Letters

Conflict of Interest

Sir.
Given the intense pharmaceutical and often controversial involvement in the treatment of anaemia in chronic kidney disease, it is surprising that the authors of the reply letter [1] to the criticism of their paper [2] fail to declare the financial support they have received from the relevant companies when they made this declaration in their original publication some months earlier [3].

This omission raises the question of the value of voluntary compliance with conflict of interest declarations when authors fail to comply with the requirements of the conflict of interest form which is very clear, detailed and comprehensive in its format. The omission of conflict of interest declarations in industry sponsored supplements in Nephrology, Dialysis Transplantation is another example of the laxity employed in the observance of full compliance.

Conflict of interest statement. The author is a consultant for Fresenius Medical Care GmbH and Nipro Corporation, Japan.

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Severe bladder dysfunction in a family with ADH receptor gene mutation responsible for X-linked nephrogenic diabetes insipidus

Sir,
We read with great interest the article by Shalev et al. [1] who reported a family affected by nephrogenic diabetes insipidus (DI) associated with hydroureteronephrosis and bladder dysfunction. The authors found a mutation of the aquaporin 2 gene (AQP2) to be responsible for the underlying concentration defect. As the authors indicate, the hyperdiuresis is thought to be responsible for the hypotonic large capacity-type bladders. We regularly see several patients affected by different forms of nephrogenic DI. We want to draw attention to one particular family with three boys affected by X-linked DI due to an R106C mutation in the AQP2 gene coding for the antidiuretic hormone (ADH) receptor. The maximal urine concentration capacity in these three patients is extremely reduced (140–215 mosm/kg) and diuresis ranges between 6 and 8 l/day. Ultrasound investigations revealed bilateral hydroureteronephrosis. Voiding cystography (VCUG) did not show any pathological reflux or outlet obstruction, but revealed an enlarged bladder (Table 1). Urinary flowmetry revealed a hypotonic large capacity-type neurogenic bladder similar to that described by Shalev et al. Clean intermittent catheterizations (CICs) are necessary in all three boys (Table 1). Undoubtedly the development of severe bladder distension in situations of extremely high amounts of hypo-osmotic urine remains rare. Nevertheless, our three patients presented with a bladder dysfunction of severity comparable with the cases reported by Shalev et al. Other authors have reported similar cases of bladder dysfunction in patients with nephrogenic DI [2,3]. In vivo studies in rats with hyperdiuresis evidenced a decrease in total bladder collagen content, but showed a normal contractile function [4]. It has not yet been elucidated if the large urine flow is the only contributing factor to the development of such urinary tract dilatation in DI. It is thought to exceed the capacity of the urinary tract, causing a functional obstruction and residual urine volume. One could hypothesize that severe distension of the bladder induces stretching of actin and myosin filaments responsible for the contractile defect in patients with severe bladder dysfunction. More complicated mechanisms might be involved in its pathogenesis, such as an independent associated urinary tract dysfunction. One could hypothesize that some gene mutations could be responsible for both the concentration defect and the bladder dysfunction in certain patients. These cases provide evidence that a similar phenotype is caused by two different gene mutations, which is a strong argument against a separate genetically mediated bladder dysfunction.

In conclusion, a mutation of the ADH receptor gene can be responsible for DI with severe bladder dysfunction, as well as a mutation of the AQP2 gene.

Conflict of interest statement. None declared.

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Table 1. Major clinical symptoms and results of radiological investigations in three male patients with a mutation of the ADH receptor gene responsible for nephrogenic DI

<table>
<thead>
<tr>
<th>Age</th>
<th>Nocturnal enuresis</th>
<th>Daytime enuresis</th>
<th>Need for CICs</th>
<th>Hydro-uretero-nephrosis</th>
<th>Bladder volume (ml) in VCUG (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>1000 (4.7)</td>
</tr>
<tr>
<td>16</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>1200 (6.3)</td>
</tr>
<tr>
<td>20</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>1200 (6.3)</td>
</tr>
</tbody>
</table>

Bladder volume (mean ± SD) in healthy children > 10 years old and adolescents measured by VCUG is 389 ± 129 ml [5].

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Hypercalcaemia from non-prescription vitamin A

Sir,

Use of over-the-counter ‘natural’ supplements may have unnatural effects. We report this case as a cautionary example.

A 67-year-old white man was admitted to hospital in late January 2004, with malaise and hypercalcaemia. He had undergone kidney transplantation 6 years earlier for kidney failure of unknown cause. Chronic allograft nephropathy occurred and the plasma creatinine rose to 400 μmol/l. He began to feel unwell in December 2003, and had a 5 kg weight loss. There was constipation, melena and haematochezia. His medications included prednisone, mycophenolate mofetil, atorvastatin, labetalol, bumetanide and potassium chloride. Blood tests showed a total plasma calcium of 4.2 mmol/l and he was admitted to hospital. On examination, there was a tremor and unsteadiness of gait. The plasma chloride was 115 mmol/l (normal 102–108). Intravenous normal saline was given mainly as antacid agents and are often used without special caution in patients with chronic renal failure (CRF) not yet on dialysis. Herein, we report a case of fatal Al-related encephalopathy in a patient with severe CRF, not on dialysis, due to the intake of large doses of antacids containing Al for at least 3 years.

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A fatal case of aluminium encephalopathy in a patient with severe chronic renal failure not on dialysis

Sir,

Aluminum (Al) toxicity in patients with end-stage renal disease is a well known adverse effect due to either dialysate Al contamination or oral intake of Al-containing phosphate binders [1]. At present, the clinical forms of Al toxicity have almost disappeared. Al-containing drugs are given mainly as antacid agents and are often used without special caution in patients with chronic renal failure (CRF) not yet on dialysis. Herein, we report a case of fatal Al-related encephalopathy in a patient with severe CRF, not on dialysis, due to the intake of large doses of antacids containing Al for at least 3 years.

Case. A 59-year-old white male patient with CRF due to diabetic nephropathy was followed as an out-patient in our chronic kidney disease clinic. When he was 47 years old, diabetes mellitus was diagnosed, and he was treated with oral antidiabetics for 2 years and thereafter with insulin. At 55, a severe polyneuropathy and distal occlusive arterial disease with foot gangrene occurred that required the amputation of the left foot. He suffered from gastric pain which he self-treated with Al hydroxide (Maalox® TC). A gastroduodenoscopy was performed that revealed antral gastritis positive for Helicobacter pylori. Despite the antibiotic treatment, the patient continued taking Al hydroxide. From the age of 57, he regularly attended our chronic kidney disease clinic. His serum creatinine was between 3 and 4 mg/dl...

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