status better than whole blood, and better reflect the actual selenium status of our critically ill patients treated with continuous haemodialysis [5].

Selenium is highly bound to plasma proteins, which prevents significant dialytic clearance. Our critically ill study patients (sepsis, organ failure) with (mean ± SD) serum albumin concentration (2.1 ± 0.72 g/dL) are illustrative of patients commonly seen in our intensive care units. The mean albumin concentration of these study patients suggests that there may have been reduced binding sites for selenium, and consequently, more unbound selenium would be available for dialytic clearance. However, during acute inflammation, plasma alpha-2 globulin concentrations are often increased as part of the acute phase response, which as Dr. Diskin points out, may also serve as a binding site for selenium. In our study, all but one patient received trace element supplementation that included selenium, either in parenteral or enteral nutrition. Consequently, an increase in free selenium or the portion cleared by continuous haemodialysis might be higher than in patients who are not supplemented with selenium. The effects of these and other changes on selenium binding to circulating plasma proteins depend on many factors and are difficult to predict.

Despite the complexities involved in trace element binding and extracorporeal removal, we reported a very low clearance rate for selenium and other trace elements during continuous haemodialysis. Although almost all of our subjects were receiving some concurrent trace element supplementation, the observed trace element clearance was considerably less than that usually administered in a typical daily trace element supplementation regimen. Our published trace element extraction coefficients and continuous dialysis clearance rates should be interpreted as what would be observed in critically ill patients receiving nutrition and continuous haemodialysis.

Conflicts of interest statement. None declared.

doi: 10.1093/ndt/gfm822

Advanced Access publication 19 November 2007

Think of oxalate when using ascorbate supplementation to optimize iron therapy in dialysis patients

Sir,

In a useful Primer on Iron Therapy recently published [1], there is an important point that should be clarified, to avoid misleading messages for the readers.

The authors wrote that supplementation of vitamin C (200 mg per day orally or 300–500 mg intravenously after each haemodialysis session) may result in the release of iron from the reticuloendothelial system, and thereby improve hypo responsiveness to ESA (erythropoiesis-stimulating agents) [1], with a reference to a short-time clinical study that did not fully address monitoring for a possible oxalate overload [2].

Any suggestion to use ascorbate supplementation to optimize iron therapy in dialysis patients cannot fail to mention the relationship between ascorbate and oxalate.

There is no doubt that ascorbate supplementation will increase oxalate overload in uraemic people. Controversies still exist on the clinical meaning of such an increase, but some key points have been clearly established [3,4].

1. The threshold of plasma saturation for oxalate corresponds to ~50 µmol/L [3].
2. Ascorbate supplementation in dialysis patients may increase oxalate plasma levels above this threshold.
3. Oxalate plasma levels showed a significant positive correlation with levels of ascorbic acid.
4. The threshold of plasma saturation may be exceeded with a dosage of ascorbate as low as 100 mg three times a week, infused intravenously after each dialysis session in 40% of patients during 6-month therapy with 500 mg/week [4].
5. A 5-fold increase in oxalate levels in the bone tissue of uraemic patients on regular dialysis has been demonstrated, even in the presence of undersaturated serum [3].

In conclusion, serum oxalate rises in uraemia because of decreased renal clearance, and crystals of calcium oxalate occur in the tissues of uraemic patients because uraemic serum is supersaturated with calcium oxalate. The possibility that hyperoxalaemia confers an increased risk of cardiac and vascular disease, even in the absence of primary hyperoxaluria, is debated and unknown, but presumably protective substances have been hypothesized to help in preventing the risk of systemic oxalosis despite increased plasma oxalate levels often to supersaturation levels, as
oxalate deposition and systemic oxalosis are uncommon in patients with chronic renal failure, as opposed to patients with primary hyperoxaluria. Furthermore, a low total vitamin C plasma level is a risk factor for cardiovascular morbidity and mortality in haemodialysis patients [5] and therefore adequate supplementation is needed.

Nonetheless, the readers of the Primer should not believe that a dosage of ascorbate as high as 500 mg per 3 weeks in uraemic patients on chronic dialysis is definitely safe, as this is not the case.

Ascorbate, as is the case with iron therapy, cannot be sco-

tomized to optimize erythropoietin therapy without looking at possible side effects.

**Conflict of interest statement.** None declared.

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doi: 10.1093/ndt/gfm819

Advanced Access publication 9 December 2007

**Reply**

Sir,

In response to our Primer on Iron Therapy, Canavese et al. point out that vitamin C supplementation might increase the risk for hyperoxalaeemia. This point is well taken, and concerns are justified that vitamin C supplementation may lead to high plasma oxalate levels in dialysis patients. When plasma concentrations of oxalate exceed 40 µmol/l, there is at least the possibility of oxalate crystals forming in various tissues (retina, skin, joints and myocardium).

Indeed, prior to the advent of reliable high-efficiency dialysis therapy, some cases of oxalosis occurred in haemodialysis patients [1,2]. However, with a weekly Kt/V > 3, oxalate deposits were not detected in a thorough biochemical analysis of biopsy and autopsy material from haemodialysis patients [3], and not a single case of oxalate deposition has been reported in recent years in dialysis patients as a result of vitamin C supplementation.

What is more, beneficial effects of intravenous vitamin C have been demonstrated in haemodialysis patients with functional iron deficiency [4] and also in dialysis patients with normal iron status [5] by augmenting iron mobilization from tissue stores. Up to 65% of dialysis patients respond to intravenous vitamin C with an increase in haemoglobin and/or a decrease in epoetin dosage [5].

When vitamin C is given orally (1000 to 1500 mg/week) or intravenously in a dosage of 250 to 500 mg after each dialysis session [6–8], plasma oxalate concentrations increase with the dose of vitamin C administered. Calcium oxalate saturation was exceeded in 40% of the haemodialysis patients during 6 months of therapy, with 500 mg vitamin C administered intravenously after each dialysis.

In summary, a short-term course of vitamin C, given either orally (1000–1500 mg/week) or intravenously, in a dosage of 250 to 500 mg after each dialysis session, appears to be inoffensive, whereas during long-term vitamin C supplementation, plasma oxalate levels should be monitored on a regular basis.

**Conflict of interest statement.** None declared.

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doi: 10.1093/ndt/gfm821