A Review of a Rare Presentation: Severe Iatrogenic Hypermagnesemia

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Abstract

**Background:** Magnesium is an essential intracellular ion that has many different functions such as, acting as a cofactor for many enzymes, a binding partner of nucleotides, stabilising nucleic acids and membranes and antagonising the actions of Ca²⁺ [1]. Unlike most other filtered solutes, only 10% of filtered magnesium is reabsorbed in the proximal tubule of the kidney and approximately 50–70% of magnesium is reabsorbed in the thick ascending limb of Henle [2]. The kidney is responsible for maintaining magnesium levels in the narrow range of 0.7–1.1 mmol/L. Therefore, hypermagnesemia is common in patients with kidney disease, and prevalence of hypermagnesemia can be as high as 59% amongst dialysis patients [3].

**Methods:** A PUBMED search of cases of severe hypermagnesemia was conducted from the year 2000 onwards.

**Results:** Eleven cases were found of severe hypermagnesemia. All 11 cases were due to administration of magnesium and eight of these were oral ingestion. Despite haemodialysis, three of the 11 cases resulted in death and one suffered hypoxic encephalopathy.

**Conclusion:** Severe hypermagnesemia is a rare cause for neuromuscular and cardiovascular presentations. Clinicians should be aware of this risk when administering or prescribing magnesium.

**Keywords:** Hypermagnesemia; Haemodialysis; Magnesium; Parathyroid Hormone

Introduction

Magnesium is an essential intracellular ion that has many different functions such as, acting as a cofactor for many enzymes, a binding partner of nucleotides, stabilising nucleic acids and membranes and antagonising the actions of Ca²⁺ [1]. Unlike most other filtered solutes, only 10% of filtered magnesium is reabsorbed in the proximal tubule of the kidney and approximately 50–70% of magnesium is reabsorbed in the thick ascending limb of Henle [2]. The kidney is responsible for maintaining magnesium levels in the narrow range of 0.7–1.1 mmol/L. Therefore, hypermagnesemia is common in patients with kidney disease, and prevalence of hypermagnesemia can be as high as 59% amongst dialysis patients [3].

Amongst dialysis patients the magnesium level rarely rises above 1.5 mmol/L and hypermagnesemia is generally asymptomatic up to 2 mmol/L [4]. Therefore, in severe hypermagnesemia exceeding 2 mmol/L the cause is often iatrogenic administration of magnesium. Above this level, hypermagnesemia can manifest in different ways. Broadly, the symptoms can be classified as neuromuscular, cardiovascular and hypocalcaemia. Neuromuscular effects occur due to decreased impulse transmission across the neuromuscular junction. Elevated magnesium has a calcium channel blocking effect which causes hypotension and bradycardia. A high level of serum magnesium also causes hypocalcaemia through negative feedback on the secretion of Parathyroid Hormone (PTH) [1,2].

Malignancy levels are sometimes routinely tested, on patient’s blood test which means that hypermagnesemia can be detected early. However, severe hypermagnesemia is uncommon and thus may not always be suspected as a cause in a severely ill patient. The aim of this literature review is to examine the cases of severe hypermagnesemia to help clinicians better understand this uncommon presentation and to appreciate the significant morbidity and mortality associated.

Methods

A literature search was conducted using Pubmed with the keyword 'hypermagnesemia' used. The initial search returned 172 articles published from the year 2000.

Results

There were 14 cases of severe hypermagnesemia found in the literature from 2000, out of which four cases ended in death of the patient and one suffered a hypoxic encephalopathy during resuscitation. In those cases, emergency dialysis was used but was insufficient to prevent mortality. These cases demonstrate the potential for significant morbidity and mortality with severe hypermagnesemia. When recommending or administering magnesium, clinicians should be aware of these risks.

Although asymptomatic hypermagnesemia is common, particularly in those with chronic kidney disease, severe hypermagnesemia is rare. In all 11 cases, hypermagnesemia was caused by administration of magnesium supplementation. In eight of the 11 cases, hypermagnesemia was caused by oral ingestion of magnesium. Clinicians should be aware of this rare complication of oral administration of magnesium. Although this is a rare complication, it is one that clinicians should consider when patients present with neuromuscular or cardiovascular symptoms and particularly if patients have a history of renal impairment. The priority in treatment for severe cases is haemodialysis which was used in eight of the 11 cases; however this was not always enough to prevent mortality. Haemodialysis is effective in addressing the aetiology of the pathology but these cases demonstrate that it must be delivered as soon as possible to prevent deterioration.

Serum magnesium does not accurately represent total levels; majority is intracellular with only 1–2% contained in extracellular fluid. The absorption of magnesium orally is inversely proportional to the dose with an average absorption of 40–60% but 15–36% at higher doses. This helps to explain why iatrogenic hypermagnesemia is uncommon despite the prevalence of oral magnesium supplementation. After absorption, 30% is bound to albumin and the excretion is via urine as magnesium [18].

Some areas do not routinely test for magnesium levels when checking electrolyte levels. In one of the cases, late diagnosis of severe hypermagnesemia caused intestinal necrosis and death [9]. However, routine testing of magnesium levels in all patients may not be cost effective and severe hypermagnesemia is an extremely rare syndrome. Further research into the efficiency of routine serum magnesium levels would be beneficial and may prevent such cases in the future.
<table>
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<th>Paper</th>
<th>Demographics</th>
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<th>Treatment</th>
<th>Outcome</th>
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<tr>
<td>McGuire et al. [5]</td>
<td>28 month old boy with severe mental retardation, spastic quadriplegia and seizure disorder. Previously normal renal function.</td>
<td>800mg of magnesium oxide four times per day for three weeks as advised by private nutritional consultant</td>
<td>Unresponsive, 5 mm nonreactive pupils, hypotonia.</td>
<td>Serum Mg 8.34 mmol/L. Creatinine 2.2 mg/dL. EGG: 3° degree heart block</td>
<td>Transoesophageal pacing. Emergency haemodialysis and continuous veno-venous haemofiltration. Patient died 20 hours after admission from refractory cardiac dysrhythmias and cardiac dysfunction.</td>
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<td>Birrer et al. [6]</td>
<td>31 year old woman, nil significant history.</td>
<td>Patient concerned with hallucis for about one month, had used entire box of Epsom Salt gurgles in preceding two days</td>
<td>Presented to emergency department with loss of consciousness (GCS 6). BP 86 / 52. HR 56 / min. RR 14 / min. Temp 33.8°C. Depressed reflexes (1 / 4). Mild abdominal distension. After intubation developed asystole punctuated by ventricular fibrillation.</td>
<td>Serum Mg 9.8 mmol/L. EGG: prolonged QT (0.453s), peaked T waves</td>
<td>Intubation and resuscitation: adrenaline and lidocaine infusion. Atropine, furosemide, dopamine, defibrillation, transvenous pacemaker. Serum Mg reported at this stage: 600 mg IV 10 % calcium chloride given. Repeated defibrillations (17 total). Emergency dialysis. Following dialysis serum Mg was 3.05 mmol/L but neurologic status was unchanged. Postdialysis arrest occurred and patient could not be resuscitated.</td>
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<td>Ali A et al. [7]</td>
<td>1080 g male neonate, preterm labour 28 weeks</td>
<td>TPN and nasogastric feeding from day two of life</td>
<td>12th day of life: apnea, bradycardia, hypotensive, hypotonic.</td>
<td>Serum Mg 22.5 mmol/L. EGG: sinus bradycardia with prolonged QT. Normal EEG and nerve conduction studies.</td>
<td>Intubation, saline and Ringer’s lactate boluses, dopamine, dobutamine, adrenaline, calcium gluconate infusion, exchange transfusion. Vitals normalized after exchange transfusion, exubated 18th day of admission, discharged on 48th day of life at 1910 g.</td>
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<td>Kontani M et al. [8]</td>
<td>76 year old female</td>
<td>Constipation and ileus. Received 34 g of magnesium citrate the day before.</td>
<td>Lethargic, systolic BP &lt; 90 mmHg, temp 35.0°C. Abdomen distended but soft, diminished bowel sounds.</td>
<td>Serum Mg 6.82 mmol/L. Emergency colonooscopy: ischaemic colitis. EGG: prolonged PR (220 ms) and QT (619 ms). Abdominal CT: suggestive of ileus.</td>
<td>Intubation, atropine, adrenaline. Inubation and resuscitation: adrenaline, dopamine, mephitropin. Haemodialysis con-traindicated due to hypotension. Enema and colonooscopy. Temporary cardiac pacing. IV calcium not used.</td>
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<td>Onishi S et al. [9]</td>
<td>89 year old male</td>
<td>Magnesium citrate 34 g for contrast enema on evening prior to admission</td>
<td>Diarrhoea and abdominal pain. Temp 34.5°C. BP: 90 / -nmHg Distended, tender abdomen with decreased bowel sounds.</td>
<td>Serum Mg 5.18 mmol/L. Creatinine 1.1 mg/dL. EGG: atrial fibrillation. CT: dilated bowel, ileus.</td>
<td>External pacemaker. Dopamine, mephitropin, calcium gluconate. Haemodialysis. Serum Mg decreased to 2.8 mmol/L. However, patient developed intestinal necrosis. Family refused surgery and patient died on 4th day of admission.</td>
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<td>Tofil N et al. [10]</td>
<td>7 year old male</td>
<td>Unknown quantity of tap water and Epsom salt enema</td>
<td>Found by family difficult to dose. Asystole on arrival to emergency.</td>
<td>Serum Mg 16.9 mmol/L. Initial blood tests showed a calcium of 0.63 mmol/L.</td>
<td>CPR, adrenaline, atropine, IV fluids. Calcium given as only low calcium level seen. Brief periods of sinus bradycardia but no development of asystole. Pronounced dead three hours after presentation.</td>
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<td>So M et al. [11]</td>
<td>64 year old male, no medical history or renal dysfunction</td>
<td>1.5 g / day of magnesium oxide (0.9 g/day of magnesium) given over a month for constipation during hospital stay for head injury</td>
<td>Initial suspected acute abdomen. Progressed to impaired consciousness, hypotension, pulseless electrical activity</td>
<td>Serum Mg 4.5 mmol/L. Initial EGG showed left BBB. After adrenaline EGG showed junctional rhythm with multifocal ventricular premature contractions. CT: megacolon, suspected free air in peritoneum around prostate.</td>
<td>1mg of fadrenaline IV restored circulation during PEA. Dopamine and saline infusion. IV calcium gluconate and glucos-e-insulin therapy. In OR volume loading and furosemide given, colostomy performed. Serum Mg 3.5 mmol/L 2 hours after admission. Discharged from ICU on post-op day 2 with serum Mg 3.2 mg / dL, nil complications.</td>
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<td>Reference</td>
<td>Description</td>
<td>Case Details</td>
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<td>Parikh H et al. [12]</td>
<td>20 year old female</td>
<td>Magnesium sulphate 4 g IV slow bolus 10g IM (total 14g) for convulsions. Given another 14 g total on morning of second day.</td>
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<td>Jhang WK et al. [13]</td>
<td>11 year old boy</td>
<td>Magnesium oxide for constipation for two weeks.</td>
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<tr>
<td>Weng YM et al. [14]</td>
<td>72 year old female</td>
<td>Magnesium oxide 1 g/day prescribed nine days earlier.</td>
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<tr>
<td>Khairi T et al. [15]</td>
<td>70 year old male</td>
<td>Four doses of milk of magnesia daily over past five days for constipation. Acute renal failure likely due to patient’s CHF.</td>
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<tr>
<td>Sugiyama M et al. [16]</td>
<td>67 year old male</td>
<td>34 g of magnesium citrate in preparation for bowel resection.</td>
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<tr>
<td>Alaini A et al. [17]</td>
<td>73 year old male</td>
<td>Multiple daily doses of milk of magnesia.</td>
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<thead>
<tr>
<th>Patient Details</th>
<th>Management</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>70 year old male</td>
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<td>Discharged in stable condition eight days after admission.</td>
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<tr>
<td>73 year old male</td>
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<td>Extubated day five after serum Mg level dropped.</td>
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<tr>
<td>20 year old female</td>
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<td>Serum magnesium lowered following dialysis and discharged in stable condition eight days after admission.</td>
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### Table 1: Summary of 11 cases of severe hypermagnesemia.

<table>
<thead>
<tr>
<th>Serum Mg (mmol/L)</th>
<th>Electrolytes and ECG</th>
<th>Management</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>4.7 mg/dL</td>
<td></td>
<td>Calcium gluconate, IV Ringer lactate. Chest physiotherapy. 4-hourly Mg withheld. Cefuroxime 1 g and metronidazole 100 mg</td>
<td>After 24 hours, patient became orientated with normal power and reflexes. Discharged on 5th day of admission.</td>
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<td>1.5 mmol/L</td>
<td></td>
<td>Serum Mg decreased to 1.5 mmol/L after 3 hours of dialysis.</td>
<td>After two days had repeated dialysis due to Mg of 4.7 mg/dL. Electrolytes and ECG normal at discharge.</td>
</tr>
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### Conflicts of Interest
The author reports no conflict of interest.

### References


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