Magnesium sulphate versus diazepam for eclampsia (Review)

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ABSTRACT

Background
Eclampsia, the occurrence of a convulsion 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 fits.

Objectives
The objective of this review was to assess the effects of magnesium sulphate compared with diazepam when used for the care of women with eclampsia. Magnesium sulphate is compared with phenytoin 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 diazepam for women with a clinical diagnosis of eclampsia.

Data collection and analysis
Both reviewers assessed and extracted data.

Main results
Seven trials involving 1441 women are included. Most of the data are from trials of good quality. Magnesium sulphate is associated with a reduction in maternal death when compared to diazepam (six trials 1336 women; relative risk (RR) 0.59, 95% confidence interval (CI) 0.37 to 0.94). There is also a substantial reduction in the risk recurrence of further fits (seven trials 1441 women; RR 0.44, 95% CI 0.34 to 0.57). There were few differences in any other measures of outcome, except for fewer Apgar scores less than seven at five minutes (two trials 597 babies; RR 0.72, 95% CI 0.55 to 0.94) and fewer babies with a length of stay in special care baby unit more than seven days (three trials 631 babies; RR 0.66, 95% CI 0.46 to 0.95) associated with magnesium sulphate.

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

PLAIN LANGUAGE SUMMARY

Magnesium sulphate saves more mothers' lives than diazepam when given 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 diazepam in reducing death and other problems for women. Other drugs have also been compared with magnesium sulphate in other reviews, magnesium sulphate was more effective than these too.

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 seizures, 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 to diazepam for the care of women with eclampsia. Magnesium sulphate is compared with phenytoin (Duley 2003) and with lytic cocktail (usually chlorpromazine, promethazine and pethidine) in other reviews (Duley 2003b).

OBJECTIVES

The aim was to evaluate the differential effects of magnesium sulphate, given either by the intramuscular or the intravenous route, when compared with diazepam 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 mortality and morbidity of the baby.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

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

Types of participants

Women with a clinical diagnosis of eclampsia at trial entry irrespective of whether they were before or after delivery, had a singleton or multiple pregnancy, or whether 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 diazepam for women with eclampsia.

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. For example, recurrence of convulsions, pulmonary oedema, renal failure, liver failure and stroke. For women randomised before delivery, additional outcomes were caesarean section, labour lasting less than eight hours and 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 search terms eclamp* anticonvuls* magnesium sul* diazepam.

METHODS OF THE REVIEW

Both reviewers extracted data from each report, without any blinding of either the results or the treatments which women received. We assessed the quality of each study. We resolved discrepancies by discussion. There was no blinding of authorship or results. Whenever possible, we sought unpublished data from investigators. We assigned a quality score for concealment of allocation to each trial, using the following criteria:
(A) adequate concealment of allocation;
(B) unclear whether adequate concealment of allocation;
(C) inadequate concealment of allocation.

Quasi-random trials were excluded, for example 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 clinician nor participant knew or were likely to guess the allocated treatment.
(B) Single blind, either the clinician 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 investigator and participant knew (or were likely to guess) the allocated treatment. Or, blinding was 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.

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

DESCRIPTION OF STUDIES

Most trials included women with both antepartum and postpartum eclampsia. Overall, about half the women in this review had also had an anticonvulsant before trial entry. The treatment regimens all included a loading dose and maintenance therapy. For magnesium sulphate, these regimens included both intravenous or intramuscular maintenance therapy. For one trial (Malaysia 1994) the treatment regimens were not described.

METHODOLOGICAL QUALITY

Three trials in this review (Zimbabwe 1990; Collab Trial 1995; Zimbabwe 1998) are of good quality. For four (Egypt 1993; Malaysia 1994; Bangladesh 1998; India 2001) it is unclear whether concealment of allocation was adequate. One study is only available as an unpublished report (India 2001), another as an abstract and an unpublished report (Egypt 1993). Blinding of the allocation 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. Follow up was more than 99% for all the trials.

RESULTS

This review includes seven trials with data from 1441 women. Magnesium sulphate is associated with a reduction in the risk of maternal death, when compared to diazepam, although the confidence intervals are wide: relative risk (RR) 0.59, 95% confidence intervals (CI) 0.37 to 0.94 (six trials 1336 women). For recurrence of convulsions, there is also a substantial reduction in risk associated with magnesium sulphate (seven trials 1441 women; RR 0.44, 95% CI 0.34 to 0.57). This means that, on average, for

every seven women treated with magnesium sulphate rather than diazepam one recurrence of convulsions will be prevented (95% CI 6 to 10 women). There are no differences in any other measure of maternal morbidity.

Some trials did not report any outcomes for the baby. Three trials (745 babies) reported perinatal mortality (RR 1.04, 95% CI 0.80 to 1.36). The only statistically significant differences are a reduction in Apgar scores less than seven at one minute (two trials 597 babies; RR 0.75, 95% CI 0.65 to 0.87) and less than seven at five minutes (two trials 597 babies; RR 0.72, 95% CI 0.55 to 0.94), and in the number of liveborn babies with a length of stay in a special care baby unit more than seven days (three trials 631 babies; RR 0.66, 95% CI 0.46 to 0.95) associated with the use of magnesium sulphate rather than diazepam.

DISCUSSION

Magnesium sulphate for women with eclampsia reduces the risk of both maternal death and further fits, compared to diazepam. There is no clear evidence of any other effects on maternal morbidity, or on perinatal morbidity or mortality.

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 phenytoin (Duley 2003) and with lytic cocktail (Duley 2003b). Overall, there is now compelling evidence in favour of magnesium sulphate, rather than diazepam, phenytoin 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 hours. 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 covered by a separate review (Duley 2003a).

AUTHORS' CONCLUSIONS

Implications for practice

There is now strong support for the routine use of magnesium sulphate, rather than diazepam, for women with eclampsia. Other reviews confirm magnesium sulphate is also better than either phenytoin or lytic cocktail (Duley 2003; Duley 2003b). Although only two relatively small trials have compared magnesium sulphate with lytic cocktail, the evidence from these studies favours magnesium sulphate. As it is an inexpensive drug, it is especially suitable for use in low- and middle-income countries. Duration of treatment should not normally exceed 24 hours, and if the intravenous route is used for maintenance therapy the dose should not exceed 1 g/hour. Serum monitoring is not necessary.

The trials in this review included women only after admission to hospital. Whether a loading dose of magnesium sulphate should be used for women at primary care level before they are transferred to hospital is unclear. Other factors in this decision are likely to include how long it will take to get the woman to hospital, and the support that is available during transfer.

Implications for research

Magnesium sulphate is now the gold standard drug against which any new anticonvulsants for women with eclampsia should be compared in properly designed randomized trials.

Eclampsia can be distinguished from other forms of seizures in that it is better controlled by magnesium sulphate than by either diazepam or phenytoin (both conventional anticonvulsants), which may offer opportunities to explore the pathogenesis of eclampsia.

POTENTIAL CONFLICT OF INTEREST

Lelia Duley was the Principal Investigator for the Collaborative Eclampsia Trial.

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- Department for International Development UK
- Medical Research Council UK

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** Indicates the major publication for the study*

TABLES

Characteristics of included studies

Study	**Bangladesh 1998**
Methods	"Consecutive patients randomly allocated" . No further information.
Participants	200 women with eclampsia. 14% postpartum.
Interventions	MgSO4: 4 g iv + 6 g im loading dose. Then 2.5 g im 4 hrly, until 24 hr after delivery or last fit. If recurrence, 2 g iv. Diazepam: 10 mg loading dose, then 40 mg in 500 ml 5% dextrose for 24 hr after delivery or last fit. If recurrence, 10 mg slowly iv.
Outcomes	Women: death, recurrence of convulsions. Baby: no denominators reported.
Notes	Data not presented separately for women randomised before delivery. MgS04 was the unfamiliar treatment.
Allocation concealment	B – Unclear

Study	**Collab Trial 1995**
Methods	Consecutively numbered sealed treatment packs, identical in size, shape, weight and feel. 5 women excluded from the analyses.
Participants	910 women with eclampsia. 54% allocated MgSO4 had had an anticonvulsant before entry, as had 50% allocated diazepam. 30% randomised after delivery.

Characteristics of included studies (*Continued*)

Interventions	Diazepam: 10 mg iv bolus. Then infusion of 40 mg/500 ml for 24 hr, rate titrated against conscious level. 20 mg/500 ml for a further 24 hr. For recurrent convulsions, 10 mg iv. MgS04: Either (a) 4/5 g iv over 5 min and 10 g im. Then 5 g im every 4 hr, for 24 hr. Or (b) 4/5 iv over 5 min, then infusion of 1 g/hr for 24 hr. For both (a) and (b), if recurrent convulsions 2 g iv.
Outcomes	All women: death, recurrent convulsions, pneumonia, respiratory depression, ventilation, cardiac arrest, arrhythmia, coagulopathy, renal failure, liver failure, cerebrovascular accident, admission intensive care, 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	For im MgS04 n = 229, for iv n = 224. Centres in Africa, Asia, and South America. In some centres MgS04 was the new treatment, in others it was the standard therapy. 99% compliance with the allocated anticonvulsant. No monitoring of serum drug levels.
Allocation concealment	A – Adequate

Study	**Egypt 1993**
Methods	"Randomly allocated", no further details.
Participants	105 women with eclampsia and 13 with imminent eclampsia. For eclampsia, 44 allocated MgSO4 were recruited before delivery, and 29 allocated diazepam.
Interventions	Diazepam: 10-20 mg iv over 2-5 min. Then 20-30 mg in 500 ml iv to keep woman drowsy until delivery. MgSO4: 4-6 g iv. Then 1-2 g/hr iv. 1 g if < 55 kg, 2 g if > 55 kg.
Outcomes	Women: death, recurrence of convulsions, caesarean section. Baby: death, Apgar scores.
Notes	Outcome not reported separately for women with eclampsia and pre-eclampsia.
Allocation concealment	D – Not used

Study	**India 2001**
Methods	"Randomly distributed", no further details.
Participants	100 women with eclampsia. 70 in first pregnancy and 79 recruited before delivery.
Interventions	Diazepam: 10 mg iv bolus. Then infusion of 40 mg/500 ml for 24 hr, rate titrated against conscious level. 20 mg/500 ml for a further 24 hr. Then 10 mg im, changed when possible to oral. For recurrent convulsions, 10 mg iv. MgSO4: 4 g in 25% MgSO4 over 10 min. The 5 g IM every 4 hr until 24 hr after delivery or, if postpartum at randomisation, for 24 hr.
Outcomes	Death, recurrence of convulsions, renal failure, pneumonia.
Notes	Outcomes related to labour and delivery not reported separately for women randomised before delivery.
Allocation concealment	B – Unclear

Study	**Malaysia 1994**
Methods	"Randomly allocated".

Characteristics of included studies (*Continued*)

Participants	39 women; 11 with eclampsia, 28 with pre-eclampsia.
Interventions	Diazepam: Not described. MgS04: "Pritchard's regime", not described further.
Outcomes	Women: death, recurrence of convulsions, caesarean section. Baby: stillbirth and neonatal death.
Notes	Published in abstract form only. Interim results of an ongoing trial. MgS04 was the unfamiliar treatment.
Allocation concealment	B – Unclear

Study	**Zimbabwe 1990**
Methods	Consecutively numbered, sealed, opaque envelopes. Prepared by someone not involved in enrolment. Blocks of 6, no stratification.
Participants	51 women with antepartum eclampsia, > 28 weeks gestation, and a live fetus at admission. 67% had diazepam before entry; 71% of those allocated MgSO4, and 63% diazepam.
Interventions	Diazepam: 10 mg iv bolus. Then infusion of 80 mg/l for 24 hr, rate titrated against conscious level. 40 mg/l for a further 24 hr. For recurrent convulsions, 10 mg iv. MgS04: 4 g iv over 3-5 min and 10 g im. Then 5 g im every 4 hr, until 24 hr after delivery. For recurrent convulsions, 2 g iv.
Outcomes	Woman: death, recurrence of convulsions, pneumonia, respiratory depression, ventilation, cardiac arrest, coagulopathy, acute renal failure, reduced urine output, caesarean section, abscess. Baby: mortality, Apgar < 7 (1,5 min), intubated, admitted NICU, days on NICU (mean), in NICU > 7 days.
Notes	Subgroup analysis by whether anticonvulsants before trial entry, but numbers very small. MgS04 was the unfamiliar treatment.
Allocation concealment	A – Adequate

Study	**Zimbabwe 1998**
Methods	Consecutively numbered sealed treatment packs.
Participants	69 women with eclampsia. 40% had already had an anticonvulsant and 43% had delivered.
Interventions	Diazepam: 10 mg iv bolus. Then infusion of 40 mg/500 ml for 24 hr, rate titrated against conscious level. 20 mg/500 ml for a further 24 hr. For recurrent convulsions, 10 mg iv. MgS04: Either (a) 4/5 g iv over 5 min and 10 g im. Then 5 g im every 4 hr, for 24 hr. Or (b) 4/5 iv over 5 min, then infusion of 1 g/hr for 24 hr. For both (a) and (b), if recurrent convulsions 2 g iv.
Outcomes	Women: death, recurrence of convulsions, respiratory depression, cardiac arrest, renal failure, coagulopathy, strike, caesarean section, blood loss > 500 ml. Baby: death, died or in SCBU > 7 days.
Notes	These data are from one hospital in the Collaborative Eclampsia Trial which continued recruitment and data collection after the end of that study.
Allocation concealment	A – Adequate

hr: hour
hrly: hourly
im: intramuscular
iv: intravenous

MgS04: magnesium sulphate
min: minutes
NICU: neonatal intensive care unit
SCBU: special care baby unit

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.

ANALYSES

Comparison 01. Magnesium sulphate versus diazepam

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Maternal death	6	1336	Relative Risk (Fixed) 95% CI	0.59 [0.37, 0.94]
02 Recurrence of convulsions	7	1441	Relative Risk (Fixed) 95% CI	0.44 [0.34, 0.57]
03 Respiratory depression	3	1025	Relative Risk (Fixed) 95% CI	0.86 [0.57, 1.30]
04 Pulmonary oedema	2	974	Relative Risk (Fixed) 95% CI	0.99 [0.39, 2.55]
05 Pneumonia	4	1125	Relative Risk (Fixed) 95% CI	0.64 [0.31, 1.33]
06 Ventilation	3	1025	Relative Risk (Fixed) 95% CI	0.73 [0.45, 1.18]
07 Renal failure	4	1125	Relative Risk (Fixed) 95% CI	0.87 [0.54, 1.39]
08 Cerebrovascular accident (stroke)	3	1025	Relative Risk (Fixed) 95% CI	0.64 [0.33, 1.23]
09 Liver failure	2	974	Relative Risk (Fixed) 95% CI	1.00 [0.48, 2.07]
10 Cardiac arrest	3	1025	Relative Risk (Fixed) 95% CI	0.94 [0.47, 1.88]
11 Coagulopathy	4	1036	Relative Risk (Fixed) 95% CI	0.89 [0.56, 1.41]
12 Woman admitted to intensive care unit	2	974	Relative Risk (Fixed) 95% CI	0.80 [0.60, 1.08]
15 Caesarean section	4	734	Relative Risk (Fixed) 95% CI	1.06 [0.96, 1.18]
17 Labour > 8 hours	1	633	Relative Risk (Fixed) 95% CI	1.15 [0.82, 1.60]
18 Blood loss at delivery > 500 ml	2	672	Relative Risk (Fixed) 95% CI	0.92 [0.70, 1.21]
19 Death of 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	2	688	Relative Risk (Fixed) 95% CI	0.95 [0.77, 1.16]
24 Intubation at place of birth	2	591	Relative Risk (Fixed) 95% CI	0.67 [0.45, 1.00]

INDEX TERMS

Medical Subject Headings (MeSH)

Anticonvulsants [*therapeutic use]; Diazepam [*therapeutic use]; Eclampsia [*drug therapy]; Magnesium Sulfate [*therapeutic use]; Randomized Controlled Trials

MeSH check words

Female; Humans; Pregnancy

COVER SHEET

Title	Magnesium sulphate versus diazepam for eclampsia
Authors	Duley L, Henderson-Smart D
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GRAPHS AND OTHER TABLES

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 01 Maternal death

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bangladesh 1998	3/100	7/100		15.8	0.43 [0.11, 1.61]
Collab Trial 1995	17/453	23/452		52.0	0.74 [0.40, 1.36]
India 2001	5/60	6/40		16.3	0.56 [0.18, 1.70]
× Malaysia 1994	0/5	0/6		0.0	Not estimable
Zimbabwe 1990	1/24	0/27		1.1	3.36 [0.14, 78.79]
Zimbabwe 1998	0/35	6/34		14.9	0.07 [0.00, 1.28]
Total (95% CI)	677	659		100.0	0.59 [0.37, 0.94]

Total events: 26 (magnesium sulphate), 42 (diazepam)

Test for heterogeneity chi-square=3.95 df=4 p=0.41 I^2 =0.0%

Test for overall effect z=2.22 p=0.03

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

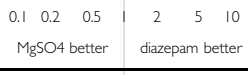
Outcome: 02 Recurrence of convulsions

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Bangladesh 1998	5/100	26/100		16.0	0.19 [0.08, 0.48]
Collab Trial 1995	60/453	125/452		76.9	0.48 [0.36, 0.63]
× Egypt 1993	0/59	0/46		0.0	Not estimable
India 2001	0/60	2/40		1.8	0.13 [0.01, 2.73]
× Malaysia 1994	0/6	0/5		0.0	Not estimable
Zimbabwe 1990	5/24	7/27		4.0	0.80 [0.29, 2.20]
Zimbabwe 1998	1/35	2/34		1.2	0.49 [0.05, 5.11]
Total (95% CI)	737	704		100.0	0.44 [0.34, 0.57]

Total events: 71 (magnesium sulphate), 162 (diazepam)

Test for heterogeneity chi-square=5.47 df=4 p=0.24 I^2 =26.8%

Test for overall effect z=6.34 p<0.00001



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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 03 Respiratory depression

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	35/453	33/452		74.1	1.06 [0.67, 1.67]
Zimbabwe 1990	0/24	1/27		3.2	0.37 [0.02, 8.75]
Zimbabwe 1998	3/35	10/34		22.7	0.29 [0.09, 0.97]
Total (95% CI)	512	513		100.0	0.86 [0.57, 1.30]

Total events: 38 (magnesium sulphate), 44 (diazepam)

Test for heterogeneity chi-square=4.18 df=2 p=0.12 I^2 =52.1%

Test for overall effect z=0.70 p=0.5

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 04 Pulmonary oedema

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	8/453	7/452		82.2	1.14 [0.42, 3.12]
Zimbabwe 1998	0/35	1/34		17.8	0.32 [0.01, 7.69]
Total (95% CI)	488	486		100.0	0.99 [0.39, 2.55]

Total events: 8 (magnesium sulphate), 8 (diazepam)

Test for heterogeneity chi-square=0.55 df=1 p=0.46 I^2 =0.0%

Test for overall effect z=0.01 p=1

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 05 Pneumonia

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	9/453	14/452		75.7	0.64 [0.28, 1.47]
India 2001	3/60	1/40		6.5	2.00 [0.22, 18.55]
Zimbabwe 1990	0/24	3/27		17.8	0.16 [0.01, 2.95]
× Zimbabwe 1998	0/35	0/34		0.0	Not estimable
Total (95% CI)	572	553		100.0	0.64 [0.31, 1.33]

Total events: 12 (magnesium sulphate), 18 (diazepam)

Test for heterogeneity chi-square=1.87 df=2 p=0.39 I^2 =0.0%

Test for overall effect z=1.19 p=0.2

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 06 Ventilation

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	25/453	27/452		73.0	0.92 [0.54, 1.57]
Zimbabwe 1990	1/24	2/27		5.1	0.56 [0.05, 5.82]
Zimbabwe 1998	1/35	8/34		21.9	0.12 [0.02, 0.92]
Total (95% CI)	512	513		100.0	0.73 [0.45, 1.18]

Total events: 27 (magnesium sulphate), 37 (diazepam)

Test for heterogeneity chi-square=3.83 df=2 p=0.15 I^2 =47.8%

Test for overall effect z=1.28 p=0.2

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 07 Renal failure

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	28/453	29/452		84.3	0.96 [0.58, 1.59]
India 2001	0/60	2/40		8.7	0.13 [0.01, 2.73]
Zimbabwe 1990	0/24	1/27		4.1	0.37 [0.02, 8.75]
Zimbabwe 1998	1/35	1/34		2.9	0.97 [0.06, 14.91]
Total (95% CI)	572	553		100.0	0.87 [0.54, 1.39]

Total events: 29 (magnesium sulphate), 33 (diazepam)

Test for heterogeneity chi-square=1.92 df=3 p=0.59 I^2 =0.0%

Test for overall effect z=0.59 p=0.6

Analysis 01.08. Comparison 01 Magnesium sulphate versus diazepam, Outcome 08 Cerebrovascular accident (stroke)

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 08 Cerebrovascular accident (stroke)

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	13/453	17/452		77.4	0.76 [0.38, 1.55]
Zimbabwe 1990	0/24	1/27		6.4	0.37 [0.02, 8.75]
Zimbabwe 1998	0/35	3/34		16.1	0.14 [0.01, 2.59]
Total (95% CI)	512	513		100.0	0.64 [0.33, 1.23]

Total events: 13 (magnesium sulphate), 21 (diazepam)

Test for heterogeneity chi-square=1.40 df=2 p=0.50 I^2 =0.0%

Test for overall effect z=1.34 p=0.2

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

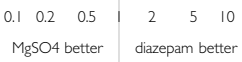
Outcome: 09 Liver failure

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	14/453	14/452		100.0	1.00 [0.48, 2.07]
× Zimbabwe 1998	0/35	0/34		0.0	Not estimable
Total (95% CI)	488	486		100.0	1.00 [0.48, 2.07]

Total events: 14 (magnesium sulphate), 14 (diazepam)

Test for heterogeneity: not applicable

Test for overall effect z=0.01 p=1



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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 10 Cardiac arrest

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	13/453	12/452		74.9	1.08 [0.50, 2.34]
Zimbabwe 1990	1/24	0/27		2.9	3.36 [0.14, 78.79]
Zimbabwe 1998	0/35	3/34		22.1	0.14 [0.01, 2.59]
Total (95% CI)	512	513		100.0	0.94 [0.47, 1.88]

Total events: 14 (magnesium sulphate), 15 (diazepam)

Test for heterogeneity chi-square=2.39 df=2 p=0.30 I^2 =16.4%

Test for overall effect z=0.18 p=0.9

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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 11 Coagulopathy

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	27/453	30/452		83.5	0.90 [0.54, 1.49]
× Malaysia 1994	0/6	0/5		0.0	Not estimable
Zimbabwe 1990	1/24	2/27		5.2	0.56 [0.05, 5.82]
Zimbabwe 1998	4/35	4/34		11.3	0.97 [0.26, 3.58]
Total (95% CI)	518	518		100.0	0.89 [0.56, 1.41]

Total events: 32 (magnesium sulphate), 36 (diazepam)

Test for heterogeneity chi-square=0.17 df=2 p=0.92 I^2 =0.0%

Test for overall effect z=0.50 p=0.6

Analysis 01.12. Comparison 01 Magnesium sulphate versus diazepam, Outcome 12 Woman admitted to intensive care unit

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

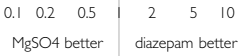
Outcome: 12 Woman admitted to intensive care unit

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	65/453	75/452		90.2	0.86 [0.64, 1.17]
Zimbabwe 1998	2/35	8/34		9.8	0.24 [0.06, 1.06]
Total (95% CI)	488	486		100.0	0.80 [0.60, 1.08]

Total events: 67 (magnesium sulphate), 83 (diazepam)

Test for heterogeneity chi-square=2.75 df=1 p=0.10 I^2 =63.6%

Test for overall effect z=1.44 p=0.1



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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 15 Caesarean section

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	215/325	198/308		87.2	1.03 [0.92, 1.15]
Malaysia 1994	2/6	3/5		1.4	0.56 [0.15, 2.12]
Zimbabwe 1990	19/24	18/27		7.3	1.19 [0.85, 1.66]
Zimbabwe 1998	18/21	9/18		4.2	1.71 [1.05, 2.81]
Total (95% CI)	376	358		100.0	1.06 [0.96, 1.18]

Total events: 254 (magnesium sulphate), 228 (diazepam)

Test for heterogeneity chi-square=5.23 df=3 p=0.16 I^2 =42.6%

Test for overall effect z=1.13 p=0.3

Analysis 01.17. Comparison 01 Magnesium sulphate versus diazepam, Outcome 17 Labour > 8 hours

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

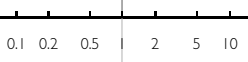
Outcome: 17 Labour > 8 hours

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	63/325	52/308		100.0	1.15 [0.82, 1.60]
Total (95% CI)	325	308		100.0	1.15 [0.82, 1.60]

Total events: 63 (magnesium sulphate), 52 (diazepam)

Test for heterogeneity: not applicable

Test for overall effect z=0.81 p=0.4



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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 18 Blood loss at delivery > 500 ml

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	75/325	76/308		97.3	0.94 [0.71, 1.24]
Zimbabwe 1998	1/21	2/18		2.7	0.43 [0.04, 4.35]
Total (95% CI)	346	326		100.0	0.92 [0.70, 1.21]
Total events: 76 (magnesium sulphate), 78 (diazepam)					
Test for heterogeneity chi-square=0.43 df=1 p=0.51 I^2 =0.0%					
Test for overall effect z=0.58 p=0.6					

Analysis 01.19. Comparison 01 Magnesium sulphate versus diazepam, Outcome 19 Death of the fetus or infant

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 19 Death of the fetus or infant

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Stillbirth					
Collab Trial 1995	49/331	47/317		84.1	1.00 [0.69, 1.44]
Malaysia 1994	1/6	0/5		0.9	2.57 [0.13, 52.12]
Zimbabwe 1990	0/27	3/30		5.8	0.16 [0.01, 2.93]
Zimbabwe 1998	1/21	5/19		9.2	0.18 [0.02, 1.41]
Subtotal (95% CI)	385	371		100.0	0.89 [0.63, 1.26]
Total events: 51 (magnesium sulphate), 55 (diazepam)					
Test for heterogeneity chi-square=4.51 df=3 p=0.21 I^2 =33.4%					
Test for overall effect z=0.66 p=0.5					
02 Perinatal death					
Collab Trial 1995	82/331	71/317		88.8	1.11 [0.84, 1.46]
Zimbabwe 1990	2/27	3/30		3.5	0.74 [0.13, 4.10]
Zimbabwe 1998	3/21	6/19		7.7	0.45 [0.13, 1.56]
Subtotal (95% CI)	379	366		100.0	1.04 [0.80, 1.36]
Total events: 87 (magnesium sulphate), 80 (diazepam)					

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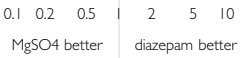
Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Test for heterogeneity chi-square=2.07 df=2 p=0.36 I² =3.4%					
Test for overall effect z=0.31 p=0.8					
03 Neonatal death					
Collab Trial 1995	35/331	26/317		94.4	1.29 [0.79, 2.09]
Malaysia 1994	1/6	1/5		3.9	0.83 [0.07, 10.20]
Zimbabwe 1990	2/27	0/30		1.7	5.54 [0.28, 110.42]
Subtotal (95% CI)	364	352		100.0	1.34 [0.84, 2.14]
Total events: 38 (magnesium sulphate), 27 (diazepam)					
Test for heterogeneity chi-square=1.03 df=2 p=0.60 I² =0.0%					
Test for overall effect z=1.24 p=0.2					



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

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 21 Apgar scores

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Apgar < 7 at 1 minute					
Collab Trial 1995	138/282	162/261		87.5	0.79 [0.68, 0.92]
Zimbabwe 1990	12/27	24/27		12.5	0.50 [0.32, 0.78]
Subtotal (95% CI)	309	288		100.0	0.75 [0.65, 0.87]
Total events: 150 (magnesium sulphate), 186 (diazepam)					
Test for heterogeneity chi-square=3.64 df=1 p=0.06 I² =72.5%					
Test for overall effect z=3.88 p=0.0001					
02 Apgar < 7 at 5 minutes					
Collab Trial 1995	63/282	76/261		84.9	0.77 [0.57, 1.02]
Zimbabwe 1990	6/27	14/27		15.1	0.43 [0.19, 0.95]
Subtotal (95% CI)	309	288		100.0	0.72 [0.55, 0.94]
Total events: 69 (magnesium sulphate), 90 (diazepam)					
Test for heterogeneity chi-square=1.83 df=1 p=0.18 I² =45.2%					
Test for overall effect z=2.42 p=0.02					

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

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

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
01 Admission to SCBU					
Collab Trial 1995	131/282	131/261		78.0	0.93 [0.78, 1.10]
Zimbabwe 1990	17/27	22/27		12.6	0.77 [0.55, 1.09]
Zimbabwe 1998	18/20	14/14		9.4	0.90 [0.78, 1.04]
Subtotal (95% CI)	329	302		100.0	0.90 [0.78, 1.04]
Total events: 166 (magnesium sulphate), 167 (diazepam)					
Test for heterogeneity chi-square=0.89 df=2 p=0.64 I² =0.0%					
Test for overall effect z=1.38 p=0.2					
03 Stay in SCBU > 7 days					
Collab Trial 1995	35/282	51/261		86.6	0.64 [0.43, 0.94]
Zimbabwe 1990	4/27	7/27		11.4	0.57 [0.19, 1.73]
Zimbabwe 1998	3/20	1/14		1.9	2.10 [0.24, 18.17]
Subtotal (95% CI)	329	302		100.0	0.66 [0.46, 0.95]
Total events: 42 (magnesium sulphate), 59 (diazepam)					
Test for heterogeneity chi-square=1.20 df=2 p=0.55 I² =0.0%					
Test for overall effect z=2.26 p=0.02					

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

Review: Magnesium sulphate versus diazepam for eclampsia
Comparison: 01 Magnesium sulphate versus diazepam
Outcome: 23 Death or in SCBU > 7 days

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	113/331	113/317		94.0	0.96 [0.78, 1.18]
Zimbabwe 1998	6/21	7/19		6.0	0.78 [0.32, 1.90]
Total (95% CI)	352	336		100.0	0.95 [0.77, 1.16]
Total events: 119 (magnesium sulphate), 120 (diazepam)					
Test for heterogeneity chi-square=0.20 df=1 p=0.65 I² =0.0%					
Test for overall effect z=0.52 p=0.6					

Analysis 01.24. Comparison 01 Magnesium sulphate versus diazepam, Outcome 24 Intubation at place of birth

Review: Magnesium sulphate versus diazepam for eclampsia

Comparison: 01 Magnesium sulphate versus diazepam

Outcome: 24 Intubation at place of birth

Study	magnesium sulphate n/N	diazepam n/N	Relative Risk (Fixed) 95% CI	Weight (%)	Relative Risk (Fixed) 95% CI
Collab Trial 1995	32/276	41/261		80.8	0.74 [0.48, 1.13]
Zimbabwe 1990	4/27	10/27		19.2	0.40 [0.14, 1.12]
Total (95% CI)	303	288		100.0	0.67 [0.45, 1.00]

Total events: 36 (magnesium sulphate), 51 (diazepam)

Test for heterogeneity chi-square=1.16 df=1 p=0.28 I^2 =13.6%

Test for overall effect z=1.97 p=0.05