WHO recommendation on magnesium sulfate regimen to prevent and treat eclampsia

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Recommendation

The full intravenous or intramuscular magnesium sulfate regimens are recommended for the prevention and treatment of eclampsia.

(moderate evidence, strong recommendation)

Publication history

First published: October 2011

Updated: no update planned

Assessed as up-to-date: October 2011

Remarks

- Magnesium sulfate is a lifesaving drug and should be available in all health-care facilities throughout the health system. The guideline development group believed that capacity for clinical surveillance of women and administration of calcium gluconate were essential components of the package of services for the delivery of magnesium sulfate.
- Clinical evidence supports the use of magnesium sulfate in all pre-eclampsia patients. In settings where there are resource constraints to manage the administration of magnesium sulfate safely in all women with pre-eclampsia, there may be a need to accord greater priority to the more severe cases. Magnesium sulfate is effective in preventing seizures in both mild and severe pre-eclampsia. However, the guideline development group noted that a higher number of women need to be treated to prevent one seizure. The group agreed on the need to treat women with severe pre-eclampsia, but the group members were divided on the use of magnesium sulfate as a prophylaxis for mild pre-eclampsia.
- Large trials have evaluated and demonstrated the effectiveness of full regimens of magnesium sulfate, which include a loading dose followed by 24-hour maintenance therapy. Specific guidance on how to administer magnesium sulfate can be found in the WHO manual entitled Managing complications in pregnancy and childbirth: a guide for midwives and doctors.(1)
- The guideline development group deliberated on the best course of action in settings in which it is not possible to administer the full magnesium sulfate regimen. The group debated the possible (but yet unproven) benefits of administering only the loading dose versus transferring women with severe preeclampsia and eclampsia without any magnesium sulfate. The group felt that that, even in cases where immediate transfer of the woman to a higher-level facility was not possible, the patient was likely to be better off with only the loading dose than without it. The group felt that since this was a
common scenario in many low-income countries, it should be given high priority for further research.

**Background**

Hypertensive disorders of pregnancy are an important cause of severe morbidity, long-term disability and death among both mothers and their babies. Worldwide, they account for approximately 14% of all maternal deaths, whereas in Latin America and the Caribbean, they contribute to approximately 22% of all maternal deaths.(2)

Among the hypertensive disorders that complicate pregnancy, pre-eclampsia and eclampsia stand out as major causes of maternal and perinatal mortality and morbidity. The majority of deaths due to pre-eclampsia and eclampsia are avoidable through the provision of timely and effective care to the women presenting with these complications.

**Methods**

The recommendation was developed using standardized operating procedures in accordance with the process described in the “WHO handbook for guideline development”, guided by the GRADE approach.(3, 4) Outcomes used for this recommendation were aligned with the prioritized outcomes from the WHO recommendations on prevention and treatment of pre-eclampsia eclampsia (2011).(5)

A Cochrane systematic review was conducted, on the comparative effects of alternative magnesium sulfate regimens for the treatment of pre-eclampsia and eclampsia.(6) In the review, randomized controlled trials relevant to the key question were screened by review authors, and data on relevant outcomes and comparisons were extracted. Evidence profiles (in the form of GRADE tables) were prepared for comparisons of interest, including the assessment and judgments for each outcome, and the estimated risks.

WHO convened a Guideline Development Group (GDG) meeting on recommendations for prevention and treatment of pre-eclampsia or eclampsia in April 2011, where this recommendation was developed. The GDG comprised of a group of independent experts, who used the evidence profiles to assess evidence on effects on the pre-specified outcomes. GDG members discussed the balance between desirable and undesirable effects, overall quality of supporting evidence, values and preferences of stakeholders, resource requirements, cost-effectiveness, acceptability, feasibility and equity, to formulate the recommendation. Remarks were added to clarify the recommendation, and aid implementation.

**Recommendation question**

For this recommendation, we aimed to answer the following question:

- in women with pre-eclampsia or eclampsia (P), what is the optimal magnesium sulfate treatment regimen (I) to improve maternal and perinatal outcomes (O)?

**Evidence Summary**

*Alternative regimens of magnesium sulfate for treatment of pre-eclampsia and eclampsia*

Evidence related to the comparative effects of alternative magnesium sulfate regimens for the treatment of pre-eclampsia and eclampsia came from a Cochrane systematic review of six RCTs involving 866
women. Two of the trials (451 women) had compared regimens for eclampsia while the other four (415 women) had compared regimens for pre-eclampsia. None of the trials had used dosages shown to be effective in large RCTs demonstrating the effectiveness of magnesium sulfate.

When loading dose alone was compared with loading dose plus maintenance regimen for women with eclampsia, one trial (401 women) showed no statistically significant differences in the critical outcomes of recurrent convulsions (RR 1.13, 95% CI 0.42–3.05) and maternal death (RR 0.89, 95% CI 0.37–2.14) and the proxy outcome for perinatal death, stillbirth (RR 1.13, 95% CI 0.66–1.92) (EB Table 44). The loading dose employed in this trial was 4 g intravenous (IV) plus 6 g intramuscular (IM), while the maintenance was 2.5 g IM every 4 hours for 24 hours. The trial had very serious limitations with regard to its quality and the resulting data were generally imprecise. A small trial (50 women) compared low-dose regimen (similar to the regimen above) with the “standard” regimen (4 g IV + 8 g IM as loading dose, then 4 g IM every 4 hours for 24 hours) for women with eclampsia. The only case of recurrent convulsion in the trial was reported among women treated with the low-dose regimen, thus generating a highly imprecise and unreliable data for this critical outcome. No statistically significant differences were observed between the two treatment groups for admission to neonatal special care unit (RR 2.36, 95% CI 0.53–10.58) and proxy outcomes of oliguria (RR 0.20, 95% CI 0.03–1.59) and any baby death (RR 0.89, 95% CI 0.41–1.93) (EB Table 45).

One small trial (17 women) had compared intravenous (2 g hourly for 24 hours) and intramuscular (5 g 4-hourly for 24 hours) maintenance regimens for women with pre-eclampsia. There was no case of eclampsia in either of the two arms of the trials. The trial was too small to yield any reliable conclusions regarding other critical and proxy outcomes reported [magnesium sulfate toxicity (RR 3.33, 95% CI 0.15–71.90); renal failure (RR 3.33, 95% CI 0.15–71.90); stillbirth (RR 1.25, 95% CI 0.09–17.02) (EB Table 46).

Three trials involving 398 women evaluated short versus 24-hour postpartum magnesium sulfate regimens for women with mild and severe pre-eclampsia or imminent eclampsia. Two of these trials, accounting for approximately two thirds of the participants, were at a low or no risk of bias while one was at a moderate risk of bias. None of the women in these trials developed any of the critical outcomes addressed: eclampsia (two trials, 394 women); magnesium sulfate toxicity (one trial, 196 women) (EB Table 47).

Implementation considerations

- The successful introduction of this recommendation into national programmes and health-care services depends on well-planned and participatory consensus-driven processes of adaptation and implementation. The adaptation and implementation processes may include the development or revision of existing national guidelines or protocols based on this recommendation.
- The recommendation should be adapted into a locally appropriate document that can meet the specific needs of each country and health service. Any changes should be made in an explicit and transparent manner.
- A set of interventions should be established to ensure that an enabling environment is created for the use of the recommendations (including, for example, the availability of magnesium sulfate and calcium gluconate), and that the behaviour of the healthcare practitioner changes towards the use of this evidence-based practice.
- In this process, the role of local professional societies is important and an all-inclusive and participatory process should be encouraged.

Research implications

The 2011 GDG identified that further research on the following high-priority questions is needed:

- There is a need to assess the safety and efficacy of the loading dose magnesium sulfate at the primary
care level flowed by transfer to higher level facility.

- Implementation research is needed to increase utilization of magnesium sulfate therapy.

Related Links

WHO recommendations on prevention and treatment of pre-eclampsia and eclampsia (2011) - full document and evidence tables (EB Tables 45-47)

Pregnancy, Childbirth, Postpartum and Newborn Care: A guide for essential practice

Managing Complications in Pregnancy and Childbirth: A guide for midwives and doctors

Supporting systematic reviews:


References


Citation


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