Original Article

Magnesium Sulphate in Eclampsia and Pre-Eclampsia - A Case Series of 103 Patients Treated with Single Loading Dose of $MgSO_4$ At Holy Family Hospital, Rawalpindi

Humaira Bilqis[1], Humera Noreen[2], Naheed Bano[3], Rizwana Chaudhri[4]

[1,2]Assistant Professor, Rawalpindi Medical University, Gynae/Obs unit I, Holy Family Hospital, Rawalpindi
[3]Associate Professor, Rawalpindi Medical University, Gynae/Obs unit I, Holy Family Hospital, Rawalpindi
[4]Professor and Dean, Gynae/Obs Department, Rawalpindi Medical University, Rawalpindi

Correspondence: *Dr. Humaira Bilqis, Assistant Professor, Rawalpindi Medical University, Gynae/Obs unit I, Holy Family Hospital, Rawalpindi*
humairabilqis@gmail.com

Abstract

Objective: To determine the efficacy of a single loading dose (14 grams) of magnesium sulphate (MgSO4) as an anti-convulsant in the management of eclampsia and severe pre-eclampsia.

Methods: A prospective study was conducted at Obs/Gynae Department, Holy Family Hospital, Rawalpindi over a period of three years. The patients who needed MgSO4 due to eampsia or severe pre-eclampsia were included in the study. The patients were given 14 grams $MgSO_4$ (4 grams I/V bolus diluted in 20 ml 0.9% normal saline + 5 grams I/M on each buttock) as the sole anticonvulsant agent. Other aspects of the management were as in the standard practice. The main outcome measure was the occurrence of seizure within 24 hours after Mgso4 therapy. All observations were recorded on a specially designed proforma.

Results: Total patients recruited were 103, including 61 eclamptics and 42 pre-eclamptics. Mean age was 27 years. In 42 (40.8%), fits occurred antenatal, 5 (4.8%) intrapartum and 14 (13.5%) postpartum. Seizures occurred in 6 (5.8%) patients within 24 hours after the loading dose of MgSO4; 5 (8.1%) among eclamptics and 1 (2.3%) among pre-eclamptics. The vaginal delivery rate was 64% and the LSCS rate was 35.9%. There were 38 (36.8%) perinatal deaths and one maternal mortality (0.97%).

Conclusions: The single loading dose of MgSO4 can be used with good seizure control and less chances of toxicity and hence a good option in low-resource countries to decrease the maternal mortality rate.

Key Words: Low dose $MgSO_4$ regimen, eclampsia, pre-eclampsia

Cite this article as: Bilqis H, Noreen H, Bano N, Chaudhri R. Magnesium Sulphate in Eclampsia and Pre-Eclampsia - A Case Series of 103 Patients Treated with Single Loading Dose of MgSO4 (14 Grams) At Holy Family Hospital, Rawalpindi. J. Soc. Obstet. Gynaecol. Pak. 2018; Vol 8(3):154-158.

Introduction

Going through the journey of being a mother might be an unpleasant rather life-threatening experience in most of the low-resource countries where almost 99% of the maternal deaths happen.[1] The Millennium Development Goals (MDGs) set by the World Health Organization (WHO) in 1990 were only partially achieved at best by most of the developing world.[2] The target goal of minimizing the maternal mortality ratio (MMR) of Pakistan to 100 maternal deaths per 100,000 live births by 2015, remained a dream which could never become a reality.[3] The hypertensive disorders of pregnancy are the second major contributor (14%) after

Authorship Contribution: [1]Conceived, designed, collected data, statistical analysis, manuscript writing, [2,3] Manuscript writing, editing of manuscript. [4]Proof Reading

Funding Source: none

Conflict of Interest: none

Received: April 28, 2018

Accepted: Sept 18, 2018

hemorrhage (27.1%) towards maternal mortality worldwide.[4]

These disorders are one of the commonest medical disorders complicating pregnancy, the spectrum ranging from gestational hypertension to eclampsia.[5] The maternal morbidity and mortality rise acutely with the progression of the disease to eclampsia. More than 10% of women develop gestational hypertension in their first pregnancy and although most of them have a successful outcome, the condition can deteriorate and can give rise to severe multisystem complications including eclampsia, cerebral haemorrhage, respiratory compromise as well as hepatic, hematological and renal impairment. Pre-eclampsia (proteinuric hypertension) complicates approximately 2-8% of pregnancies.[6] The maternal and fetal outcome is badly affected with the development of seizures and the maternal and perinatal mortality acutely rises with each convulsion.

In developed countries, the incidence of eclamptic convulsions are reported around 1/2000 whereas in the developing countries, its incidence varies from 1/100 to 1/1500 deliveries.[7] According to an Indian study, the incidence of eclampsia varies from 0.5% to 1.8%.[8] The burden of disease is reflected by the WHO estimates which indicate that over 63,000 mothers die because of pre-eclampsia and its complications each year worldwide, with 98% of these occurring in the developing countries.[9] In Nigeria, two studies concluded eclampsia to be the major maternal killer being the cause of 46.3% and 31.3% maternal deaths respectively.[10,11]

The exact incidence is not known in our country due to the lack of a centralized integrated data but the hospital statistics available at individual centers are quite distressing.[12] Furthermore, these statistics, if available, are only representing the data of tertiary care level. The primary and secondary level hospitals are not playing their very fundamental and vital role in the initial management especially the use of magnesium sulphate ($MgSO_4$), proper referral and record keeping of these patients. This may partly be due to the lack of facilities especially the inadequate supply of $MgSO_4$ and partly due to the lack of adequate, trained and motivated staff who can administer and monitor it in these hospitals. As a consequence, the people have lost confidence in these health centers and they prefer to bring these fitting women to bigger but distant hospitals which can cause much of the precious time to be wasted during this transfer and delay in the management. In addition, according to the PDHS 2017-18, only 86% of the pregnant women seek antenatal care and only 66% women deliver at any health care facility.[13] Seizures during labour are related by some to be due to evil forces rather than any disease process, thus treated by other means instead of providing any medical treatment. In all these circumstances, a large number of cases complicated with pre-eclampsia/eclampsia are not even reported. Multiple delays ultimately result in the high rates of maternal and neonatal morbidity and mortality.

Eclampsia, unlike pre-eclampsia, is considered to be a preventable condition.[14] In addition to the utilization of health care facilities, provision of antenatal and postnatal services at the community level, addressing the delays in the management of these deprived women and the use of $MgSO_4$ in the prevention and treatment of convulsions can improve this grim situation. According to the results of the Magpie Trial, the risk of convulsions was halved in high risk pre-eclamptics with the use of $MgSO_4$.[15] In the Collaborative Eclampsia Trial, a large multicentric trial conducted at 27 centers in 9 developing countries, $MgSO^4$ was found to be a better anticonvulsant for eclamptic patients as compared to phenytoin and diazepam.[16] The Cochrane reviews have also reported that $MgSO_4$ is superior to diazepam and phenytoin in terms of seizure control.[17] But in spite of all the above evidence regarding $MgSO_4$, there has been a constant discussion in the literature regarding its dosage regimen.

In 1984, Pritchard published his standardized regimen which consists of the initial loading dose of 14 grams (gms) [4 gms IV + 5 gms IM on each buttock] followed by 4 hourly IM doses of 5 gms $MgSO^4$ for 24 hrs after the last convulsion or delivery whichever is later. Thus a minimum total dose would be 44 gms provided no convulsion occurs after delivery. This dose will be increased if a patient is not delivered soon after the loading dose or she has further fits before or after delivery. This high dose administration not only increases the risk of toxicity but also enhances the cost of treatment, requires more vigilant monitoring and needs adequate trained staff to monitor. These issues can become a great hurdle in the routine use of this gold standard drug. In recent years, several studies although on a smaller scale have been conducted especially in the low-income countries using different low dose regimens to overcome these issues.[6,8,18,19,20] Almost all these studies have shown promising results

in terms of control of convulsions as well as maternal and fetal outcomes.

In our study, we aimed to see the efficacy of the single loading dose of 14 gms $MgSO_4$, both for the prophylaxis and treatment of eclampsia.

Methodology

The study was conducted over a period of 3 years i.e. January 2012 to December 2014 at Holy Family Hospital, Rawalpindi.

Detection of significant proteinuria (+1 on dipstick/>300 mgs per 24 hrs) in hypertensive patients having 2 or more readings of raised blood pressure (≥ 140/90 mmHg) after 20 weeks gestation was used as the criteria to diagnose pre-eclampsia. Signs and symptoms of imminent eclampsia i.e. uncontrolled hypertension, headache, dizziness, blurring of vision, excessive generalized edema and hyper-reflexia were considered to be indications for $MgSO^4$ prophylaxis in patients with severe pre-eclampsia. An occurrence of tonic-clonic seizures in such patients having no previous history of any seizure disorder was included in the therapeutic limb of the study. These patients might already be admitted in the ward due to pre-eclampsia and developed new symptoms, newly admitted or referred from other hospitals without $MgSO_4$ therapy. For exclusion criteria, see Table I.

Table 1. Exclusion criteria	
>3 seizures	DIC
Deranged RFTs/ Low urine output	$MgSO_4$ given before admission
Respiratory depression	Any other anticonvulsant given
Jaundice/Deranged LFTs/HELLP syndrome	H/O seizures other than eclampsia
Unconsciousness	

Initial emergency management was started in all these patients taking care of airway, breathing and circulation. Patients were kept in left lateral position, catheterized and intermittent suction was done when required. 14 grams $MgSO_4$ was given as the sole anticonvulsant agent (4 grams slow IV bolus diluted in 20 ml of 0.9% normal saline plus 10 grams IM stat dose i.e. 5 grams on each buttock). Other aspects of the management were followed as per protocol and were strictly monitored for clinical signs of magnesium toxicity. After stabilizing, the patients were assessed for vaginal / abdominal delivery. The patients who were not in spontaneous labour, were assessed for inducibility and induction of labour was started according to the Bishop Score. All the labour events and neonatal outcomes were observed and recorded on a specially designed proforma. In case of seizure after loading dose, 2 grams $MgSO^4$ slow IV followed by the standard IM regimen was started which continued for 24 hours after last seizure. Our main outcome measure was the recurrence of seizures in eclamptics or occurrence of first seizure in pre-eclamptics within first 24 hours after loading dose.

Results

We recruited 103 patients in the study including 61 with eclampsia and 42 with severe pre-eclampsia. The mean age was 27.0 years. Demographic characteristics of the study participants are given in Table II.

Table II. Demographic Features		
Demographic Factors	Total number (n= 103)	% age
Residence		
a. Urban	47	45.6
b. Rural	56	54.3
Parity		
a. Primigravida	49	47.5
b. P1-P4	48	46.6
c. P5 or more	6	5.8
Gestational age		
a. Term	44	42.7
b. Pre-term	59	57.2
Categories of patients:		
a. Pre-eclampsia	42	40.8
b. Eclampsia	61	59.2
• Antenatal	42	40.8
• Intrapartum	5	4.8
• Postpartum	14	13.5

Seizures ocurred in 6 (5.8%) patients within 24 hours after this therapy; 5 out of 61 (8.1%) among eclamptics and 1 out of 42 (2.3%) among pre-eclamptics (Figure 1).

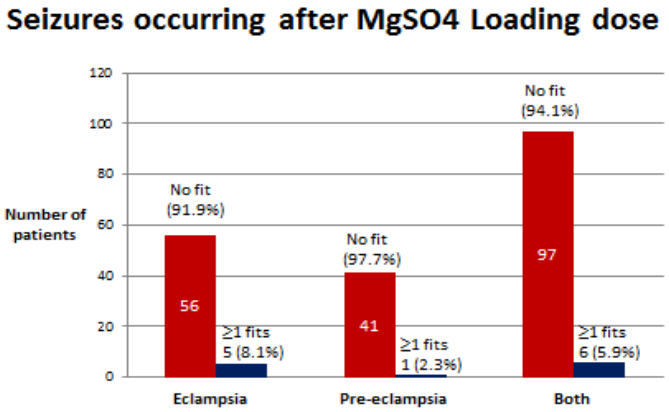

Figure 1. Main outcome - seizures occurring within 24 hours after loading dose of $MgSO_4$

Twenty (19.4%) patients underwent LSCS directly due to certain indications just after stabilizing them. Out of the remaining 83 patients, labour started spontaneously in 33 (32%) and induced in 50 (48.5%) patients. 66(64%)

patients delivered vaginally while 17 (16.5%) patients ended up in emergency LSCS. Overall, the vaginal delivery rate was 64% and LSCS rate was 35.9%. In 65 (63.1%) deliveries, the neonates were alive till 24 hours follow up after delivery while there were 38 (36.8%) perinatal deaths. There was only one maternal mortality (0.97%) which happened in an eclamptic patient.

Table III: Labour Events

Labour Events	Total number (n= 103)	% age
Induction of labour		
a. Yes	50	48.5
b. No	53	51.4
MOD		
a. SVD	66	64.0
b. LSCS	37	35.9
• After trial	17	16.5
• Without trial	20	19.4
Perinatal outcome		
a. Discharged alive	65	63.1
b. Perinatal deaths	38	36.8
Maternal outcome		
a. Stable	102	99.0
b. Expired	1	0.97

Discussion

Magnesium sulphate is considered to be the gold standard drug to prevent or control the eclamptic convulsions but what should be the optimal dose of this potentially dangerous drug is still questionable. The need to answer this question is even more necessary for the low resource settings because of the significant biological, racial, climatic, logistic, economic and social differences from the high-income settings where the trials for this drug are usually conducted and dosage regimens are recommended.

We found very promising results in our study using the single loading dosage regimen of magnesium sulphate, both in terms of prevention and control of eclamptic convulsions. The results of our study compare well with many other studies, conducted at the low resource settings in Asia and Africa using the same regimen.

Dasgupta et al[21] conducted a comparative, prospective, randomized study in Kolkata, India. In this trial, a total of 500 eclmaptic and pre-eclamptic women were randomized to treat with single loading dose or the standard Pritchard regimen. The incidence of appearance or recurrence of convulsions, pulmonary complications, maternal mortality, C-section and postpartum haemorrhage was almost similar between two groups. Moreover, the perinatal outcomes were also similar. The results were encouraging in terms of significantly lower incidences of toxicity, less time to return to postnatal wards and to return home, less number of health care staffs required in the single loading dose group.

Another study conducted by Noor et al.[20] using only a single loading dose of $MgSO_4$ in eclamptics and pre-eclamptics also revealed very promising results.

Al-Khayat et al.[22] in Egypt and Shoaib et al.[23] at Jinnah Postgraduate Medical College, Karachi, in two different trials concluded this dosage regimen to be effective in the prevention of eclampsia.

Results from the randomized controlled trial in Bengladesh by Begum et al.[24] has strengthened the evidence regarding similar efficacy of loading dose when compared with the standard Pritchard regimen.

There are certain studies in which shorter regimens are used both in terms of the amount of drug and duration of therapy.[25,26,27] The results of almost all these studies are showing good efficacy and safety profiles.

In a community-based study carried out in the rural set-up of Bangladesh.[28], the investigators used the loading dose at the time of referral of hypertensive mothers. Most of them remained fit-free and the morbidity was much less.

Furthermore, less manpower, less monitoring, less laboratory tests and less hospital stay was required in our study sample. These benefits make this regimen to be an alternate option in our low-resource and over-populated settings. The reluctance in its use at the lower level hospitals can be overcome by the use of this simple intervention which might in turn be quite helpful in lowering the graph of morbidity and mortality rates of these poor patients.

Though most studies report ecalmpsia common in primigravidae[19,29], 47.5% of the patients were primigravidae in our study.

The incidence of abdominal deliveries in our study was 36% which is much lower than 50% incidence found in study by Shrestha et al.[30] The most probable reason for this is that our study population included stable eclamptics only who had up to three fits so that more time could be given for trial of vaginal delivery. Maternal mortality of eclamptics in our study was 0.97%, which is much less than that in many studies.[29,31]

Our study was unique in the sense that it was a pilot study which has added the evidence in favour of

efficacy and safety of single loading dose of magnesium sulphate especially in the population of Northern Punjab. There were certain limitations of the study. It was conducted at a single center of this region, having shorter follow up period and not comparative. So a larger, multi-centric, randomized, controlled trial is needed in its continuation to generate more evidence.

Conclusion

This low dose regimen can be used safely with good seizure control and less chances of toxicity and is a good option in low-resource countries to decrease the maternal mortality rate. Further randomized controlled trials are required to be conducted.

References

1. WHO Maternal mortality-Fact sheet. 16 February 2018
2. Maternal and perinatal health challenges in Pakistan. Farrukh MJ, Tariq MH, Shah KU. Journal of Pharmacy Practice and Community Medicine. 2017; 3(2): 76-77
3. Pakistan Millennium Development Goals report 2010. Islamabad, Pakistan
4. Global causes of maternal death: A WHO systematic analysis. Say L, Chou D, Gen MA, Tuncalp O, Mollar AB, Daniels JD et al. Lancet Global Health. 2014; 2(6): e323-e333
5. National Institute for Health and Clinical Excellence. Hypertension in pregnancy. The management of hypertensive disorders during pregnancy. NICE clinical guidelines 107. 2010
6. Soni BL. Alternative magnesium sulphate regimens for women with pre-eclampsia and eclampsia: RHL commentary. The WHO Reproductive Health Library, Geneva: World Health Organization
7. Suchitra R, Nissi Vinuthna K, Shyamala Devi, Shantha Bai K, Begum S. Comparison of low dose, single loading dose and standard Pritchard regimen of magnesium sulphate inantepartum eclampsia. International journal of current research. 7(9). 20204-20207; September 2015
8. Ahar GS, Gavali U. Body friendly, safe and effective regimen of magnesium sulphate for eclampsia. Int J Med Res Health Sci. 2013; 2(1): 83-86
9. World Health Organization. Trends in Maternal Mortality: 1990-2008. Geneva: WHO 2010
10. Status of emergency obstetric service in six states of Nigeria—A need assessment report. Society of Gynaecology and Obstetrics of Nigeria. 2004
11. Adamu YM, Salihu HM, Sathiakumar N, Alexander R. Maternal mortality in Northern Nigeria: a P……. study. Eur J Obstet Gynaecol Reprod Biol. 2003; 109: 153-159
12. Bano, N, R Chaudhri, L Yasmeen, F Shafi, L Ejaz. A Study of Maternal Mortality in 8 Principal Hospitals in Pakistan in 2009." International Journal of Gynecology and Obstetrics 114 (3): 255–59.
13. National Institute of Population Studies (NIPS) [Pakistan] and ICF. 2018. Pakistan Demographic and Health Survey 2017-18. Islamabad, Pakistan, and Rockville, Maryland, USA: NIPS and ICF
14. Duley L. The global impact of pre-eclampsia and eclampsia. Semin perinatal 2009; 33 (3): 130-7
15. Magpie Trial Collaboration Group. Do women with pre-eclampsia and their babies benefit from magnesium sulphate? The Magpie Trial: a randomized placebo-controlled trial. The Lancet 2002; 359: 1877-1890
16. The Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from Collaborative Eclampsia Trial. The Lancet. 1995; 345: 1445-63
17. Duley L, Gulmezoglu AM, Henderson-Smart DJ, Chou D. Magnesium sulphate and other anticonvulsants for women with pre-eclampsia. Cochrane Database Syst Rev 2010; (11): CD 000025
18. Seth S, Nagrath A, Singh DK. Comparison of low dose, single loading dose and standard Pritchard regimen of magnesium sulphate in antepartum eclampsia. Anatol J Obstet Gynaecol 2010; 1:1
19. Ekele BA, Muhammad D, Bello LN, Namadina IM. Magnesium sulphate therapy in eclampsia: the Sokoto (ultrashort) regimen. BMC Res Notes 2009 Aug 19; 2: 165
20. Noor S, Halimi M, Faiz NR, Gull F, Akbar N. Magnesium sulphate in the prophylaxis and treatment of eclampsia. J Ayub Med Coll Abbottabad. 2004 Apr-Jun; 16 (2): 50-4
21. Dasgupta S, Sarkhel A, Jain A. Single loading dose of magnesium sulphate in severe pre-eclampsia and eclampsia-Is it effective? A randomized prospective study. Obstet Gynaecol Int J 2015, 2 (6): 00059
22. El-Khayat W, Atef A, Abdelatty S, El-Semary A. A novel protocol for postpartum magnesium sulphate in severe pre-eclampsia: a randomized controlled pilot trial. J Matern Fetal Neonatal Med 2014 (27): 1-5
23. Shoaib T, Khan S, Javed I, Bhutta SZ. Loading dose of magnesium sulphate versus standard regimen for prophylaxis of pre-eclampsia. J Coll Physicians Surg Pak 2009, 19 (1): 30-33
24. Begum MR, Begum A, Quadir E. Loading dose versus standard regimen of magnesium sulphate in the management of eclampsia: a randomized trial. J Obstet Gynaecol Res 2002, 28 (3): 154-159
25. Ehrenberg HM, Mercer BM. Abbreviated postpartum magnesium sulphate therapy for women with mild pre-eclampsia: a randomized controlled trial. Obstet Gynaecol 2006, 108 (4): 833-838
26. Darngawn L. Jose R, Regi A, Bansal R, Jeyaseelan L. A shortened postpsrtum magnesium sulphate prophylaxis regimenin pre-eclamptic women at low risk of eclampsia. Int J Gynaecol Obstet 2012, 116 (3): 237-239
27. Mala SB, Katz L, Neto CN, Calado BV, Azevedo AP, et al. Abbreviated (12-hour) postpartum magnesium sulphate therapy in severe pre-eclampsia. Int J Gynaecol Obstet 2014, 126 (3): 260-264
28. Shamsuddin L, Nahar K, Nasrin B, Nahar S, Tamanna S, et al. Use of parenteral magnesium sulphate in eclampsia and severe pre-eclampsia cases in a rural set up of Bangladesh. Bangladesh Med Res Counc Bull 2005, 31(2): 75-82
29. Regmi MC, Aggrawal A, Pradhan T, Rijal P, Subedi A, Uprety D. Loading dose versus standard regimen of magnesium sulphate in eclampsia- a randomized trial. Nepal Med Coll J 2010, 12 (4): 244-247
30. Shrestha A. Low dose magnesium sulphate in eclampsia. Nepal Med Coll J 2015, 17 (3-4): 136-140
31. Begum MR, Begum A, Johanson R, Ali MN, Akhtar SA. Low dose (Dhaka) magnesium sulphate regimen foe eclampsia. Acta Obstet Gynaecol Scand 2001, 80: 998-1002.