Red Cell Lipid Peroxidation and Antioxidant System in Chronic Renal Failure Patients Treated with Recombinant Human Erythropoietin

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Dear Sir,

Erythropoietin (EPO) deficiency and shortened red cell survival are considered as main factors known to contribute to the pathogenesis of anemia almost invariably observed in chronic renal failure (CRF) [1]. Shortened red cell life span has been attributed to the susceptibility of red cell membrane lipids to autoxidation [2], and to the alteration of the antioxidant system [3]. Indeed, elevated red cell lipid peroxide levels have been observed in CRF [2]. Although the use of recombinant human EPO (rhEPO) for the correction of anemia in patients on regular hemodialysis has been reported to be effective [4], its actions on red cell lipid peroxidation and antioxidant system elements like glutathione peroxidase (GSH Px) and GSH, are not clearly established. In a recent study [5], EPO deficiency due to starvation has been reported to increase red cell lipid peroxidation and depress antioxidant system. Replenishment of EPO has been observed to reverse these effects.

In order to determine the role of correcting anemia with rhEPO on the susceptibility of red cells to lipid peroxidation and on GSH Px activity and GSH levels, 9 patients (5 women, 4 men; age 20-65 years), on maintenance hemodialysis three times weekly for 1-8 years, were included in the study. The primary renal diseases were: 5 with chronic glomerulonephritis; 2 with chronic pyelonephritis; 1 with primary nephrosclerosis, and 1 with diabetic nephropathy. All patients were anemic, the mean hemoglobin value being 7.0 ± 1.1 g/dl. No other obvious cause for anemia besides uremia was observed. EPO (Cilag AG, International) was applied intravenously at the end of hemodialysis. The starting dose was 50 U/kg body weight three times a week. The target hemoglobin level was 10-12 g/dl. If the desired level was not reached, the rhEPO dose was increased to 75 U/kg body weight after 4 weeks. Finally 100 U/kg body weight was used.

Blood counts were monitored using Technicon H 6000 analyzer. Red cell diene conjugate levels were measured according to Goldstein and Harber [6]. The amount of thiobarbituric acid (TBA) reactive substances was determined by the method of Cynamon et al. [7]. Red cell suspensions in phosphate buffer with sodium azide were incubated with 0.75% H2O2 for 1 h at 37 °C. Red cell
GSH content was measured with Ellman’s reagent [8]. GSH Px activity in hemodialysates was determined by the assay procedure described by Hafe-man et al. [9]. Enzyme activity was expressed as a decrease in log GSH of 0.001/min/mg hemoglobin after subtracting the decrease in log GSH per minute of the nonenzymatic reaction. Statistical analysis was performed by Student’s t test.

Table 1 shows the hemoglobin, hematocrit, red cell diene conjugate, TBA-reactive substance levels, GSH content and GSH Px activity before and 1, 2, 3 and 4 months after treatment with rhEPO. Although hemoglobin and hematocrit values after 1- and 4-months treatment were increased significantly compared to the pretreatment values, elevated pretreatment red cell diene conjugate and TBA-reactive substances were not found decreased after rhEPO treatment. On the other hand GSH levels have been reported to remain unchanged, whereas GSH Px activities were observed to be decreased in CRF [3,10]. In our study, GSH Px activities have not been found to reach normal levels after treatment with rhEPO.

Although the use of rhEPO has been considered very effective in elevating the hemoglobin levels of patients with CRF, a 4-month treatment does not seem to alter red cell lipid peroxide levels and GSH Px activity.

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Table 1. Hemoglobin, hematocrit, red cell diene conjugate and TBA-reactive substance levels, GSH content and GSH Px activities in controls and patients before and after treatment with rhEPO (n = 9; mean ± SD)

*p < 0.01 compared to pretreatment values; ** p < 0.001 compared to pretreatment values.

References


