Increased Ultrafiltration after Erythropoietin-Induced Correction of Renal Anemia in Patients on Continuous Ambulatory Peritoneal Dialysis

H.B.		Steinhauer
I.		Lubrich-Birkner
K.W.		Dreyling
W.H.		Hör
P.		Schollmeyer

Department of Internal Medicine, Division of Nephrology, University of Freiburg, FRG

Dr. Hjalmar B. Steinbauer, Medizinische Universitätsklinik, Abteilung Nephrologie, Hugstetter Strasse 55, D-7800 Freiburg, (FRG)

Dear Sir,

Recombinant human erythropoietin (rHuEPO) has been shown to be effective in correcting renal anemia of patients with chronic renal failure undergoing hemodialysis [1–4]. Despite that anemia is usually less severe in patients on continuous ambulatory peritoneal dialysis (CAPD) compared to hemodialysis, the correction of anemia will improve the clinical condition of CAPD patients. In order to study the effect of rHuEPO on anemia and peritoneal dialysis efficiency, 8 CAPD patients (aged 26–67 years) were treated with rHuEPO (Cilag Ltd., Schaffhausen, Switzerland) subcutaneously twice weekly with an initial dose of 50 U/kg body weight. Every 4 weeks the rHuEPO dose was increased for 25 U/kg body weight till the target hematocrit (HKT) of 35% had been achieved. In case this HKT was exceeded, rHuEPO was reduced by 25 U/kg body weight. CAPD study exchanges with 4 h dwell time were performed twice weekly in the morning with 1.5 liters 1.5% dextrose monohydrate (Fresenius AG, Bad Homburg, FRG; Baxter, Deerfield, Ill., USA).

Subcutaneous administration of rHuEPO was tolerated without severe side effects (short-lasting local pain after subcutaneous injection in 4 patients, increased anti-hypertensive treatment in 2 patients, transient flu-like

syndrome in 1 patient). The results are summarized in table 1. rHuEPO-induced correction of anemia was associated with increased peritoneal ultrafiltration (UF). UF/4 h dwell time rose from 156 ± 105 to 264 ± 138 ml after 12 weeks of rHuEPO treatment. Urea clearance increased from 5.5 ± 0.8 to 6.3 ± 1.5 ml/min/1.73 m². Since urea serum and dialysate concentrations remained unchanged, the augmented clearance of urea is due to the rise in UF.

Increased peritoneal UF can be achieved by (1) augmented mesenteric blood flow, (2) raised peritoneal permeability, (3) decreased lymphatic absorption from the abdominal cavity, and (4) increased osmotic gradient between dialysis solution and plasma [5,6]. rHuEPO-induced correction of anemia may rise mesenteric perfusion by improved cardiac function [7,8]. A corresponding observation was described in CAPD patients with congestive heart disease after effective digitalis therapy [9]. No data are available on the effect of anemia correction on peritoneal transport, peritoneal lymphatic absorption and osmotic gradient.

In summary, renal anemia in CAPD patients can be corrected effectively by subcutaneous administration of rHuEPO. The observed rise in UF after rHuEPO-induced correction of anemia might improve dialysis efficiency in patients undergoing CAPD.

*p < 0.05, **p < 0.03, ***p < 0.005 vs. data before rHuEPO treatment, analyzed by Wilcoxon's test for combined data. CI = Peritoneal clearance.

92

Steinhauer/Lubrich-Birkner/Dreyling/Hörl/Schollmeyer

References

- Winearls, C.G.; Oliver, D.O.; Pippard, M.J.; Reid, C.; Downing, M.R.; Cotes, P.M.: Effect of human erythropoietin derived from recombinant DNA on the anemia of patients maintained by chronic hemodialysis. *Lancet* ii: 1175–1178 (1986).
- Eschbach, J.W.; Ergle, J.C.; Downing, M.R.; Browne, J.K.; Adamson, J.W.: Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. *New Engl. J. Med.* 3/6:73–78(1987).
- Bommer, J.; Alexiou, C; Müller-Bühl, E.; Eifert, J.; Ritz, E.: Recombinant human erythropoietin therapy in hemodialysis patients – dose determination and clinical experience. *Nephrol. Dial. Transplant.* 2:238–242 (1987).
- Casati, S.; Passerini, P.; Campise, M.R.; Graziani, G.; Cesana, B.; Perisic, M.; Ponticelli, C: Benefits and risks of protracted treatment with human recombinant erythropoietin in patients having hemodialysis. *Br. med. J.* 295:1017–1020 (1987).
- Steinhauer, H.B.: Pharmacological manipulation of peritoneal transport in CAPD. *Clin. Nephrol.* 50:S29–S33 (1988).
- Mactier, R.A.; Khanna, R.; Twardowski, Z.; Moore, H.; Nolph, K.D.: Contribution of lymphatic absorption to loss of ultrafiltration and solute clearances in continuous ambulatory peritoneal dialysis. *J. clin. Invest.* 50:1311–1316 (1987).
- Grützmacher, P.; Scheuermann, E.; Low, I.; Bergmann, M.; Rauber, K.; Baum, R.; Heuser, J.; Schoeppe, W.: Correction of renal anaemia by recombinant human erythropoietin: Effects on myocardial function. *Contr. Nephrol.*, vol. 66, pp. 176–184 (Karger, Basel 1988).
- Verbeelen, D.; Bossuyt, A.; Smitz, J.; Herman, A.; Dratwa, M.; Jonckheer, M.H.: Hemodynamics of patients with renal failure treated with recombinant human erythropoietin. *Clin. Nephrol.* 31:6–11 (1989).
- Maher, J.F.: Pharmacologic manipulation of peritoneal transport; in Nolph, Peritoneal dialysis, pp. 213–239 (Nijhoff, The Hague 1981).
- Announcement
- Charles E. Culpeper Foundation Scholarships in Medical Science
- The Charles E. Culpeper Foundation is currently accepting applications for its 1990 Scholarships in Medical Science Program designed to support the career development of academic physicians. Up to three awards of \$100,000 per year for 3 years will be made to United States medical schools on behalf of candidates who are US citizens, who have received the MD degree from a US medical school in 1981 or later, and who are judged worthy of support by virtue of the quality of their research proposals. All scientific research relevant to human health is eligible for consideration. No institution may nominate more than one candidate.

In selecting awardees, emphasis will be on identifying young physicians with clear potential for making substantial contributions to science as academic-physicians. Since January 1988, 6 physicians have been selected as Charles E. Culpeper Foundation Medical Scholars, 3 each in the years 1988 and 1989.

The deadline for applications is August 15, 1989. Awards will be announced by January 15 1990

for activation on or about July 1

1990. Application forms and instructions may be obtained by contacting the Charles E. Culpeper Foundation

866 United Nations Plaza

New York

NY 10017 (USA)