Management of Eclampsia and Magnesium Toxicity

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Objectives

- Eclampsia
  - Define and review epidemiology
  - Prevention
  - Diagnosis, treatment, and management

- Magnesium toxicity
  - Symptoms
  - Review the management

- Perform simulation activities
  - Eclampsia
  - Magnesium toxicity
Eclampsia

- Definition: grand mal seizures or coma in pt w/preeclampsia
- Incidence: 1 in 2000 to 1 in 3448 Pregnancies
  1-2% of all pre-eclampsia
- Predicting features (59-75%):
  - Persistent headache (50-75%)
  - Blurred vision (19-32%)
  - Epigastric or RUQ pain
  - Altered mental status
  - Sudden onset
- Timing: antepartum, intrapartum, postpartum
  - Majority occur after 28 weeks (91%)
Eclampsia

- HTN hallmark for diagnosis
  - Severe in 20-54%
  - Mild in 30-60%
  - Absent in 16%

- Proteinuria
  - Usually associated with at least 1+ proteinuria
  - Case series of 399 eclamptics
    - $\geq$3+ protein in 48%
    - No proteinuria in 14%
Eclampsia

- **Timing**
  - 91% after 28 weeks
  - 7.5% 21-27 weeks

- **Lopez-Liera Classification**
  - Antepartum: 38-53%
  - Intrapartum
  - Postpartum (<7 days): 11-44%
  - Intercurrent (stabilization and continued pregnancy > 1 week)

- **Other notes**
  - 40% occur prior to hospitalization
  - 16% >48 hours postpartum

Witlin AG Sibai BM. Obstet Gynecol 1998
Late Postpartum Eclampsia

- 48 hours to 4 weeks out
- Up to 16%
- Have s/sx’s preeclampsia IP/PP in 56%
- New onset s/sx’s in 44%
- Late onset eclampsia occurs despite h/o Mg use

Witlin AG Sibai BM. Obstet Gynecol 1998
Lubarsky et al. Obstet Gynecol 1994
Eclampsia: Differential Diagnosis

- Epilepsy
- Intracranial masses
- Metabolic disorders
- Infectious disease (i.e., HIV)
- Psychogenic non-epileptic seizures
- Drug abuse
Eclampsia: Risks and Sequelae

- Maternal death (0-2%, up to 14%)
- Perinatal death (5-10%)
- Abruption (7-10%)
- DIC (7-11%)
- Pulmonary edema (3-5%)
- Acute renal failure (5-9%)
- Aspiration pneumonia (2-3%)
- Cardiopulmonary arrest (2-5%)

Sibai BM. Obstet Gynecol 2005
Eclampsia: Risks Sequelae

- Intracranial hemorrhage
- Retinal detachment
- Transient neurologic deficits (3.1%)
- Transient cortical blindness (2.3%)
  - More common with PP eclampsia

Matter F and Sibai B. AJOG 1999
Eclampsia: Cerebral Pathology

- CT/MRI Head: edema/infarction within the subcortical white matter and adjacent gray matter—PARIETO-OCCIPITAL LOBES
  - PRES: posterior reversible encephalopathy syndrome
- Cerebral imaging is not necessary for diagnosis/management
- Similar findings in patients who have hypertensive encephalopathy
an ounce of prevention is worth a pound of cure
Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomised placebo-controlled trial

The Magpie Trial Collaborative Group*
To Mg or not to Mg?

**Magnesium Sulfate Prophylaxis**
There are only two double-blind, placebo controlled trials that have evaluated the use of magnesium sulfate in women with preeclampsia without severe features (17, 18). No instances of eclampsia occurred among 181 women assigned to placebo, and no differences occurred in the percentage of women who progressed to severe preeclampsia (12.5% in magnesium group versus 13.8% in the placebo group; RR, 0.90; 95% CI, 0.52–1.54). However, the number of
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Magnesium sulphate (n=5068)</th>
<th>Placebo (n=5068)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD) (years)</td>
<td>27.1 (6.7)</td>
<td>27.2 (6.7)</td>
</tr>
<tr>
<td>Primiparous‡</td>
<td>2604 (52%)</td>
<td>2591 (51%)</td>
</tr>
<tr>
<td>Multiple pregnancy</td>
<td>217 (4%)</td>
<td>203 (4%)</td>
</tr>
<tr>
<td>History of epilepsy</td>
<td>56 (1%)</td>
<td>56 (1%)</td>
</tr>
<tr>
<td>Systolic BP at entry</td>
<td>801 (16%)</td>
<td>808 (16%)</td>
</tr>
<tr>
<td>$\geq$170 mm Hg</td>
<td>1119 (22%)</td>
<td>1146 (23%)</td>
</tr>
<tr>
<td>Diastolic BP at entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$\geq$110 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proteinuria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trace/none</td>
<td>2 (0.04%)</td>
<td>5 (0.1%)</td>
</tr>
<tr>
<td>1+</td>
<td>1571 (31%)</td>
<td>1568 (31%)</td>
</tr>
<tr>
<td>2+</td>
<td>1704 (34%)</td>
<td>1721 (34%)</td>
</tr>
<tr>
<td>3+</td>
<td>1310 (26%)</td>
<td>1270 (25%)</td>
</tr>
<tr>
<td>4+</td>
<td>481 (9%)</td>
<td>504 (10%)</td>
</tr>
<tr>
<td>Severe pre-eclampsia</td>
<td>1303 (26%)</td>
<td>1349 (27%)</td>
</tr>
<tr>
<td>Imminent eclampsia§</td>
<td>816 (16%)</td>
<td>833 (16%)</td>
</tr>
<tr>
<td>Oliguria</td>
<td>131 (3%)</td>
<td>129 (3%)</td>
</tr>
<tr>
<td>Previous treatment with anticonvulsant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium sulphate</td>
<td>440 (9%)</td>
<td>435 (9%)</td>
</tr>
<tr>
<td>Other anticonvulsant</td>
<td>242 (5%)</td>
<td>241 (5%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>196 (4%)</td>
<td>192 (4%)</td>
</tr>
<tr>
<td>Previous treatment with antihypertensive</td>
<td>2508 (49%)</td>
<td>2502 (49%)</td>
</tr>
<tr>
<td>If treated with antihypertensive, highest BP before entry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP $\geq$170 mm Hg</td>
<td>1149 (23%)</td>
<td>1172 (23%)</td>
</tr>
<tr>
<td>Diastolic BP $\geq$110 mm Hg</td>
<td>1540 (30%)</td>
<td>1554 (31%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>8 (0.2%)</td>
<td>4 (0.1%)</td>
</tr>
<tr>
<td>Postpartum at randomisation</td>
<td>640 (13%)</td>
<td>697 (14%)</td>
</tr>
</tbody>
</table>

2 frontal/severe headache
Epigastric pain
Blurred vision
Hyper-reflexia
Irrespective of BP or proteinuria
<table>
<thead>
<tr>
<th></th>
<th>Magnesium sulphate (n=5055)</th>
<th>Placebo (n=5055)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Eclampsia</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>4 (0.08%)</td>
<td>3 (0.06%)</td>
<td>0.42 (0.29 to 0.60)*</td>
</tr>
<tr>
<td>Number of fits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>27</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>$\geq$4</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Maternal death</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (0.04%)</td>
<td>2 (0.04%)</td>
<td>0.55 (0.26 to 1.14)†</td>
</tr>
<tr>
<td>Main cause of death</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest or failure</td>
<td>4</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Eclampsia or pre-eclampsia</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Anaemia or postpartum haemorrhage</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Anaesthetic death</td>
<td>1</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Respiratory failure or pneumonia</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Renal failure</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>0</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Risk difference (95% CI) is *$-1.1$ ($-1.6$ to $-0.7$), †$-0.2$ ($-0.4$ to 0.04).

Table 6: **Eclampsia and maternal death**
<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative risk (95% CI)</th>
<th>Number of events</th>
<th>Magnesium sulphate</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe pre-eclampsia</td>
<td>0.42 (0.23–0.76)</td>
<td>15/1297</td>
<td>37/1345</td>
<td></td>
</tr>
<tr>
<td>Not severe pre-eclampsia</td>
<td>0.42 (0.26–0.67)</td>
<td>25/3758</td>
<td>59/3710</td>
<td></td>
</tr>
<tr>
<td>Randomised before delivery</td>
<td>0.40 (0.27–0.59)</td>
<td>36/4416</td>
<td>88/4359</td>
<td></td>
</tr>
<tr>
<td>&lt;34 weeks</td>
<td>0.54 (0.28–1.06)</td>
<td>13/1206</td>
<td>24/1206</td>
<td></td>
</tr>
<tr>
<td>≥34 weeks</td>
<td>0.35 (0.22–0.57)</td>
<td>23/3210</td>
<td>64/3153</td>
<td></td>
</tr>
<tr>
<td>Randomised after delivery</td>
<td>0.54 (0.16–1.80)</td>
<td>4/639</td>
<td>8/696</td>
<td></td>
</tr>
<tr>
<td>Anticonvulsant before trial*</td>
<td>1.24 (0.49–3.11)</td>
<td>10/439</td>
<td>8/435</td>
<td></td>
</tr>
<tr>
<td>No anticonvulsant before trial*</td>
<td>0.34 (0.23–0.51)</td>
<td>30/4590</td>
<td>88/4583</td>
<td></td>
</tr>
<tr>
<td>Imminent eclampsia</td>
<td>0.26 (0.12–0.57)</td>
<td>8/810</td>
<td>31/829</td>
<td></td>
</tr>
<tr>
<td>No imminent eclampsia</td>
<td>0.49 (0.32–0.75)</td>
<td>32/4245</td>
<td>65/4226</td>
<td></td>
</tr>
<tr>
<td>High PMR country</td>
<td>0.34 (0.21–0.56)</td>
<td>22/2814</td>
<td>64/2812</td>
<td></td>
</tr>
<tr>
<td>Middle PMR country</td>
<td>0.54 (0.28–1.03)</td>
<td>14/1463</td>
<td>26/1461</td>
<td></td>
</tr>
<tr>
<td>Low PMR country</td>
<td>0.67 (0.19–2.37)</td>
<td>4/778</td>
<td>6/782</td>
<td></td>
</tr>
<tr>
<td>All women</td>
<td>0.42 (0.29–0.60)</td>
<td>40/5055</td>
<td>96/5055</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 2: Effects of treatment on eclampsia**

PMR=Perinatal mortality rate. *Not known whether previous anticonvulsant was given to 26 women allocated magnesium sulphate and to 37 allocated placebo.
MAGPIE

- NNT for Severe Preeclampsia: 63
- NNT for Non-severe preeclampsia: 91
Management

- Goals of management
  - Prevention of injury
  - Support respiratory and cardiovascular functions
  - Prevention of morbidity
  - Stop seizure (?)

- Modes of management
  - Medical
  - Non-medical
Management

- Nonmedical management
  - Bedrails up
  - Recovery position
  - Supplemental O2 at 8-10 L/min
  - Physical restraints
  - Telemetry

- Medical management
  - MgSO4
  - 10% will have a second seizure on Mg
  - Antihypertensive therapy
Eclampsia: Management

- Magnesium administration
  - 4-6 gm bolus over 15-20 minutes
  - 1-2 gm/hour

- Neuroleptics
  - Diazepam/Lorazepam
  - Levetiracetam
  - Phenytoin
Eclampsia: Management

- Hypertension
  - Goal is to reduce BP to a stable range (usually about 15-20%)
    - 140-160 systolic BP
    - 90-110 diastolic BP
  - BP does not have to be normalized especially in patients with previously severe range blood pressures
Eclampsia: Management

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labetalol</td>
<td>10–20 mg IV, then 20–80 mg every 20–30 min to a maximum dose of 300 mg or Constant infusion 1–2 mg/min IV</td>
<td>Considered a first-line agent, tachycardia is less common and fewer adverse effects, contraindicated in patients with asthma, heart disease, or congestive heart failure</td>
</tr>
<tr>
<td>Hydralazine</td>
<td>5 mg IV or IM, then 5–10 mg IV every 20–40 min or Constant infusion 0.5–10 mg/h</td>
<td>Higher or frequent dosage associated with maternal hypotension, headaches, and fetal distress—may be more common than other agents</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>10–20 mg orally, repeat in 30 minutes if needed; then 10–20 mg every 2–6 hours</td>
<td>May observe reflex tachycardia and headaches</td>
</tr>
</tbody>
</table>

Abbreviations: IM, intramuscularly; IV, intravenously.
Eclampsia: Fetal Management

- To deliver or not deliver?
  - Stabilize mother first
- Cesarean section not indicated by eclampsia alone
- FHR changes typically resolve
  - After convulsions have stopped
  - Correction of maternal hypoxemia
- Induction of labor when stable
  - Typically quick
- Early pregnancy, unfavorable cervix
Eclampsia: Post-partum

- Continue Magnesium infusion
  - Length of duration is variable
  - Ensure stable vital signs, adequate urine output

- Control hypertension

- Counseling for future pregnancies and long-term health counseling
Magnesium Toxicity
Magnesium Sulfate: What is it?

- Calcium antagonist
  - Slows muscular conduction, specifically smooth muscle, and can depress CNS irritability
- Cleared through the renal system
  - In patients with normal renal function, the half-time for excretion is about 4-5 hours
Magnesium Toxicity

- Symptoms can vary but commonly include some of the following:
  - Difficulty speaking or moving
  - Blurry vision
  - Weakness
  - Unresponsive
  - Loss of deep tendon reflexes
  - Respiratory compromise
  - Cardiac arrest
## Magnesium Toxicity

Effects Associated with Various Serum Magnesium Levels

<table>
<thead>
<tr>
<th>Effect</th>
<th>Serum Level (mEq/liter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticonvulsant prophylaxis</td>
<td>4-7</td>
</tr>
<tr>
<td>EKG changes</td>
<td>5-10</td>
</tr>
<tr>
<td>Loss of deep tendon reflexes</td>
<td>10</td>
</tr>
<tr>
<td>Respiratory paralysis</td>
<td>12-15</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>15</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>&gt;25</td>
</tr>
</tbody>
</table>
Therapeutic MgSO4

- Serum concentration b/t 2-3.5 mmol/l (4-7 mEq/l)
- Okusanya et al
  - 4-6g bolus rapid doubling within 30 minutes
  - 1g/hr: 1-2 mmol/l
  - 2g/hr: higher likelihood of 2-3 mmol/l
  - Mg levels <2 mmol/l are likely protective
Magnesium Toxicity

- Treatment:
  - Stop magnesium sulfate infusion/administration
  - Fetal assessment
  - Administer *calcium gluconate* (10 mL of 10% solution over 10 minutes or 1 gm IV)
  - Review for errors (i.e., dosing, incorrect orders, etc.)
Magnesium Toxicity

- Why does this happen?
  - Impaired renal function (i.e., patients with decreased glomerular filtration rate)
  - Administration of improper dose
  - Overexposure or long exposure
Magnesium Toxicity

- How can you prevent this?
  - Frequent evaluations of the patient for signs/symptoms of toxicity by the RN staff and Physicians or other providers
  - Serial serum magnesium serum levels along with your basic labs in patients who are being treated with magnesium
Questions?