Increasing uptake and correct use of Magnesium Sulfate Administration for Management of Severe Preeclampsia and Eclampsia

Photo: PATH/Evelyn Hockstein
Objectives

At the end of the workshop, participants will be able to:

- Describe new WHO guidelines for management of severe pre-eclampsia and eclampsia, including the recommended regimen for MgSO4
- Describe new findings on prevalence of magnesium toxicity
- Use a phone application to assist with calculating the dose for loading and maintenance doses of MgSO4
- Correctly dilute MgSO4 doses for IV administration
- Correctly add lignocaine to MgSO4 for IM administration
- Use a simple monitoring tool for women
- Correctly use checklists and simple job aids for MgSO4 use that can be shared with peers
Causes of maternal deaths

WHAT ARE PREGNANT WOMEN DYING FROM?

- **28%** Pre-existing medical conditions exacerbated by pregnancy (such as diabetes, malaria, HIV, obesity)
- **27%** Severe bleeding
- **14%** Pregnancy-induced high blood pressure
- **11%** Infections (mostly after childbirth)
- **8%** Abortion complications
- **9%** Obstructed labour and other direct causes

© World Health Organization 2014
Price of preeclampsia and eclampsia

A woman in a developing country:

- **Is 7 times** more likely to develop PE (2.8% of live births) than in developed countries (0.4% of live births).
- **Is 3 times** more likely to progress to eclampsia if she develops PE (2.3% of pre-eclamptic women in the developing world compared with 0.8%).
- **Is up to 14 times** more likely to die of eclampsia should she develop it—even in hospital settings.
- **Has an approximately 300 times higher** risk of dying of PE and eclampsia than a woman in a developed country.
Severe preeclampsia and eclampsia

- **Diagnostic criteria – severe pre-eclampsia**
  - Diastolic BP 110 mm Hg or more
  - Proteinuria 3+ or more

- **Diagnostic criteria – eclampsia**
  - A pregnant woman or a woman who has recently given birth is found unconscious or having convulsions (fits), diastolic BP 110 mm Hg or more
  - Proteinuria 2+ or more

A small proportion of women with eclampsia have normal blood pressure. Treat all pregnant/postpartum women with convulsions as if they have eclampsia until another diagnosis is confirmed.
Time of eclampsia occurrence

- Approximately 38 to 55% of all cases of eclampsia occur antepartum
- 13-36% occur intrapartum
- 5-39% occur within the first 48 hours following childbirth
- 5-17% occur greater than 48 hours postpartum
Management of severe preeclampsia and eclampsia

The goals of management are to:

- Stabilize the woman
- Prevent onset of eclampsia or recurrent convulsions in cases of eclampsia
- Treat severe hypertension to prevent cerebral hemorrhage
- Ensure optimal timing of childbirth (based upon gestational age, the severity of preeclampsia, and maternal and fetal condition) to prevent development of maternal or fetal complications from disease progression.
While comprehensive management of women with PE and eclampsia should include anticonvulsant drugs, antihypertensive drugs, and timed childbirth, we are focusing on MgSO$_4$ today.
Aspirational goals

All women with severe preeclampsia receive MgSO$_4$ for prevention of eclamptic seizures.

MgSO$_4$ is administered as soon as possible after the first eclamptic seizure, wherever that occurs, to prevent recurrent fits.
Evidence for using MgSO₄

Two randomized control trials provided the scientific evidence needed to promote MgSO₄ as the anticonvulsant of choice for the treatment of severe preeclampsia and eclampsia:

- The Magnesium Sulfate for Prevention of Eclampsia (MAGPIE) Trial for women with preeclampsia (2002).
Comparative benefits of MgSO$_4$

- Compared to phenytoin and diazepam, MgSO$_4$:
  - Reduces the rate of recurrent seizures by one-half to two-thirds
  - Reduces the rate of maternal death by one-third
Current situation

Despite its endorsement by WHO and its presence on most essential medicines lists, MgSO₄ is still:

- Underutilized;
- Incorrectly administered; or
- Unavailable in many low-resource settings due to:
  - Stockouts.
  - Procurement of concentrations of MgSO₄ other than 50%.
  - Policies restricting use to certain cadres or types of health care facilities.
Barriers to uptake of MgSO$_4$

Low coverage of MgSO$_4$ for management of severe preeclampsia and eclampsia is due to a combination of factors:

- Policy
- Provider
- Supply/Logistics

Photo: PATH/Evelyn Hockstein
Barriers to uptake of MgSO₄: Complex dosing

The current regimen is complex and requires:

- Different **dilutions** for initial intravenous (IV) loading dose (20%), IV additional dose for recurrent seizures after loading dose (50%), and intramuscular (IM) doses (50%):
  - Requires calculating the amount of diluent to add to the solution to get the correct dilution.

- Different **doses** for:
  - IV and IM doses.
  - Loading and maintenance doses.
WHO regimen for MgSO₄ (Pritchard regimen)

**Loading Dose**

1. Give magnesium sulfate 20% solution, 4 g IV over 5 minutes
2. Follow promptly with 10 g of 50% MgSO₄ solution, 5 g in each buttock via deep IM injections with 1 mL of 2% lignocaine in the same syringe.
3. If convulsions recur after 15 minutes, give 2 g magnesium sulfate (50% solution) IV over 5 minutes.
WHO regimen for MgSO₄ (Pritchard regimen) - (cont.)

Maintenance Dose
Give 5 g magnesium sulfate (50% solution) + 1 mL lignocaine 2% IM every 4 hours into alternate buttocks.

Delay MgSO₄ dose if:
• Respiratory rate is less than 16 per minute.
• Patellar reflexes are absent.
• Urinary output is less than 30 mL per hour over 4 hours
WHO regimen for MgSO₄ (Zuspan regimen)

- **Loading dose:** 4 grams (20% solution) intravenously over 5 minutes followed by
- **Maintenance dose:** 1 gram (20% solution) per hour as a continuous infusion

Withhold MgSO₄ if:
- Respiratory rate is less than 16 per minute.
- Patellar reflexes are absent.
- Urinary output is less than 30 mL per hour over 4 hours

Photo: http://nats.ie/doc/Magnesium_Sulphate_Powerpoint_Presentation.pdf
Barriers to uptake of MgSO₄: Multiple product presentations of MgSO₄

Available presentations:
- 1% (10 mg/mL)
- 2% (20 mg/mL)
- 10% (100 mg/mL)
- 15% (150 mg/mL)
- 20% (200 mg/mL)
- 50% (500 mg/mL)

WHO recommended presentation of MgSO₄:
- 500 mg/mL in 2-mL ampoule (50%)
- 500 mg/mL in 10-mL ampoule (50%)

Photo: PATH/Evelyn Hockstein
Barriers to uptake of MgSO₄: Perception of risk of magnesium toxicity

Evidence

- Review of literature shows very few cases of toxicity.
- Toxicity mostly related to medication errors or in cases of renal insufficiency.

Provider Reluctance

- Providers may be reluctant to administer maintenance dosing because of fear of toxicity.
- Administering maintenance dosing requires careful monitoring which may be difficult when there are shortages of qualified health care providers.
- Providers may have difficulty remembering signs of toxicity and how to assess for them.
Complaints of pain and side effects during IM injections may negatively influence:

- A health care provider’s decision to initiate or continue treatment
- A patient’s acceptance of ongoing treatment
- The repeated IM maintenance injections could potentially lead to development of abscess
Barriers to uptake of MgSO₄: Lack of reliable IV infusion pumps for delivery of MgSO₄

- Pump devices that facilitate continuous IV infusion of MgSO₄ may not be available or may not be reliable.
- IM dosing is therefore favored because of the relative safety over IV doses in settings that do not have pumps to control the IV infusion.
Barriers to uptake of MgSO₄:
Confusing data on MgSO₄

- Published dosage regimens for MgSO₄ vary widely
- There does not appear to be a clear threshold concentration for ensuring the prevention of convulsions
- Timing of drug discontinuation has been arbitrary; there are no high quality data to guide therapy
There are four key opportunities for increasing uptake of MgSO$_4$

1. Improve product presentation
2. Increase provider confidence and comfort
3. Develop simplified regimen to reduce complexity
4. Task shift

Photo: PATH/Susheela Engelbrecht
1 - Improve product presentation

- Develop package(s) with the correct strengths of MgSO₄ for loading and maintenance doses with an appropriate identification (e.g., color coding).
- There is ongoing work under the UN Commission on Life-Saving Commodities for Women and Children (UNCoLSC) recommendation 10 to revise product presentation.
1 - Improve product presentation

- Challenges:
  - Many companies produce MgSO₄ as contract manufacturers.
  - Improvements to existing product presentation, such as adding an additional strength of MgSO₄, require investment and/or additional regulatory approval.
  - Some manufacturers do not have a strong willingness to be involved in efforts to improve the existing product presentation without explicit demand.
2 – Increase provider confidence and comfort: Use of apps to assist with dosing

- Interactive mobile phone application guides providers through the steps for safe preparation and administration using the current WHO protocol.

- Based on demand, it can be revised for country-specific dosing regimens and translated into other languages.
2 – Increase provider confidence and comfort: Use checklists to guide administration of MgSO₄

Checklists:

- Break down complex tasks into steps.
- Facilitate standardization of procedures.
- Provide prompts / reminders for students and veteran providers.
- Can be used for training and quality improvement initiatives.

### Checklist: Administering Maintenance Dose of Magnesium Sulfate

<table>
<thead>
<tr>
<th>Monitor women for toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before repeating the 4-hourly dose of magnesium sulfate:</td>
</tr>
<tr>
<td>1. Count respiration rate for one minute.</td>
</tr>
<tr>
<td>2. Calculate urinary output over the last 4 hours.</td>
</tr>
<tr>
<td>3. Check patellar reflexes.</td>
</tr>
<tr>
<td>4. WITHHOLD or DELAY drug if there are signs of toxicity.</td>
</tr>
<tr>
<td>5. Provide maintenance dose of magnesium sulfate if no signs of toxicity.</td>
</tr>
</tbody>
</table>

If respiratory arrest occurs:

6. Assist ventilation.

7. Give calcium gluconate 1 g (10 mL of 10% solution) by IV injection SLOWLY (over 3 minutes) until respiration begins.

8. Record findings on the woman’s record.

9. Explain findings to the woman.

### Administer Maintenance Dose of Magnesium Sulfate

1. Wash hands thoroughly with soap and water and dry with a clean, dry cloth or air dry.

2. Take one 20 mL sterile syringe.

3. Draw 10 mL (5 g) of MgSO₄ 50% into the syringe.

4. Add 1 mL of 2% lignocaine into the syringe.

5. Put on clean exam gloves on both hands.

6. Verify in which buttock the last magnesium sulfate injection was given.

7. Carefully clean the injection site with an alcohol wipe.

8. Give 5 g by DEEP IM injection in the alternate buttock from the most previous injection.

9. Dispose of used needle and syringe in a sharps disposal box.

10. Dispose of gloves in a 0.5% decontamination solution.

11. Wash hands thoroughly with soap and water and dry with a clean, dry cloth or air dry.

12. Record drug administration, injection site, and findings on the woman’s record.

13. Explain findings and drug administration to the woman.
2 – Increase provider confidence and comfort: Use interactive case studies to improve diagnosis and management decisions

- Designed to assess and strengthen a provider’s ability to apply knowledge about diagnosing and managing pre-eclampsia and eclampsia.
- “Decision pages” present choices about what should happen next
- Subsequent pages teach whether the decision made increases or decreases the likelihood of a positive health outcome for the woman and her baby

Decide, Save Lives!
An Interactive Case Study on the Diagnosis and Management of Eclampsia

August 2011
Field-Test Draft

Jhpiego
an affiliate of Johns Hopkins University
2 – Increase provider confidence and comfort: Use simple tools to monitor women receiving MgSO₄

- Contains all parameters to be monitored
- Provides space for administration of medications
- Provides a “snapshot” of the woman and baby’s conditions
- Currently being evaluated in both basic and comprehensive emergency obstetric care facilities in sub-Saharan African countries

### Monitoring a woman with severe preeclampsia/eclampsia (adapted from the LUVKAN Chart)

<table>
<thead>
<tr>
<th>Date</th>
<th>Hours on MgSO₄</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FHR (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>250</td>
</tr>
<tr>
<td>240</td>
</tr>
<tr>
<td>230</td>
</tr>
<tr>
<td>220</td>
</tr>
<tr>
<td>210</td>
</tr>
<tr>
<td>200</td>
</tr>
<tr>
<td>190</td>
</tr>
<tr>
<td>180</td>
</tr>
<tr>
<td>170</td>
</tr>
<tr>
<td>160</td>
</tr>
<tr>
<td>150</td>
</tr>
<tr>
<td>140</td>
</tr>
<tr>
<td>130</td>
</tr>
<tr>
<td>120</td>
</tr>
<tr>
<td>110</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>90</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>70</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BP (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>210</td>
</tr>
<tr>
<td>200</td>
</tr>
<tr>
<td>190</td>
</tr>
<tr>
<td>180</td>
</tr>
<tr>
<td>170</td>
</tr>
<tr>
<td>160</td>
</tr>
<tr>
<td>150</td>
</tr>
<tr>
<td>140</td>
</tr>
<tr>
<td>130</td>
</tr>
<tr>
<td>120</td>
</tr>
<tr>
<td>110</td>
</tr>
<tr>
<td>100</td>
</tr>
<tr>
<td>90</td>
</tr>
<tr>
<td>80</td>
</tr>
<tr>
<td>70</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pupil (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>19</td>
</tr>
<tr>
<td>18</td>
</tr>
<tr>
<td>17</td>
</tr>
<tr>
<td>16</td>
</tr>
<tr>
<td>15</td>
</tr>
<tr>
<td>14</td>
</tr>
<tr>
<td>13</td>
</tr>
<tr>
<td>12</td>
</tr>
<tr>
<td>11</td>
</tr>
<tr>
<td>10</td>
</tr>
<tr>
<td>9</td>
</tr>
<tr>
<td>8</td>
</tr>
<tr>
<td>7</td>
</tr>
<tr>
<td>6</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level of consciousness</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
</tr>
<tr>
<td>V</td>
</tr>
<tr>
<td>P</td>
</tr>
<tr>
<td>U</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Input (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV solution:</td>
</tr>
<tr>
<td>IV rate</td>
</tr>
<tr>
<td>Output (mL)</td>
</tr>
<tr>
<td>Proteins</td>
</tr>
<tr>
<td>Respiratory rate</td>
</tr>
<tr>
<td>Lung sounds</td>
</tr>
<tr>
<td>Temperature</td>
</tr>
<tr>
<td>Deep tendon reflex</td>
</tr>
<tr>
<td>MgSO₄ dose</td>
</tr>
<tr>
<td>MgSO₄ route</td>
</tr>
<tr>
<td>Calcium gluconate</td>
</tr>
</tbody>
</table>

Please determine hourly urine output, deep tendon reflex, and respiratory rate prior to administering a dose of magnesium sulphate
2 - Increase provider confidence and comfort: Develop simplified delivery mechanisms

Fig. 1. Springfusor® pump (Go Medical, Australia).

Mundle et al, 2012
3 - Develop simplified regimen to reduce complexity

Simplified regimen will lead to:

**Increased Uptake**
- Increased uptake of a safe, effective dosing regimen of MgSO$_4$.

**Reduced Mortality**
- Reduced mortality (perinatal/maternal).
Simplified MgSO₄ regimen: 50% dilution for all routes and doses

- Study in India used 50% solution for loading and continuous maintenance IV infusion.
- Women receiving continuous IV infusion (50%) vs. maintenance IM dosing:
  - Were less likely to stop treatment due to side effects, toxicity, oliguria or renal failure, or personal request (4% vs. 6.5%).
  - Reported significantly less nausea, headache, and pain.
Simplified dosing: Loading dose only regimen for treatment of eclampsia

- Approximately 10 percent of eclamptic women will have repeated seizures if managed expectantly.
- Some researchers observed that many patients with eclampsia who did not receive maintenance therapy due to suspicion/fear of toxicity or stockouts of MgSO₄ did not convulse any further.
- This led to conducting small studies in Bangladesh, Nigeria, Pakistan, Nepal, and India.
Results of loading dose only regimen for treatment of eclampsia

- The studies showed the effectiveness of using a loading dose only regimen of MgSO$_4$ for eclampsia.
- Unfortunately, the studies were too small to draw any statistically reliable conclusions about the differential effects on the two reported primary outcomes recurrence of convulsion and maternal death.
- In order to change global recommendations, we need to have an evidence base with enough power to:
  - Support a simplified MgSO$_4$ regimen.
  - Promote changes in practice, including the possibility of task shifting.
4 – Task shift

Task shifting administration of initial dose of MgSO4 to community- or peripheral facility-based providers will lead to:

**Increased Uptake**
- Increased uptake of MgSO$_4$.

**Timely administration**
- Earlier administration of MgSO4.

**Reduced Mortality**
- Prevention of eclampsia and recurrent fits.
- Reduced mortality (perinatal / maternal).
Together we can make a difference and ensure that every woman who needs MgSO4 receives it in a safe, timely manner.
Comments?

Questions?
Stations

- Station 1: Mobile application with monitoring tool
- Station 2: Calculating IV infusion rates
- Station 3: Interactive case study
- Station 4: Checklists

Please spend 15 minutes in each station.
Thank you!

Photo credit: Susheela Engelbrecht
For more information, please contact Susheela Engelbrecht (sengelbrecht@path.org)


References


References


References
