NDT Plus (2008) 4: 270–278

NDT PLUS
Nephrology Dialysis Transplantation

Letters

Advance Access publication 10 June 2008

Are segments of the developing world competing in end-stage renal disease (ESRD)?

Sir,

Trinidad and Tobago are the southernmost islands in the Caribbean archipelago with a population of 1.3 million, consisting of two major diaspora Africans and Southeast Asians. An economy buoyant by petroleum exports is responsible for a GDP per capita of 10 894.4 ($US). The number of patients ($n = 436$) with ESRD receiving dialysis is the highest in comparison with Jamaica ($n = 366$), Bahamas ($n = 211$), Barbados ($n = 185$), Cayman Islands ($n = 41$) and the British Virgin Islands ($n = 27$) [1].

In Jamaica and Trinidad, the two most common causes of ESRD are diabetes and hypertension. The management of ESRD in Trinidad is mainly by dialysis provided by the state at two major tertiary centres on the island. To receive dialysis, patients must only be hepatitis B surface antigen negative; patients infected with the human immunodeficiency virus (HIV) or those who are hepatitis C virus (HCV) seropositive are not excluded. A study of the trends in the prevalence and epidemiology of ESRD during the period 1999–2007 at one of these haemodialysis sites was conducted using a retrospective cohort design. Between 1999 and 2004 the number of new cases seeking dialysis was 5 per annum; however, in 2005, 2006 and 2007, there were 14, 16 and 26 new cases, respectively. During this period there were no unusual patterns of disease occurrences or any special interventions, either clinical or promotional, to detect renal disease. The mean age among men was 52 (SD $\pm$ 13.9) years as compared to women 46.8 (SD $\pm$ 14.9) years; a similar finding was reported by Soyibo and Barton [1]. In contrast, Reikes showed in 2000 that, in the United States, the highest incidence rate of ESRD occurs in patients 64 years and older [2]. This implies that in the Caribbean population ESRD occurs at an earlier age.

There were more Africans (45.7%) than Southeast Asians (39.5%), and hypertension (70.4%) and diabetes (40.7%) were the commonest comorbid conditions, similar to findings reported by Brown [3] and Lane *et al.* [4]. In conclusion, we provide epidemiological evidence of ESRD of epidemic proportions in Trinidad.

Conflict of interest statement. None declared.

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doi: 10.1093/ndtplus/sfn067

Advance Access publication 10 April 2008

Ibuprofen codeine combination precipitating severe hypokalaemia in a patient with pre-existing type 1 renal tubular acidosis

Sir,

A 36-year-old lady presented to the A&E with a 2-day history of generalized, severe progressive weakness of her limbs. Two days prior to her presentation, she had been exercising vigorously at the gym and subsequently developed muscle pain. In the hours following, she developed progressive weakness in her upper and lower limbs. She became unable to walk or stand. She described several previous episodes of leg weakness and numbness, especially at night, over a few months. On further questioning, she stated that she had been taking up to eight tablets of an ibuprofen codeine combination (200 mg + 12.8 mg respectively) everyday for 3 months for backache. She had been admitted previously with profound iron deficiency anaemia and weakness but mild hypokalaemia 19 months before, which had resolved completely with oral supplementation. There was no other relevant family or drug history. On examination, the patient was dehydrated, afebrile (37.4°C), with a regular pulse rate of 90 bpm and blood pressure 123/83 mmHg. She had decreased power in all four limbs (MRC score of 3/5 in the lower limbs and 4/5 in the upper limbs). Blood tests on admission showed a serum potassium of 1.7 mmol/L and a high serum creatinine level of 282 mmol/L and urea 12.8 mmol/L (sodium 130 mmol/L, chloride 95 mmol/L, creatinine kinase 289 i.u./mL). Arterial blood gas sampling revealed a metabolic acidosis (pH 7.20, pCO_2 3.04 kPa (23 mmHg), pO_2 15.7 kPa (118 mmHg), HCO_3 11.0 mmol/L, base deficit 18) with an anion gap of 25 mmol/L. Serum lactate was normal (0.9 mmol/L) and salicylate was undetected. An *E. coli* UTI was discovered and treated. ECG changes were consistent with severe hypokalaemia. Her urine sodium at presentation

was 42 mmol/L, potassium 12.4 mmol/L, urea 27 mmol/L and osmolality of 134 mOsm/kg. The urine osmolal 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 hyperchloraemic metabolic acidosis (pH 7.23, HCO_3 14.7 mmol/L, base deficit 12.6). Her serum anion gap was normal (13 mmol/L). Whilst acidotic, her urine anion gap was + 7 mmol/L and urine pH 6.52. 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.

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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 metabolities 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 m^2. 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 m^2 and proteinuria 1.13 g/24 h) and proximal tubular kidney dysfunction with hypophosphataemia, hypouricaemia, hyperchloraemic 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 m^2) 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