Lesson of the Week

Severe hypermagnesaemia due to magnesium sulphate enemas in patients with hepatic coma

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Magnesium sulphate enemas are commonly used as purgatives and are recommended in the treatment of hepatic encephalopathy and coma. We describe two patients in whom their administration produced severe hypermagnesaemia and hypercalcaemia. The peak serum magnesium concentrations were in the range reported as causing fatal toxicity.[1]

Magnesium sulphate enemas should not be used in patients with liver disease at risk of renal failure

Case reports

CASE 1

A 20 year old previously fit man presented to the referring hospital with jaundice. Clinical features and investigations suggested acute viral hepatitis, and he was sent home to rest. He was admitted to hospital 11 days later with increasing jaundice, vomiting, and hepatic drowsiness and subsequently transferred.

On admission he was deeply jaundiced and in grade 3 hepatic coma. The liver span was reduced at 5 cm. Serological markers for hepatitis B, hepatitis A, cytomegalovirus, and Epstein-Barr virus were absent. Bilirubin concentration was 582 μmol/l (34 mg/100 ml) (reference range 5-17 μmol; 0·29-1·0 mg/100 ml), aspartate transaminase 654 U/l (15-40 μU/l), albumin 30 g/l (35-50 g/l), prothrombin time 55 s (11-14 s), and partial thromboplastin time 55 s (30-40 s). Renal function was normal. He was treated with our regimen for liver failure, which includes magnesium sulphate enemas twice daily. His neurological condition deteriorated despite use of 20% mannitol infusions and good urine output, and he was transferred to the intensive care unit 29 hours after admission for ventilation.

Serum magnesium concentration was measured as part of routine monitoring on the second day after admission and was raised at 5 mmol/l (12·2 mg/100 ml) (reference range 0·7-1·0 mmol/l; 1·7-2·4 mg/100 ml). At this point five magnesium sulphate enemas had been given (fig 1). Two further enemas were given before this result became known and the enemas were stopped. Hypercalcaemia of 3·16 mmol/l (12·6 mg/100 ml) (2·1-2·6 mmol/l; 8·4-10·4 mg/100 ml) was first noted on the second day with a phosphate concentration of 0·42 mmol/l (1·3 mg/100 ml) (0·7-1·25 mmol/l; 2·2-3·9 mg/100 ml).

He developed progressive renal failure, with low urinary sodium output typical of the hepatorenal syndrome. Haemodialysis was begun because of oliguria and a continued rise in creatinine and magnesium concentrations. Hypotension developed, which was unresponsive to inotropic agents, and he died after asystole on the sixth day after transfer. Histological examination of the liver post mortem confirmed severe acute hepatitis with bridging necrosis.

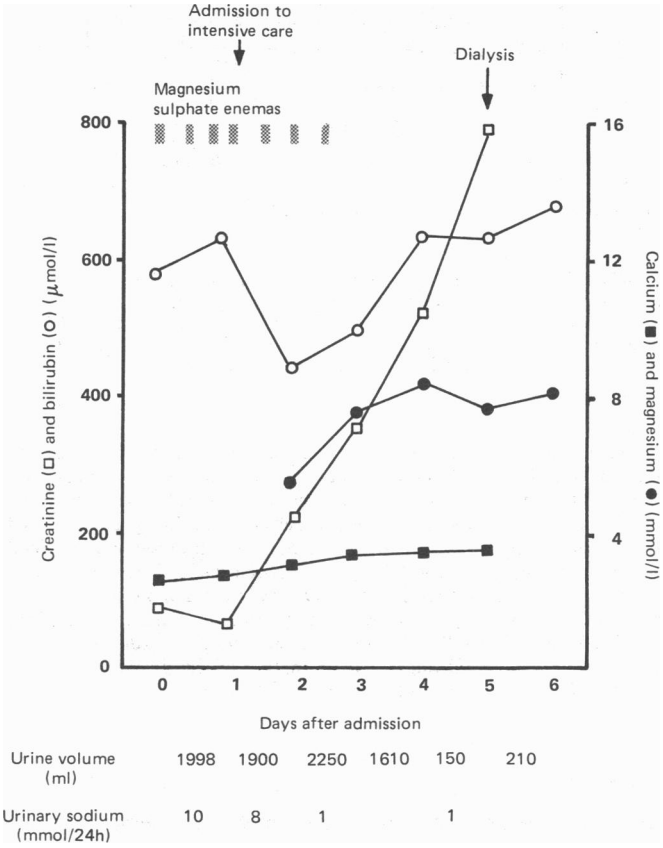

FIG 1—Serial concentrations of magnesium, calcium, creatinine, and bilirubin and urine output related to administration of enemas (case 1).

Conversion: SI to traditional units—Bilirubin: 1 μmol/l≈58·5 μg/100 ml. Creatinine: 1 μmol/l≈11·3 μg/100 ml. Magnesium: 1 mmol/l≈2·4 mg/100 ml. Calcium: 1 mmol/l≈4 mg/100 ml. Sodium: 1 mmol=1 mEq.

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CASE 2

A 36 year old housewife was admitted with variceal bleeding. She had a four year history of chronic alcohol abuse (100-150 g/day). She had jaundice and mild encephalopathy with hepatosplenomegaly and ascites. Bilirubin concentration was 74 μmol/l (4·3 mg/100 ml), aspartate transaminase 178 U/l, albumin 27 g/l, prothrombin time 20 s, and partial thromboplastin

time 48 s. She was initially managed medically and was given neutral phosphate enemas twice a day, but after a further episode of haematemesis oesophageal stapling transection was performed on the second day after admission.

Pulmonary oedema developed in the immediate postoperative period, and she was admitted to the intensive care unit for artificial ventilation. Hepatic encephalopathy developed on the third day after surgery and was treated with magnesium sulphate enemas twice daily. Despite septicaemia on the fifth and pancreatitis on the sixth postoperative days, urine output and creatinine concentration remained normal (fig 2). Magnesium concentrations were measured because she was receiving parenteral nutrition. On the ninth day she developed acute tubular necrosis and her conscious level deteriorated suddenly, progressing to coma. Computed tomography of the brain did not show a localising lesion, and electroencephalography showed little electrical activity. The serum magnesium concentration had remained within the reference range until this point, when it rose to 14·6 mmol/l (35·5 mg/100 ml). This was accompanied by hypercalcaemia of 3·0 mmol/l (12·2 mg/100 ml) and a marginal increase in phosphate concentration (1·34 mmol/l; 4·1 mg/100 ml). She developed refractory bradycardia and died in asystole that evening. Histological examination of the liver post mortem showed cirrhosis and severe fatty change.

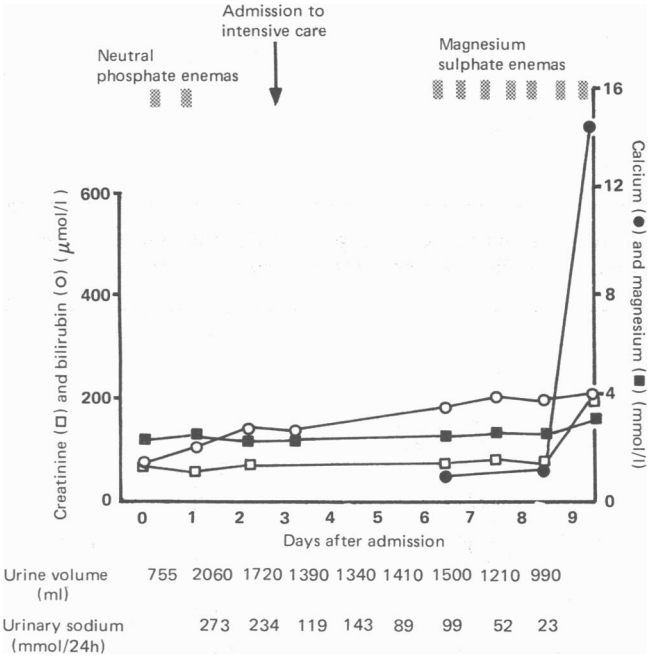

FIG 2—Serial concentrations of magnesium, calcium, creatinine, and bilirubin and urine output related to administration of enemas (case 2).

Conversion: SI to traditional units—Bilirubin: 1 μmol/l≈58·5 μg/100 ml. Creatinine: 1 μmol/l≈11·3 μg/100 ml. Magnesium: 1 mmol/l≈2·4 mg/100 ml. Calcium: 1 mmol/l≈4 mg/100 ml. Sodium: 1 mmol=1 mEq.

Discussion

In both patients detection of the hypermagnesaemia was fortuitous as the reason for measuring the magnesium concentration was to establish the baseline value before the start of parenteral nutrition.

The common factor in both cases was purgation with magnesium sulphate enemas. Hypermagnesaemia developed as renal function deteriorated. We therefore presume that the hypermagnesaemia resulted from failure of renal excretion of magnesium. Hypermagnesaemia is well documented in renal impairment but only in association with exogenous magnesium intake[1]; it is not a recognised feature of acute hepatic impairment. We measured serial magnesium concentrations in seven patients with acute hepatic necrosis (median aspartate transaminase activity 3971 U/l (range 1250-9000 U/l) not given magnesium sulphate enemas: all concentrations were within the reference range.

Hypermagnesaemia due to absorption of magnesium from an intact gastrointestinal tract is rare but has been reported in patients with normal and impaired renal function.[2-4] We measured serial serum magnesium concentrations in five subsequent cases of the hepatorenal syndrome when sodium phosphate enemas were administered. No values exceeding the reference range were detected despite progressive deterioration in renal function. We have traced only one, unreviewed report of hypermagnesaemia in a patient with hepatic failure treated with enemas containing magnesium.[5] None of the major textbooks on liver disease,[6-9] a recent review of acute and chronic hepatic failure,[10] or an important manual of intensive care[11] mention this possible complication. Two of the textbooks specifically recommend purgation with magnesium sulphate enemas in hepatic coma,[6,7] and the others recommend purgation without mentioning that magnesium sulphate enemas may cause hypermagnesaemia in patients with renal impairment.[8-11] In both acute liver failure and acute decompensation of chronic liver disease renal impairment is common, whether due to the hepatorenal syndrome or to acute tubular necrosis.

Each magnesium sulphate enema used in our hospital contains 263 mmol (6·4 g) magnesium. Appreciable absorption could rapidly give rise to toxic concentrations. In case 2 serum magnesium concentrations increased rapidly to toxic values when renal function deteriorated terminally. All signs of magnesium toxicity except arrhythmias would be masked in ventilated and paralysed patients. The refractory bradycardia progressing to asystole and death in case 2 was probably due to magnesium toxicity. As suitable alternatives to magnesium sulphate enemas such as lactulose and neutral phosphate enemas exist these should be prescribed. Other electrolyte disturbances such as hypocalcaemia and hyperphosphataemia, however, may occur with neutral phosphate enemas.[12]

In both of our cases hypercalcaemia occurred. This biochemical feature is unusual, although hypercalcaemia in the progeny of mothers treated with magnesium sulphate enemas has been reported.[13] Both of our patients had hypermagnesaemia, renal failure, and normal or only mildly raised phosphate concentrations; in these circumstances exchange of calcium for magnesium at the bone surface, combined with failure of renal calcium excretion, could produce hypercalcaemia.

In conclusion, we recommend that patients with liver disease who might develop renal impairment or in whom renal failure is established should not be prescribed enemas containing magnesium for treatment of hepatic encephalopathy as serious magnesium toxicity can occur, which may contribute to death.

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