Antenatal Magnesium Sulfate Decreases Risk of Cerebral Palsy

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CONTEXT
Infants born prematurely have high risk to develop cerebral palsy. Antenatal interventions that have the potential to prevent premature delivery shall also aim to reduce risks to both mother and their infants. At the current time, there are limited data to suggest that such intervention exists. This study by Rouse et al. aimed to prevent death or cerebral palsy by administering MgSO₄ antenatally to women at high risk for spontaneous or indicated premature delivery.

METHODS
Multicenter randomized controlled trial in the United States.
Table 1: Main results

| Outcome                                           | MgSO4 (N=1041) (%) | Control (N=1095) (%) | RR (95% CI) |
|---------------------------------------------------|--------------------|----------------------|-------------|
| Death or moderate or severe cerebral palsy        | 118/1041 (11.3)    | 128/1095 (11.7)      | 0.97 (0.77–1.23) |
| Moderate or severe cerebral palsy alone           | 20/1041 (1.9)      | 38/1095 (3.5)        | 0.55 (0.32–0.95) |
| Death alone                                       | 99/1041 (9.5)      | 93/1095 (8.5)        | 1.12 (0.85–1.47) |

Population

Inclusion
Pregnant women (singletons/twins) at 24 to 31 weeks’ gestation at high risk of spontaneous premature delivery due to rupture of membrane (ROM) (22–31 wk) or advanced labor (cervix 2–8 cm dilated) or planned to deliver within 2–24 hours.

Exclusion
Anticipated delivery within 2 hours; Dilated cervix >8 cm; ROM before 22 week’s gestation; Unwillingness of the obstetrician to intervene for the benefit of the fetus; Major fetal anomalies or death; Hypertension/preeclampsia; Contraindications to magnesium sulfate; IV magnesium sulfate given within the previous 12 hours.

Intervention

MgSO4 group
6 g of IV MgSO4 over 20–30 min followed by 2 g/h continuous infusion and stopped after 12 hours if delivery is not imminent (no uterine contractions) and restarted if it is imminent. If stopped longer than 6 hours, then same bolus dose will be repeated as well.

Control group
Identical placebo
Intervention will be discontinued if patient developed preeclampsia/eclampsia or reached 34 week’s gestation.

Outcomes

Primary
Composites of stillbirth/infant death at 1 year or moderate or severe cerebral palsy at 2 years.

Secondary
Various maternal and neonatal outcomes and complications including adverse side effects of MgSO4, death, various degrees of cerebral palsy, and developmental delay measured by Gross Motor Function Classification System and Bayley Scales of Infants development II, respectively.

Allocation
Computer generated and stratified according to gestation, twins.

Blinding
Blinded (mothers, healthcare givers, outcome assessors).

Follow-up
Primary outcome was done in 95.6% of fetuses.

RESULTS

Although there was no statistical significant difference between groups in the main composite outcome of death or moderate or severe cerebral palsy, the risk of moderate or severe cerebral palsy was significantly lower in the MgSO4 group. Moreover, there were no significant differences in other outcomes such death or other neonatal outcomes except for the need for mechanical ventilation, which was less in MgSO4 group (relative risk (RR): 0.92, confidence interval (CI): 0.85–0.99). Administering MgSO4 to women at less than 28 week’s gestation had much better effect on moderate or severe cerebral palsy (RR: 0.45, CI: 0.23–0.87) but no effect when given at 28 week’s gestation or more (RR: 1.00, CI: 0.38–2.65). In regard to the side effect, this study did not find any serious maternal or neonatal adverse outcome.

COMMENTARY

This study has shown the neuroprotective benefit of antenatal MgSO4 given to women at risk of premature delivery. Previously, there was doubt regarding the efficacy and safety. However, Cochrane Systematic Review has confirmed this effect.[1]

Clinical practice guidelines have been developed in Australia and Canada.[2,3] The guidelines are similar but vary in some aspects such as doses and indications, but neuroprotection was their main aim. It is worth mentioning that the American College of Obstetric and Gynaecology has not yet recommended it routinely.[4]

Currently, MgSO4 is not an effective tocolytic agent. However, if the aim of prolonging gestation is to minimize maternal and neonatal mortality and morbidity, then it
is sound to recommend MgSO₄ as it is the only potential tocolytic agent that has neuroprotective effect.

In summary, MgSO₄ is being used in obstetric care for different indications. It has been shown to be effective for neuroprophalxis to decrease the risk of moderate to severe cerebral palsy. Based on the current evidence, we recommend administering MgSO₄ antenatally to women at high risk of premature delivery under individualized clinical practice guidelines.

Abstracted from
Rouse DJ, Hirtz DG, Thorn E, Varner MW, Spong CY, Mercer BM, et al. for the Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine units Network. A randomised, controlled trial of magnesium sulphate for the prevention of cerebral palsy. N Engl J Med 2008;359:895-905. ClinicalTrials.gov number, NCT00014989

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2. Magee L, Sawchuck D, Synnes A, von Dadelszen P. SOGC Clinical Practice Guideline. Magnesium sulphate for fetal neuroprotection. J Obstet Gynaecol Can 2011;33:516-29.
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4. Committee Opinion No. 455: Magnesium sulfate before anticipated preterm birth for neuroprotection. Obstet Gynecol 2010; 115:669-71.