Case Report

Encephalopathy caused by lanthanum carbonate

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Abstract

Lanthanum carbonate is a nonaluminum, noncalcium phosphate-binding agent, which is widely used in patients with end-stage chronic kidney disease. Until now, no significant side-effects have been described for the clinical use of lanthanum carbonate, and there are no available clinical data regarding its tissue stores. Here we report the case of a 59-year-old patient who was admitted with confusional syndrome. The patient received 3750 mg of lanthanum carbonate daily. Examinations were carried out, and the etiology of the encephalopathy of the patient could not be singled out. The lanthanum carbonate levels in serum and cerebrospinal fluid were high, and the syndrome eased after the drug was removed. The results of our study confirm that, in our case, the lanthanum carbonate did cross the blood-brain barrier (BBB).

Although lanthanum carbonate seems a safe drug with minimal absorption, this work reveals the problem derived from the increase of serum levels of lanthanum carbonate, and the possibility that it may cross the BBB. Further research is required on the possible pathologies that increase serum levels of lanthanum carbonate, as well as the risks and side-effects derived from its absorption.

Keywords: chronic kidney disease; encephalopathy; lanthanum carbonate; phosphate-binding agent

Background

Hyperphosphatemia is an established risk factor for cardiovascular mortality, renal osteodystrophy and secondary hyperparathyroidism in patients with end-stage chronic kidney disease (CKD) under renal replacement therapy. Limitations in the phosphate of the diet have been the cornerstone of the treatment, but this measure is not enough for the control of hyperphosphatemia, and the use of phosphate-binding agents (calcium carbonate, calcium acetate, aluminium hydroxide or sevelamer) is necessary [1]. The ideal phosphate-binding agent should offer a minimal absorption, few side effects, a minimal pill load and low cost. Aluminium hydroxide may cause encephalopathy, osteomalacia and anaemia [2]. Therefore, it must be used with caution. Calcium carbonate or calcium acetate increase vascular and valvular calcification. Sevelamer is a nonabsorbable ion-exchange resin that does not contain calcium or aluminium, and its use is only restricted by gastrointestinal tolerance, metabolic acidosis and the high pill load required for an adequate control of phosphate levels.

Two years ago, a new and powerful noncalcium non-aluminium phosphate-binding agent appeared on the market, lanthanum carbonate (LaCO₃), which allows for a potential improvement of the control of serum phosphate levels in patients with CKD, and no significant side effects have been described to date [3, 4].

We report here the case of a patient with end-stage CKD under periodic haemodialysis with confusional syndrome, probably secondary to LaCO₃ intake.

Case report

We present the case of a 59-year-old male patient with a history of cystic thyroid nodules, arterial hypertension, portal hypertension of unknown origin with esophageal varices, Barrett’s esophagus, left ventricular hypertrophy, secondary hyperparathyroidism and end-stage CKD of unknown origin, under haemodialysis since 1998 with cadaveric renal transplantation in 1999. The patient started haemodialysis again in April 2002 with Kt/V >1.2. His usual treatment included omeprazole (20 mg/day), prednisone (2.5 mg/day) and darbepoetin alpha (50 µg/14 days). For adequate control of secondary hyperparathyroidism, the patient was prescribed in stages, treatment with calcium acetate (3000 mg/day), paricalcitol (1 µg/48 h), cinacalcet (60 mg/day) and LaCO₃ (3750 mg/day) since September 2009, with poor gastrointestinal tolerance, which led to weight loss. The patient started treatment with LaCO₃ in November 2008 with a dose of 2000 mg/day, at which time analysis showed Ca 7.9 mg/dL, P 6.9 mg/dL, PTH 603 pg/mL; in July 2009, we increased the dose of cinacalcet to 90 mg/day, but the patient developed gastrointestinal intolerance and we decreased the dose to 60 mg/day and LaCO₃ was increased to 3500 mg/day because the patient had poor control of mineral metabolism with Ca 8.4 mg/dL,
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LaCO$_3$ is highly insoluble, and its absorption, which is intestine, and it acts as a phosphate-binding agent [3, 4]. Its dissociation in the gastric area and the first stretch of the elements. It is the first element of the lanthanides. LaCO$_3$ Lanthanum is an element that belongs to the rare earth elements. It is the first element of the lanthanides. LaCO$_3$ is highly insoluble, and its absorption, which is enhanced in uremic patients, is therefore minimal (0.002%). It shows a 99% binding to plasmatic proteins, and it is excreted biliary. Although it does not metabolize with hepatic enzymes, there are no data regarding cases of severe hepatopathy. Its elimination half-life is 53 h. Disorders that lead to a significant reduction of the bile flow, as portosystemic shunt, may be associated to a slower elimination of lanthanum, which would involve an increase of its plasmatic concentrations and a higher tissue deposition [6].

Experimental studies have detected the presence of LaCO$_3$ in several tissues, such as the alimentary canal, bones and liver [6, 7]. No brain deposit or cognitive disorders have been described.

The only significant adverse effects that have been found are gastrointestinal problems, in ~6% of the cases, whereas the main adverse reactions described for the central nervous system are nausea, headaches or taste alterations. At an experimental level, the impact of lanthanides on the central nervous system is not insignificant: they can cross the blood-brain barrier [8] (BBB) and accumulate on the hippocampus, the cortex and the cerebellum, with the subsequent risks of cognitive and conduct alterations [9]. LaCO$_3$ inhibits the activity of the Ca$_{2+}$-ATPase, it reduces the concentration of monoamine neurotransmitters [10] and it alters the function of the cholinergic system. There is limited experience of treatments for >2 years.

We present the case of a patient that was under treatment with LaCO$_3$ for 18 months. Gastrointestinal upsets derived from its intake led to anorexia, malnutrition, which was seen in retrospect, and an increase of the free fraction of the compound. This fact, together with a delay in the biliary excretion as a consequence of the portosystemic shunt, proved because the patient had portal hypertension of unknown origin with esophageal varices and led to increased levels of LaCO$_3$. Normal levels of ammonium ruled that the delirium was attributed to hepatic encephalopathy. We do not know if LaCO$_3$ altered the permeability of the BBB [10] or if it was previously altered, which would explain the spinal fluid protein concentration of our patient that could not be ascribed to any existing neurological pathology. Our clinical case showed that the high serum levels of LaCO$_3$ explain the fact that it crossed the BBB and led to confusional syndrome and hypotension, which disappeared when the drug was removed.

Although LaCO$_3$ seems a safe drug with minimal absorption, our work reveals the problems derived from the increase of LaCO$_3$ serum levels, after increasing the LaCO$_3$ dose in a patient with malnutrition and hepatopathy, and the possibility that LaCO$_3$ may cross the BBB. Further research is required on the possible pathologies that increase the serum levels of LaCO$_3$ and on the risks and side effects derived from its absorption.

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Conflict of interest statement. None declared.

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