Topiramate-induced metabolic acidosis: a case study
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To the Editor,
We present the case of a 75 year-old male with hypertension and chronic obstructive pulmonary disease who was diagnosed with chronic delusional disorder and mixed personality disorder, along with partial epilepsy due to a left parietal haematoma from several years prior. The patient was under treatment with topiramate, levetiracetam, quetiapine, sertraline, clobazam, and bronchodilators. He sought treatment for a respiratory infection and functional deterioration consisting of apathy, drowsiness, and periods of aggressive behaviour. A physical examination revealed that the patient had no fever, although he did suffer from disorientation and slurred speech, and would drift off to sleep, but with no apparent focal loss of motor function. The patient also had shallow tachypnoea, widespread rhonchi, and crackles in the left base, with radiological images indicative of superinfection of the abnormally widened bronchial tubes. We performed a laboratory analysis, revealing mildly elevated chlorine (114 mEq/l), with nor-
mal renal function and all other ion parameters (sodium: 138mEq/l; potassium: 4.2mEq/l), and baseline arterial gases compatible with a diagnosis of metabolic acidosis (pH: 7.24; pCO₂: 33mm Hg; pO₂: 67mm Hg; bicarbonate: 17mMol/l; base excess [BE]: -9.1mMol/l). The anion GAP value (difference between serum sodium and the sum of chloride and bicarbonate) was 7mEq/l. The patient received treatment with systemic steroids and quinolones, with rapid clinical improvement until reaching a normal baseline levels. However, later controls revealed persistent hyperchloremic metabolic acidosis; after ruling out other possibilities, we attributed this fact to the chronic treatment with topiramate, which was suspended and replaced with phenytoin, which completely resolved the altered laboratory values by the time the patient was discharged.

Topiramate is a sulphamate with antiepileptic effects, and is indicated in preventive treatment of migraine,1,2 the treatment of neuropathic pain3, bipolar disorder,4 tobacco dependence, and bulimia nervosa,4 among other pathologies. Its most common secondary side effects3,5 are asthenia, dizziness, drowsiness, emotional lability, and weight loss. The development of urolithiasis and hyperchloremic metabolic acidosis with a normal anion GAP is much less common, but has been reported. Topiramate has a molecular structure very similar to acetazolamide2,6 and inhibits the carbonic anhydrase enzyme,7,8 especially the type II isoenzyme that predominates in human kidneys.2,6 This can lead to mixed renal tubular acidosis10 (type 3) as a result of ultrafiltration and reabsorption of bicarbonate in both proximal and distal tubules,4 thus altering urine acidification and provoking a decrease in serum bicarbonate and CO₂ concentrations,7 which is usually mild and asymptomatic,3,9 although can produce hyperventilation1,4 neurological symptoms,3 nephrolithiasis, osteoporosis, and osteomalacia in the long term. The circumstances that predispose patients to developing this complication are not well established, but patients are more likely to develop it if they have other conditions that cause acidosis, such as infections, diabetic ketoacidosis, chronic renal failure, or surgery.4,5 Certain genetic polymorphisms in the involved carbonic anhydrase isoenzymes may explain a greater or lesser susceptibility of certain patients to develop this complication.3,9 Some authors have suggested the possibility of monitoring bicarbonate1,6 or CO₂1,5 levels to predict these cases, although this is not a completely validated method. The development of metabolic acidosis during chronic treatment with topiramate is a reversible condition, regardless of the dosage9 and duration of treatment.9 The only treatment is to suspend the use of the drug10 (there is no antidote) and replace it with a substitute. When the withdrawal of the drug is not possible, and the patient maintains acceptable levels of pH and serum bicarbonate, with no symptoms, indefinite treatment with oral alkaline supplements can be administered (sodium citrate or citric acid1).

Conflicts of interest
The authors affirm that they have no conflicts of interest related to the content of this article.


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Giant true aneurysm of the radial artery following ligation of an arteriovenous fistula for haemodialysis

To the Editor,
Aneurysms and pseudoaneurysms develop in approximately 8% of arteriovenous fistulas (AVF) created for haemodialysis.1 They are potential sources of embolisation and thrombosis, and can occasionally erode the skin, giving rise to infection and local bleeding, and can even deform the af-