Does long-term administration of sodium thiosulphate inhibit progression to renal failure in nephrocalcinosis?

Sir,

In a previous communication, about 10 years ago, we presented two patients with erythrocytosis associated with renal tubular acidosis type-I (RTA-I). At that time their work-up had revealed severe metabolic acidosis, alkaline urine, hypokalaemia, hypocitraturia, extensive nephrocalcinosis and increased serum erythropoietin levels, despite abnormally elevated haematocrit values. Therefore, erythrocytosis was attributed to increased production of erythropoietin due to localized areas of tissue hypoxia at the areas of nephrocalcinosis [1–3]. One of those patients was lost to follow up a few years later. The other one has attended our outpatient clinic, periodically, for the past 18 years, and is on oral supplementation with the original regimen of sodium bicarbonate, potassium gluconate and sodium thiosulphate. Nephrocalcinosis persisted during this prolonged period of time, without evidence of further calcium deposition. Of particular interest is the fact that renal function remained stable, with serum creatinine fluctuating from 1.8 to 2.1 mg/dl. During his last laboratory evaluation (December 2000), serum creatinine was 1.8 mg/dl, BUN was 25 mg/dl,
sodium was 144 mEq/l, potassium was 3.9 mEq/l, calcium was 9.4 mg/dl, phosphate was 3.6 mg/dl and magnesium was 2.3 mg/dl. Haematocrit values have been constantly elevated above 55%, with the patient requiring phlebotomy whenever they reached 60%. Otherwise the patient feels well and carries on with his life without problems.

RTA-I is associated with specific defects in renal tubular hydrogen ion secretion and causes metabolic acidosis, alkaline urine, hypercalciuria and hypocitraturia due to acid-aemia and to a primary defect in citrate excretion. Occasionally, hyperuricosuria is also found. These abnormalities favour the nucleation of calcium oxalate and phosphate and the development of nephrolithiasis and nephrocalcinosis. Although nephrocalcinosis is a common feature and a serious cause of morbidity in adults and adolescents with RTA-I, its pathophysiology and therapy have not received the appropriate attention.

Similarly the pathogenesis of renal insufficiency in RTA-I remains unclear. However, interstitial nephritis due to a combination of calcium deposition, tubular obstruction, infection and immune injury seem to play a pivotal role in the progression of patients with RTA-I to renal failure. Alkali therapy has a beneficial effect on stone formation, since it corrects metabolic acidosis, reduces urinary calcium excretion and increases urinary citrate excretion. Oral potassium supplements are also used in patients with hypokalaemia [4,5]. Our patient, in addition to sodium bicarbonate and potassium gluconate, received sodium thiosulphate for 18 years at a dose of 15–20 mmol daily from a 2 M solution (10 mmol/5 ml) [6]. This therapy seemed to prevent any further deposition of calcium and has been associated with stable renal function for the past 2 decades.

The mechanism by which sodium thiosulphate could have affected nephrocalcinosis and interstitial nephritis is not fully understood. Sodium thiosulphate results in the formation of calcium thiosulphate in the urine, a compound with much higher solubility than the other calcium salts (phosphate, oxalate). Thus, sodium thiosulphate could not only inhibit further nephrocalcinosis, but in some degree it could contribute to decalcification of renal parenchyma [6]. In addition, sodium thiosulphate could attenuate toxicities from chemicals and metabolites due to its ability to stabilize glutathione (GSH) levels in various tissues, including brain, liver and kidney. GSH plays an important role in host defense, since it limits the action of oxygen free radicals and protects cells from oxidative stress. In this regard, sodium thiosulphate injection 1 h before, or 30 min after, cisplatin infusion attenuated renal injury in experimental animals. Similar sodium thiosulphate-associated protection has been found after exposure to paraquat, hypochlorous acid and other drugs and chemicals [7].

In conclusion, oral supplementation of sodium thiosulphate in addition to alkali and potassium in the case of RTA-I seems to offer protection against progression to nephrocalcinosis and to renal failure.

Department of Nephrology Aretaieion Hospital Athens Greece

B. Agroyannis H. Tzanatos D. V. Vlahakos E. Mallas