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Review Article

Antenatal administration of Magnesium sulphate for pre-eclampsia- cons and pros in tocolysis

[1]Rajkishor Pandit, [2]Ruby Singh, [3]Brijmohan Kumar Rajak

[1]Senior Consultant and Head of Department, Department of Obstetric and Gynecology, MIHS, Provincial Hospital, Janakpur, Madhesh Pradesh, Nepal;
[2,3]Consultant Obstetrician and Gynecologist, MIHS, Provincial Hospital, Janakpur, Madhesh Pradesh, Nepal

ABSTRACT:
Pre-eclampsia affects 3–5% of pregnancies and is traditionally diagnosed by the combined presentation of high blood pressure and proteinuria. Eclampsia is a very serious complication of preeclampsia that presents after 20 weeks of gestation.Literature reports many trials that proved the efficacy of $MgSO_4$ in the treatment of maternal eclampsia and reported that the mortality rate has decreased and the risk of eclampsia was reduced by half in patients receiving treatment with $MgSO_4$. Several mechanisms are presented, including the effects of magnesium sulfate on peripheral and cerebral vasodilation, blood-brain barrier protection, and as an anticonvulsant. The present paper aimed to assess cons and pros of antenatal administration of magnesium sulphate for management of pre-eclampsia
Keywords: Eclampsia; Magnesium sulphate; Pritchard regimen; Zuspanregimen

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Corresponding author: Rajkishor Pandit, Senior Consultant and Head of Department, Department of Obstetric and Gynecology, MIHS, Provincial Hospital, Janakpur, Madhesh Pradesh, Nepal

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INTRODUCTION

Preterm birth is the leading cause of neonatal mortality and the most common reason for antenatal hospitalization.[1]Pre-eclampsia affects 3–5% of pregnancies and is traditionally diagnosed by the combined presentation of high blood pressure and proteinuria. New definitions also include maternal organ dysfunction, such as renal insufficiency, liver involvement, neurological or haematological complications, uteroplacental dysfunction, or fetal growth restriction. When left untreated, pre-eclampsia can be lethal, and in low-resource settings, this disorder is one of the main causes of maternal and child mortality.[2]

In the absence of curative treatment, the management of pre-eclampsia involves stabilisation of the mother and fetus, followed by delivery at an optimal time.[2]Magnesium sulphate is extensively used in obstetrics for the treatment and prevention of eclampsia.[3] The use of magnesium sulphate as an anticonvulsant started during the Magpie trial in 1998-2001 when being one of the participating centres, women with pre-eclampsia were randomized to receive magnesium sulphate or placebo. Its routine use as an anticonvulsant in the management of pre-eclampsia started in 2002 after publication of Magpie trial.[4]

Babies born to mothers who experience complications during pregnancy such as preterm birth (early birth before 37 weeks of pregnancy) and intrauterine infection (infections in the uterus) have a higher risk of a movement disorder called cerebral palsy. Cerebral palsy is a broad term used to describe a non□progressive physical disorder of movement or posture that is acquired in early life, and that results from complications in brain development. It may also be associated with intellectual disabilities, behavioural disorders, sensory defects (blindness and deafness) and seizures.[3]Therefore, the present paper aimed to assess cons and pros of antenatal administration of Magnesium sulphate for management of pre-eclampsia.

MODE OF ACTION OF MAGNESIUM SULPHATE FOR PRE-ECLAMPSIA

Several mechanisms are presented, including the effects of magnesium sulfate on peripheral and cerebral vasodilation, blood-brain barrier protection, and as an anticonvulsant.Though the specific mechanisms of action remain unclear, the effect of magnesium sulfate in the prevention of eclampsia is likely multi-factorial.[5]Magnesium, which has a beneficial effect in eclampsia, may act by opposing calcium-dependent arterial constriction, thereby relieving vasospasm. Magnesium may also antagonize the increase in intracellular calcium concentration caused by ischemia and thus prevent cell damage and death.[6]Magnesium sulfate may act as a vasodilator, with actions in the peripheral vasculature or the cerebrovasculature, to decrease peripheral vascular resistance and/or relieve vasoconstriction. Additionally, magnesium sulfate may also protect the blood-brain barrier and limit cerebral edema formation, or it may act through a central anticonvulsant action.[5]

RECOMMENDED DOSAGE

A plasma concentration of 1.8-3.0 mmol/L is recommended for the treatment of eclamptic seizures while carefully monitoring for toxicity beyond this recommended concentration. The first warning of imminent toxicity in the mother is the loss of the patellar reflex at concentrations between 3.5 and 5 mmol/L. Respiratory paralysis and cardiac arrest may occur at supratherapeutic concentrations beyond 5 mmol/L. Therefore, close monitoring for the loss of deep tendon reflexes, respiratory rate <12 breaths/minute, urine output <30 mL/hour, and high plasma concentrations are of paramount importance.[7]

AVAILABLE REGIMEN

The two recommended regimens (Zuspan and Pritchard) have been internationally accepted as standard regimens on the basis of their proven clinical efficacy in the two largest $MgSO_4$ trials. Although these trials showed comparable clinical efficacy for the predominantly intramuscular (Pritchard) and intravenous (Zuspan) regimens, they also highlighted the lack of understanding of the minimum effective dose for eclampsia prevention and treatment.[8]Magnesium sulphate was given according to Pritchard regime. It was observed that many patients did not receive maintenance therapy due to suspicion of toxicity but they did not convulse any further. Later on, there was a period when magnesium sulphate was out of stock and it was almost impossible to get magnesium sulphate. At that time Pritchard regime could only be used in eclamptic women, whereas pre-eclamptics received only single bolus dose. It was observed that none of the patients with pre-eclampsia developed seizure even after the single bolus dose.[4]

Begum R et al[9] determined the recurrent convulsion rate with the low dose 'Dhaka' magnesium sulphate regime. The loading dose of magnesium sulphate was 10 gm. Following this 2.5 gm was given intramuscularly 4 hourly, for 24 hours after administration of the first dose. Half of the standard dose of magnesium sulphate appeared to be sufficient to control convulsions effectively and serum levels of magnesium remained lower than levels which produce toxicity.[9] Mahajan NN et al[10] described 'Padhar Regime' which is a low-dose magnesium sulphate treatment for eclampsia in their study and found that the low-dose regime appears to control and prevent convulsions effectively in Indian women.[10]

Various low dose magnesium sulphate regimens have been described principally because of small size of Indian women & concern about toxicity in circumstances where facility for measurement of serum level of magnesium is not available. Low dose magnesium sulphate regimen has shown promise in terms of decrease in side effects without a significant decrease in its therapeutic benefits. In India, Pritchard's regimen has been modified in various places and found that low dose regimen was as efficacious as standard dose regimen in convulsion control with less of magnesium toxicity but neither a long term statistical data has been reported nor standardisation of protocol has been framed.[11]The two widely used regimes for magnesium sulphate are continuous intravenous infusion, and combined intravenous (IV) and intramuscular regime (IM). The IV regimen achieves more stable serum levels of magnesium but requires the use of an infusion pump for safe delivery and has a greater potential for inadvertent overdose.[4]Lower-dose and loading dose-only regimens could be as safe and efficacious as standard regimens.[12]

Furthermore, Magnesium sulphate for pre-eclampsia costs less and prevents more eclampsia in low gross national income (GNI) than in high GNI countries. Cost-effectiveness substantially improves if it is used only for severe pre-eclampsia, or the purchase price is reduced in low GNI countries.[13]

MATERNAL RISKS ASSOCIATED WITH MAGNESIUM SULFATE

The 'well recognised' and more commonly reported maternal adverse effects of magnesium sulphate include flushing, increased warmth and sweating due to the peripheral vasodilatory effects of magnesium, and nausea, vomiting, headaches, muscle weakness, blurred vision, and intravenous (IV) or intramuscular (IM) site pain or discomfort. Though such maternal adverse effects may be considered comparatively 'minor,' they have been associated with the need for early cessation of this therapy, which has benefits when used for maternal and fetal neuroprotection.[14]

MATERNAL EFFECTS OF MAGNESIUM SULFATE

In a study by Bozhinova S et al,[1] authors reported on very good effect in cases with pains and increased uterine tone (36.73%), as well as in cases with pains and irregular uterine contractions (10.21%), while the treatment was without any effect in cases with uterine contractions on 15-20 min, increased uterine tone, bleeding and Pelvic score 1-3 points in spite of high dosages of MgSO4 and longer duration of treatment. In another study by Noor S et al,[15] the magnesium sulphate regimen consisted of 4 gm loading dose as 20% solution intravenously over 10-15 minutes followed immediately by 5 gm into each buttock and dose of 5gm intramuscularly was repeated only if the patient developed convulsions and the study reported that themagnesium sulphate is an effective drug to prevent and control seizures. It is easy to administer and subsequent nursing is easy. Seizures usually terminate after the initial loading dose of magnesium sulphate.[15]

FETAL EFFECTS OF MAGNESIUM SULFATE

Elevated maternal magnesium sulphate concentrations are associated with toxic effects that range from diminished deep tendon reflexes to apnoea and electromechanical dissociation.[16-19] Riaz M et al[20]reported that neonates born to mothers who received magnesium sulphate were more likely to be hypotonic and had lower Apgar scores at birth.Hypocalcaemia can result from inhibition of parathyroid hormone, and many non-specific, but unpleasant, symptoms are commonly observed, such as nausea, vomiting and flushing.[21]

Marret S et al[22]reported thatthe role for antenatal magnesium sulphate therapy as a neuroprotective agent for the preterm fetus is not yet established.On the contrary, Chollat C et al[23] reported that neuroprotective effect of magnesium sulphate to reduce cerebral palsy in infants born preterm when administered to females at risk of imminent preterm birth. Neuroprotection regardless of gestational age, cause of preterm birth, and total dose. Antenatal magnesium sulphate treatment has good cost-effectiveness.[23]Antenatal magnesium sulphate given prior to preterm birth for fetal neuroprotection prevents CP and reduces the combined risk of fetal/infant death or CP. Benefit is seen regardless of the reason for preterm birth, with similar effects across a range of preterm gestational ages and different treatment regimens. Widespread adoption worldwide of this relatively inexpensive, easy-to-administer treatment would lead to important global health benefits for infants born preterm.[24]

CONCLUSION

Eclampsia is a very serious complication of preeclampsia that presents after 20 weeks of gestation. Appropriate administration of antenatal magnesium sulphate was not shown to be associated with serious maternal adverse effects. Literaturereports many trials that proved the efficacy of $MgSO_4$ in the treatment of maternal eclampsia and reported that the mortality rate has decreased and the risk of eclampsia was reduced by half in patients receiving treatment with $MgSO_4$. Thus, it can be suggested that if $MgSO_4$ is given to all mildly preeclamptic patients, the risk of progressing to severe preeclampsia and eclampsia will decrease substantially.

REFERENCES

1. Bozhinova S, Markova S, Tsvetkov Ts, Penkov V, Ivanova I. Za iprotivmagnezieviiatsulfatkatotokolitichnosredstvo [Pros and cons of magnesium sulfate as a tocolytic]. AkushGinekol (Sofiia). 2002;41(6):17-22.
2. Mol BW, Roberts CT, Thangaratinam S, Magee LA, De Groot CJ, Hofmeyr GJ. Pre-eclampsia. The Lancet. 2016 Mar 5;387(10022):999-1011.
3. Nguyen TM, Crowther CA, Wilkinson D, Bain E. Magnesium sulphate for women at term for neuroprotection of the fetus. Cochrane Database of Systematic Reviews. 2013(2).
4. Shoaib T, Khan S, Javed I, Bhutta SZ. Loading dose of magnesium sulphate versus standard regime for prophylaxis of pre-eclampsia. J Coll Physicians Surg Pak. 2009 Jan 1;19(1):30-3.
5. Euser AG, Cipolla MJ. Magnesium sulfate for the treatment of eclampsia: a brief review. Stroke. 2009 Apr;40(4):1169-75.
6. Sadeh M. Action of magnesium sulfate in the treatment of preeclampsia-eclampsia. Stroke. 1989 Sep;20(9):1273-5.
7. Padda J, Khalid K, Colaco LB, Padda S, Boddeti NL, Khan AS, Cooper AC, Jean-Charles G. Efficacy of Magnesium Sulfate on Maternal Mortality in Eclampsia. Cureus. 2021 Aug 20;13(8):e17322.
8. Okusanya BO, Oladapo OT, Long Q, Lumbiganon P, Carroli G, Qureshi Z, Duley L, Souza JP, Gülmezoglu AM. Clinical pharmacokinetic properties of magnesium sulphate in women with pre□eclampsia and eclampsia. BJOG: An International Journal of Obstetrics & Gynaecology. 2016 Feb;123(3):356-66.
9. Begum R, Begum A, Johanson R, Ali MN, Akhter S. A low dose ('Dhaka') magnesium sulphate regime for eclampsia: Clinical findings and serum magnesium levels. Acta obstetricia et gynecologica Scandinavica. 2001 Jan 1;80(11):998-1002.
10. Mahajan NN, Thomas A, Soni RN, Gaikwad NL, Jain SM. 'Padhar Regime'–A Low-Dose Magnesium Sulphate Treatment for Eclampsia. Gynecologic and obstetric investigation. 2009 Sep 30;67(1):20-4.
11. Sahu L, Singh S, Tempe A, Koner BC. A randomized comparative study between low-dose magnesium sulphate and standard dose regimen for management of eclampsia. Int J Reprod Contracept Obstet Gynecol. 2014 Mar 1;3(1):79-86.
12. Pratt JJ, Niedle PS, Vogel JP, Oladapo OT, Bohren M, Tunçalp Ö, Gülmezoglu AM. Alternative regimens of magnesium sulfate for treatment of preeclampsia and eclampsia: a systematic review of non□randomized studies. Acta obstetricia et gynecologica Scandinavica. 2016 Feb;95(2):144-56.
13. Simon J, Gray A, Duley L, Magpie Trial Collaborative Group. Cost□effectiveness of prophylactic magnesium sulphate for 9996 women with pre□eclampsia from 33

countries: economic evaluation of the Magpie Trial. BJOG: An International Journal of Obstetrics & Gynaecology. 2006 Feb;113(2):144-51.
14. Bain ES, Middleton PF, Crowther CA. Maternal adverse effects of different antenatal magnesium sulphate regimens for improving maternal and infant outcomes: a systematic review. BMC Pregnancy Childbirth. 2013 Oct 21;13:195.
15. Noor S, Halimi M, Faiz NR, Gull F, Akbar N. Magnesium sulphate in the prophylaxis and treatment of eclampsia. Journal of Ayub Medical College Abbottabad. 2004;16(2).
16. Agus ZS, Morad M. Modulation of cardiac ion channels by magnesium. Annu Rev Physiol 1991; 53: 299– 307.
17. Bashuk RG, Krendel DA. Myasthenia gravis presenting as weakness after magnesium administration. Muscle Nerve 1990; 13: 708– 12.
18. Altura BM, Altura BT, Carella A. Magnesium deficiency-induced spasms of umbilical vessels: relation to preeclampsia, hypertension, growth retardation. Science 1983; 221: 376– 8.
19. Elin RJ. Assessment of magnesium status. Clin Chem 1987; 33: 1965– 70.
20. Riaz M, Porat R, Brodsky NL, Hurt H. The effects of maternal magnesium sulfate treatment on newborns: a prospective controlled study. *J Perinatol* 1998; 18: 449– 54.
21. Cholst IN, Steinberg SF, Tropper PJ, Fox HE, Segre GV, Bilezikian JP. The influence of hypermagnesemia on serum calcium and parathyroid hormone levels in human subjects. N Engl J Med 1984; 310: 1221– 5
22. Marret S, Doyle LW, Crowther CA, Middleton P. Antenatal magnesium sulphate neuroprotection in the preterm infant. InSeminars in Fetal and Neonatal Medicine 2007 Aug 1 (Vol. 12, No. 4, pp. 311-317). WB Saunders.
23. Chollat C, Sentilhes L, Marret S. Protection of brain development by antenatal magnesium sulphate for infants born preterm. Developmental Medicine & Child Neurology. 2019 Jan;61(1):25-30.
24. Crowther CA, Middleton PF, Voysey M, Askie L, Duley L, Pryde PG, Marret S, Doyle LW, AMICABLE Group. Assessing the neuroprotective benefits for babies of antenatal magnesium sulphate: an individual participant data meta-analysis. PLoS medicine. 2017 Oct 4;14(10):e1002398.