

## Magnesium Sulfate and Other Anticonvulsants for Women with Preeclampsia

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The Cochrane Abstract on the next page is a summary of a review from the Cochrane Library. It is accompanied by an interpretation that will help clinicians put evidence into practice. Dr. Fogleman presents a clinical scenario and question based on the Cochrane Abstract, followed by an evidence-based answer and a critique of the review. The practice recommendations in this activity are available at <http://www.cochrane.org/reviews/en/ab000025.html>.



This clinical content conforms to AAFP criteria for evidence-based continuing medical education (EB CME). See CME Quiz on page 1265.

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A collection of Cochrane for Clinicians published in *AFP* is available at <http://www.aafp.org/afp/cochrane>.

### Clinical Scenario

A 24-year-old primiparous woman presents at term in active labor. She has a headache, a blood pressure reading of 150/100 mm Hg, and an elevated protein/creatinine ratio. Further laboratory studies show normal complete blood count and liver function tests. She is diagnosed with preeclampsia.

### Clinical Question

Should magnesium sulfate or a different anticonvulsant be given to prevent eclamptic seizures during labor?

### Evidence-Based Answer

Magnesium sulfate should be considered first-line treatment to prevent eclamptic seizures during labor. (Strength of Recommendation = A, based on consistent, good-quality patient-oriented evidence)

### Practice Pointers

Preeclampsia is common, occurring in 3 to 8 percent of U.S. pregnancies.<sup>1</sup> Eclampsia, however, is a less common complication characterized by seizures; it occurs as often as once in 100 pregnancies in some low-income countries, but affects only one in 2,000 pregnancies in the United Kingdom.<sup>1</sup> Severe preeclampsia is typically defined as blood pressure greater than 160/100 mm Hg and/or protein level greater than 5 g on a 24-hour urine collection. These patients may have a platelet count less than  $100 \times 10^3$  per  $\mu\text{L}$  ( $100 \times 10^9$  per L); increased transaminase or lactate dehydrogenase levels; persistent headache; right upper quadrant pain; visual changes; less than 500 mL of urine output over 24 hours; or a fetus with intrauterine growth restriction.<sup>1</sup>

Although severe preeclampsia can adversely affect multiple maternal systems,

predicting who will have a seizure is difficult. Because the treatment of choice for eclamptic seizures is magnesium sulfate, it seems reasonable to also consider using it for prevention.<sup>2</sup> However, a number of other medications are available for seizure prevention, including phenytoin (Dilantin) and nimodipine (Nimotop).

This Cochrane review supports the use of magnesium sulfate over other medications for the prevention of eclamptic seizures.<sup>2</sup> Since the last review update in 2003, the authors added two studies: one from 1998 in Mexico involving 36 women, and one from 2008 in India involving 50 women with preeclampsia. The results of both studies were consistent with the previous review's conclusions. Further, they contributed to the heterogeneity of the review, which featured several large and small studies from a variety of different-sized and geographically diverse hospitals. Therefore, these results have broad implications.

Women with mild preeclampsia seize less often than those with severe preeclampsia, and a 2004 review of trials suggested no benefit to prophylactic use of magnesium sulfate in those with mild preeclampsia.<sup>3</sup> However, this Cochrane review found a statistically significant reduction in eclampsia for women with severe preeclampsia (number needed to treat = 50; 95% confidence interval, 34 to 100), as well as for women with "not severe" preeclampsia (number needed to treat = 100; 95% confidence interval, 100 to 500).<sup>2</sup>

Compared with no treatment or another form of seizure prevention, magnesium sulfate increases the risk of cesarean delivery and adverse effects ranging from flushing and nausea to respiratory and cardiac

## Cochrane Abstract

**Background:** Eclampsia, the occurrence of a seizure in association with preeclampsia, is rare but potentially life-threatening. Magnesium sulfate is the drug of choice for treating eclampsia. This review assesses its use for preventing eclampsia.

**Objectives:** To assess the effects of magnesium sulfate and other anticonvulsants for prevention of eclampsia.

**Search Strategy:** The authors searched the Cochrane Pregnancy and Childbirth Group's Trials Register (June 4, 2010), and the Cochrane Central Register of Controlled Trials Register (*The Cochrane Library* 2010, Issue 3).

**Selection Criteria:** Randomized trials comparing anticonvulsants with placebo or no anticonvulsant, or comparisons of different drugs, for preeclampsia.

**Data Collection and Analysis:** Two authors assessed trial quality and extracted data independently.

**Main Results:** The authors included 15 trials. Six ( $n = 11,444$  women) compared magnesium sulfate with placebo or no anticonvulsant: magnesium sulfate reduced the risk of eclampsia by more than one-half (risk ratio [RR] = 0.41; 95% confidence interval [CI], 0.29 to 0.58; number needed to treat for an additional beneficial outcome [NNTB] = 100; 95% CI, 50 to 100), with a nonsignificant reduction in maternal death (RR = 0.54; 95% CI, 0.26 to 1.10) but no clear difference in serious

maternal morbidity (RR = 1.08; 95% CI, 0.89 to 1.32). It reduced the risk of placental abruption (RR = 0.64; 95% CI, 0.50 to 0.83; NNTB = 100; 95% CI, 50 to 1,000) and increased cesarean delivery (RR = 1.05; 95% CI, 1.01 to 1.10). There was no clear difference in stillbirth or neonatal death (RR = 1.04; 95% CI, 0.93 to 1.15).

Adverse effects, primarily flushing, were more common with magnesium sulfate (24 versus 5 percent; RR = 5.26; 95% CI, 4.59 to 6.03; number need to treat for an additional harmful outcome = 6; 95% CI, 5 to 6). Follow-up was reported by one trial comparing magnesium sulfate with placebo: for 3,375 women there was no clear difference in death (RR = 1.79; 95% CI, 0.71 to 4.53) or morbidity potentially related to preeclampsia (RR = 0.84; 95% CI, 0.55 to 1.26; median follow-up of 26 months); for 3,283 children exposed in utero, there was no clear difference in death (RR = 1.02; 95% CI, 0.57 to 1.84) or neurosensory disability (RR = 0.77; 95% CI, 0.38 to 1.58) at 18 months of age. Magnesium sulfate reduced eclampsia compared with phenytoin (three trials, 2,291 women; RR = 0.08; 95% CI, 0.01 to 0.60) and nimodipine (one trial, 1,650 women; RR = 0.33; 95% CI, 0.14 to 0.77).

**Authors' Conclusions:** Magnesium sulfate reduces the risk of eclampsia by more than one-half, and probably reduces maternal death. There is no clear effect on outcome after hospital discharge. One-fourth of women report adverse effects with magnesium sulfate.



These summaries have been derived from Cochrane reviews published in the Cochrane Database of Systematic Reviews in the Cochrane Library. Their content has, as far as possible, been checked with the authors of the original reviews, but the summaries should not be regarded as an official product of the Cochrane Collaboration; minor editing changes have been made to the text (<http://www.cochrane.org>).

suppression and death. However, there was no increased risk of negative long-term outcomes to the child at 18 months of age. Although cost-effectiveness is higher if treatment is limited to women with severe preeclampsia, magnesium sulfate remains a low-cost, widely available therapy.<sup>4</sup> The American College of Obstetricians and Gynecologists recommends the use of magnesium sulfate as first-line therapy to prevent seizures in women with preeclampsia.<sup>1</sup>

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## Cochrane Briefs

### Pre-employment Examinations for Preventing Occupational Injury and Disease

#### Clinical Question

Do pre-employment examinations improve workers' occupational health outcomes?

#### Evidence-Based Answer

There is limited evidence that task-focused examinations reduce sick leave and the incidence of musculoskeletal injuries; however, general pre-employment examinations have no effect on health outcomes. (Strength of Recommendation = B, based on

inconsistent or limited-quality patient-oriented evidence)

### Practice Pointers

Employers often ask family physicians to examine prospective employees to certify job fitness and to detect health risks that may be exacerbated by occupational factors. Prospective employees at increased risk of occupational diseases or injuries may be provided work accommodations or not offered employment. However, it is uncertain if pre-employment examinations actually improve workers' occupational health outcomes and, if so, which components of the examination are beneficial.

In this Cochrane review, the authors searched multiple electronic databases through December 2009 for randomized controlled trials, controlled before-after studies, and interrupted time-series that evaluated the effectiveness of pre-employment examinations in reducing occupational diseases or injuries, sickness absences, and/or medical visits. Nine studies met the inclusion criteria; six of these studies were conducted in the United States. Numbers of participants ranged from 71 to 6,125. Most studies had at least one year of follow-up.

One randomized trial found that Army recruits undergoing an examination that focused on the ability to perform specific work tasks had a mean of 36 fewer sick days (95% confidence interval, 3.76 to 68.24) than recruits undergoing a general examination. Another trial that randomized telephone company employees who underwent general examinations into groups in which results were or were not reported to the employer found no statistical difference

in sick days taken. Several controlled before-after studies found that job-focused pre-employment examinations were associated with a reduced incidence of musculoskeletal injuries and medical visits. Evidence was conflicting about the effect of pre-employment examinations on the proportion of rejected job applicants.

An estimated one-half of U.S. workers undergo pre-employment examinations.<sup>1</sup> The Americans with Disabilities Act forbids employers from requiring prospective employees to undergo a health examination before extending a job offer. However, employers may make job offers conditional on passing a pre-employment examination if this policy is applied consistently to all employees in a certain job category.<sup>2</sup> Based on this Cochrane review, family physicians who are asked to perform pre-employment examinations should request detailed information from the patient or employer regarding essential job-related tasks and focus the examination on detecting existing conditions or injury risks that are relevant to those tasks.

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