Review: Recombinant human erythropoietin decreases the need for blood transfusions and may delay dialysis in chronic renal failure

Cody J, Daly C, Campbell M, et al. **Recombinant human erythropoietin for chronic renal failure anaemia in pre-dialysis patients.** Cochrane Database Syst Rev. 2001(4):CD003266 (latest version 27 Aug 2001).

QUESTION

In patients with chronic renal failure (CRF) and renal anemia, does recombinant human erythropoietin (rHu EPO) delay the need for dialysis?

DATA SOURCES

Studies were identified by searching 13 databases, including MEDLINE (1980 to May 2001), EMBASE/Excerpta Medica (1984 to June 2001), and the Cochrane Controlled Trials Register; hand searching *Kidney International*; scanning reference lists of relevant articles, reviews, and book chapters; searching the Internet; and contacting experts in the field and at relevant biomedical companies.

STUDY SELECTION

Studies were selected if they were randomized controlled trials (RCTs) or quasi-RCTs that compared rHu EPO with placebo or no rHu EPO in patients with CRF and renal anemia who had not started dialysis.

DATA EXTRACTION

2 investigators independently assessed trials for methodologic quality and subject relevance. Data were extracted on participants, intervention, and outcomes (time to dialysis, glomerular filtration rate [GFR], serum creatinine level, hemoglobin or hematocrit values, blood transfusions, quality-of-life measures, hypertension, other adverse events, and mortality).

MAIN RESULTS

12 RCTs (232 patients) were included. 9 trials were 8 to 12 weeks in duration; 3 trials ranged from 36 weeks to 1 year. 5 trials reported progression of renal failure; groups did not differ for the proportion of patients starting dialysis (Table). The groups did not differ for GFR (4 trials) (weighted mean difference [WMD] 1.59 mL/min, 95% CI –0.49 to 3.66) or serum creatinine levels (5 trials) (WMD 76.12 µmol/L, CI –7.94 to 160.17). Fewer patients who received rHu EPO required blood transfusions (Table). 1 trial that measured hemoglobin level showed that rHu EPO was beneficial (mean difference 2.3 g/dL, CI 1.37 to 3.23), and 7 trials showed a benefit of rHu EPO in increasing hematocrit levels (WMD 9.92%, CI 8.7% to 11.05%). 2 trials that measured quality of life showed improvement with rHu EPO at 12 and 48 weeks. More patients who received rHu EPO had to start antihypertensive therapy than did control-group patients (Table). Incidences of withdrawal because of adverse effects (4 trials) and mortality (3 trials) were low and did not differ between groups.

CONCLUSION

In patients with chronic renal failure and renal anemia, recombinant human erythropoietin corrects anemia and reduces the need for blood transfusions but increases blood pressure and does not reduce the need to start dialysis.

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For correspondence: Ms. J. Cody, University of Aberdeen, Aberdeen, Scotland, UK. E-mail j.cody@abdn.ac.uk.

Recombinant human erythropoietin (rHu EPO) vs placebo or no rHu EPO (control) for chronic renal failure with renal anemia*

Outcomes at 8 wk to 1 y	Number of trials	Weighted event rates		RRR (95% CI)	NNT (CI)
		rHu EPO	Control		
Dialysis	5	31%	43%	28% (–3 to 50)	Not significant
Blood transfusion	3	7.0%	26%	69% (21 to 88)	6 (3 to 23)
				RRI (CI)	NNH (CI)
Antihypertensive therapy	4	47%	33%	42% (0 to 102)	8 (4 to 100)

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article using a fixed-effects model.

COMMENTARY

In the past decade, rHu EPO therapy has probably been the most important advance in the treatment of patients with end-stage renal disease. The drug is simple to use, is safe, and leads to consistent improvement in patients' quality of life (1). Among patients with chronic renal insufficiency, the drug is used with many of the same benefits. Nonetheless, anemia in this patient population is underrecognized and undertreated. Obrador and colleagues (2) found that 51% of patients starting dialysis in the United States have a hematocrit level < 28%, and among these patients only 20% were treated with rHu EPO.

Cody and colleagues reviewed the literature to investigate the relation between rHu EPO therapy and the rate of progression of the underlying renal disease. In theory, rHu EPO therapy could hasten disease progression by worsening blood pressure control. Alternatively, improved oxygen delivery could have a renoprotective effect, and rHu EPO might actually delay loss of renal function and the eventual need for dialysis.

The studies, when combined, showed a 28% reduction in the need to start dialysis, with these data being consistent with both a 3% increase and a 50% reduction in the need to start dialysis. Although not statistically significant, the magnitude of effect, if confirmed, has great clinical significance. Therefore, I see these results not as negative but rather as a strong stimulus for further research in this area.

Steven Fishbane, MD
Winthrop-University Hospital
Mineola, New York, USA

References

1. **Korbet SM.** Anemia and erythropoietin in hemodialysis and continuous ambulatory peritoneal dialysis. Kidney Int Suppl. 1993;40:S111-9.
2. **Obrador GT, Ruthazer R, Arora P, Kausz AT, Pereira BJ.** Prevalence of and factors associated with suboptimal care before initiation of dialysis in the United States. J Am Soc Nephrol. 1999;10:1793-800.

