Dent’s disease

Sir,

The letter by Burgess and co-workers [1] gives interesting details on thiazide treatment in two patients with Dent’s disease. They conclude that this therapy is safe and may influence the natural course of the disease in patients with mild chronic renal failure. This cannot be confirmed by our results of two patients with Dent’s disease and long-term thiazide therapy. Both showed severe adverse effects with symptomatic hypokalaemia soon after the start of the therapy and signs of progression of renal disease were found in one patient. However, global renal function remained normal up to the age of 20 years in both.
The first patient was diagnosed with low molecular weight tubular proteinuria (total proteinuria 30 mg/m²/h), nephrocalcinosis and hypercalciuria (20 mg/kg/day) at the age of 5 years. Later on the diagnosis of Dent's disease was confirmed by molecular analysis detecting a point mutation which created a novel donor splice side [2]. The patient was treated with hydrochlorothiazide (0.5 mg/kg/day) which resulted in a decrease of calcium excretion to 5 mg/kg/day. However, he developed severe hypokalaemia (serum potassium 2.8 mmol/l) with clinical symptoms which was treated with oral potassium substitution. This medication was unchanged for the next 10 years, and calcium excretion was stable with values of 4–6 mg/kg/day. However, during this time total proteinuria increased further to 82 mg/m²/h and he developed renal cysts. Nephrocalcinosis was not progressing and renal function remained normal until the age of 20 years. An attempt to withdraw thiazide medication led to an increase in calcium excretion to 8.5 mg/kg/day.

The second patient was diagnosed with low molecular weight proteinuria (total proteinuria 67 mg/m²/day), nephrocalcinosis, renal cysts and hypercalciuria (9 mg/kg/day) at the age of 9 years. Due to compliance problems, thiazide medication (0.5 mg/kg/day) was taken regularly only after the age of 14 years. While calcium excretion declined to values between 3.5 and 5 mg/kg/day, severe hypokalaemia (serum potassium 2.9 mmol/l) developed which was treated with potassium supplementation (2.5 mmol/kg/day). During 4 years of thiazide medication, total proteinuria remained stable at values of 90–100 mg/m²/day and nephrocalcinosis did not progress. Renal function remained normal until now. After withdrawal of the medication, calcium excretion increased to 9 mg/kg/day.

Our data show that hydrochlorothiazide is effective in reducing hypercalciuria to normal values in patients with Dent’s disease over a long period of time supporting the data presented by Burgess et al. [1]. However, this medication led to symptomatic hypokalaemia in both patients. This has also been reported in other patients with Dent’s disease [3]. Thiazide therapy leads to profound potassium wasting in patients with normal renal function, whereas this probably occurs much less often in patients with renal insufficiency.

In spite of thiazide medication, proteinuria increased in patient 1 and the formation of renal cysts indicated progression of renal disease. The fact that none of our two patients had renal function deterioration at the age of 20 years points to a slow natural course of the disease rather than to the effect of thiazide treatment, as most patients with Dent’s disease will develop renal insufficiency not before the third or fourth decade of life [4].

Therefore, although thiazide medication may be effective in reducing hypercalciuria in patients with Dent’s disease, starting with small doses and regular electrolyte controls are mandatory, especially in patients with normal renal function. Hypokalaemia may be severe with only moderate doses of diuretics. Our data give no support to the opinion that this medication slows the natural course of the disease and prevents chronic renal failure.

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