The dark side of antenatal magnesium sulfate: High-dose regimen is associated with brain damage in the preterm caprine model of chorioamnionitis

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Objectives

Magnesium sulfate is currently the standard antenatal treatment for neuroprotection in early-preterm infants. However, some clinical studies in pregnancies complicated by chorioamnionitis have shown no significant reduction in cerebral palsy rates with magnesium sulfate therapy. Moreover, recent experimental data have suggested neurotoxicity at supraphysiological magnesium concentrations. We aimed to investigate the effects of magnesium sulfate administered at low and high doses on preterm goat fetuses in endotoxin-induced experimental chorioamnionitis.

Methods

With or without intra-amniotic endotoxin (n=5 in each of the 4 groups), low-dose (0.14 g/kg loading, 0.035 g/kg maternal bodyweight maintenance) and high-dose (0.2 g/kg loading, 0.07 g/kg maternal bodyweight maintenance) magnesium sulfate were administered within 24 hours, corresponding to a cumulative maternal dose of 0.35 g/kg and 0.62 g/kg bodyweight, respectively. Preterm delivery was induced by cesarean section at 0.80 gestation (day 120). Fetal brain tissues were then harvested.

Results

There were 3 stillbirths (60%) in the endotoxin plus high-dose magnesium-exposed pregnancies, whereas all the fetuses in the remaining 3 groups (n=15) were live born (p=0.167).

Histopathology revealed marked hyperemia, edema, and brain damage characterized by necrotic and apoptotic cells in various parts of fetal brains with increased caspase-3 immunoreaction (p<0.05) following endotoxin and high-dose regimen. These effects were not evident in other groups, including low-dose treatment with endotoxin and high-dose treatment without endotoxin.

Conclusion

Our experimental data reveal that high-dose magnesium sulfate regimens can cause fetal brain injury in the setting of chorioamnionitis.