Effect of Magnesium Sulphate on Fetal Heart Rate Parameters: A Systematic Review

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Abstract

Objective: To examine the potential effects of intravenous magnesium sulphate ($MgSO_4$) administration on antepartum and intrapartum fetal heart rate (FHR) parameters measured by cardiotocography (CTG) or electronic fetal monitoring (EFM).

Methods: We undertook a systematic review of randomized controlled trials, observational studies, and case series. Studies were reviewed independently by two reviewers and qualitatively analyzed with regard to CTG/EFM parameters (baseline FHR, variability and acceleration-deceleration patterns), types of participants, interventions offered, and outcomes reported.

Results: Of 18 included studies, two were RCTs (72 women); 12 were prospective observational studies (269 women), 10 of which were of a pre- and post-intervention design; one was a prospective cohort study (36 women) and three were retrospective cohort studies (555 women). Lower baseline FHR was associated with $MgSO_4$ exposure in seven of nine relevant studies. Decreased FHR variability was reported in nine of 12 relevant studies. Reductions in reactivity or acceleration pattern were seen in four of six relevant studies without an increase in decelerative patterns. All changes were small and not associated with adverse clinical outcomes.

Conclusion: Maternal administration of $MgSO_4$ for eclampsia prophylaxis/treatment, tocolysis or fetal neuroprotection appears to have a small negative effect on FHR, variability, and accelerative pattern, but is not sufficient clinically to warrant medical intervention.

Key Words: Magnesium sulphate, fetal heart rate, non-stress test, cardiotocograph

Competing Interests: None declared.

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Résumé

Objectif : Examiner les effets potentiels de l'administration de sulfate de magnésium ($MgSO_4$) par voie intraveineuse sur les paramètres de la fréquence cardiaque fœtale (FCF) antepartum et intrapartum mesurés par cardiotocographie (CTG) ou monitorage fœtal électronique (MFÉ).

Méthodes : Nous avons mené une analyse systématique ayant porté sur des essais comparatifs randomisés, des études observationnelles et des séries de cas. Ces études ont été analysées de façon indépendante par deux arbitres scientifiques; de plus, elles ont fait l'objet d'une analyse qualitative en fonction des paramètres de la CTG / du MFÉ (FCF initiale, variabilité et profils d'accélération-décélération), des types de participantes, des interventions offertes et des issues signalées.

Résultats : Parmi les 18 études admises à l'analyse systématique, on comptait deux ECR (72 femmes); 12 études observationnelles prospectives (269 femmes), dont 10 comptaient un devis préintervention et postintervention; une étude de cohorte prospective (36 femmes); et trois études de cohorte rétrospectives (555 femmes). Une FCF initiale moindre a été associée à l'exposition au $MgSO_4$ dans le cadre de sept des neuf études pertinentes. Une variabilité moindre de la FCF a été signalée dans neuf des 12 études pertinentes. Des baisses des profils de réactivité ou d'accélération ont été constatées dans quatre des six études pertinentes, sans hausse des profils de décélération. Toutes les modifications ont été faibles et n'ont pas été associées à des issues cliniques indésirables.

Conclusion : Bien que l'administration de $MgSO_4$ à la mère à des fins de prophylaxie / prise en charge de l'éclampsie, de tocolyse ou de neuroprotection fœtale semble exercer un faible effet négatif sur la FCF, la variabilité et le profil d'accélération, cet effet n'est pas suffisant sur le plan clinique pour justifier la tenue d'une intervention médicale.

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INTRODUCTION

Magnesium sulphate has been used for a variety of obstetrical indications, including tocolysis for preterm labour for which it is now recognized to be ineffective.[1] At present, $MgSO_4$ is used for the prevention of eclampsia, for treatment in women with preeclampsia and eclampsia, and for fetal neuroprotection in the setting of imminent preterm birth for any indication at < 32 weeks' gestation in Canada.[2,3]

Cardiotocography, or electronic fetal monitoring, is a routine technique for monitoring fetal well-being during the antenatal and intrapartum periods in pregnancies considered at risk for adverse perinatal outcome. Antenatal EFM is considered a "non-stress test" because the fetus is not subjected to the usual stresses associated with regular uterine contractions. EFM records normal and altered fetal cardiovascular function by documenting the baseline fetal heart rate, fetal heart rate variability, and the presence and pattern of fetal heart rate accelerations and/or decelerations along with their temporal relationship to uterine contractions.[4] EFM is used to detect fetal compromise related to fetoplacental pathology, cord compression, or other processes that may result in altered fetal cardiovascular function, such as fetal immaturity or maternal administration of central nervous system-depressant drugs.[5]

While EFM is deeply embedded in Canadian obstetrical practice, evidence indicates that when compared with intermittent auscultation, EFM has been shown only to decrease the incidence of neonatal seizures (without a proven benefit for infant mortality, other standard indicators of newborn wellbeing, or cerebral palsy), and it increases the incidence of Caesarean section and instrumental vaginal deliveries.[6] As such, EFM is recommended only for women with risk factors for adverse perinatal outcome, such as those requiring $MgSO_4$ for either prevention of eclampsia or fetal neuroprotection.[7]

The use of $MgSO_4$ for fetal neuroprotection in the setting of imminent preterm birth for any indication at < 32 weeks is a relatively recent recommendation from the Society of Obstetricians and Gynaecologists of Canada,[7] and a Canada-wide knowledge translation initiative has been undertaken within a quality assurance framework for tertiary obstetrical facilities.[8] This initiative has included educational site visits to these facilities, where questions were raised by physicians, midwives, and nurses about the effects of $MgSO_4$ on EFM, especially related to FHR variability.[8] The current SOGC Fetal Health Surveillance Guidelines (published in 2007) recommend use of EFM for women with risk factors for adverse perinatal outcome (including preeclampsia, eclampsia, and preterm labour), but do not discuss the effect of $MgSO_4$ on EFM parameters.[2]

An effect of magnesium on FHR patterns is plausible because magnesium ions (Mg^{++}) cross the fetal-placental membranes and fetal serum Mg^{++} levels rapidly equilibrate with maternal levels.[9] Magnesium is a peripheral vasodilator and is assumed to cross the fetal blood-brain barrier, as it does in the mother. The FHR could potentially be affected through peripheral and central mechanisms. Although some observational studies have reported adverse effects of $MgSO_4$ on EFM parameters, this may represent "confounding by indication," in that women who are receiving $MgSO_4$ have conditions that may themselves be associated with abnormalities in FHR and FHR pattern.

We undertook a systematic review of controlled studies of $MgSO_4$ administration during pregnancy, in order to understand the potential effects of $MgSO_4$ on EFM.

METHODS

We searched PubMed (Medline) (1963 to March 2014), the Cochrane Library (1991 to March 2014), EMBASE (1974 to March 2014), and the bibliographies of retrieved articles addressing the effect of $MgSO_4$ on FHR or FHR pattern. The literature search was conducted using the following search terms: ("magnesium sulfate" OR magnesium sulphate OR "$MgSO_4$") AND ("fetus" OR "fetal" OR "foetus" OR "foetal") AND "heart" OR "fetal cardiotocography" OR "fetal electronic monitoring" OR "fetus heart rate" OR "fetus monitoring" OR "fetus distress." Studies were considered if:

1. they were original articles published in English;
2. they were controlled studies published as randomized controlled trials (RCTs), observational studies, or case series;
3. they described human subjects being exposed to $MgSO_4$ during pregnancy for any indication; and
4. they examined FHR effects by any continuous electronic method, including Doppler, following $MgSO_4$ administration.

Excluded were case reports and studies that measured only parameters other than FHR, FHR variability, and/or FHR accelerations and decelerations after maternal exposure to $MgSO_4$.

ABBREVIATIONS

EFM	electronic fetal monitoring
FHR	fetal heart rate
Mg	magnesium
$MgSO_4$	magnesium sulphate