

Review Demonstrates Very Low Incidence of Side Effects from Magnesium Sulfate

Background: Pre-eclampsia/eclampsia (PE/E) is a life-threatening multisystem disorder of pregnancy, and among the most common causes of maternal and perinatal morbidity and mortality in low- and middle-income countries. Globally, as many as 1 in 12 pregnant women develop PE annually, and in Asia and Africa, PE/E accounts for 9% of maternal deaths, and about one-quarter of such deaths in Latin America and the Caribbean. Untreated PE can lead to seizures, kidney and liver damage and, in severe cases, death.

Evidence-based treatment: Global evidence and World Health Organization recommendations include magnesium sulfate ($MgSO_4$) treatment for eclampsia among the 56 interventions that, together, could prevent the needless deaths of 358,000 women and 7.6 million children in low- and middle-income countries. However, despite consensus that $MgSO_4$ is significantly more effective than diazepam or phenytoin in preventing seizures in PE/E, universal and consistent use of the drug has been slow to take hold. Concerns have persisted about its toxicity, particularly among providers in low- and middle-income countries.



Photo by: Kate Holt/Jhpiego

A newly published article in the journal *BMC Pregnancy and Childbirth*¹ presents the results of a review of the global literature to document the known occurrences of side effects resulting from $MgSO_4$ use. “An integrative review of the side effects related to the use of magnesium sulfate for pre-eclampsia and eclampsia management” summarizes the rates of side effects when $MgSO_4$ was used as part of a clinical trial in low- or middle-income countries. It attempts to answer the question: “Is magnesium sulfate a dangerous drug?”

Methodology

Three screening criteria were used for inclusion in the review:

- $MgSO_4$ was used to manage PE/E in a prospective clinical study;
- Study was conducted in a low- or middle income country; and
- Study methodology recorded the incidence of adverse side effects resulting from $MgSO_4$ use.

Four research questions were asked through the review:

- Incidences of absent patellar reflex or respiratory depression;
- Frequency of use of calcium gluconate to counteract the effects of $MgSO_4$ in response to detected side effects;
- Frequency of skipped or delayed doses of $MgSO_4$ in response to development of side effects; and

¹ *BMC Pregnancy and Childbirth* 2013, 13:34; online at: www.biomedcentral.com/1471-2393/13/34. Authored by Jeffrey Michael Smith, Richard F Lowe, Judith Fullerton, Sheena M Currie, Laura Harris, Erica Felker-Kantor.

- Number of maternal deaths among women with severe PE/E reported to be attributed to toxicity of MgSO₄ rather than from manifestations of the underlying disease.

In addition, the review summarized the incidence of oliguria among women undergoing MgSO₄ therapy, as this manifestation of severe pre-eclampsia can alter the administration schedule of the drug.

Results: Women who receive MgSO₄ commonly may experience non-serious effects of the drug, including a feeling of warmth, flushing, nausea and vomiting, muscle weakness, somnolence and dizziness. More substantial side effects of the drug include a loss of the patellar reflex and respiratory depression. The usual monitoring of a woman on MgSO₄ includes assessment for these signs. This review of 24 studies comparing a MgSO₄ regimen against other drug regimens summarized the incidence of the key factors noted above in order to provide real evidence to guide clinical practices and aid clinicians.

Overall Outcome Rates from All Studies in 9,556 Subjects

	Affected Patellar Reflex	Respiratory Depression	Oliguria	Delayed or Skipped Dose	Calcium Gluconate Use
Incidence	1.6%	1.3%	2.5%	3.6%	0.2%
One maternal death reported by authors as due to MgSO ₄					

The results, summarized in the table above, reveal that:

- The incidence of depressed or absent patellar reflex is very low, at less than 2%.
- The incidence of respiratory depression—meaning a respiratory rate of less than 16 breaths per minute—was even more uncommon, occurring in 1.3% of cases.
- The incidence of oliguria, a manifestation of the disease that may require less frequent dosing of MgSO₄, was also uncommon, occurring for 2.5% of women.
- The need to delay or skip a scheduled dose of magnesium was approximately 3.6%, reflecting an uncommon need to alter the prescribed drug regimen. This is an interesting observation that may reflect provider confidence since the feeling that side effects should be managed (i.e., delaying the next dose) is more common than the side effects themselves.
- The need to use calcium gluconate to reverse the effects of magnesium was extremely rare, occurring in only 2 per 1,000 cases.
- Most importantly, this review showed only one maternal death due to use of MgSO₄ among more than 9,500 women. Indeed, this one death, due to inappropriate administration of the medication, should be compared to the frequent deaths caused when the medication is not used in the management of women with pre-eclampsia.

Conclusions: This review of the side effects of MgSO₄ clearly demonstrates that MgSO₄ is, in fact, not a dangerous drug. The findings indicate a low incidence of severe side effects (generally 1-2%) directly attributable to use of MgSO₄. When adverse effects did occur, delaying the next scheduled dose was generally sufficient to mitigate the effect.

As a result, clinical leaders in maternal health should adopt, promote and support the use of MgSO₄ as the anticonvulsant of choice in treating and managing PE/E. Women under treatment with MgSO₄ should be provided with appropriate vigilance for side effects and clinical conditions, and simple protocols should be in place and understood by all staff. Midwives, nurses and other clinicians who provide basic emergency obstetric care should be empowered to administer MgSO₄ in an effort to expand the use of this lifesaving, safe intervention.