

Clinical Report

## Lanthanum, constipation, baffling X-rays and a perforated colonic diverticulum

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### Abstract

Lanthanum carbonate (LC) is used as a phosphate binder in dialysed patients. Abdominal pain and constipation are known side effects of its use. Furthermore, in radiological studies, LC tablets are seen as intense radio-opaque deposits within the entire gastrointestinal tract—findings which can lead to diagnostic misinterpretations. An elderly patient on peritoneal dialysis and taking LC presented with peritonitis, secondary to a perforated colonic diverticulum. The possible association between the use of LC, worsening constipation and complications arising from colonic diverticular disease, are discussed.

**Keywords:** constipation; dialysis; diverticular disease; lanthanum carbonate

### Introduction

Lanthanum carbonate (LC) has become an accepted phosphate binder in patients with chronic kidney disease (CKD). After chewing and then swallowing the tablets, LC dissociates in the upper gastrointestinal tract into its trivalent cation. This cation then forms insoluble complexes with phosphate throughout a wide range of gastrointestinal pH [1–3]. These complexes are excreted fecally, resulting in reduced serum phosphorous levels. As a phosphate binder, LC is as good as aluminum hydroxide and possibly superior to other phosphate binders [4, 5].

In 2011, Damment performed short-term animal studies using pharmacological doses of LC and other phosphate binders. No adverse pharmacological effects were observed in animals with normal renal function. In particular, no problems were seen within the gastrointestinal tract [5]. However, a number of reports have emerged in which LC is possibly associated with complications associated with colonic diverticulosis [3, 6]. Recently, an elderly patient in our peritoneal dialysis (PD) unit was prescribed LC. Shortly afterwards, the patient presented with peritonitis and perforation of a colonic diverticulum. Her case report follows.

### Case report

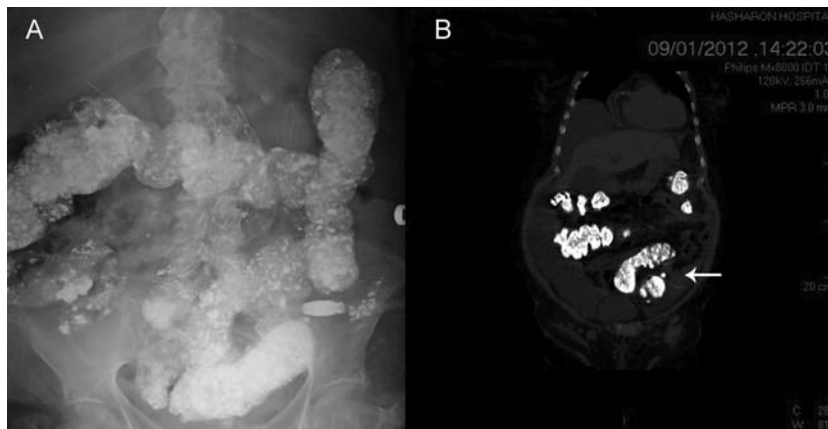
In January 2012, a 78-year-old woman was admitted with 3 days of abdominal pain and worsening

constipation. Relevant past history included CKD Stage 5 of unknown origin. PD was commenced in December 2008. Other medical problems included recurrent gastrointestinal bleeding, left colonic diverticulosis and bone pain which necessitated the commencement of chronic narcotic therapy (oxycodone 20 mg daily) in September 2009.

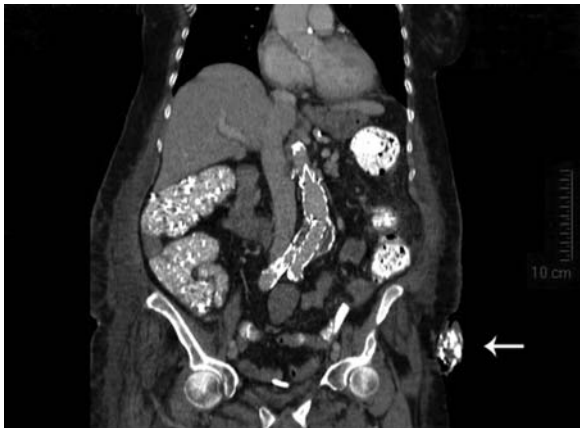
During her 3 years on PD, hyperphosphatemia and a high calcium-phosphate product did not respond adequately to calcium-containing phosphate binders. Subsequently, the patient was commenced on LC, at a daily dose of 3 g in September 2011. The LC dose was increased to 4.5 g daily in November 2011. The patient was instructed on how to chew the tablets and given a 'crushing device' to help her break down the tablets before ingestion.

On admission, the patient was afebrile. Tenderness, without peritoneal irritation, was present over the left lower abdominal quadrant. Leukocytosis was prominent—serum white blood cell count (WBC) of 24 000/mm<sup>3</sup>, as was hypoalbuminemia (serum albumin level: 32 gm/L). The PD effluent had a WBC of 260/mm<sup>3</sup> (38% neutrophils, 33% monocytes). A plain abdominal X-ray (Figure 1A) was incorrectly interpreted as showing residual contrast dye within the gastrointestinal tract. What in fact the X-ray showed was widespread radio-opaque LC deposits, of varying sizes, within both the small and large bowels.

Peritonitis was diagnosed, possibly as a result of colonic diverticulitis. Intravenous ceftriaxone and metronidazole were commenced. Over the following 24 h, abdominal tenderness increased, and the PD effluent



**Fig. 1.** (A) Plain abdominal X-ray (supine position) showing multiple hyperdense deposits of varying sizes throughout the gastrointestinal tract. A diffuse number of deposits are seen in the large bowel. (B) Abdominal CT examination (coronal section), taken without the oral administration of positive contrast media. Radio-opaque deposits with a very high density (Hounsfield units: 200–600) are seen throughout the colon and also lodged within a colonic diverticulum (arrow).



**Fig. 2.** Abdominal CT examination, taken 9 days after cessation of the LC and 5 days after the operative Hartsmann procedure. Radio-opaque deposits are still present within the colon and also visible within the colostomy (arrow).

WBC count rose to  $720 \text{ cells/mm}^3$ . An abdominal computed tomography (CT), performed without the addition of oral contrast dye, demonstrated extensive radio-opaque deposits within the colonic lumen, and also within colonic diverticulae (Figure 1B). Intravenous vancomycin and gentamycin were added to the therapeutic regime. Over the next 2 days, the patient improved clinically and all blood and PD fluid cultures had remained negative.

On the fifth day, the patient's condition deteriorated. She complained of increasing abdominal pain, and signs of peritoneal irritation were evident. The WBC count of the PD fluid was  $12\,000/\text{mm}^3$ . Urgent open laparotomy disclosed a ruptured colonic diverticulum and free purulent peritoneal fluid. A Hartsmann procedure with draining of the colostomy was performed. The Tenckhoff catheter was removed. Intraoperative cultures grew *Enterococcus avium* Group D and *Bacteroides*.

Postoperative recovery was slow and necessitated hemodialysis and prolonged antibiotic therapy and intradialytic parenteral nutrition. The patient complained of constant abdominal pain and repeat CT examination, carried out 9 days after admission (and 5 days

postoperatively), still showed fragments of LC within the colon and within the colostomy (Figure 2). Successful closure of the colostomy was carried out in late April 2012. The patient remains on narcotics. Phosphate binders have not yet been recommended.

## Discussion

CKD patients with hyperphosphatemia have high rates of vascular calcifications and death [7]. Treating hyperphosphatemia is extremely difficult. For this reason, therapeutic options are varied and commonly include the use of 'phosphate binders'—agents that decrease gastrointestinal absorption of dietary phosphate.

LC is a fourth-generation phosphate binder. Despite early fears as to bone, liver and brain toxicities [8], the drug has been used extensively, and successfully, in dialysis patients [9, 10]. However, gastrointestinal side effects are common [2]. Indeed, a company pamphlet on the drug (Fosrenol™, Shire Pharmaceuticals Inc.) warns about constipation, abdominal pain and diarrhea as possible adverse reactions associated with the drug. Listed contraindications to the use of LC include bowel obstruction and fecal impaction [11].

An increased prevalence of colonic diverticular disease is thought to be present in CKD patients, especially in patients with polycystic kidney disease [12, 13]. Three reports suggest caution in using LC in dialysis patients with diverticular disease [3, 6, 14]. In 2009, Muller *et al.* described an elderly woman on hemodialysis, who was receiving LC at a low dose. She presented with fever, confusion and abdominal pain. Diverticular sigmoiditis was diagnosed, with rectosigmoidoscopy showing LC tablets within the bowel [6]. This patient recovered with conservative therapy. In 2012, Camarero-Temino *et al.* described a 55-year-old hemodialysis patient who was taking 3 g LC daily. She presented on three separate occasions with abdominal pain and constipation [3]. Sigmoidal diverticulitis and intestinal obstruction resolved with conservative therapy and cessation of LC. Finally, Kato *et al.* examined abdominal CT scans in nine asymptomatic hemodialysis patients on LC. Not only were multiple 'calcium-like' deposits seen throughout the digestive tract, but also

digested LC tablets had accumulated within colonic diverticulae [14].

As with all phosphate binders, constipation may become troublesome in patients taking LC, especially if they are on other medications known to cause constipation. Traditionally, an association between constipation and diverticular disease exists [15]. Constipation possibly aggravates colonic diverticular disease by raising intraluminal pressure within the colonic bowel. Therefore, it seems prudent that phosphate binders should be used with caution in dialysis patients with colonic diverticulosis. If these drugs are to be given in such patients, then they should be initiated with (i) strict instructions on how to take the drug, (ii) low initial doses and slow dose titration, (iii) constant clinical supervision, so as to detect constipation at an early stage and (iv) the use of high fiber diet and/or laxatives. Importantly, our patient had constipation which may have been aggravated by the simultaneous use of narcotics and the high dose of LC.

LC tablets appear as radio-opaque deposits within the entire gastrointestinal tract, but especially in the colon [1–4, 14, 16, 17]. This fact is irrefutable, and the presence of such deposits has been suggested as a way in which compliance to the drug can be ascertained [17]! Lanthanum has an atomic weight nearly identical to that of barium, it absorbs X-ray and it has a density 4-fold greater than calcium [18]. These properties lead to its contrast-agent like features and its ability to be seen as radio-opaque deposits, both on plain X-rays and on CT examinations [2, 4]. Stopping the use of LC and adding laxatives are thought to clear these deposits 'quickly' [1]. However, in this studied patient, repeat CT examination performed 9 days after stopping LC still showed widespread lanthanum deposits within the colon. Radiologists must be informed if the patient is taking LC, and the drug should be stopped if elective abdominal radiological studies are to be performed [1, 4]. The real problem arises when urgent radiological studies of the abdomen have to be performed in these patients. Then, an incorrect interpretation of the radiological findings may lead to both erroneous diagnostic and therapeutic decisions.

In 2005, caution was advocated over the widespread use of LC [18]. In 2007, Druke [19] emphasized that the long-term clinical implications in using LC must be continually monitored as the drug does accumulate within tissues and is poorly cleared. In 2008, Hutchison *et al.* [10] detailed LC administration in dialysis patients for up to 6 years, without evidence of toxicity. However, in 2009, Hutchison [20] further added that 'it would be wrong to be complacent, and continued clinical vigilance is essential'. We concur completely with these statements.

*Conflict of interest statement.* None declared.

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Received for publication: 13.5.12; Accepted in revised form: 30.5.12