Magnesium sulphate versus phenytoin for eclampsia (Review)

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ABSTRACT

Background
Eclampsia, the occurrence of a convulsion (fit) in association with pre-eclampsia, remains a rare but serious complication of pregnancy. A number of different anticonvulsants are used to control eclamptic fits and to prevent further convulsions.

Objectives
The objective of this review was to assess the effects of magnesium sulphate compared with phenytoin when used for the care of women with eclampsia. Magnesium sulphate is compared with diazepam and with lytic cocktail in other Cochrane reviews.

Search strategy
We searched the Cochrane Pregnancy and Childbirth trials register (28 November 2002) and the Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 4, 2002).

Selection criteria
Randomised trials comparing magnesium sulphate (intravenous or intramuscular administration) with phenytoin for women with a clinical diagnosis of eclampsia.

Data collection and analysis
Both reviewers assessed trial quality and extracted data.

Main results
Six trials involving 897 women are included. Most of the data are from trials of good quality. Magnesium sulphate is associated with a substantial reduction in the recurrence of convulsions, when compared to phenytoin (five trials, 895 women; relative risk (RR) 0.31, 95% confidence interval (CI) 0.20 to 0.47). The trend in maternal mortality favours magnesium sulphate, but this difference is not statistically significant (two trials, 797 women; RR 0.50, 95% CI 0.24 to 1.05). There are also reductions in the risk of pneumonia (RR 0.44, 95% CI 0.24 to 0.79), ventilation (RR 0.66, 95% CI 0.49 to 0.90) and admission to an intensive care unit (RR 0.67, 95% CI 0.50 to 0.89) associated with the use of magnesium sulphate. For the baby, magnesium sulphate was associated with fewer admissions to a special care baby unit (SCBU) (one trial, 518 babies; RR 0.73, 95% CI 0.58 to 0.91) and fewer babies who died or were in SCBU for more than seven days (one trial, 665 babies; RR 0.77, 95% CI 0.63 to 0.95).

Authors' conclusions
Magnesium sulphate appears to be substantially more effective than phenytoin for treatment of eclampsia.

PLAIN LANGUAGE SUMMARY

Magnesium sulphate reduces the number of repeat fits in mothers' given phenytoin for eclamptic fits

Some women develop raised blood pressure along with protein in the urine (pre-eclampsia, or 'toxaemia') in pregnancy, and this can cause considerable ill health for those women and their babies. A few of these women have fits or convulsions (eclampsia), either in

pregnancy or shortly after birth. Some of these women die, particularly those in income-poor countries. The review of trials found that magnesium sulphate was more effective than phenytoin in reducing the number of repeat fits and other problems for women. Other drugs have also been compared with magnesium sulphate in other reviews; magnesium sulphate was more effective than these.

BACKGROUND

Pre-eclampsia is a multisystem disorder that is usually associated with raised blood pressure and proteinuria but, when severe, can involve the woman's liver, kidneys, clotting system, or brain. The placenta is also often involved, with an increased risk of poor growth and early delivery for the baby. It is a relatively common complication of pregnancy, and can occur at any time during the second half of pregnancy or the first few weeks after delivery.

Eclampsia, the occurrence of a convulsion (fit) in association with pre-eclampsia, remains a rare but serious complication of pregnancy. Estimated to complicate around one in 2000 deliveries in Europe and other high-income countries (Douglas 1994), and from one in 100 to 1700 deliveries in low- and middle-income countries (Crowther 1985), eclampsia is associated with around 10% of maternal deaths and an estimated 50,000 women die each year having had an eclamptic convulsion (Duley 1992).

Currently, standard practice is to use an anticonvulsant to control the immediate fit and to prevent further convulsions, but the choice of anticonvulsant has been controversial. Until recently, there has been little adequately controlled evidence to support the use of any of the options, and there has been enormous variation in clinical practice. For example, although magnesium sulphate has long been the drug of choice in the United States (Gifford 1990), until recently only 2% of obstetricians in the United Kingdom reported using it (Hutton 1992). The data presented in earlier versions of this review have had a considerable impact on clinical practice, and increasingly magnesium sulphate is being used for treatment of eclampsia. In a recent survey in the UK and Ireland, for example, 60% of clinicians reported using magnesium sulphate (Gülmezoglu 1998). Other anticonvulsants still reported to be in use for eclampsia include diazepam (valium) and phenytoin, with lytic cocktail still available in some parts of the developing world.

The aim of this review is to summarise the evidence about the differential effects of magnesium sulphate when compared with phenytoin for the care of women with eclampsia. Magnesium sulphate is compared with diazepam (Duley 2003a) and with lytic cocktail (usually chlorpromazine, promethazine and pethidine) (Duley 2003c) in other reviews.

OBJECTIVES

The aim was to evaluate the differential effects of magnesium sulphate, given either by the intramuscular or intravenous route, when compared with phenytoin for the care of women with eclampsia. The comparison was in terms of maternal mortality, recurrence of convulsions, other serious morbidity that could lead to death, and use of health service resources. For women who were entered into the trials before delivery, additional outcomes were those related to labour, delivery, and morbidity and mortality for the baby.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

All known randomised trials that compare magnesium sulphate with phenytoin when used for the care of women with eclampsia. Quasi-randomised studies were excluded.

Types of participants

Women with a clinical diagnosis of eclampsia at randomisation irrespective of whether they were before or after delivery, had a singleton or multiple pregnancy, or an anticonvulsant had been given before trial entry. If women with pre-eclampsia had also been entered into the trial, only data for women with eclampsia were included in this review.

Types of intervention

All randomised comparisons of magnesium sulphate (intravenous or intramuscular administration) with phenytoin for women with eclampsia. As phenytoin is only used for prevention of further fits, another agent (usually a benzodiazapine) may have been used for control of the acute convulsion.

Types of outcome measures

The most important outcome is maternal death but as this is relatively rare, even for women with eclampsia, other measures of serious morbidity, which could lead to death, were also included, eg recurrence of convulsions, pulmonary oedema, renal failure, liver failure, stroke. For women randomised before delivery, additional outcomes were caesarean section, labour less than eight hours, blood loss at delivery more than 500 ml, mortality for the baby, and morbidity for liveborn babies. Measures of use of health service resources were also included.

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

We searched the Cochrane Pregnancy and Childbirth Group trials register (28 November 2002).

The Cochrane Pregnancy and Childbirth Group's trials register is maintained by the Trials Search Co-ordinator and contains trials identified from:
1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. monthly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness search of a further 37 journals.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Search strategies for identification of studies' section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are given a code (or codes) depending on the topic. The codes are linked to review topics. The Trials Search Co-ordinator searches the register for each review using these codes rather than keywords.

The Cochrane Central Register of Controlled Trials, (The Cochrane Library, Issue 4, 2002) was also searched using the terms eclamp* anticonvuls* magnesium sul* phenyt*.

METHODS OF THE REVIEW

Two reviewers, LD and DHS, extracted and checked the data independently. We resolved discrepancies by discussion. There was no blinding of authorship or results. Whenever possible, we sought unpublished data from investigators.

A quality score for concealment of allocation was assigned to each trial, using the following criteria:
(A) adequate concealment of allocation;
(B) unclear whether adequate concealment of allocation;
(C) inadequate concealment of allocation.

We excluded quasi-randomised trials, eg those using alternate allocation.

In addition, we assigned to each reported outcome quality scores for completeness of follow up and blinding of the assessment of outcome using the following criteria:
For completeness of follow up:
(A) less than 3% of participants excluded;
(B) 3% to 9.9% of participants excluded;
(C) 10% to 19.9% of participants excluded.

Excluded: if not possible to enter data based on intention to treat, and/or 20% of participants were excluded from that outcome.

For blinding of assessment of outcome:
(A) Double blind, neither clinicians nor participant knew or were likely to guess the allocated treatment.
(B) Single blind, either the clinicians or the participant knew the allocation. Or, the trial is described as double blind, but side effects of one or other treatment mean that it is likely that for a significant proportion (more than 20%) of participants the allocation could be correctly identified.
(C) No blinding, both clinicians/investigators and participant knew (or were likely to guess) the allocated treatment. Or, blinding not mentioned.

Excluded: no blinding, and the outcomes were very subjective.

Subgroup analyses planned for future updates of this review will be by whether the women was randomised before delivery, and by whether she had received an anticonvulsant before randomisation.

We performed statistical analyses using the Review Manager software (RevMan 2000), with results presented as relative risks (RR) and risk difference (RD). We calculated from 1/RD the number needed to treat (NNT) for benefits and for harmful or adverse effects. The 95% confidence intervals are given for each measure. We used the fixed effects model for calculating relative risk. If there was clear heterogeneity between the studies in any one outcome, we used a random effects model. We also explored possible factors in the heterogeneity, including study quality, clinical factors as determined by the prespecified subgroup analyses, and the play of chance.

DESCRIPTION OF STUDIES

This review largely includes women with antepartum eclampsia, 17% were postpartum. About 80% of the women had had an anticonvulsant before trial entry. The magnesium sulphate regimens included both intravenous and intramuscular maintenance therapy. In one trial, immediate control of fits for women allocated phenytoin was with diazepam (Collab Trial 1995). In another study all women received clonazepam before trial entry (Cape Town 1990) and, in another, nifedipine was given to all women after recruitment (India 1999). One study (South Africa 1996) used a loading dose only. For this study, the only outcome included in this review is recurrence of convulsions.

METHODOLOGICAL QUALITY

Six trials were identified. Five were small, and one was large (Collab Trial 1995). This large study included 777 of the 897 women in this review (87%). The methodological quality of the large Collaborative Eclampsia Trial (Collab Trial 1995) was good, but for the small trials concealment of allocation was either inadequate or unclear. Blinding after randomisation was not possible in any of the trials, due to the nature of the drugs. In the large trial

(Collab Trial 1995), assessment of outcome was by the attending clinicians. Although this was not discussed in most of the other studies, it is likely the same is true for them all.

There were no major discrepancies in the data extraction.

RESULTS

Six trials (897 women) compare magnesium sulphate with phenytoin. Magnesium sulphate is associated with a substantial reduction in the recurrence of convulsions, when compared with phenytoin, relative risk (RR) 0.31, 95% confidence intervals (CI) 0.20 to 0.47 (five trials, 895 women). This means that, on average, for every eight women treated with magnesium sulphate rather than phenytoin, one recurrence of convulsions will be prevented (95% CI 6 to 13 women). The trend in maternal mortality also favours magnesium sulphate, but this difference is not statistically significant (two trials, 797 women; RR 0.50, 95% CI 0.24 to 1.05). For the women there are also reductions in the risk of pneumonia (one trial, 775 women, RR 0.44, 95% CI 0.24 to 0.79), ventilation (one trial, 775 women; RR 0.66, 95% CI 0.49 to 0.90) and admission to an intensive care unit (one trial, 775 women; RR 0.67, 95% CI 0.50 to 0.89) associated with the use of magnesium sulphate, rather than phenytoin.

For the baby, most of the outcome data in this review come from the single large trial (Collab Trial 1995). Two trials (665 babies) reported perinatal mortality (RR 0.85, 95% CI 0.67 to 1.09). Magnesium sulphate was associated with fewer liveborn babies being admitted to a special care baby unit (one trial, 518 babies; RR 0.73, 95% CI 0.58 to 0.91) and fewer babies who had the composite outcome of death or in special care for more than seven days (one trial, 643 babies; RR 0.77, 95% CI 0.63 to 0.95).

DISCUSSION

Magnesium sulphate for women with eclampsia reduces the risk of further fits, compared with phenytoin. The trend in maternal mortality is also in favour of magnesium sulphate. These benefits of magnesium sulphate when compared with phenytoin are also reflected in reductions in other measures of maternal and perinatal morbidity.

Once women were randomised, the allocated treatments could not be blinded in any of these studies. It is unlikely that any subsequent bias will have substantially influenced the results, however. The main outcomes assessed were objective, and the strength and consistency of the data indicate they represent true effects.

This review should be viewed in conjunction with those comparing magnesium sulphate with diazepam (Duley 2003a) and with lytic cocktail (Duley 2003c). Overall, there is now compelling evidence in favour of magnesium sulphate, rather than phenytoin, diazepam, or lytic cocktail for the treatment of eclampsia. Magnesium sulphate is cheap and relatively easy to produce, and so making it readily available for the care of women with eclampsia in both high-income and low- to middle-income countries should be a high priority.

Most of the women who received magnesium sulphate in these trials had 4 g as a loading dose, and then maintenance therapy was either the intramuscular regimen or an infusion of 1 g/hour. For most women duration of treatment was 24 hour. Women were monitored using respiration rate, urine output and tendon reflexes. Serum monitoring was not used. Administration and clinical monitoring of magnesium sulphate can be done by medical, midwifery or nursing staff, provided they are appropriately trained.

Magnesium sulphate is also the drug of choice for prevention of eclampsia for women with pre-eclampsia. This topic is also covered by a separate review (Duley 2003b).

AUTHORS' CONCLUSIONS

Implications for practice

There is now strong support for the routine use of magnesium sulphate rather than either phenytoin for women with eclampsia. The evidence from this review suggests that phenytoin is less effective than magnesium sulphate, and that it may even be harmful. Other reviews confirm magnesium sulphate is also better than either diazepam or lytic cocktail (Duley 2003a; Duley 2003c). Although only two relatively small trials have compared magnesium sulphate with lytic cocktail, the evidence from these studies favours magnesium sulphate. Magnesium sulphate is cheap and easy to produce, and so it should be a priority to make this readily available for the care of women with eclampsia in both high-income and low- to middle-income countries.

Implications for research

Magnesium sulphate is now the gold standard against which any new anticonvulsants for women with eclampsia should be compared in properly designed randomised trials. Eclampsia can be distinguished from other forms of seizures in that it is better controlled by magnesium sulphate than by either phenytoin or diazepam (both conventional anticonvulsants), which may offer opportunities to explore the pathogenesis of eclampsia.

POTENTIAL CONFLICT OF INTEREST

Lelia Duley was principal investigator for the Collaborative Eclampsia Trial.

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- Medical Research Council UK

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* *Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Baltimore 1993**
Methods	Sealed opaque envelopes. 3 envelopes lost, 2 after women entered in error. 8 women with twins excluded, plus 1 lost to follow up (not clear if eclampsia).
Participants	2 women with antenatal eclampsia (103 with PE not included in this review).
Interventions	Phenytoin: infusion of 1000, 1250 or 1500 mg. MgSO4: 6 gm IV bolus, followed by infusion of 2 g/hr.
Outcomes	Women: recurrence of convulsions. Baby: none reported.
Notes	Outcome for 2 women with eclampsia only reported separately for convulsions. Both women allocated phenytoin and had eclampsia. Not possible to enter data in meta-analysis, as no one in MgSO4 group. Phenytoin was unfamiliar treatment.
Allocation concealment	B – Unclear

Study	**Cape Town 1990**
Methods	Random number tables. No information about concealment of allocation.
Participants	22 women with antenatal eclampsia and no previous anticonvulsant (1 had phenobarbitone and was entered in error).
Interventions	All women had clonazepam at entry.

Characteristics of included studies (*Continued*)

	Phenytoin: 500 or 1000 mg IV at maximum rate of 50 mg/min. Then 500 mg over 4 hr. 12 hr later, 500 mg over 4 hr. MgS04: 4 g IV over 20-30 min. Then 1-2 g/hr for 24 hr.
Outcomes	Women: death, recurrence of convulsions, caesarean section. Baby: mortality.
Notes	Trial stopped early, after 4 fits in phenytoin group. No information about whether this was a planned interim analysis. Phenytoin was the unfamiliar treatment.
Allocation concealment	C – Inadequate

Study	**Collab Trial 1995**
Methods	Consecutively numbered sealed treatment packs, identical in size, shape, weight and feel. Sequence generated by computer with variable block size and stratified by centre. 2 women lost to follow up.
Participants	777 women with clinical diagnosis of eclampsia. 76% allocated MgSO4 had an anticonvulsant before trial entry, and 80% allocated phenytoin. 19% postpartum.
Interventions	Phenytoin: diazepam 10 mg IV for control of seizures (PRN). 1 g phenytoin IV over 20 min, then 100 mg every 6 hr for 24 hr. MgS04: Either (a) 4 g IV over 5 min and 10 g IM. Then 5 g IM every 4 hr for 24 hr. Or (b) 4 g IV over 5 min, then infusion of 1 g/hr for 24 hr. For both (a) and (b), if recurrent convulsions 2 g IV. Clinical monitoring alone, no serum monitoring.
Outcomes	All women: death, recurrent convulsions, pneumonia, respiratory depression, ventilation, cardiac arrest, arrhythmia, coagulopathy, renal failure, liver failure, cerebrovascular accident, admission intensive care unit, abscess. Women randomized before delivery: transfusion, induction, labour > 8 hr, caesarean section, blood loss. Baby: mortality, Apgar < 7 (1, 5 min), intubated, admitted SCBU, in SCBU > 7 days, death or in SCBU > 7 days.
Notes	4 centres in South Africa and India. For IM MgS04 n = 336, for IV n = 52. Phenytoin was the unfamiliar treatment. 99% compliance with the allocated anticonvulsant. 48/387 (12%) allocated phenytoin also had diazepam.
Allocation concealment	A – Adequate

Study	**India 1999**
Methods	Sealed envelopes. Sequence generated by computer.
Participants	50 consecutive women with eclampsia. 29 had an anticonvulsant before entry.
Interventions	Phenytoin: 15 mg/kg loading dose, given at 50 mg/min. 10 mg/kg initially then 5 mg/kg 2 hr later. Maintenance 500 mg IV 12 hours later. Then 250 mg either IV or oral, 12 hrly for 4 doses. MgSO4: 4 g IV and 8 g IM. Then 4 g IV every 4 hr, until 24 hr after delivery. Both groups: if fit given 10 mg diazepam.
Outcomes	Recurrence of convulsions, renal failure, pulmonary oedema.
Notes	Not stated whether all women randomised before delivery. Data on labour and outcome for the baby not included. All women had 5 mg nifedipine sl after recruitment.

Allocation concealment	C – Inadequate

Study	**Memphis 1995**
Methods	"Randomly allocated". No further details.
Participants	24 women with eclampsia. 14 women have MgSO4 before trial entry, 9 allocated MgSO4 and 5 allocated phenytoin.
Interventions	Phenytoin: 1-1.5 g IV. Additional doses to keep serum levels 10-20 microg/ml. MgSO4: 6 g IV over 15 min. Then infusion of 2 g/hr, adjusted to keep serum levels 4.8-9.6 mg/dl.
Outcomes	Women: recurrence of convulsions. Baby: none.
Notes	Published in abstract only. 79% of women randomized before delivery.
Allocation concealment	B – Unclear

Study	**South Africa 1996**
Methods	Computer generated random numbers in sealed envelopes.
Participants	24 women with eclampsia.
Interventions	Phenytoin: 1 g in 200 ml over 15-20 min. MgSO4: 4 g IV and 10 g IM.
Outcomes	Women: fits, Doppler measurements on middle cerebral artery.
Notes	Intervention described is loading dose only.
Allocation concealment	C – Inadequate

hr: hour
hrly: hourly
IM: intramuscular
IV: intravenous
min: minute
MgS04: magnesium sulphate
PE: pre-eclampsia
PRN: as required
SCBU: special care baby unit
sl: sublingual

Characteristics of excluded studies

Study	**Reason for exclusion**
India 1997	Not a randomised trial. Case series of 100 women with eclampsia. 40 received phenytoin, 28 lytic cocktail, 16 diazepam and 16 MgSO4.
Texas 1991	One woman with eclampsia, 49 women with pre-eclampsia. Outcome not reported separately, but no women had a convulsion after trial entry.

MgS04: magnesium sulphate

ANALYSES

Comparison 01. Magnesium sulphate versus phenytoin

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	2	797	Relative Risk (Fixed) 95% CI	0.50 [0.24, 1.05]
02 Recurrence of convulsions	5	895	Relative Risk (Fixed) 95% CI	0.31 [0.20, 0.47]
03 Respiratory depression	1	775	Relative Risk (Fixed) 95% CI	0.71 [0.46, 1.09]
04 Pulmonary oedema	2	825	Relative Risk (Fixed) 95% CI	1.00 [0.47, 2.10]
05 Pneumonia	1	775	Relative Risk (Fixed) 95% CI	0.44 [0.24, 0.79]
06 Ventilation	1	775	Relative Risk (Fixed) 95% CI	0.66 [0.49, 0.90]
07 Renal failure	2	825	Relative Risk (Fixed) 95% CI	1.48 [0.94, 2.32]
08 Cerebrovascular accident	1	775	Relative Risk (Fixed) 95% CI	0.54 [0.20, 1.46]
09 Liver failure	1	775	Relative Risk (Fixed) 95% CI	1.50 [0.54, 4.16]
10 Cardiac arrest	1	775	Relative Risk (Fixed) 95% CI	1.16 [0.39, 3.43]
11 Coagulopathy	1	775	Relative Risk (Fixed) 95% CI	0.88 [0.66, 1.16]
12 Admission to intensive care unit	1	775	Relative Risk (Fixed) 95% CI	0.67 [0.50, 0.89]
15 Caesarean section	2	650	Relative Risk (Fixed) 95% CI	0.94 [0.86, 1.03]
16 Labour > 8 hours	1	628	Relative Risk (Fixed) 95% CI	1.19 [0.85, 1.67]
18 Blood loss at delivery > 500 ml	1	628	Relative Risk (Fixed) 95% CI	0.98 [0.74, 1.30]
20 Mortality for the fetus or infant			Relative Risk (Fixed) 95% CI	Subtotals only
21 Apgar scores			Relative Risk (Fixed) 95% CI	Subtotals only
22 Utilization of special care baby unit (SCBU)			Relative Risk (Fixed) 95% CI	Subtotals only
23 Death or in SCBU > 7 days	1	643	Relative Risk (Fixed) 95% CI	0.77 [0.63, 0.95]

INDEX TERMS

Medical Subject Headings (MeSH)

Anticonvulsants [*therapeutic use]; Chlorpromazine [therapeutic use]; Drug Combinations; Eclampsia [*drug therapy]; Magnesium Sulfate [*therapeutic use]; Meperidine [therapeutic use]; Phenytoin [*therapeutic use]; Promethazine [therapeutic use]; Randomized Controlled Trials

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title Magnesium sulphate versus phenytoin for eclampsia

Authors Duley L, Henderson-Smart D

Contribution of author(s) Both reviewers contributed to the design, and conducted data extraction. Lelia Duley entered the data and drafted the text of the review, with comments and input from David Henderson-Smart.

Issue protocol first published 1995/2

Review first published 1995/2

Date of most recent amendment 19 August 2005

Date of most recent SUBSTANTIVE amendment	01 July 2003
What's New	One new trial added, India 1999, with 50 women.
Date new studies sought but none found	Information not supplied by author
Date new studies found but not yet included/excluded	Information not supplied by author
Date new studies found and included/excluded	06 January 2003
Date authors' conclusions section amended	05 March 2003
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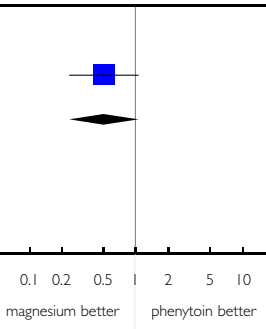
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 01 Maternal death

Review: Magnesium sulphate versus phenytoin for eclampsia
Comparison: 01 Magnesium sulphate versus phenytoin
Outcome: 01 Maternal death

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
× Cape Town 1990	0/11	0/11		0.0	Not estimable
Collab Trial 1995	10/388	20/387		100.0	0.50 [0.24, 1.05]
Total (95% CI)	399	398		100.0	0.50 [0.24, 1.05]
Total events: 10 (Treatment), 20 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.83 p=0.07					



Analysis 01.02. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 02 Recurrence of convulsions

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 02 Recurrence of convulsions

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cape Town 1990	0/11	4/11		5.4	0.11 [0.01, 1.85]
Collab Trial 1995	22/388	66/387		78.7	0.33 [0.21, 0.53]
India 1999	2/25	10/25		11.9	0.20 [0.05, 0.82]
Memphis 1995	0/11	2/13		2.7	0.23 [0.01, 4.40]
South Africa 1996	1/13	1/11		1.3	0.85 [0.06, 12.01]
Total (95% CI)	448	447		100.0	0.31 [0.20, 0.47]

Total events: 25 (Treatment), 83 (Control)

Test for heterogeneity chi-square=1.56 df=4 p=0.82 I^2 =0.0%

Test for overall effect z=5.48 p<0.00001

Analysis 01.03. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 03 Respiratory depression

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 03 Respiratory depression

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	32/388	45/387		100.0	0.71 [0.46, 1.09]
Total (95% CI)	388	387		100.0	0.71 [0.46, 1.09]

Total events: 32 (Treatment), 45 (Control)

Test for heterogeneity: not applicable

Test for overall effect z=1.56 p=0.1

Analysis 01.04. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 04 Pulmonary oedema

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 04 Pulmonary oedema

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	12/388	13/387		96.3	0.92 [0.43, 1.99]
India 1999	1/25	0/25		3.7	3.00 [0.13, 70.30]
Total (95% CI)	413	412		100.0	1.00 [0.47, 2.10]
Total events: 13 (Treatment), 13 (Control)					
Test for heterogeneity chi-square=0.51 df=1 p=0.48 I^2 =0.0%					
Test for overall effect z=0.01 p=1					

Analysis 01.05. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 05 Pneumonia

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 05 Pneumonia

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	15/388	34/387		100.0	0.44 [0.24, 0.79]
Total (95% CI)	388	387		100.0	0.44 [0.24, 0.79]
Total events: 15 (Treatment), 34 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.72 p=0.006					

Analysis 01.06. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 06 Ventilation

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 06 Ventilation

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	58/388	87/387		100.0	0.66 [0.49, 0.90]
Total (95% CI)	388	387		100.0	0.66 [0.49, 0.90]
Total events: 58 (Treatment), 87 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.66 p=0.008					

Analysis 01.07. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 07 Renal failure

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 07 Renal failure

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	40/388	28/387		96.6	1.42 [0.90, 2.26]
India 1999	3/25	1/25		3.4	3.00 [0.33, 26.92]
Total (95% CI)	413	412		100.0	1.48 [0.94, 2.32]
Total events: 43 (Treatment), 29 (Control)					
Test for heterogeneity chi-square=0.42 df=1 p=0.51 I^2 =0.0%					
Test for overall effect z=1.70 p=0.09					

Analysis 01.08. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 08 Cerebrovascular accident

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 08 Cerebrovascular accident

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	6/388	11/387		100.0	0.54 [0.20, 1.46]
Total (95% CI)	388	387		100.0	0.54 [0.20, 1.46]
Total events: 6 (Treatment), 11 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.21 p=0.2					

Analysis 01.09. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 09 Liver failure

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 09 Liver failure

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	9/388	6/387		100.0	1.50 [0.54, 4.16]
Total (95% CI)	388	387		100.0	1.50 [0.54, 4.16]
Total events: 9 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.77 p=0.4					

Analysis 01.10. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 10 Cardiac arrest

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 10 Cardiac arrest

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	7/388	6/387		100.0	1.16 [0.39, 3.43]
Total (95% CI)	388	387		100.0	1.16 [0.39, 3.43]
Total events: 7 (Treatment), 6 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.27 p=0.8					

Analysis 01.11. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 11 Coagulopathy

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 11 Coagulopathy

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	73/388	83/387		100.0	0.88 [0.66, 1.16]
Total (95% CI)	388	387		100.0	0.88 [0.66, 1.16]
Total events: 73 (Treatment), 83 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.91 p=0.4					

Analysis 01.12. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 12 Admission to intensive care unit

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 12 Admission to intensive care unit

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	65/388	97/387		100.0	0.67 [0.50, 0.89]
Total (95% CI)	388	387		100.0	0.67 [0.50, 0.89]
Total events: 65 (Treatment), 97 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.81 p=0.005					

Analysis 01.15. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 15 Caesarean section

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 15 Caesarean section

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Cape Town 1990	8/11	7/11		2.8	1.14 [0.64, 2.03]
Collab Trial 1995	224/309	247/319		97.2	0.94 [0.86, 1.03]
Total (95% CI)	320	330		100.0	0.94 [0.86, 1.03]
Total events: 232 (Treatment), 254 (Control)					
Test for heterogeneity chi-square=0.45 df=1 p=0.50 I^2 =0.0%					
Test for overall effect z=1.31 p=0.2					

Analysis 01.16. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 16 Labour > 8 hours

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 16 Labour > 8 hours

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	60/309	52/319		100.0	1.19 [0.85, 1.67]
Total (95% CI)	309	319		100.0	1.19 [0.85, 1.67]
Total events: 60 (Treatment), 52 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=1.02 p=0.3					

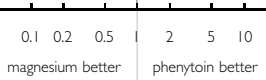
Analysis 01.18. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 18 Blood loss at delivery > 500 ml

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 18 Blood loss at delivery > 500 ml

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	71/309	75/319		100.0	0.98 [0.74, 1.30]
Total (95% CI)	309	319		100.0	0.98 [0.74, 1.30]
Total events: 71 (Treatment), 75 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.16 p=0.9					



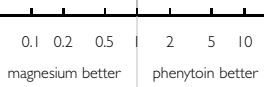
Analysis 01.20. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 20 Mortality for the fetus or infant

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 20 Mortality for the fetus or infant

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Stillbirth					
Cape Town 1990	2/11	2/11		2.8	1.00 [0.17, 5.89]
Collab Trial 1995	55/314	70/329		97.2	0.82 [0.60, 1.13]
Subtotal (95% CI)	325	340		100.0	0.83 [0.61, 1.13]
Total events: 57 (Treatment), 72 (Control)					
Test for heterogeneity chi-square=0.04 df=1 p=0.83 I^2 =0.0%					
Test for overall effect z=1.18 p=0.2					
02 Perinatal death					
Cape Town 1990	2/11	2/11		2.0	1.00 [0.17, 5.89]
Collab Trial 1995	82/314	101/329		98.0	0.85 [0.66, 1.09]
Subtotal (95% CI)	325	340		100.0	0.85 [0.67, 1.09]
Total events: 84 (Treatment), 103 (Control)					
Test for heterogeneity chi-square=0.03 df=1 p=0.86 I^2 =0.0%					
Test for overall effect z=1.27 p=0.2					
03 Neonatal death					
× Cape Town 1990	0/11	0/11		0.0	Not estimable
Collab Trial 1995	29/314	32/329		100.0	0.95 [0.59, 1.53]
Subtotal (95% CI)	325	340		100.0	0.95 [0.59, 1.53]
Total events: 29 (Treatment), 32 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.21 p=0.8					



Analysis 01.21. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 21 Apgar scores

Review: Magnesium sulphate versus phenytoin for eclampsia
Comparison: 01 Magnesium sulphate versus phenytoin
Outcome: 21 Apgar scores

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Apgar < 7 at 1 minute					
Collab Trial 1995	116/259	148/259		100.0	0.78 [0.66, 0.93]
Subtotal (95% CI)	259	259		100.0	0.78 [0.66, 0.93]
Total events: 116 (Treatment), 148 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.78 p=0.005					
02 Apgar < 7 at 5 minutes					
Collab Trial 1995	25/259	29/259		100.0	0.86 [0.52, 1.43]
Subtotal (95% CI)	259	259		100.0	0.86 [0.52, 1.43]
Total events: 25 (Treatment), 29 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=0.57 p=0.6					

Analysis 01.22. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 22 Utilization of special care baby unit (SCBU)

Review: Magnesium sulphate versus phenytoin for eclampsia
Comparison: 01 Magnesium sulphate versus phenytoin
Outcome: 22 Utilization of special care baby unit (SCBU)

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Admission to SCBU					
Collab Trial 1995	82/259	113/259		100.0	0.73 [0.58, 0.91]
Subtotal (95% CI)	259	259		100.0	0.73 [0.58, 0.91]
Total events: 82 (Treatment), 113 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.78 p=0.005					
03 In SCBU > 7 days					
Collab Trial 1995	23/259	43/259		100.0	0.53 [0.33, 0.86]
Subtotal (95% CI)	259	259		100.0	0.53 [0.33, 0.86]
Total events: 23 (Treatment), 43 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.58 p=0.01					

Analysis 01.23. Comparison 01 Magnesium sulphate versus phenytoin, Outcome 23 Death or in SCBU > 7 days

Review: Magnesium sulphate versus phenytoin for eclampsia

Comparison: 01 Magnesium sulphate versus phenytoin

Outcome: 23 Death or in SCBU > 7 days

Study	Treatment n/N	Control n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	105/314	142/329		100.0	0.77 [0.63, 0.95]
Total (95% CI)	314	329		100.0	0.77 [0.63, 0.95]
Total events: 105 (Treatment), 142 (Control)					
Test for heterogeneity: not applicable					
Test for overall effect z=2.51 p=0.01