Case Report

Lanthanum carbonate possibly responsible for acute liver failure in a patient with Child–Pugh stage A liver cirrhosis

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Abstract

The majority of patients with end-stage renal disease have hyperphosphataemia, which is associated with significant morbidity and mortality. Lanthanum carbonate has been introduced as a new treatment modality to lower serum phosphorus. But there has been ongoing concern about lanthanum accumulation in tissues, especially in liver. We describe the case of a woman with pre-existing liver disease, who presented with acute liver failure after introduction of lanthanum carbonate to her treatment. The condition was fully reversible after stopping lanthanum carbonate.

Keywords: chronic renal failure; lanthanum carbonate; liver disease; phosphorus

Introduction

Treatment of hyperphosphataemia in kidney patients remains a challenge for the nephrologist. Aluminium salts have been abandoned because of central nervous and bone toxicity. Calcium carbonate is associated with a high incidence of hypercalcaemia and vascular calcification. Calcium- and aluminium-free alternative treatments have been developed recently. Lanthanum carbonate (Fosrenol®, Shire, Hampshire, UK) has been recently introduced as a highly effective phosphorus-lowering drug. In the present case report, we describe the disturbances caused by lanthanum carbonate in a patient with pre-existent liver disease on regular haemodialysis.

Case report

The patient is a 58-year-old woman with a history of alcoholic hepatitis, pancreatitis and secondary diabetes mellitus. She was treated with haemodialysis for end-stage kidney disease since May 2007. In December 2007, she suddenly presented with decreased consciousness and somnolence, needing admission to the hospital.

On physical examination at admission, the temperature was 36.4°C, the blood pressure was 110/81 mmHg and the heart rate was regular, 114 beats/min. The heart and breath sounds were normal. Abdominal examination revealed neither hepatosplenomegaly nor ascites; there was no distension or tenderness. Her skin and conjunctivae appeared mildly icteric. On neurological examination, the patient was somnolent but could be roused with mild stimulation. Her speech was slurred. The pupils were equal and light responsive; there was no nystagmus. She had generalized hyporeflexia but no focal deficits. Alcohol intake was denied.

She had been treated with calcium carbonate, vitamin D supplements and lorazepam for several months. Because of persistence of high serum phosphorus on calcium carbonate, a treatment with lanthanum carbonate (Fosrenol, 750 mg once daily) was initiated 3 weeks earlier.

Laboratory findings on admission after dialysis revealed disturbed liver tests: LDH 612 U/l (range 181–502 U/l), total alkaline phosphatases 118 U/l (range 34–76 U/l), bilirubin 2.33 mg/dl (range 0.2–1 mg/dl) and ammonia 166 µg/dl (range 20–60 µg/dl). Phosphorus was 1.5 mg/dl (range 2.7–4.5 mg/dl) and calcium was 10.4 mg/dl (normal range 8.6–9.8 mg/dl). Serum creatinine was 3.82 mg/dl (range 0.40–1.20 mg/dl), and blood urea and glucose were normal. C-reactive protein and white blood cell count were within the normal range. Haemoglobin was unchanged at 10.9 g/dl (range 11.8–14.5 g/dl), and platelet count was 114 × 10³/mm³ (range 158–450 × 10³/mm³). Ethanol test was negative.

CT -scan of the brain was normal and ultrasound of the abdomen showed, apart from the cirrhosis, no other abnormalities.

The patient was given lactulose enemas during 5 days and treatment with lanthanum carbonate was discontinued. After 2 days, ammonia and liver tests had returned to normal and the patient did fully recover. Up to 6 months after stopping lanthanum carbonate, no recurrence of liver failure episodes has been observed. Intake of other drugs or toxic substances was denied by the patient and her family. Retrospective testing for paracetamol in serum samples that were saved was negative.
Discussion

Our patient, who had pre-existing liver damage, was treated with lanthanum for 3 weeks when she was admitted with decompensated liver cirrhosis with mainly neurological symptoms. No other recent changes in treatment nor in daily habits were documented. Other common causes of acute liver failure were excluded; ethanol test was negative and there was no presence of infectious disease. Oral lorazepam is not hepatotoxic. After interruption of lanthanum carbonate intake, the plasma concentration of ammonia returned to normal and our patient became asymptomatic. We assume that the recent introduction of lanthanum carbonate to her therapy can be considered as the responsible factor for this episode of liver failure. In animal models, it has been shown that lanthanum is absorbed in the intestine and accumulates in different tissues, primarily in liver, but also in bone, kidney and brain [1,2]. This accumulation has been shown to be markedly enhanced in chronic kidney disease, and seems to occur in a time-dependent manner. The liver is also the main excretory organ of lanthanum and it has been demonstrated that of all cellular components of the hepatocytes, only the lysosomes contain large amounts of lanthanum [3]. Plasma levels of lanthanum are virtually undetectable, suggesting that they are a poor indicator of tissue burden. No tests in animals with liver disease have been reported.

A clinical study with 4 years of follow-up could not show hepatotoxicity regarding liver enzymes; however, no patients with pre-existing liver disease were included [4]. It should also be kept in mind that cases of cirrhosis have been seen despite the presence of normal liver enzymes, and a liver biopsy should be considered to assess hepatic integrity. Furthermore, prolonged exposure of the liver to other metals such as copper and iron has been shown to cause hepatotoxicity, cirrhosis and progression to hepatocellular carcinoma [5,6]. All these data confirm the need for determination of potential long-term toxic effects of lanthanum in larger patient numbers, with special attention to the liver.

According to the prescribing information of lanthanum carbonate [7], liver disease is not mentioned as being absolutely contraindicated. The present observation illustrates that in patients with pre-existent liver disease using lanthanum carbonate, careful monitoring of liver function is mandatory.

Conflict of interest statement: None declared.

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