Safe and Appropriate Use of Magnesium in Obstetrics

Jeffrey L Ecker, MD
Massachusetts General Hospital
Harvard Medical School

Disclosures

• I left San Francisco for Boston
• I use magnesium (less and less)
• I have no financial or other disclosures

Epsom Salts: Take a Soak?

• Can soothe the body, mind and soul
  – Relax the nervous system
  – Cure skin problems
  – Draw toxins from the body
• Not actually a salt but a compound
  – Magnesium sulfate
Could Lady Sybil have been saved? I honestly do not know, as I am not a doctor, or medical historian, but I am very much fascinated by the subject. Based on my readings, a C-section done early enough could have possibly saved her, so long as the hospital conditions and surgical instruments didn’t give her a terrible illness. As said before, this was a risky procedure back then. Another possibility is intravenous magnesium sulfate, which had just been recently introduced as a treatment for pre-eclampsia.

Magnesium In Obstetrics

- 1906: Horn in Germany suggests treatment of eclamptic seizures with magnesium
- 1926: Lazard uses and publishes series of IV magnesium to treat eclamptic seizures
  - 12% v 36% Mortality
- 1974: Pritchard reports 154 consecutive cases of IV+IM magnesium treatment of eclampsia without a death

Safe and Appropriate Use of Magnesium in Obstetrics

- Uses
  - Prevention of eclamptic seizures
  - Tocolysis
  - Neuroprotection
- FDA and other warnings
  - ACOG response
- Safety measures
Prevention of Eclampsia: Does It Work?

- Cochrane Review 2011:
  - Prevents Maternal Death (2 studies, 10K women)
    - RR: 0.54 (.26-1.1)
  - Prevents Eclampsia (6 studies, 11K women)
    - RR: 0.41 (.29-.58)
    - Risk Difference: -.01

Magnesium for Seizure Prophylaxis: What Dose?

- No one dosing regimen demonstrably better than another
  - Loading 4-6 mg/hr IVB
  - Continuous: 1-3 mg/hr
- Be mindful of urine output

Magnesium for Seizure Prophylaxis: Which Patients?

- It’s all about NNT
  - MAGPIE/Cochrane
    - Mild PE: NNT=100
    - Severe PE: NNT=60
- “Active” labor has nothing to do with it
- Evaluate /weigh (in your facility) the downside of a seizure
Magnesium for Seizure Prophylaxis: Which Patients?

- Some experts recommend treating all with PE
- ACOG 2013:

  “for women with preeclampsia with systolic blood pressure of less than 160 mmHg and a diastolic blood pressure less than 110 mmHg and no maternal symptoms, it is suggested that magnesium sulfate not be administered universally for the prevention of eclampsia”
  Quality of Evidence—Low, Strength of Recommendation—qualified

Magnesium for Tocolysis

- Smooth muscle relaxant
- Observational series suggest a benefit
  - “Magnesium sulfate was found to be a successful, inexpensive and relatively non-toxic tocolytic agent that had few side effects.”
We conclude that it is appropriate to withhold tocolysis with magnesium sulfate or other agents from women presenting in preterm labor as newborn benefits has not been demonstrated.

Table 7. Analysis of Pregnancy and Newborn Outcomes After Magnesium Sulfate Treatment Compared With Calcium Channel Blockers for Preterm Labor (Five Trials) (24–28)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Magnesium Sulfate</th>
<th>Calcium Channel Blockers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delivery less than 34 wk</td>
<td>23/246 (9.4%)</td>
<td>22/246 (8.9%)</td>
</tr>
<tr>
<td>Delivery less than 28 wk</td>
<td>9/246 (3.6%)</td>
<td>9/246 (3.6%)</td>
</tr>
<tr>
<td>Delivery less than 24 wk</td>
<td>1/246 (0.4%)</td>
<td>2/246 (0.8%)</td>
</tr>
<tr>
<td>Birth weight less than 2500 g</td>
<td>238/246 (97.0%)</td>
<td>236/246 (96.2%)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>6/246 (2.4%)</td>
<td>6/246 (2.4%)</td>
</tr>
<tr>
<td>Necrotizing enterocolitis</td>
<td>2/246 (0.8%)</td>
<td>2/246 (0.8%)</td>
</tr>
<tr>
<td>Respiratory distress</td>
<td>11/246 (4.5%)</td>
<td>11/246 (4.5%)</td>
</tr>
<tr>
<td>Respiratory distress within 72 h</td>
<td>4/246 (1.6%)</td>
<td>4/246 (1.6%)</td>
</tr>
<tr>
<td>Vaginal birth</td>
<td>230/246 (92.9%)</td>
<td>231/246 (93.9%)</td>
</tr>
</tbody>
</table>

We conclude that it is appropriate to withhold tocolysis with magnesium sulfate or other agents from women presenting in preterm labor as newborn benefits has not been demonstrated.
Magnesium for Neuroprotection

• (Some) Observational studies suggest protection against cerebral palsy among VLBW babies if mothers received MgSO4 prior to delivery (for seizure protection or tocolysis)
  – OR 0.14

Magnesium for Neuroprotection: Three RCT’s

Reduction of moderate/severe CP but not Death

<table>
<thead>
<tr>
<th>Study</th>
<th>Overall CP</th>
<th>Moderate/Severe CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>MgSO4</td>
<td>100.8%</td>
<td>191.4%</td>
</tr>
<tr>
<td>Placebo</td>
<td>120.4%</td>
<td>211.6%</td>
</tr>
</tbody>
</table>

"The neuroprotective effect of magnesium is now established."
NNT=63

A More Temperate Conclusion

The American College of Obstetricians and Gynecologists

COMMITTEE OPINION

Number 450 • March 2010

Committee on Obstetric Practice

Magnesium Sulfate Before Anticipated Preterm Birth for Neuroprotection

Abstract: Numerous large clinical studies have evaluated the evidence regarding magnesium sulfate, neuroprotection, and preterm birth. The Committee on Obstetric Practice and the Society for Maternal-Fetal Medicine recognize that none of the individual studies found a benefit with regard to their primary outcomes. However, this

committee endorses the need for magnesium sulfate in the management of preterm labor. Physicians electing to use magnesium sulfate for neuroprotection should develop specific guidelines regarding inclusion criteria, treatment regimens, consent process, and monitoring in accordance with one of the larger trials.
What Is ACOG’s Favorite Undergarment?

Where Are We?

- Magnesium for….
  - Seizure prophylaxis? **YES**
  - Especially severe PE
  - Tocolysis?: **NO**
  - Neuroprotection: **YES**
  - Any of three regimens appropriate

And Then the FDA (5/30/13)….

- Advises against use > 5-7 days for preterm labor
  - Concern about fetal and neonatal bone changes
- Changes category from **A** to **D**
But, but......

- No one uses it that long
- Few absolute number of cases of adverse outcome
- Lots of people just look at the letter D
- Some benefits

In all of these conditions, prolonged use of magnesium sulfate is never indicated. Therefore, the FDA’s change in the pregnancy classification of magnesium sulfate addresses an unindicated and non-standard use of this medication.

Using Magnesium Safely

- Avoid inadvertent toxicity
  - Pump not free flowing drip
  - Bolus but not continuous infusion if oliguria or decreased renal function
- Know signs and levels of toxicity
- Know the antidote
  - Calcium gluconate 1 gm IVP

Magnesium Toxicity

<table>
<thead>
<tr>
<th>Serum magnesium</th>
<th>mmol/L</th>
<th>mEq/L</th>
<th>mg/dL</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.75</td>
<td>2.25</td>
<td>1.5</td>
<td>20</td>
<td>Therapeutic range</td>
</tr>
<tr>
<td>0.76 - 3.5</td>
<td>&gt; 2.5</td>
<td>&gt; 1.5</td>
<td>3.6 - 9</td>
<td>Loss of skeletal muscle</td>
</tr>
<tr>
<td>3.6 - 9</td>
<td>&gt; 3</td>
<td>&gt; 9</td>
<td>&gt; 9</td>
<td>Respiratory paralysis</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>&gt; 12</td>
<td>&gt; 25</td>
<td>&gt; 25</td>
<td>Cardiac arrest</td>
</tr>
</tbody>
</table>

Perinatology.com
Safe Use of Magnesium in Obstetrics

- For seizure prophylaxis
- For neuroprotections
- For less than 48-72 hours

Questions? Objections? Toxic Reactions?

Chill with epsom salts & lavender