficient information about the review process to rule out the possibility of reviewer error and bias. A validity assessment did not appear to have been carried out. The authors did note limitations in the available evidence, in terms of small sample size and the possibility of measurement bias. Given the clinical heterogeneity between included studies, the decision to combine the studies in a narrative synthesis was appropriate. In light of the possibility of error and bias in the review process, and the unclear quality of the included studies, the authors’ conclusions should be treated with caution.

Implications of the review for practice and research
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Research: The authors did not state any implications for research.
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