

Magnesium sulphate regimens for women with eclampsia: messages from the Collaborative Eclampsia Trial

Eclampsia remains an important cause of maternal mortality throughout the world. Although it has long been standard practice to use an anti-convulsant for the care of women with eclampsia, the choice of agent has been controversial for more than 70 years. This situation changed recently with the publication of the Collaborative Eclampsia Trial, involving nearly 1700 women with eclampsia¹. In this study, roughly half the women were randomised to receive either magnesium sulphate or diazepam, and the other half were randomised to either magnesium sulphate or phenytoin. In the diazepam arm of the trial, women allocated magnesium sulphate had a 52% lower risk of recurrent convulsions (95% CI 64% to 37%) than those on diazepam. In the phenytoin arm, women allocated magnesium had a 67% lower risk of recurrent convulsions (95% CI 79% to 47%) than those on phenytoin. There is now, for the first time, compelling evidence in favour of magnesium sulphate, rather than diazepam or phenytoin, for the treatment of women with eclampsia.

Although magnesium sulphate is already part of routine clinical practice in some parts of the world^{2,3}, in others it is rarely used or not available. For example, only 2% of UK obstetricians said they used it in a recent survey⁴, and for the trial magnesium sulphate had to be imported into Ghana, Uganda and Zimbabwe, as it was not available locally. This suggests that many clinicians, both in the UK and elsewhere, will now be facing the challenges of first getting access to a drug they have not previously needed, and then of introducing it into their clinical management of a condition that they see only very rarely.

As the evidence to support the use of magnesium sulphate for women with eclampsia comes from this recent study it is important that, as far as possible, the way in which magnesium sulphate was administered and its safety monitored within the trial are reflected in clinical practice. There were two separate regimens (see below) for giving magnesium sulphate, and clinicians at each centre chose which they would use. Women were allocated to an anti-convulsant by opening the next in a series of sealed treatment packs, a system which also has implications for routine clinical practice.

The aim of this paper is to help clinicians responsible for the care of women with eclampsia by providing additional information about the treatment regimens, and the packs, for magnesium sulphate that were used in the Collaborative Eclampsia Trial.

Treatment regimens for magnesium sulphate

Both regimens were based on current recommendations, and reflected clinical practice in the collaborating centres. An initial intravenous (IV) loading dose was followed for 24 h by either an IV infusion, or regular intramuscular (IM) injections. At centres where the clinicians were unfamiliar with the use of magnesium sulphate, the regimen that was to be used locally was presented and discussed in detail at meetings attended by both midwives and doctors.

Intramuscular maintenance regimen

This was administered as described by Pritchard and colleagues⁵. A loading dose of 4 g IV (usually in 20% solution) over 5 min (minimum, preferably 10–15 min) was followed immediately by 5 g (usually in 50% solution) as a deep IM injection into the upper outer quadrant of each buttock. Maintenance therapy was a further 5 g IM every 4 h, continued for 24 h after the last fit.

Intravenous maintenance regimen

The IV regimen was as described by Zuspan⁶. A loading dose of 4 g IV (or in some cases 5 g IV), as described above, was followed by an infusion of 1 g/h continued for 24 h after the last fit. In most centres, the rate of infusion was controlled manually.

Recurrent convulsions

In both the intramuscular and intravenous regimens, if convulsions recurred, a further 2–4 g (depending on the woman's weight, 2 g if less than 70 kg) was given IV over 5 min.

Monitoring during magnesium sulphate therapy

Magnesium sulphate has no sedative effect, so on recovering from the post-ictal phase the woman should be alert and orientated. However, magnesium can depress neuromuscular transmission at the myoneural junction, causing muscular

Table 1. Clinical monitoring during administration of magnesium sulphate.

Only give the next IM dose, or only continue the IV infusion if:

- Respiratory rate > 16/min
- Urine output > 25 ml/h
- Patellar reflexes are present

paralysis as serum levels increase. The rationale for clinical monitoring is that loss of the patellar reflex (knee jerk) precedes respiratory depression and respiratory arrest. Frequent monitoring of the patellar reflex and respiratory rate are therefore essential if complications of therapy are to be minimised. Also, magnesium is cleared by the kidney so, if renal function is impaired, less magnesium will be required. Monitoring during the administration of magnesium sulphate in this trial was clinical, and was based on ensuring that respiration was not depressed, the patellar reflex was present, and renal function was adequate (Table 1). There was no monitoring of serum magnesium levels. Urine output was measured every hour for all women. Observation charts included spaces to record the patellar reflexes and respiratory rate every 15 min. For the IM regimen it was essential to recheck all these observations before giving the next dose. For the IV regimen, more frequent monitoring (every 5–10 min) was recommended during the first 2 h of therapy.

Magnesium toxicity

The following guidelines were provided for management of the potential complications of magnesium sulphate:

1. Respiratory arrest

Intubate and ventilate immediately, and stop magnesium therapy. Give 1 g IV of calcium gluconate, the antidote for magnesium toxicity. Ventilation should be continued until the resumption of normal, spontaneous respiration.

2. Respiratory depression

Given oxygen by mask, 1 g IV of calcium gluconate, and stop magnesium therapy. Maintain the airway and nurse in the recovery position.

3. Absent patellar reflexes

If respiration is normal, withhold further doses of magnesium sulphate until the reflexes return. If respiration is depressed, manage as in 2. above. Magnesium sulphate can be restarted if considered necessary (at a reduced dose unless there have been further convulsions) once reflexes have returned.

4. Urine output < 100 ml in 4 h

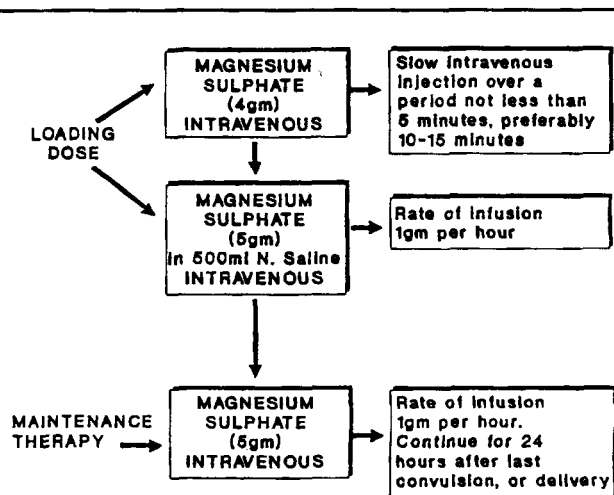
If there are no other signs of magnesium toxicity, reduce the next IM dose of magnesium sulphate to 2.5 g, or the IV infusion to 0.5 g/h. When there are other signs of magnesium toxicity, manage as for the appropriate section above. Review the overall management with particular attention to fluid balance and blood loss.

Treatment packs

These were simply sealed shoebox-sized cardboard boxes. Each contained enough magnesium sulphate for the loading dose, 24 h maintenance therapy, and treatment of one recurrent convulsion. In addition, each had 1 g calcium gluconate as well as everything required to initiate therapy (for description of contents see Table 2). On the box lid was a flow chart summarising how to administer magnesium sulphate (Figs 1 and 2).

Table 2. Contents of the magnesium sulphate (intramuscular regimen) packs.

Intravenous infusion	500 ml normal saline Giving set Intravenous cannula Tape (to secure cannula) Swab (to clean skin for cannula)
Magnesium sulphate	14 g (for loading dose) 5 × 5 g (for maintenance therapy) 5 g (for recurrent convulsions)
Syringes and needles	(For loading dose)
Calcium gluconate	1 g (for toxicity)
Syringe and needle	(For calcium gluconate)
Charts	Fluid balance Observations
Protocol	Summary flow chart (on lid) Detailed regimen Guidelines for other aspects of care

**Fig. 1.** Flow chart for the IV magnesium sulphate regimen.

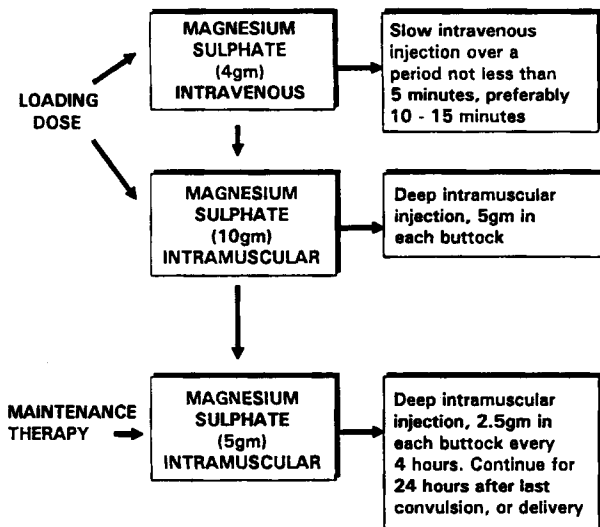


Fig. 2. Flow chart for the intramuscular magnesium sulphate regimen.

For the trial this was on the inside, but in clinical practice it would be more appropriate to have it on the outside. A more detailed description of the treatment regimen was on an A4 sheet folded inside the box, along with a sheet for recording fluid balance, an observation chart, and guidelines for maintaining the airway, blood pressure control and timing of delivery.

Discussion

It is rational and sensible for clinicians to adopt the treatment regimens for magnesium sulphate used in the Collaborative Eclampsia Trial. This has the considerable practical (and economic) advantage that serum monitoring is not required. Although some authors have advocated 2 g/h for IV maintenance therapy⁷, this should not be considered for routine practice until it has been adequately evaluated in comparison to the intravenous regimen described here. It is quite plausible that higher doses will increase the hazards (such as respiratory arrest) without any increase in the benefits associated with the use of magnesium sulphate when given as described in the trial.

The treatment packs used in this study also have considerable practical implications, for both developed and developing countries. They are

a simple, relatively cheap but effective way of ensuring that magnesium sulphate is always readily at hand when required. In developing countries, the problem is the familiar one of maintaining a regular supply of any essential drug. In developed countries, the issue is getting rapid access to a drug which is only rarely required. An additional advantage in all centres, and particularly those where individual clinicians rarely see a woman with eclampsia, is that the pack is self-explanatory and includes a quick and easy to follow protocol.

Magnesium sulphate is a simple salt, and it should be feasible to make it clearly and readily available for the care of all women with eclampsia, regardless of where they live. In countries (including the UK) where until now magnesium sulphate has not been routinely used for eclampsia, there should be some regional or national strategy to ensure affordable and regular supplies. Providing it in the context of treatment packs, as described here, would also help to promote safe and appropriate use.

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Dr L. Duley, Senior Research Fellow

National Perinatal Epidemiology Unit, Radcliffe Infirmary, Oxford OX2 6HE

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