Treatment Approaches for Preeclampsia in Low-Resource Settings: The Springfusor pump for delivery of magnesium sulfate

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Background

- MgSO$_4$ is inexpensive and effectively prevents and treats seizures associated with preeclampsia
- IM administration
  - painful and associated with patient and provider dissatisfaction, limiting utilization.
- Electric infusion pumps
  - expensive and not available in many low-resource settings
- Gravity-driven IV drip systems
  - higher risk of under or over-dosing given imprecise flow rates and lack of monitoring
- Springfusor pump offers alternative to IM or gravity-driven IV drip systems in settings where electronic pumps not available
Springfusor Pump

- Manufactured by GoMedical (Australia)
- Costs:
  - ($35) Springfusor pump - durable/reusable
  - ($3) Disposable flow control tubing set including syringe
  - Pump is portable and may be worn attached to the arm or on a lanyard around the neck
"A randomized trial comparing treatment of severe preeclampsia with a magnesium sulfate regimen administered with the Springfusor infusion pump to a continuous (IV) regimen"

Authors: T Easterling, M Hebert, H Bracken, MC Ramadan, S Shaarawy, E Darwish, D Charles and B. Winikoff
# Summary of Gynuity Springfusor studies

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<thead>
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<tbody>
<tr>
<td><strong>Setting</strong></td>
<td>2 tertiary hospitals in urban India</td>
<td>2 secondary hospitals in urban India</td>
<td>2 tertiary hospitals in urban Egypt</td>
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<tr>
<td><strong>Study design</strong></td>
<td>RCT</td>
<td>Open label</td>
<td>RCT</td>
</tr>
<tr>
<td><strong>Sample size</strong></td>
<td>300</td>
<td>85</td>
<td>200</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>4g IV over 20 min +10g IM +5g IM every 4h</td>
<td>--</td>
<td>4g IV over 20 min+1g per hour</td>
</tr>
<tr>
<td><strong>MgSO4 regimen with Springfusor</strong></td>
<td>4g IV over 20 min+4g every 4 hours up to 24 hours</td>
<td>4g IV over 20 min+4g every 4 hours up to 24 hours</td>
<td>6g loading dose IV over 30 min +2g over 10 min every 2 hours up to 12 hours</td>
</tr>
<tr>
<td><strong># of flow control tubings req’d</strong></td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td><strong>Provider administering MgSO4.</strong></td>
<td>Physicians, residents</td>
<td>Physicians, residents</td>
<td>Physicians (Cairo), nurses (Alexandria)</td>
</tr>
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</table>
## Springfusor offers safe alternative to IM administration

<table>
<thead>
<tr>
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<th>SPRINGFUSOR (n=147)</th>
<th>IV/IM (n=153)</th>
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<tbody>
<tr>
<td>Completed 24h of treatment</td>
<td>91.2% (134)</td>
<td>92.2% (141)</td>
</tr>
<tr>
<td>Stopped early due to woman’s request, side effects, oliguria or renal failure, or signs of toxicity (n, %)</td>
<td>4.0% (6)</td>
<td>6.5% (10)</td>
</tr>
<tr>
<td>Stopped early due to staff error or provider preference (n, %)</td>
<td>4.8% (7)</td>
<td>1.3% (2)</td>
</tr>
</tbody>
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Mundle et al. 2012. Differences not statistically significant (p>0.05)
## Maternal outcomes

<table>
<thead>
<tr>
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<th>SPRINGFUSOR (n=147)</th>
<th>IV/IM (n=153)</th>
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<tbody>
<tr>
<td><strong>Caesarean delivery (%(n))</strong></td>
<td>49.3% (72)</td>
<td>43.0% (65)</td>
</tr>
<tr>
<td><strong>Seizures post-treatment (%(n))</strong></td>
<td>0.6% (1)</td>
<td>0.6% (1)</td>
</tr>
<tr>
<td><strong>Woman’s status at discharge (%(n))</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recovered</td>
<td>95.9% (141)</td>
<td>91.5% (140)</td>
</tr>
<tr>
<td>Improving</td>
<td>3.4% (5)</td>
<td>7.2% (11)</td>
</tr>
<tr>
<td>Unchanged</td>
<td>0.7% (1)</td>
<td>1.3% (2)</td>
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Mundle et al. 2012. Differences not statistically significant (p>0.05)
Springfusor reduces side effects associated with IM administration

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<thead>
<tr>
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<th>SPRINGFUSOR (n=147)</th>
<th>IV/IM (n=153)</th>
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<tbody>
<tr>
<td>Flushing^</td>
<td>63.3% (94)</td>
<td>75.2% (115)*</td>
</tr>
<tr>
<td>Nausea^</td>
<td>18.4% (27)</td>
<td>32.7% (50)*</td>
</tr>
<tr>
<td>Vomiting^</td>
<td>10.2% (15)</td>
<td>11.8% (18)</td>
</tr>
<tr>
<td>Headache</td>
<td>4.8% (7)</td>
<td>12.4% (19)*</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>15.6% (23)</td>
<td>49.0% (75)*</td>
</tr>
<tr>
<td>Diplopia</td>
<td>3.4% (5)</td>
<td>7.8% (12)*</td>
</tr>
</tbody>
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^ Sides effects frequently associated with rapid infusion of loading dose
Mundle et al (2012). Differences statistically significant (p<0.05)
Springfusor: Patient acceptability

**Pain**

- Springfusor Pump (n=147): 97% Acceptable, 2% Neutral, 1% Unacceptable
- IV/IM (n=153): 31% Acceptable, 38% Neutral, 31% Unacceptable

**Side Effects**

- Springfusor Pump (n=147): 93% Acceptable, 5% Neutral, 2% Unacceptable
- IV/IM (n=153): 39% Acceptable, 34% Neutral, 26% Unacceptable

Mundle et al. 2012. Differences statistically significant (p<0.05)
Can Springfusor be used outside a tertiary-care center?

- Open-label trial conducted at secondary care centers in India (n=85)
- Almost all women (82 of 85 or 96.5%) completed the full course of MgSO$_4$ treatment.
- No case received an excessive dose of MgSO$_4$
- No eclamptic seizures after study entry
- One woman was successfully referred to tertiary care center with the pump in situ.

Refining the Springfusor regimen: Results from a PK analysis

An increased loading dose could provide a higher-concentration time profile in the first 6-8 hours, more comparable to IM

Figure 4. Typical concentration–time profiles for the intravenous and intramuscular dose groups, superimposed with simulations of intravenous dosing with loading dose increased from 4 g to 5, 6, 7 and 8 g.

Conclusions

• Springfusor can be used by health care personnel (nurses and MD) in low resource settings
• Requires little technical support: Providers received three hour training on use of Springfusor pump
• Standardized protocols eliminate the need for user to program a pump or calculate an error rate for magnesium sulfate
• Serial bolus protocol and continuous IV pharmacologically equivalent
  • Serial bolus may offer a “third option” to continuous IV or IM magnesium sulfate
  • decreases cost of Springfusor tubing by 50%
Thank you!
Opportunities to Improve Care of Hypertensive Pregnant Women

- Diagnosis
- Blood Pressure Control
- Induction of Labor
- Delivery
- Postpartum Care

MgSO₄
A randomized open-label study to compare the clinical outcomes and magnesium serum concentrations obtained in the treatment of severe pre-eclampsia with a repeat bolus intravenous magnesium sulfate regimen administered with the Springfusor infusion pump to the MAGPIE intramuscular magnesium sulfate regimen.
**Diagnosis**

**Blood Pressure Control**

**Postpartum Care**

**Delivery**

**Induction of Labor**

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**MgSO₄**

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**A pilot study of three oral antihypertensive regimens for management of hypertension in pregnancy**

- **Primary aim:** To determine the efficacy of oral medications for management of acute, severe hypertension in pregnant women.
- **Secondary aims:**
  - To assess adverse outcomes and necessity for additional hypertensive treatment.
  - To assess maternal and fetal outcomes.
**Diagnosis**

- **MgSO₄**: Used in the management of preeclampsia.

**Blood Pressure Control**

- Nifedipine (Extended-release Tablets, USP 30 mg)
- Methylxoprop (Methylxoprop Tablets, USP 250 mcg)

**Delivery**

- Induction of Labor

**Postpartum Care**

- Induction of labour in pre-eclamptic women: a randomised trial comparing the Foley balloon catheter with oral misoprostol.

**Study Design**

- Open-label randomized trial
- Study sites: Government Medical College, Nagpur, India; Daya Women's Hospital, Nagpur, India
- Sample size: 602 women

**Rationale**

- Prompt delivery of the baby, preferably by vaginal route, is vital in order to achieve good maternal and neonatal outcomes.
- WHO recommends two low cost interventions for induction of labour [1]: oral misoprostol tablets and transcervical Foley catheterization [1]
- Both misoprostol and Foley catheter are used in low resource settings, but their relative risks and benefits are not known.

Future Directions

- Protocols require use of MgSO4 50% solution, which may not be available in all settings
  - Springfusor could be pre-packaged in a treatment pack with a supply of 50% solution
- Test use in primary health care facilities where burden of disease may be greatest
- Test use in all women requiring MgSO4 including eclamptic patients