Lipoperoxidation and Glutathione-Dependent Enzymes in Uremic Anemia of CAPD Patients

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Dear Sir,

Oxidative stress appears to participate in the genesis of uremic anemia of chronic renal failure (CRF) patients both undergoing he-modialysis (HD) or chronic ambulatory peritoneal dialysis (CAPD), by shortening red blood cell (RBC) life span [1]. However, little information is available to date on the modification of glutathione-dependent antiperoxi-dative enzymes in uremia and above all in CAPD, a procedure which allows a better control of the uremic condition and induces a less severe anemia as compared to HD [2]. We therefore investigated the levels of glutathione-dependent enzymes in a group of patients undergoing CAPD (n = 29) in comparison with those of a group of healthy controls (n = 12). The glutathione redox levels (as GSH/GSSG), glutathione peroxidase (GPX) and glutathione transferase (GST) enzyme activities were determined. Plasma lipoperoxidation levels [3], as measured by thiobarbi-turic acid reactants (TBAR) and in the form of directly detectable malonaldehyde (MDA) were determined by HPLC technique. These parameters were compared with the anemia severity, estimated by the most common he-matological parameters and by the serum erythropoietin (EPO) concentration.

A sub-

group of CAPD patients with severe anemic conditions, refractory to the rhEPO therapy (EPO+ group, n = 7), was also investigated. The results obtained revealed increased GST (206%, p < 0.001) and GPx (124%, p = 0.065) activities in the presence of a decreased glutathione redox (59%, p < 0.01) and increased lipid peroxidation (187%, p < 0.05) in the CAPD population in comparison with the control group. The higher GST activity in CAPD patients can be ascribed to a proportional increase in the expression of the enzyme, as was demonstrated by immu-noblotting of RBC lysate proteins after partial purification, using an antiserum against the human placenta GST-III form. GPx activity positively correlated with TBAR levels (p = 0.0048, n = 26), while a negative relationship was observed between GST and TBAR (p = 0.0312). A positive relationship between GPx levels (p < 0.001, n ≈ 29) and the severity of the anemia, in terms of RBC number, was observed. In the EPO+ subgroup, the antianemic therapy does not appear to influence the GST and GPx expression levels.

These preliminary data are in agreement with previous observations [2] and are consistent with the presence of oxidative stress conditions in CAPD patients which are linked to an overexpression of glutathione-related enzymes and particularly GST protein in the RBC. The overexpression of glutathione-related enzymes can be presumed to be a compensatory mechanism against the overproduction of subproducts of lipoperoxidation, many of which are harmful toxins [3].

References

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