Individualize the duration of postpartum magnesium treatment for patients with preeclampsia to best balance the benefits and harms of treatment

Magnesium treatment reduces the risk of seizure in patients with preeclampsia. However, prolonged postpartum magnesium infusion may cause harm, including a delay in early ambulation, return to full diet, discontinuation of a bladder catheter, and initiation of breastfeeding.

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Preeclampsia complicates 3% to 8% of pregnancies.[1-3] The incidence of preeclampsia is influenced by the clinical characteristics of the pregnant population, including the prevalence of overweight, obesity, chronic hypertension, diabetes, nulliparity, advanced maternal age, multiple gestations, kidney disease, and a history of preeclampsia in a prior pregnancy.[4]

Magnesium treatment reduces the rate of eclampsia among patients with preeclampsia

For patients with preeclampsia, magnesium treatment reduces the risk of seizure. In the Magpie trial, 9,992 pregnant patients were treated for 24 hours with magnesium or placebo.[5] The magnesium treatment regimen was either a 4-g IV bolus over 10 to 15 minutes followed by a continuous infusion of 1 g/hr or an intramuscular regimen (10-g intramuscular loading dose followed by 5 g IM every 4 hours). Eclamptic seizures occurred in 0.8% and 1.9% of patients treated with magnesium or placebo, respectively (relative risk [RR], 0.42; 95% confidence interval [CI], 0.29 to 0.60). Among patients with a multiple gestation, the rate of eclampsia was 2% and 6% in the patients treated with magnesium or placebo, respectively. The number of patients who needed to be treated to prevent one eclamptic event was 63 and 109 for patients with preeclampsia with and without severe features, respectively. Intrapartum treatment with magnesium also reduced the risk of placental abruption from 3.2% for the patients receiving placebo to 2.0% among the patients treated with magnesium (RR, 0.67; 99% CI, 0.45-0.89). Maternal death was reduced with magnesium treatment compared with placebo (0.2% vs 0.4%), but the difference was not statistically significant.

In the Magpie trial, side effects were reported by 24% and 5% of patients treated with magnesium and placebo, respectively. The most common side effects were flushing, nausea, vomiting, and muscle weakness. Of note, magnesium treatment is contraindicated in patients with myasthenia gravis because it can cause muscle weakness and hypoventilation.[6] For patients with preeclampsia and myasthenia gravis, levetiracetam may be utilized to reduce the risk of seizure.[6]

Duration of postpartum magnesium treatment

There are no studies with a sufficient number of participants to definitively determine the optimal duration of postpartum magnesium therapy. A

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TABLE Postpartum seizures among patients with preeclampsia treated with no postpartum magnesium,[15] a short course of 6 or 12 hours of postpartum magnesium,[10-14] or 24 hours of postpartum magnesium[10-15]

Study	No. of participants included in study data	Clinical diagnosis of participants	Duration of postpartum magnesium infusion	No. of eclamptic seizures among all participants
Ehrenberg, 2006[10]	196	PET without severe features	12 vs 24 hours	No seizures
Maia, 2014[11]	112	PET with severe features	12 vs 24 hours	No seizures
Anjum, 2016[12]	119	PET with severe features	6 vs 24 hours	No seizures
El-Khayat, 2016[13]	160	PET with severe features	12 vs 24 hours	1 seizure in group receiving 12 hours of treatment; no seizures in 24-hour treatment group
Vigil-DeGracia, 2017[14]	284	PET with severe features	6 vs 24 hours	No seizures
Vigil-DeGracia, 2018[15]	1,113	PET with severe features	No postpartum magnesium vs 24 hours of magnesium treatment	2 seizures in group with no postpartum magnesium; 1 seizure in group receiving 24 hours of treatment

properly powered study would likely require more than 16,000 to 20,000 participants to identify clinically meaningful differences in the rate of postpartum eclampsia among patients treated with magnesium for 12 or 24 hours.[7,8] It is unlikely that such a study will be completed. **Hence, the duration of postpartum magnesium must be based on clinical judgment, balancing the risks and benefits of treatment.**

The American College of Obstetricians and Gynecologists (ACOG) recommends continuing magnesium treatment for 24 hours postpartum. They advise, "For patients requiring cesarean delivery (before the onset of labor), the infusion should ideally begin before surgery and continue during surgery, as well as 24 hours afterwards. For patients who deliver vaginally, the infusion should continue for 24 hours after delivery."[9]

Multiple randomized trials have reported on the outcomes associated with 12 hours versus 24 hours of postpartum magnesium therapy (**TABLE**). Because the rate of postpartum eclamptic seizure is very low, none of the studies were sufficiently powered to provide a definitive answer to the benefits and harms of the shorter versus longer time frame of magnesium therapy.[10-15]

The harms of prolonged postpartum magnesium infusion

The harms of prolonging treatment with postpartum magnesium infusion are generally not emphasized in the medical literature. However, side effects that can occur are flushing, nausea, vomiting, and muscle weakness, delayed early ambulation, delayed return to full diet, delayed discontinuation of a bladder catheter, and delayed initiation of breastfeeding.[5,15] In one large clinical trial, 1,113 patients with preeclampsia with severe features who received intrapartum magnesium for ≥8 hours were randomized after birth to immediate discontinuation of magnesium or continuation of magnesium for 24 hours.[15] There was 1 seizure in the group of 555 patients who received 24 hours of postpartum magnesium and 2 seizures in the group of 558 patients who received no magnesium after birth. In this trial, continuation of magnesium postpartum resulted in delayed initiation of breastfeeding and delayed ambulation.[15]

Balancing the benefits and harms of postpartum magnesium infusion

An important clinical point is that magnesium treatment will not prevent all seizures associated with preeclampsia; in the Magpie trial, among the 5,055 patients with preeclampsia treated with magnesium there were 40 (0.8%) seizures.[5]

Magnesium treatment will reduce but not eliminate the risk of seizure. Clinicians should have a plan to treat seizures that occur while a woman is being treated with magnesium.

In the absence of high-quality data to guide the duration of postpartum magnesium therapy it is best to use clinical parameters to balance the benefits and harms of postpartum magnesium treatment.[16-18] Patients may want to participate in the decision about the duration of postpartum magnesium treatment after receiving counseling about the benefits and harms.

For patients with preeclampsia without severe features, many clinicians are no longer ordering intrapartum magnesium for prevention of seizures because they believe the risk of seizure in patients without severe disease is very low. Hence, these patients will not receive postpartum magnesium treatment unless they evolve to preeclampsia with severe features or develop a "red flag" warning postpartum (see below).

For patients with preeclampsia without severe features who received intrapartum magnesium, after birth, the magnesium infusion could be stopped immediately or within 12 hours of birth. For patients with preeclampsia without severe features, early termination of the magnesium infusion best balances the benefit of seizure reduction with the harms of delayed early ambulation, return to full diet, discontinuation of the bladder catheter, and initiation of breastfeeding.

For patients with preeclampsia with severe features, 24 hours of magnesium may best balance the benefits and harms of treatment. However, if the patient continues to have "red flag" findings, continued magnesium treatment beyond 24 hours may be warranted.

Red flag findings include: an eclamptic seizure before or after birth, ongoing or recurring severe headaches, visual scotomata, nausea, vomiting, epigastric pain, severe hypertension, oliguria, rising creatinine, or liver transaminases and declining platelet count.

The hypertensive diseases of pregnancy, including preeclampsia often appear suddenly and may evolve rapidly, threatening the health of both mother and fetus. A high level of suspicion that a hypertensive disease might be the cause of vague symptoms such as epigastric discomfort or headache may accelerate early diagnosis. Rapid treatment of severe hypertension with intravenous labetalol and hydralazine, and intrapartum plus postpartum administration of magnesium to prevent placental abruption and eclampsia will optimize patient outcomes. No patient, patient's family members, or clinician, wants to experience the grief of a preventable maternal, fetal, or newborn death due to hypertension.[19] Obstetricians, midwives, labor nurses, obstetrical anesthesiologists and doulas play key roles in preventing maternal, fetal, and newborn morbidity and death from hypertensive diseases of pregnancy. As a team we are the last line of defense protecting the health of our patients. ●

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