A confusional state associated with use of lanthanum carbonate in a dialysis patient: a case report

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Abstract

A 75-year-old woman was admitted with febrile confusion and abdominal pain. She was taking medications that included lanthanum carbonate. Examination, biology, a cerebral scan, and a review of her medications could not explain the confusion. The plain film of the abdomen revealed multiple diffuse calcium-like deposits throughout the digestive tract. The plasma levels of lanthanum were higher than normal. The confusion resolved after discontinuation of the lanthanum carbonate.

This case raises the problem of the potential role played by lanthanum tablet residue in the genesis or aggravation of diverticular flare-up and the problem of the potential permeability of the blood–brain barrier with lanthanum use in case of its digestive accumulation, leading to increased serum concentrations.

Keywords: adverse event; confusion; therapeutic

A 75-year-old woman undergoing haemodialysis since December 2004 was admitted to our Nephrology Unit on 7th May 2007 with febrile confusion and abdominal pain. She had a history of end-stage renal disease consecutive to chronic interstitial nephropathy, hypertension, atrial fibrillation, ischaemic heart disease, situs inversus and bowel occlusion in 2000 due to sigmoid diverticulosis.

Medications included bisoprolol, amiodarone, bromazepam, sodium bicarbonate, sodium alginic, calcium carbonate and lanthanum carbonate 750 mg twice a day.

She had become febrile for a few days prior to admission. Upon arrival, her body temperature was 38.5°C. She complained of dizziness associated with falls but had not experienced loss of consciousness. Neurological examination revealed confusion with no focal abnormality, the osteotendinous reflexes were quick, but there was no sign of localization or motor deficiency. Abdominal examination revealed diffuse abdominal pain but no vomiting or diarrhoea.

Predialytic blood tests showed normal blood count, serum sodium 141 mmol/L, serum potassium 5.7 mmol/L, blood urea nitrogen 45.6 mmol/L and serum creatinine 733 µmol/L. Liver tests and serum glucose were normal.

C-reactive protein was 74 mg/L. Rare colonies of Candida tropicalis were found in stool cultures. A brain CT scan showed cerebral atrophy without any recent lesion.

The ECG showed sinus rhythm with no repolarization or conduction abnormality. The plain film of the abdomen (Figure 1) revealed multiple diffuse calcium-like deposits throughout the digestive tract, especially in the rectosigmoid region. Repeated radiographs showed that these deposits continued to migrate through the digestive tract after withdrawal of the lanthanum carbonate. The abdominal CT scan (Figure 2) showed no mesenteric vascular abnormalities, but rectosigmoid distension with perirectal fat infiltration. Rectosigmoidoscopy revealed diverticular sigmoiditis with bowel mucous membrane inflammation, and the presence of off-white foreign bodies on the bowel wall. Upon analysis these were found to be lanthanum carbonate tablet residues.
Fig. 1. Plain film of the abdomen: multiple diffuse calcium-like deposits throughout the digestive tract, especially in the rectosigmoid region.

Fig. 2. Abdominal CT scan: no mesenteric vascular abnormalities, but rectosigmoid distension with perirectal fat infiltration.

Laboratory workup signs of inflammation regressed after initiation of antibiotics (ceftriaxone, gentamicin, and metronidazole). The patient’s confusion resolved after the discontinuation of lanthanum carbonate. The plasma levels of lanthanum (ICP-MS method) markedly decreased in parallel to the clinical improvement: from 2.13 µg/L on the first day following the discontinuation to 1.05 µg/L and 0.25 µg/L on Days 4 and 7, respectively.

Discussion

Lanthanum carbonate is a phosphate binder that is active in the colon and minimally absorbed in the bloodstream. Its phosphate binding effect is optimal at pH 3–5 (stomach and upper small intestine) but can occur throughout the digestive tract. The small absorbed fraction is excreted via the bile. The recommended daily dosage is 500–1500 mg [1].

A previous case was reported by Kurtz et al. in ‘Kongress der Gesellschaft für Nephrologie 2008 September Tübingen, Germany’, who described a 70-year-old man on chronic dialysis in Göttingen presenting ascending colon ischaemia associated with peritonitis. Pathologic examination of the resected colon disclosed multiple undissolved lanthanum carbonate tablets. Another case of acute hepatitis associated with encephalopathy after lanthanum carbonate use has been reported in a patient with Child Pugh stage A cirrhosis [2].

In a randomized study conducted on healthy subjects, lanthanum was shown to be minimally absorbed in the intestinal tract (0.00127%) [3]. However, in animal models lanthanum was found to accumulate in different organs, especially in liver, but also in bone, kidney and brain [3–5].

The bone lanthanum content in biopsies from a group treated with lanthanum carbonate and collected at the end of the 1-year study correlated significantly with plasma lanthanum at the 1- and 2-year follow-up visits.

In one study, maximal plasma levels of lanthanum were reached after 24 weeks and then stabilized [6]. This accumulation has been shown to be markedly enhanced in chronic kidney disease and seems to occur in a time-dependent manner [2,7].

A toxicology study (animal experiments on rats) [8] showed that long-term lanthanum carbonate exposure leads to persistent alteration of nervous function: lanthanides can penetrate the blood–brain barrier and higher concentrations of lanthanum accumulate in the cerebral cortex, hippocampus and cerebellum, with a risk of cognitive and behavioural alterations as well as learning and memory disabilities. Lanthanum inhibits the activity of Ca²⁺-ATPase, alters the function of the central cholinergic system and decreases the concentration of some neurotransmitter monoamines.

Tissue concentrations are higher than plasma levels. Lacour et al. [4] found that the plasma levels of lanthanum were a poor indicator of lanthanum accumulation in tissues. Although the daily dose usually given to patients is lower than that found to lead to neurological symptoms in Feng’s study [8], these toxic levels may be reached in renal failure due to the accumulation.

The case reported herein raises the problem of the potential role of the lanthanum tablet residue in the genesis or aggravation of diverticular flare-up and, on the other hand, the problem of the potential permeability of the blood–brain barrier with lanthanum use in the case of its digestive accumulation, leading to increased serum concentrations.

Our observation is certainly not a formal proof of these hypotheses. However, lanthanum carbonate should be used with caution in patients with diverticular colitis and/or those not able to completely chew tablets before swallowing. In our patient, mucosal inflammation due to sigmoiditis...
Lanthanum deposition in a dialysis patient

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Abstract

Lanthanum carbonate (LaCO₃) is an oral phosphate binder widely used in end-stage renal disease (ESRD). Preclinical animal studies reported the highest La concentrations outside the gut to be in mesenteric lymph nodes. We observed previously unreported La deposition visible by light microscopy and confirmed by scanning electron microscopy with energy dispersive x-ray spectroscopy in a mesenteric lymph node at autopsy of a 38-year-old female ESRD patient 3 years following LaCO₃ administration. Although LaCO₃ is generally thought to be minimally absorbed, this demonstration suggests the need for further investigation of the extent and potential effects of such absorption.

Keywords: end-stage renal disease; lanthanum; lymph node; scanning electron microscopy/energy dispersive x-ray spectroscopy

Introduction

Lanthanum carbonate (Fosrenol®) (LaCO₃) is used as an orally administered phosphate-binding agent to reduce the gastrointestinal absorption of phosphate and ameliorate hyperphosphataemia in end-stage renal disease (ESRD). It is minimally absorbed in normal individuals, but markedly increased absorption has been demonstrated in uraemic rats [1]. Plasma and bone levels of La have been seen to rise during therapeutic administration in humans, with long-term gradual mobilization from bone stores during a year after discontinuation of therapy [2]. Interestingly, La deposition at levels higher than in bone or liver has been reported in mesenteric lymph nodes of rats given oral LaCO₃ (personal communication, M. Smythe, PhD, Shire corporation, 13 May 2009).

Case report

We report substantial, readily detected La deposits in a mesenteric lymph node several years after the oral ingestion of LaCO₃. The patient was a 38-year-old woman with IgA nephropathy and ESRD beginning in 1996. She received a cadaveric kidney transplant in 1999, which was rejected and removed in 2003, and began peritoneal dialysis (PD) which continued through September/October 2005. She received LaCO₃ (one tablet after each meal) from April through October of 2005 (most or all of which time she was on PD), then haemodialysis (HD) from September/October to early December, returning to PD in early December 2005. In