



The American College of
Obstetricians and Gynecologists
WOMEN'S HEALTH CARE PHYSICIANS



Society for
Maternal-Fetal
Medicine

COMMITTEE OPINION

Number 652 • January 2016
(Reaffirmed 2018)

(Replaces Committee Opinion Number 573, September 2013)

The American College of Obstetricians and Gynecologists Committee on Obstetric Practice Society for Maternal-Fetal Medicine

This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.

INTERIM UPDATE: This Committee Opinion is updated to reflect a limited, focused change in gestational age at which to consider tocolysis.

Magnesium Sulfate Use in Obstetrics

ABSTRACT: The U.S. Food and Drug Administration advises against the use of magnesium sulfate injections for more than 5–7 days to stop preterm labor in pregnant women. Based on this, the drug classification was changed from Category A to Category D, and the labeling was changed to include this new warning information. However, the U.S. Food and Drug Administration's change in classification addresses an unindicated and non-standard use of magnesium sulfate in obstetric care. The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine continue to support the short-term (usually less than 48 hours) use of magnesium sulfate in obstetric care for appropriate conditions and for appropriate durations of treatment, which includes the prevention and treatment of seizures in women with preeclampsia or eclampsia, fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery, and short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal corticosteroids in pregnant women who are at risk of preterm delivery within 7 days.

The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine have long supported the short-term use of magnesium sulfate in obstetric care for appropriate conditions and for appropriate durations of treatment. The U.S. Food and Drug Administration (FDA) advises against use of magnesium sulfate injection for more than 5–7 days to stop preterm labor in pregnant women. Based on this, the drug classification was changed from Category A to Category D, and the labeling was changed to include this new warning information (1). The change was prompted by concern for fetal and neonatal bone demineralization and fractures associated with long-term in utero exposure to magnesium sulfate. These concerns are based both on unsolicited reports to the FDA's Adverse Event Reporting System and results from a number of epidemiologic analyses, although these studies have important limitations in design (2–7). There are 18 cases in the Adverse Event Reporting System database that report fetal and neonatal long bone demineralization and fractures. It is important to note that in these cases, the average duration

of prenatal magnesium sulfate exposure was 9.6 weeks, with an average total maternal dose of 3,700 g, a much longer duration and much higher dose than is currently recommended for obstetric use. In addition, sample sizes in available population studies were generally small, making the conclusions of these studies subject to confounding and bias (2–7).

Magnesium sulfate has been used in obstetrics for decades, and thousands of women have been enrolled in clinical trials that studied the efficacy of prenatal magnesium sulfate for a variety of conditions (8–11). Concerns about fetal and neonatal bone demineralization and fracture have not been raised from these studies, including recent trials of magnesium for neuroprotection. The uses of magnesium sulfate in the context of appropriate clinical obstetric practice include, in particular, prevention and treatment of seizures in women with preeclampsia or eclampsia and fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery (8, 9, 12). Magnesium sulfate also may be used for the short-term prolongation of pregnancy (up to 48 hours)

to allow for the administration of antenatal corticosteroids. Tocolysis is not recommended beyond 34 weeks of gestation, and it is generally not recommended before 24 weeks of gestation but may be considered based on individual circumstances at 23 weeks (13). Practitioners should not stop using magnesium sulfate for these indications based on the FDA reclassification. In all of these conditions, prolonged use of magnesium sulfate is never indicated. Therefore, the FDA's change in the pregnancy classification of magnesium sulfate addresses an unindicated and nonstandard use of this medication.

Conclusions

The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine continue to support the short-term (usually less than 48 hours) use of magnesium sulfate in obstetric care for appropriate conditions and for appropriate durations of treatment, which include the following:

- Prevention and treatment of seizures in women with preeclampsia or eclampsia.
- Fetal neuroprotection before anticipated early preterm (less than 32 weeks of gestation) delivery.
- Short-term prolongation of pregnancy (up to 48 hours) to allow for the administration of antenatal corticosteroids in pregnant women who are at risk of preterm delivery within 7 days.

References

1. Food and Drug Administration. FDA recommends against prolonged use of magnesium sulfate to stop pre-term labor due to bone changes in exposed babies. FDA Drug Safety Communication. Silver Spring (MD): FDA; 2013. Available at: <http://www.fda.gov/downloads/Drugs/DrugSafety/UCM353335.pdf>. Retrieved June 12, 2013. ↵
2. Yokoyama K, Takahashi N, Yada Y, Koike Y, Kawamata R, Uehara R, et al. Prolonged maternal magnesium administration and bone metabolism in neonates. *Early Hum Dev* 2010;86:187–91. [PubMed] [Full Text] ↵
3. McGuinness GA, Weinstein MM, Cruikshank DP, Pitkin RM. Effects of magnesium sulfate treatment on perinatal calcium metabolism. II. Neonatal responses. *Obstet Gynecol* 1980;56:595–600. [PubMed] [Obstetrics & Gynecology] ↵
4. Holcomb WL Jr, Shackelford GD, Petrie RH. Magnesium tocolysis and neonatal bone abnormalities: a controlled study. *Obstet Gynecol* 1991;78:611–4. [PubMed] [Obstetrics & Gynecology] ↵
5. Schanler RJ, Smith LG Jr, Burns PA. Effects of long-term maternal intravenous magnesium sulfate therapy on neonatal calcium metabolism and bone mineral content. *Gynecol Obstet Invest* 1997;43:236–41. [PubMed] ↵
6. Matsuda Y, Maeda Y, Ito M, Sakamoto H, Masaoka N, Takada M, et al. Effect of magnesium sulfate treatment on neonatal bone abnormalities. *Gynecol Obstet Invest* 1997;44:82–8. [PubMed] ↵
7. Nassar AH, Sakhel K, Maarouf H, Naassan GR, Usta IM. Adverse maternal and neonatal outcome of prolonged course of magnesium sulfate tocolysis. *Acta Obstet Gynecol Scand* 2006;85:1099–103. [PubMed] [Full Text] ↵
8. Magnesium sulfate before anticipated preterm birth for neuroprotection. Committee Opinion No. 455. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2010;115:669–71. [PubMed] [Obstetrics & Gynecology] ↵
9. Diagnosis and management of preeclampsia and eclampsia. ACOG Practice Bulletin No. 33. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2002;99:159–67. [PubMed] [Obstetrics & Gynecology] ↵
10. Mercer BM, Merlino AA, Society for Maternal-Fetal Medicine. Magnesium sulfate for preterm labor and preterm birth. *Obstet Gynecol* 2009;114:650–68. [PubMed] [Obstetrics & Gynecology] ↵
11. Chronic hypertension in pregnancy. Practice Bulletin No. 125. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2012;119:396–407. [PubMed] [Obstetrics & Gynecology] ↵
12. Management of preterm labor. Practice Bulletin No. 127. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2012;119:1308–17. [PubMed] [Obstetrics & Gynecology] ↵
13. Periviable birth. Obstetric Care Consensus No. 3. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2015;126:e82–94. [PubMed] [Obstetrics & Gynecology] ↵

Copyright January 2016 by the American College of Obstetricians and Gynecologists, 409 12th Street, SW, PO Box 96920, Washington, DC 20090-6920. All rights reserved.

ISSN 1074-861X

Magnesium sulfate use in obstetrics. Committee Opinion No. 652. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2016;127:e52–3.