Table 1. Itch score (median; range) 1 week before treatment (week 0), during (week 1–4) and after treatment (week 5–6) treatment with pentoxyfilline

Week of treatment	Patient A	Patient B	Patient C
0	3 (3–5)	6 (5–6)	4 (2–7)
1	3 (2–4)	5 (5)	3 (2–5)
2	3 (2–4)	4 (3–4)	5 (1–6)
3	1.5 (0–3)	3 (3–5)	1 (0–5)
4	0 (0–3)	1 (2–3)	2 (1–3)
5	0 (0–3)	1 (1)	2 (0–4)
6	0 (0)	No data	0 (0–4)

developed after 1 week of treatment. The treatment course was completely administered in three patients and in these three, pruritus was reduced dramatically (Table 1 showing mean and range of VAS each week in the patients were followed). While in the first week almost no effect could be noted, reduction of pruritus started in the second week and reached its peak during the third week. In two patients, the effect continued over at least two more weeks after discontinuation of the treatment.

In view of the high rate of side effects, PTX will not be of help for all patients. However, in patients tolerating the drug, the therapeutic effect seems to be very promising. Hopefully, modifications in dose and infusion rate will lead to greater tolerability without a loss of efficacy.

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Why we should subdivide CKD stage 3 into early (3a) and late (3b) components

Sir,

According to the DOQI estimate of chronic kidney disease (CKD) populations in the US, CKD stage 3 patients outnumbered those in the following stage (stage 4) almost 20-fold. The reported absolute numbers were 7.6 and 0.4 million for patients in stages 3 and 4, respectively. I feel that this unexpected difference between the two successive CKD stages did not raise sufficient questions, research and analysis. Such a huge difference can either be due to a high mortality rate during the late periods of stage 3, so that only a minority of patients reach stage 4, or it is due to a very high mortality rate during stage 4. It should be indicated that stage 3 extends over a glomerular filtration rate (GFR) range (59–30) that is twice the GFR range of stage 4 (29–15). At the same rate of GFR loss, this latter range difference would result in halving the residence time of CKD patients on stage 4 compared to stage 3. This alone can account for only half (i.e. for a factor of 2× out of 20×) of the overall patient count difference between the two stages. However, current available evidence suggests that the combination of high mortality in these two stages is the main explanation for the sudden drop in patient numbers between the two stages. It could be indicated here that the CKD stage 5 patient count would also have been negligible compared to that of stage 4, as it is the case in fact in many developing countries, except for the availability of the renal replacement therapy (RRT). Such therapy has allowed for longer residence time within (dialysis) or after (transplantation) this stage.

Robert N. Foley *et al*. [1] reported a renal replacement rate of 1.6% and 3.4% among CKD patients with no DM, or with DM. However, they reported much higher mortality rates of 8.1, 17.7, respectively, among the same patients, during only a 2 year follow-up period. Keith *et al*. [2] reported 5 year mortality of 24.3% and 45.7% in CKD stages 3 and 4, respectively. Only 1.3% of the patients in stage 3 reached the end stage renal disease (ESRD) stage during this 5 year follow-up period. As is now appreciated, mortality is a much more likely fate for CKD stage 3 patients than reaching ESRD. 'Recent data have shown that CKD patients are 5–10 times more likely to die than to reach ESRD.'[3]. Similar findings have been also reported by several other studies.

We can safely hypothesize that most of this high mortality within stage 3 is toward the end of stage 3 itself and is the result of the developing uraemic milieu after the progressive reduction of GFR below 60 ml/min. Few uraemia-related pathological changes are expected to have developed prior to reaching GFR range value of 60 ml/min. How to equate GFR of 59 ml/min with 30 ml/min? Such patients are truly heterogeneous, regarding the degree of the developing 'uraemia' associated pathological changes.

I believe that stage 3 should be subdivided into two 15 m/min ranged components: 3a (GFR 59–45 ml/min) and 3b (GFR 44–30 ml/min). This would help to define more precisely the edge within stage 3 at which mortality becomes the main worry. Higher efforts to reverse or even abort the developing pathological processes can then be targeted, prior to that edge. For example, considering renal transplantation as the only modality among RRT modalities that can truly reverse this uraemic milieu, we might be justified in considering the introduction of this modality, not as a RRT, but as a mean to save patients organs and lives prior to that lethal edge. Prospective studies for such utilization of renal transplantation or any other therapeutic maneuvers directed to stage 3 will of course be needed. This hypothesis concerns the existence of an edge or a jump in mortality rate within stage 3, that is expected to be within the latter part of stage 3 (3b). Defining that point might help in directing our intervention more appropriately. In addition, as CKD is

essentially defined by estimated GFR below 60 ml/min, having our data on CKD patients, reported on equally divided stages (each of 15 ml/min range) would allow for better comprehension and comparative evaluation of the changing trends of morbidity and mortality during the CKD journey.

Conflict of interest statement. None declared.

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Hypokalaemic paralysis induced by large amounts of cola consumption

Sir,

Cola includes large amounts of caffeine. It is well known that caffeine intoxication induces neuro-psychiatric, cardiovascular, respiratory, gastrointestinal and metabolic abnormalities. Metabolic complications include hyponatraemia, metabolic acidosis, hyperglycaemia, respiratory alkalosis and hypokalaemia [1]. Only three cases of hypokalaemia by cola intoxication have been reported in the literature. However, in one case, the hypokalaemia was associated with metabolic alkalosis induced by chronic vomiting, rather than only cola intoxication [2]. The other two cases occurred in pregnant women [3,4]. We report a case of hypokalaemic paralysis induced only by large amounts of cola consumption in a man.

A 52-year-old man was admitted to our emergency room with progressive paralysis in both extremities. He had started medication for alcoholism and major depression 30 months previously. He was intermittently treated in an adjacent psychiatric hospital for resolution of his psychiatric problems. Whenever he was admitted, he drank large amounts of cola without the permission of hospital staff. Due to symptomatic aggravation, he was readmitted to the psychiatric hospital, 1.5 months before admission to our hospital. On admission to the psychiatric hospital, his initial potassium level was 4.0 mmol/l; since then, he had drunk 4–5 l of cola per day. He felt numbness in his fingers and toes 3 days prior to admission at our hospital. He could not grip his fingers tightly and walk by himself, following the consumption of 9 l of cola 1 day before. He could not move his arms and legs nor rotate his neck, and had difficulty in breathing on admission. He had no history of vomiting and diarrhoea. On admission to our hospital, he looked agitated and acutely ill. His volume status was normal. Body temperature was 36.5°C, heart rate was 84 bpm, respiration rate was 18 per minute and blood pressure was 130/80 mmHg. There was no pitting oedema in the legs. There was muscle weakness as grade IV/V and deep tendon reflex was decreased at both legs. Peripheral WBC count was 13 870/mm^3 and the polymorphonuclear leukocyte (PMN) was 67.4%. The haemoglobin level was 17.1 g/dl and platelet level was 317 000/mm^3. Total protein level was 7.3 g/dl and albumin level was 4.5 g/dl. Serum electrolyte showed that sodium level was 141.6 mmol/l and potassium level 2.3 mmol/l and magnesium level was 1.9 mmol/l. His serum osmolality was 288 mosm/kg. Metabolic acidosis and respiratory acidosis were observed on his arterial blood gas analysis (pH 7.30, PCO_2 37 mmHg, HCO_3^- 17 mmol/l). His urine potassium level was 6.6 mmol/l and urine osmolality was 228 mosm/kg. His renin and aldosterone level in a supine position was within normal range. His thyroid function test was normal (TSH 1.04 μU/ml (0.17–5.00), free T4 0.91 ng/dl (0.89–1.80) and free T3 2.57 pg/ml (1.62–3.80). There were no explanations for the hypokalaemia, other than excessive consumption of cola. After cola was withdrawn and only 170 mmol of potassium chloride was replaced via intravenous site, his serum potassium level was 4.2 mmol/l and paralysis was completely improved 48 h later.

It is known that an oral intake of only 180–360 mg caffeine can provoke serious hypokalaemia [5]. Cola includes 130 mg caffeine per litre; this patient thus consumed approximately 1000 mg caffeine. There are several potential mechanisms by which caffeine may induce hypokalaemia [2]:

(i) Redistribution of potassium into cells.
(ii) Caffeine induces catecholamine release, probably by means of adenosine antagonism.
(iii) Caffeine may increase renal excretion of potassium.
(iv) Caffeine-induced hyperventilation with respiratory alkalosis.

Caffeine-induced hypokalaemia may well be an overlooked cause. When faced with unexplained hypokalaemia, patients should be asked to provide a thorough history of caffeine intake, such as cola, coffee, cocoa and oriental tea.

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