

MAGNESIUM

Magnesium: Fetal neuroprotection against cerebral palsy

SUMMARY: Magnesium sulfate (MgSO₄) for fetal neuroprotection is an intervention with substantial potential for safely, effectively, and inexpensively improving the neurologic prognosis of fetuses facing early preterm birth. Uniform administration to women at risk for preterm birth has the potential to prevent more than 1,000 cases of cerebral palsy every year in the US alone. The safety profile of magnesium sulfate is excellent and well known given its liberal use historically in both tocolysis and maternal seizure prophylaxis for pre-eclampsia.

Rationale: Preterm birth is a major risk factor for cerebral palsy, with infants born at the threshold of viability being 70 times more likely to be diagnosed with the disease than those born at term. Karin Nelson, MD, and Judith Grether, MD, were the first to report that MgSO₄ administered to mothers delivering prematurely protects their offspring against cerebral palsy. This protective association was robust, persisted after controlling for multiple confounders, and is biologically plausible because magnesium can reduce vascular instability, lessen hypoxic damage, and protect against cytokine or excitatory amino acid damage—all threats to the vulnerable preterm brain. In addition, 3 large, randomized, placebo-controlled trials of antenatal MgSO₄ for fetal neuroprotection, including one through the NICHD Maternal Fetal Medicine Unit (MFMU) Network, individually and collectively, support the use of MgSO₄ to lower the risk for moderate to severe cerebral palsy in surviving infants born at the earliest gestational ages.

Eligible patients: Women presenting with anticipated preterm delivery within the next 12 hours of singleton or twin pregnancies at gestational ages of 23 through 31 6/7 weeks. Typical candidates will have advanced preterm labor (ie, cervix dilated at least 3 cm) with intact membranes, preterm premature rupture of membranes (PPROM), or be those for whom delivery is planned within 24 hours (eg, women with severe fetal growth restriction or pre-eclampsia with severe features). If delivery does not occur and the patient has received this treatment prior to 32 weeks' gestation, she is a candidate for repeat administration up to 33 6/7 weeks' gestation. If she has not received this intervention prior to 32 weeks' gestation, she is NOT a candidate at all.

Contraindications:

- Cervical dilation > 8 cm
- Delivery anticipated within 2 hours
- Patients with other medical contraindications to MgSO₄ such as myasthenia gravis, should not receive this treatment.

Technique: Administer a 6-g IV loading dose of magnesium sulfate (MgSO₄) over the course of 20 to 30 minutes. Follow this with a constant infusion of 2 g per hour for up to 12 hours or delivery. If delivery is not imminent after 12 hours, terminate the infusion. Infusion may be repeated as often as preterm delivery threatens. A MgSO₄ bolus of 6 g is administered if 6 hours have elapsed since the constant

infusion was terminated and delivery is again imminent. If less than 6 hours has elapsed, a constant infusion of 2 g per hour is restarted.

Special Considerations:

- Concomitant use of a calcium channel blocker and MgSO₄ has been theorized to be associated with potentially severe hypotension but recent studies suggest safety with co-administration of nifedipine.
- Magnesium is excreted renally. Extra vigilance is required if the agent is used in patients with renal dysfunction.
- Deep tendon reflexes should be assessed regularly in all patients (neuromuscular depression occurs at magnesium concentrations of 10 mEq/L and above) and urine output should be monitored.
- If hypermagnesemia is suspected, the patient's serum magnesium concentration should be measured, and, depending on the circumstances, the MgSO₄ infusion discontinued. If severe (e.g. respiratory depression), consider administration of 1 gram IV calcium gluconate (10 mL of a 10% solution) over 2 minutes.

Reference(s):

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3. Constantine M, Weiner J. Effects of Antenatal Exposure to Magnesium Sulfate on Neuroprotection and Mortality in Preterm Infants, A Meta-analysis. *Obstetrics and Gynecology* 2009;114:354-64
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5. American College of Obstetricians and Gynecologists Committee on Obstetric Practice; Society for Maternal-Fetal Medicine. Committee Opinion No. 455: magnesium sulfate before anticipated preterm birth for neuroprotection. *Obstet Gynecol*. 2010;115(3):669-671. Reaffirmed 2015.
6. Magee LA, et al. Therapy with both magnesium and nifedipine does not increase the risk of serious magnesium-related maternal side effects in women with pre-eclampsia. *Am J Obstet Gynecol*. 2005; 193, 153-63.

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