Iatrogenic Hypermagnesemia Following an Epsom Salt Enema

Michael Prystajecky
Habib ur Rehman
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OBJECTIVES

Learners will be able to:

• State etiologies of hypermagnesemia
• Identify risk factors for magnesium toxicity
• Recognize signs of hypermagnesemia
• Manage magnesium toxicity
HISTORY OF PRESENTING ILLNESS

• 85 female 3 day history constipation, bloating, diffuse abdo pain

• Prior admissions for abdominal distension/ constipation

• No prior abdominal surgeries, hernias, diverticulitis, or abnormal colonoscopies

• ROS unremarkable
PAST MEDICAL HISTORY

- AL Amyloidosis (2010)
- ESRD (IHD)
- Dysplipidemia
- Angiodysplasia
- Anemia
- Osteoarthritis
MEDICATIONS

- epoetin alfa
- lasix
- alfacalcidol
- renagel
- replavite

- atorvasatin
- rabeprazole
- lactulose
- folic acid
PHYSICAL EXAMINATION

- 36.5° C – p75 – 100/48 – 97% R/A
- ABDO: soft, non-distended, non-tender, no masses/HSM, no rebound tenderness
- CV: normal S1S2, no murmur/EHS
- RESP: no increased WOB, no adventitious sounds
## INVESTIGATIONS

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb</td>
<td>99</td>
</tr>
<tr>
<td>WBC</td>
<td>5</td>
</tr>
<tr>
<td>Plt</td>
<td>152</td>
</tr>
<tr>
<td>INR</td>
<td>0.9</td>
</tr>
<tr>
<td>PTT</td>
<td>29</td>
</tr>
<tr>
<td>Na</td>
<td>133</td>
</tr>
<tr>
<td>K</td>
<td>4.6</td>
</tr>
<tr>
<td>Cl</td>
<td>99</td>
</tr>
<tr>
<td>Mg</td>
<td>0.81</td>
</tr>
<tr>
<td>Ca</td>
<td>2.36</td>
</tr>
<tr>
<td>PO₄</td>
<td>1.79</td>
</tr>
<tr>
<td>ALP</td>
<td>71</td>
</tr>
<tr>
<td>ALT</td>
<td>19</td>
</tr>
<tr>
<td>Bili</td>
<td>9</td>
</tr>
<tr>
<td>Alb</td>
<td>27</td>
</tr>
<tr>
<td>HCO₃</td>
<td>19</td>
</tr>
<tr>
<td>Cr</td>
<td>1029</td>
</tr>
<tr>
<td>Urea</td>
<td>18.6</td>
</tr>
<tr>
<td>Gluc</td>
<td>5.4</td>
</tr>
<tr>
<td>AXR: minimally distended colon, fecal loading, no free air</td>
<td></td>
</tr>
</tbody>
</table>
COURSE IN HOSPITAL

- 2-4-6 enema
- Vag/PR bleeding, skeletal paralysis, bruising, 34.1°C
- PipTazo, DDAVP, cryoprecipitate, plts, crystalloid
- Ca 2.94, Mg >7.8, 7.23/47/18 (v), lactate 1.2
- Abdominal distension, muscle weakness
COURSE IN HOSPITAL

Shallow respirations, NRB, 33.8°C

Dialysis initiated

99% 3L, 36.5°C speaking Power 4-/5

Dialysis completed

Ca 2.58, Mg >7.8, 7.12/57/16 (v)

Ca 2.16, Mg 2.47, 7.24/58/21 (v)
04:00
66bpm
PR 240ms
QRS 80ms
QTc 443ms

PAD 3
84bpm
PR 200ms
QRS 80ms
QTc 447ms
Serum Magnesium (mmol/L)

Rate (per min)

Hours from Presentation

Dialysis start

2-4-6 enema

- HR
- RR
- Mg

Serum Magnesium (mmol/L)

Rate (per min)

Hours from Presentation
Serum Magnesium and Calcium (mmol/L)

Temperature (Celsius)

Hours from Presentation

2-4-6 enema

Dialysis start

Temp

Mg

Ca

Dialysis start

2-4-6 enema
Discussion: 2-4-6 Enema

- 60mL Epsom Salts + 120mL glycerine + water
- 60mL Epsom Salts = 28g
  Epsom Salts = 2.8g
  elemental Mg
- RDA = 300-400mg/d $\rightarrow$ Mg
dose 8x RDA
- Identical solution in 1949 case report of fatal
  hypermagnesemia

Discussion: Mg Physiology

• 2\textsuperscript{nd} most abundant intracellular ion
• Multitude of physiologic roles
  • Enzyme substrate (CK, PK, AC, ATPases)
  • Enzyme activation (PFK-1, CK, AC, N/K ATPase)
  • Membrane function
  • Calcium antagonization (muscle, neuron, nodal tissue)
  • Structural function (proteins, nucleic acids, mitochondria)

Magnesium Physiology

Dietary Intake: 360mg

Fecal Output: 260mg

Renal Excretion: 100mg

Body Reserves: 24,000mg
Hypermagnesemia: Etiology

HYPERMAGNESEMA

Increased Intake
- Cathartics
- Enemas
- Parenteral

Mobilization
- Trauma
- Burns
- Sepsis
- Cardiac arrest
- Shock

Impaired Excretion
- Renal Failure
- FHH

Other
- Hypothyroidism
- Hypothermia
- Adrenal Insufficiency

Significant hypermagnesemia: massive Mg load +/- renal impairment and/or impaired gastrointestinal motility

Longo et al. (2012). Harrison’s Principles of Internal Medicine (18th ed.)
# Hypermagnesemia: Case Reports

<table>
<thead>
<tr>
<th>CASE REPORT</th>
<th>PATIENT</th>
<th>SOURCE</th>
<th>SERUM Mg</th>
<th>TREATMENT</th>
<th>OUTCOME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collins 1949</td>
<td>4M Hirschsprung disease</td>
<td>MgSO4 enema</td>
<td>12.5 mmol/L</td>
<td>prostigmine, nikethamide, calcium gluconate, caffeine</td>
<td>Fatal</td>
</tr>
<tr>
<td>Brown 1978</td>
<td>4M functional constipation</td>
<td>MgSO4 enema</td>
<td>5.87 mmol/L</td>
<td>calcium gluconate, forced diuresis PD</td>
<td>Fatal</td>
</tr>
<tr>
<td>Ashton 1990</td>
<td>2F chronic constipation</td>
<td>MgSO4 enema</td>
<td>7.1 mmol/L</td>
<td>mannitol</td>
<td>Complete recovery</td>
</tr>
<tr>
<td>Collinson 1986</td>
<td>20M acute liver failure, renal failure (HRS)</td>
<td>MgSO4 enema</td>
<td>5 mmol/L</td>
<td>HD</td>
<td>Fatal</td>
</tr>
<tr>
<td>Collinson 1986</td>
<td>36M acute liver failure, renal failure (HRS)</td>
<td>MgSO4 enema</td>
<td>14.6 mmol/L</td>
<td>none</td>
<td>Fatal</td>
</tr>
<tr>
<td>Harker 2000</td>
<td>18mo F chronic constipation, multiple congenital abnormalities</td>
<td>MgSO4 enema</td>
<td>14.8 mmol/L</td>
<td>calcium gluconate, lasix, bicarb, HD</td>
<td>Recovery</td>
</tr>
<tr>
<td>Tofil 2005</td>
<td>7M constipation</td>
<td>MgSO4 enema</td>
<td>16.9</td>
<td>Calcium</td>
<td>Fatal</td>
</tr>
</tbody>
</table>
# Hypermagnesemia: Manifestations

<table>
<thead>
<tr>
<th>2-5 mmol/L</th>
<th>5.1-8 mmol/L</th>
<th>&gt;8 mmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CARDIAC</strong></td>
<td>Bradycardia</td>
<td>1&lt;sup&gt;st&lt;/sup&gt; degree AV block</td>
</tr>
<tr>
<td></td>
<td>Vasodilation</td>
<td>Atrial fibrillation</td>
</tr>
<tr>
<td></td>
<td>Hypotension</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prolonged QRS</td>
<td></td>
</tr>
<tr>
<td><strong>RESPIRATORY</strong></td>
<td>Shallow respirations</td>
<td>Respiratory arrest</td>
</tr>
<tr>
<td></td>
<td>↑ Respiratory rate</td>
<td></td>
</tr>
<tr>
<td><strong>NEUROLOGIC</strong></td>
<td>Lethargy</td>
<td>Paralysis</td>
</tr>
<tr>
<td></td>
<td>Weakness</td>
<td>Coma</td>
</tr>
<tr>
<td></td>
<td>Slurred Speech</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓/Absent DTRs</td>
<td></td>
</tr>
<tr>
<td><strong>GASTROINTESTINAL</strong></td>
<td>Paralytic ileus</td>
<td></td>
</tr>
</tbody>
</table>

Hypercalcemia

- Hypocalcemia and hypercalcemia reported in magnesium toxicity
  - Hypocalcemia: likely via CaSR activation / PTH suppression\(^1\)
  - Hypercalcemia
    - 2 prior case reports\(^2,3\)
    - Ca/Mg exchange at bone surface\(^4\)

Bleeding Diathesis

• Mucocutaneous bleeding and bruising
• Predisposing factors
  • Uremia $\rightarrow$ platelet dysfunction
  • Amyloidosis $\rightarrow$ Factor X def., acquired vWD, liver impairment, blood vessel fragility
  • Hypothermia $\rightarrow$ platelet dysfunction
• Hypermagnesemia associated with platelet dysfunction
  *in vitro* and *in vivo*
  • Decreased platelet aggregation

Hypothermia

• Described in 4 case reports of hypermagnesemia\textsuperscript{1-4}

\textbf{Body Temp} = \textbf{Heat From Metabolism} - \textbf{Radiative Heat Loss} - \textbf{Convective Heat Loss} - \textbf{Evaporative Heat Loss}

• Proposed mechanism
  • Initial drop in core temperature from peripheral vasodilation $\pm$ alteration metabolic activity
  • Blunting of compensatory vasoconstriction/shivering

\textsuperscript{1}Clin Chim Acta. 2002 Dec;326(1-2):201-3
\textsuperscript{3}J Emerg Med. 2002;22(2):185-188.
Hypermagnesemia: Treatment

• Cardiovascular and respiratory support
• Intravenous calcium gluconate/chloride
  • Competitive binding of magnesium binding sites
• Forced diuresis (crystalloid ± furosemide)
• Magnesium-free cathartics
• Hemodialysis
Conclusion

- Severe hypermagnesemia arises from massive magnesium load, usually in context of impaired renal function/increased intestinal absorption.
- Magnesium toxicity presents with non-specific cardiac, respiratory, neurologic, and GI manifestations.
- Hypocalcemia, hypothermia, and bleeding are rare manifestations of hypermagnesemia.
- Tx consists temporizing measures (IV Ca) and enhancing renal excretion (forced diuresis, dialysis).
References


Ashton MR, Sutton D, Nielsen M. Severe magnesium toxicity after magnesium sulphate enema in a chronically constipated child. BMJ. 1990;300(6723):541


Acknowledgements

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