was 42 mmol/L, potassium 12.4 mmol/L, urea 27 mmol/L and osmolality of 134 mOsm/kg. The urine osmolar gap was −1.8, making recent toluene abuse unlikely. Immunological tests were negative (inter alia, Hep 2 cells, ANA, and autoimmune profile negative). Subsequent investigations showed transient polyuria (urine volume up to 4.3 L/day), high 24-h urinary K⁺ wasting (175 mmol/day). CT scan of the abdomen showed marked bilateral nephrocalcinosis, but no other abnormalities.

The patient re-presented to the emergency department with similar symptoms a month later. On this occasion, she was also found to be hypokalaemic (2.1 mmol/L) with similar symptoms a month later. On this occasion, she was again treated with fluid resuscitation and potassium repletion. She denied further NSAID or diuretic use. In view of the recurrent hypokalaemia, advanced nephrocalcinosis, urine pH, positive urine anion gap and normal anion gap metabolic acidosis, a diagnosis of longstanding type 1 RTA was made. She made a full recovery and was discharged 5 days later on potassium citrate supplementation, and remained potassium replete on follow-up.

There have been reports of ibuprofen codeine combination, particularly in excess doses, causing acute and transient RTA [1–4]; when characterized it has been reported to be type 2. Our patient now meets criteria for a diagnosis of type 1 RTA. This pre-existing condition was not diagnosed until her admission with life-threatening hypokalaemia, after taking an ibuprofen codeine combination for 3 months. This presentation with far graver hypokalaemia than before was accompanied by no alternative explanation for the development of 0.76 mol potassium deficit, and was associated with transient hypophosphataemia. We speculate that at the time of presentation she had developed a proximal tubulopathy, attributable to the ibuprofen codeine combination, resulting in a combined renal tubular acidosis with dramatic consequences. Vigilance in eliciting a detailed analgesic history remains important in patients with acute acidoses, especially in patients with pre-existing renal conditions.

Conflict of interest statement. None declared.

1 School of Medicine
King’s College, London
2 Department of Renal Medicine
Mayday University Hospital
Thornton Heath, UK
E-mail: charles.soper@mayday.nhs.uk


doi: 10.1093/ndtplus/sfn025

Advance Access publication 29 April 2008

Proximal tubular dysfunction associated with tenofovir in an HVC-HIV co-infected patient undergoing HVC therapy

Sir,

Tenofovir is an adenosine analogue, and exposure to ribavirin (RBV) could increase the intracellular phosphorylated metabolites of tenofovir. Nucleoside analogues essentially have mitochondrial toxicity. Nephrotoxicity of these nucleoside analogues in combination with HVC therapy is a rare complication [1].

We present the case of a 40-year-old white man, with HIV infection diagnosed in 2001 and VHC in 2006. The HIV infection was asymptomatic with a CD4+ lymphocyte count of 711 cells/µl and undetectable plasma HIV-RNA. The antiretroviral treatment was efavirenz (600 mg/day), emtricitabine (200 mg/day) and tenofovir disoproxil fumarate (300 mg/day). In November 2006, the patient initiated therapy for the VHC infection consisting of pegylated interferon and RBV therapy. The renal function was normal, with a serum creatinine of 86 µmol/l and a creatinine clearance of 100 ml/min/1.73 m². Five months after initiation of treatment for the VHC infection, the patient showed general weakness and dyspnea. Blood and urine analyses on admission indicated the presence of anaemia (haemoglobin 6.4 g/dl and haematocrit 20.6%), renal failure (creatinine of 424 µmol/l, urea 10.7 mmol/l, MDRD 12.3 ml/min/1.73 m² and proteinuria 1.13 g/24 h) and proximal tubular kidney dysfunction with hypophosphataemia, hypouricaemia, hyperchloremic metabolic acidosis with normal anion gap and a low-molecular-weight proteinuria. A renal biopsy showed the presence of chronic tubulo-interstitial lesions and focal-segmental glomerulosclerosis (Figure 1).

The patient was diagnosed with HIV nephropathy and proximal tubular dysfunction secondary to tenofovir and RBV treatment. The administration of these drugs was stopped. Two months later the metabolic disorders completely regressed with partial recovery of renal function (creatinine of 186 µmol/l and MDRD of 37 ml/min/1.73 m²) and reduction of proteinuria (0.40 g/24 h).

Some cases of acute tubular necrosis, isolated tubular defects such as Fanconi syndrome, distal tubular acidosis and nephrogenic diabetes insipidus, have been reported with reverse transcriptase inhibitors [2]. Tenofovir is eliminated by glomerular filtration and active tubular secretion. Hypothetically, this effect could enhance the risk of kidney tubular dysfunction in HVC-HIV co-infected patients undergoing HVC therapy, although tenofovir-related nephrotoxicity
is apparently rare and mainly seen in patients with mild pre-existing renal impairment [3,4]. In the same manner as other reverse transcriptase inhibitors, RBV could compete with tenofovir for the human organic anion transporter-1 (hOAT1), on the basolateral membrane of the proximal tubules, resulting in an increased tenofovir concentration and tubular toxicity [1,5].

Conflict of interest statement. None declared.

1Department of Nephrology
2Department of Internal Medicine
Hospital de Terrassa, Terrassa
3Department of Pathology
Hospital Clinic
Barcelona, Spain
E-mail: 34989nfb@comb.es

Néstor Fontseré1
Carolina Guérero2
Vincent Esteve1
Manel Solé3
Manel Ramírez de Arellano1

Sir,
The children affected by Finnish-type congenital nephrotic syndrome (FCNS) frequently show muscular hypotonia and neurological development retardation, which usually ameliorate after kidney transplantation [1,2,3,4]. However, Laakkonen H et al. recently described six FCNS patients with a severe dyskinetic cerebral palsy-like syndrome with dystonic features, athetosis and a hearing defect. Four of the patients died between 1 and 4 years of age in different circumstances; the others survived with severe neurological deficits. In spite of normal metabolic investigations, Laakkonen et al. hypothesize that the complex neurological picture was due to mitochondrial dysfunction [5].

We observed a child with FCNS and similar dyskinetic symptoms who died suddenly when he was 4.5 years. He was born at 34 weeks; elevated α-feto-protein was detected in maternal serum (1100 ng/ml) and amniotic fluid; the placenta was 1200 g with a placenta weight/newborn weight ratio of 0.44. Neonatal hyperbilirubinaemia, max 5.5 mg/dl (5.3 mg/dl non-conjugated and 0.2 mg/dl conjugated), was observed. At the age of 3 weeks, secondary hypothyroidism (T4 0.63 ng/dl and TSH 13.1 µU/ml; nv: T4 0.8–1.9 ng/dl, TSH 0.4–4 µU/ml) was diagnosed; thyroxine 37.5 µg/day normalized thyroid hormones (T4 1.2 ng/dl and TSH 3.4 µU/ml). Laboratory parameters also showed heavy proteinuria (>300 mg/Kg/day) and severe hypoalbuminaemia (0.78 g/dl). The clinical diagnosis of FCNS was later confirmed by molecular study for NPHS1 locus. At the age of 3

doi: 10.1093/ndtplus/sfn043

Advance Access publication 13 May 2008

A new case of Finnish-type congenital nephrotic syndrome, neuromuscular symptoms and early death