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Journal of Women Health Care and Issues
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Mini Review Article

Antenatal magnesium Sulphate for fetal Neuroprotection- A mini review.

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Received Date: November 26, 2019; **Accepted Date:** December 06, 2019; **Published Date:** December 10, 2019
Citation: Chopra K. (2019) Antenatal magnesium sulphate for fetal neuroprotection- A mini review. J Women Health Care Issues, 2(3); Doi/10.31579/2642-9756/016

Abstract
Prematurity is one of the leading causes of neurological impairment and thus morbidity and mortality. Various preventive strategies are available to prevent preterm birth and fetal morbidity associated with prematurity. Magnesium sulphate was proposed for its benefits on fetal neuroprotection. Various randomised studies were done emphasising its use, the appropriate gestational age and dosing regimen. Hospital based protocols are required to implement its efficient usage.

Kew Words: fetal neuroprotection; antenatal magnesium sulphate

Introduction
Babies delivering before 37 weeks of gestation have significantly higher rates of early, late and post neonatal mortality as compared to babies born at term. The disability in preterm babies range from cerebral palsy to less severe cognitive abnormalities. Approximately, 75 % of preterm deliveries are due to spontaneous preterm birth, cause for which is not known in majority. In the remaining, infections, preterm premature rupture of membranes, early induction of labour due to maternal conditions like pre-eclampsia are the causes. There are various treatment regimens and strategies to reduce the risk of babies delivering prematurely. These includes progesterone prophylaxis, cervical cerclage, tocolytics to subside the uterine contractions till the steroids can be administered to ensure fetal lung maturation and recently magnesium sulphate for fetal neuroprotection.

Magnesium sulphate as neuroprotective agent

Babies born preterm are at risk of intraventricular haemorrhage and periventricular leukomalacia, responsible for causing cerebral palsy. Oligodendrocytes injury is responsible for glial injury and thus cerebral damage. [1]

Exact mechanism of action of magnesium sulphate is not known, but many possible ways do exist. Magnesium sulphate blocks NMDA receptors on oligodendrocytes thus reducing the risk of injury. It also acts as calcium antagonist and reduce calcium influx in the cells. It acts as a vasodilator and protect tissues against free radical injury. It also protects tissues against hypoxic damage and has positive synergistic effect with steroids administration. [2,3,4]

In one animal-based study, it was ascertained that magnesium crosses the placenta within 2 hours of achieving desired serum levels and later concentrates in forebrain. [5] It was thus, concluded as per Australian guidelines to give magnesium sulphate even if expected time of delivery is less than 4 hours. [6]

Lex W Doyle et al, did a review including five trials and including 6145 babies. They used magnesium sulphate therapy in women at risk of delivering preterm and they found that its administration significantly decreased the risk of cerebral palsy in infant with relative risk of 0.68; 95% CI, 0.54-0.87. [7]

Five randomized controlled trials were included in a meta-analysis and it reported that among infants surviving till 18-24 months of age, number needed to treat one case of cerebral palsy was 46 when magnesium sulphate was given to less than 30 weeks gestational age and 56 when given to gestational age of 32-34 weeks. [8] Administration of magnesium sulphate is thus recommended by United States and Canadian guidelines as well.

Patients who were at high risk of delivering at 30 weeks of gestational age or less, were considered appropriate for giving magnesium sulphate for fetal neuroprotection as recommended by the University of Adelaide. [6] It was found in a study by Rouse et al, that giving magnesium sulphate to women with gestational age of less than 28 weeks, significantly reduced the risk of moderate or severe cerebral palsy. [4] A study was planned with the aim of assessing the difficulties encountered in the implementation of giving magnesium sulphate for its neuroprotective effects in preterm infants. The study enrolled 119 women, out of which 81 (68.1%) received magnesium sulphate with an average gestational age of 29.6 weeks +/- 2.1 days. It was seen that the risk of neonatal mortality before hospital discharge was lower in infants who received magnesium sulphate. [9]

So, there should be hospital-based protocols formulated after the discussion with obstetricians and paediatricians regarding the gestational age below which magnesium sulphate should be given for its neuroprotective effect.

Dosing regimen
Dose of magnesium sulphate is 4-6 gm loading dose followed by maintenance dose of 1-3 gm/hour as suggested in various studies. University of Adelaide suggested, an I/V dose of 4 gm as loading dose and 1 gm/ hour as maintenance dose for 24 hours or delivery, whichever is sooner. [6] In another study by Rouse et al, the maintenance dose was continued till 12 hours and stopped if delivery didn't happen. [4] More
randomised control trials are required to well establish the protocol of dosing regimen of magnesium sulphate in antenatal period in patients at high risk of delivering preterm. Monitoring of women

receiving magnesium sulphate is important and should be done judiciously. Respiratory rate, urine output and deep tendon reflexes should be seen. There can be flushing, feeling of warmth, nausea, vomiting and sweating. Major side effects leading to its discontinuation are hypotension and tachycardia. Magnesium sulphate should not be given to patients with known neuromuscular disorders and with calcium channel blocker.

Conclusion

Magnesium sulphate definitely have a significant role in the neuroprotection of the fetus born premature. There should be an emphasis regarding its implementation in national, state and hospital guidelines in order to extend benefit to the unborn premature fetus and reduce the burden of cerebral palsy and neurological impairment.

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