Magnesium Sulfate for People at Risk of Preterm Birth for Neuroprotection of the Fetus and Concomitant Tocolysis

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This document has been updated to change bolus dose from 6g to 4-6g to account for hospital variation in Magnesium Sulfate policies.

Summary

- Magnesium Sulfate reduces the risk of cerebral palsy in preterm infants prior to 32 weeks gestation
- Tocolysis should only be used short term during antenatal corticosteroid administration
- Magnesium nor Terbutaline should be used as tocolytics for preterm labor

Discussion of Evidence

Approximately one third of cases of cerebral palsy (CP) are associated with early preterm birth. Available evidence suggests that magnesium sulfate given before anticipated early preterm birth reduces the risk of CP in surviving infants. A recent Cochrane review on the use of magnesium sulfate for neuroprotection of the fetus in people at risk for preterm birth included six randomized, placebo-controlled trials involving 6759 babies, and demonstrated a reduction in CP for all six studies who recruited people at less than 34 weeks gestation (RR 0.71; 95% CI 0.71 to 0.89; six trials; 6107 infants) .[1] The number of people needed to be treated to prevent once case of CP among those who survive until age 18-24 months is 46 (95% CI 26-187) in infants exposed to magnesium sulfate in utero before 30 weeks, and 56 (95% CI 34-164) in infants exposed to magnesium sulfate in utero before 32-34 weeks.[2]

Of the 3 large randomized clinical trials designed to evaluate the effect of magnesium sulfate treatment on neurodevelopmental outcomes,[3-5] the only one to show a significant reduction in CP (the "Rouse Regimen") enrolled people at imminent risk for preterm birth between 24 and 31 6/7 weeks of gestation [because of PPROM (87%), advanced preterm labor (10%), or indicated preterm delivery (3%)], randomly assigned them to receive either IV magnesium sulfate or placebo and, in contrast to previous trials, permitted retreatment with magnesium sulfate (up to 34 weeks of gestation).[5]

In people at risk for preterm birth secondary to preterm labor, tocolytic agents are often used to inhibit myometrial contractions. **An evaluation of 19 randomized clinical trials, however, revealed that magnesium sulfate tocolysis did not reduce the frequencies of delivery within 48 hours, 7 days, or early/late preterm birth, and was not associated with improvements in newborn morbidities or mortalities**.[6] Alternatively, beta-mimetics (i.e., terbutaline), calcium channel blockers (i.e., nifedipine), and cyclooxygenase inhibitors (i.e., indomethacin) were not found to be superior when compared with magnesium sulfate treatment.[6] Based on these data:

1. It is appropriate to withhold tocolysis from people presenting in preterm labor as neonatal benefit has not been demonstrated with such treatment.

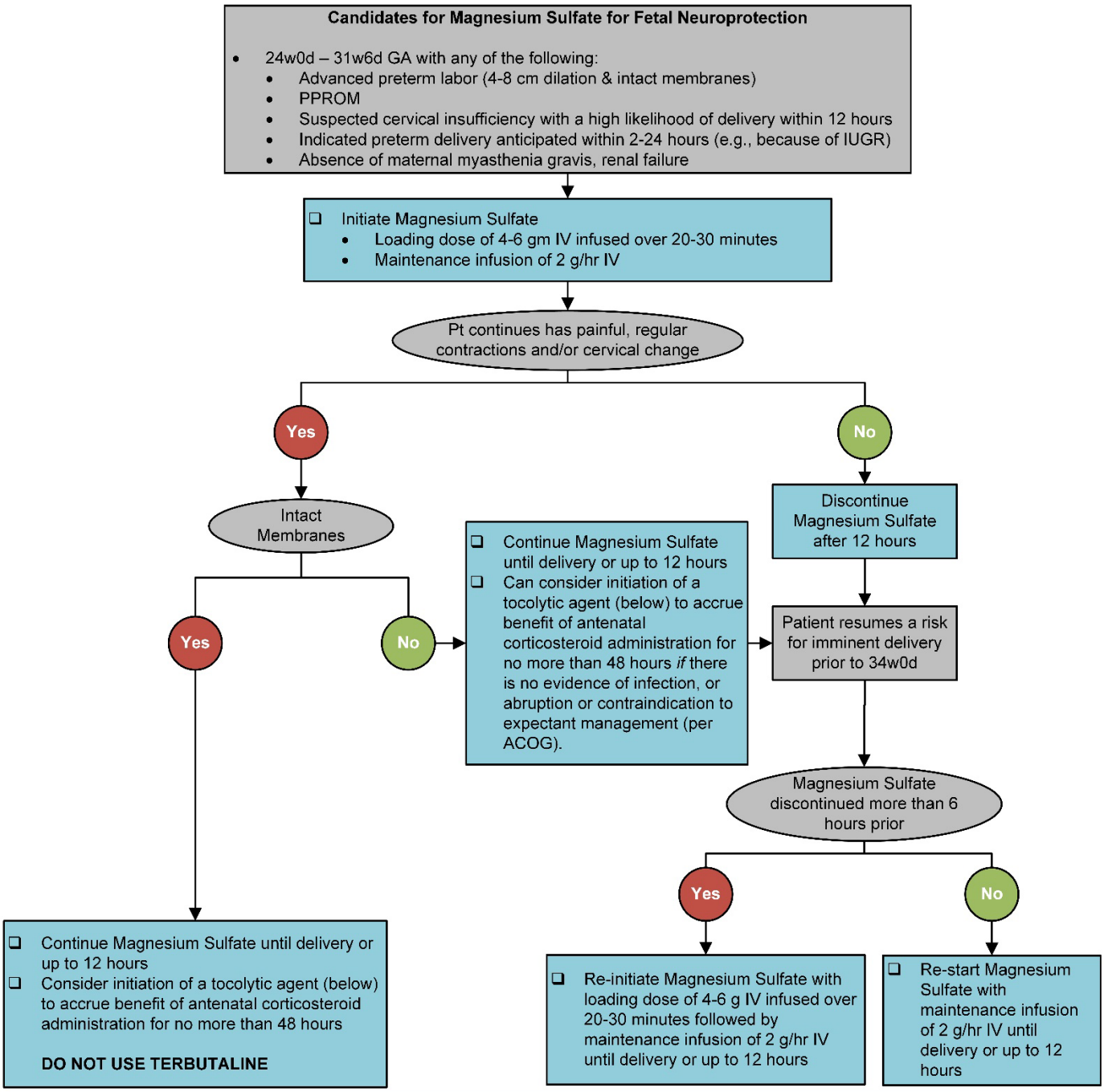
2. **If tocolysis is initiated to achieve time to accrue the benefits of antenatal corticosteroid administration, to facilitate patient transport, or during treatment of reversible causes of preterm labor, the tocolytic agent can be discontinued once these goals have been achieved.**

3. It is appropriate to withhold tocolysis from people with recurrent preterm labor unless used to effect administration of a "rescue course" of antenatal corticosteroids (please refer to BCM Ob/Gyn Perinatal Guideline on "Management of Periviability and the Use of Antenatal Corticosteroids in the Management of Pregnancies at Risk for Preterm Birth") as brief pregnancy prolongation is unlikely to improve neonatal outcomes.

4. **TERBUTALINE SHOULD NOT BE ADMINISTERED ROUTINELY FOR PRETERM LABOR, USED CONTINUOUSLY, USED IN OBSTETRIC TRIAGE AREAS, OR PRESCRIBED ON AN OUTPATIENT BASIS BECAUSE OF THE POTENTIAL FOR SERIOUS MATERNAL HEART PROBLEMS AND DEATH.**

Figure 1 outlines the BCM OB/Gyn Perinatal Guidelines Committee recommendations regarding the use of magnesium sulfate for people at risk of preterm birth for neuroprotection of the fetus and the use of concomitant tocolysis[7].

Figure 1. Use of Magnesium Sulfate for Fetal Neuroprotection and concomitant use of tocolysis[1,6,8]



Recommended Tocolytics

- **Indomethacin**: 25 mg po every 6 hours
  if GA <32w0d, no oligohydramnios, no maternal renal/hepatic impairment
- **Nifedipine Immediate Release**: Initial po dose of 10 mg; repeat dose every 20 min to a max dose of 40 mg po in the first hour, then start 10-20 mg po every 4-6 hours
  if BP >90/50 mm Hg & no maternal cardiac disease or renal impairment

Indications for Terbutaline

- Single dose of 0.25 mg SQ for tocolysis for ECV
- 0.25 mg IV or SQ for management of acute intrapartum fetal distress from suspected uterine tachysystole **or** management of acute intrapartum fetal distress to abolish uterine contractions in preparation for emergent cesarean delivery
- **TERBUTALINE SHOULD NOT BE ADMINISTERED ROUTINELY FOR PRETERM LABOR, USED CONTINUOUSLY, USED IN OBSTETRIC TRIAGE AREAS, OR PRESCRIBED ON AN OUTPATIENT BASIS BECAUSE OF THE POTENTIAL FOR SERIOUS MATERNAL HEART PROBLEMS AND DEATH**

References

References

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