Effect of Hyperoxalaemia on Factor VIII-Related Antigen in Uremia

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Sir,

Oxalate is known to accumulate in patients receiving dialysis, but we have been unable to confirm earlier reports of extrarenal tissue deposition of calcium oxalate in patients receiving dialysis [1], and the clinical relevance of hyperoxalaemia remains uncertain. Oxalate has been reported to have a toxic effect on endothelial cells in culture [2], leading to suggestions that hyperoxalaemia may contribute to endothelial damage and thus to arterial disease in patients receiving dialysis. We studied this possibility during a study of the effects of ascorbate supplementation on plasma oxalate in patients receiving dialysis.

We recruited 11 dialysis patients [6 haemodialysis, 5 continuous ambulatory peritoneal dialysis, mean age $42 \pm$ (SD) 13.5 years, and five control subjects, mean age 37 ± 7.2 years]. Fasting venous blood samples were taken without venous stasis before and after a 3-week course of oral ascorbic acid, 500 mg/day. Plasma oxalate measured using an enzyme/bioluminescent assay [3] rose from 1.4 (SEM 0.2) to 6.8 (0.9) $\mu\text{mol/l}$ in controls ($p < 0.01$) and from 30.3 (3.5) to 48.4 (6.1) $\mu\text{mol/l}$ in patients ($p < 0.01$). Whole blood ascorbate (2,4-dinitrophenylhydrazine method) rose from 9.3 (1.2) to 17.8 (1.8) mg/l in controls ($p < 0.05$) and from 7.0 (SEM 0.7) to 26.6 (SEM 2.5) mg/l in patients ($p < 0.01$). Factor VIII-related antigen levels (rocket immunoelectrophoresis) were higher in patients than controls both before [367 (79) vs. 99 (19)%; $p = 0.007$] and after [279 (67) vs. 109 (16)%; $p = 0.032$] ascorbate, but no significant change was observed within either group as a result of the rise in plasma oxalate.

Endothelial damage in vivo in a variety of diseases has recently been reported to be associated with a rise in the plasma level of factor VIII-related antigen (von Willebrand factor, vWF), which is synthesised by vascular endothelium [4]. Although vWF levels are known to be increased in uraemia [5], a report of elevated vWF levels associated with ciclosporin toxicity in renal transplant

recipients, with reduction towards normal as the dose of ciclosporin was reduced [6], suggests that this measurement remains a valid marker of endothelial damage in uraemic patients.

Whatever the cause of the raised levels of vWF in renal disease, ascorbic acid has no known

effect on vWF levels, and paired comparison of measurements taken from the same subject before and after an ascorbate-induced rise in plasma oxalate is therefore a valid way of looking for oxalate-induced changes in vWF levels. Our study thus provides no support for the suggestion that hyperoxalaemia results in endothelial damage in vivo.

References

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