Original Article

Efficacy of Loading Dose of Magnesium Sulphate versus Standard Pritchard Regimen for Controlling of Fits in Eclampsia

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ABSTRACT

Objective: To determine the efficacy of loading dose of magnesium sulphate verses standard Pritchard regime for controlling of fits in eclampsia.

Study Design: Randomized controlled trial study

Place and Duration of Study: This study was conducted at the department of Obstetrics and Gynaecology Unit II Civil Hospital Karachi from July 2016 to December 2016 for a period of six months.

Materials and Methods: There were 132 women with antepartum, intrapartum and postpartum eclampsia irrespective of age, parity and gestational age were included in the study. Women with known case of epilepsy, space occupying lesion, magnesium sulphate sensitivity, renal failure, history of administration of magnesium sulphate prior to admission and those with contraindication of magnesium sulphate like myasthenia gravis were excluded. Women who fulfilled the inclusion and exclusion criteria were randomly allocated into two groups. Group A comprise of 66 women who received Standard Pritchard regimen (loading dose and maintenance dose). Group B also comprise 66 women who received only loading dose. The efficacy of drug i.e. occurrence of convulsion after completion of therapy was observed.

Results: The mean age of the participants in group A was 29±5.2 years and 27±3.6 years in group B. The average BMI in group A and group B was 28.51±1.6 kg/m^2 and 28.40±1.5 kg/m^2 respectively. Majority of the participants in group A were nulliparous 22(33.33%) and multiparous 28(42.42%) in group B. Postpartum eclampsia was observed in 49(37.1%), followed by antepartum 44(33%) and intrapartum 39(29.5%). Women who were treated with standard Pritchard regimen, fits was controlled in 62(93.94%) only 4(6.06%) had recurrence of convulsions while in loading dose group 8(12.12%) had recurrence of convulsions and 58(87.87%) women remained fits free. Single loading dose is equally effective as standard Pritchard regimen.

Conclusion: Magnesium sulphate is the most preferable drug for prevention and treatment of eclamptic patients. The single loading dose of magnesium sulphate is equally effective as standard Pritchard regimen in prevention of convulsions with the added advantage of reduced toxicity, fewer side effects and ease of monitoring.

Key Words: Eclampsia, Magnesium sulphate, standard Pritchard regime

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INTRODUCTION

Eclampsia is the occurrence of sudden onset of generalized tonic clonic seizures in a hypertensive woman after 20 weeks of pregnancy".[1]

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Globally it is a major cause of feto-maternal morbidity and mortality.[2] Currently, the incidence of eclampsia in United states and United Kingdom is 0.04 to 0.1%.[3] In comparison, the reported rate of eclampsia in developing countries is approximately 15%.[4] Worldwide, each year 50000 women died due to eclampsia and it accounts for 10% of maternal death in developed countries.[5] According to Tariq and Rehman and USA based studies, prevalence of preeclampsia and eclampsia in Pakistan and USA is 19% and 1-24% respectively.[6] Another study conducted which state that hemorrhage, hypertensive disorders and unsafe abortion are the three leading causes of direct maternal deaths and preeclampsia and eclampisa is account for 10 t0 25%.[7,8]

Since the publication of the collaborative multicentre study on eclampsia in 1995, the most preferable anticonvulsant drug for the treatment of eclampsia is

magnesium sulphate.[9] MgSO4 is also recognized by WHO and United Nations as a lifesaving drug for the management of preeclampsia and eclampsia.[10]

Currently standard intramuscular (IM) Pritchard regimen (1975) and intravenous Zuspan regimen (1978) are two common regimens which are in current used.[11] The dosage of magnesium sulphate as recommended by Pritchard is a loading dose of 4g intravenously and 10g intramuscularly; 5g on each buttock. This is followed by a maintenance dose of 5gm intramuscularly on alternate buttocks every 4 hours for up to 24 hours after delivery or last fit.[11-12.] There is a 25% risk of postpartum eclampsia especially during the first 12-24 hours therefore continue magnesium sulphate for 24 hours after last fit.[11-12]

It was observed in a study conducted in Jinnah postgraduate medical centre (JPMC) Karachi that maintenance therapy was not given to majority of patients due to risk of side effects and they did not develop any further convulsion. Several studies have been done on magnesium sulphate in terms of reducing dose and duration of treatment in order to avoid side effects, reduce costs and decrease patient discomfort.[13,14] Use of magnesium sulphate is not common due to its cost, non-availability and clinician's inexperience on its use.[15]

Currently there is only one study available at the local level and shows no significance difference in the effectiveness of either drug. We know that we are dealing with eclampsia frequently. This study will contribute the data in medical institute which may be helpful in selecting the better treatment option. The aim of this study is to improve the quality of treatment in our population.

MATERIALS AND METHODS

This is a prospective randomized controlled trial study conducted in the department of Obstetrics and Gynacology Unit II Civil Hospital Karachi from July 2016 to December 2016. Ethical approval was taken from College of Physicians and Surgeons Pakistan. There were 132 women with antepartum, intrapartum and postpartum eclampsia irrespective of age, parity and gestational age were included in the study. Women with known case of epilepsy, space occupying lesion, magnesium sulphate sensitivity, renal failure, history of administration of magnesium sulphate prior to admission and those with contraindication of magnesium sulphate like myasthenia gravis were excluded. Women who fulfilled the inclusion and exclusion criteria were randomly allocated into two groups by envelop method. Sample size calculated by using WHO statistical size calculator by using two proportion sample size formula. Proportion 1 for standard regime group (100%) proportion 2 for loading dose group (88%), assuming power 90% and 95% confidence interval sample size was calculated as 132 and randomized in two groups 66 in each group.

Group A comprise of 66 women who received Standard Pitchard regimen (loading dose and maintenance dose). Group B also comprise of 66 women who received only loading dose. Informed consent was taken from spouse or nearest family member. The efficacy of drug i.e. occurrence of convulsion after completion of therapy was observed and recorded in a self-designed proforma. Data was analyzed by using SPSS version 20. Mean and standard deviation calculated for age and BMI. Frequency and percentages were calculated for parity, types of eclampsia, number of fits and efficacy of drug. Chi square test was applied and P value <0.05 considered significant.

Loading Dose: Loading dose 4gram of Magnesium sulphate (MgSO4) diluted in 12cc distilled water slowly intravenously given in 15-20 mins plus 10g intramuscularly; 5g on each buttock.[11,12]

Pritchard Regime: loading dose 4gram of Magnesium sulphate (MgSO4) diluted in 12cc distilled water slowly intravenously given in 15-20 mins plus 10g intramuscularly; 5g on each buttock followed by a maintenance dose of 5gm intramuscularly on alternate buttocks every 4 hours for up to 24 hours after last fit.[11,12]

Null Hypothesis: There is no significant difference between two regimens.

Alternate Hypothesis: There is a significant difference between two regimens**.**

RESULTS

There were 132 women with eclampsia randomly allocated into two groups. Sixty six women were treated with loading and maintenance dose called group A and 66 were treated with loading dose only called group B. Mean age of the participants in group A was 29$\pm$5.2 years and 27$\pm$3.6 years in group B. The average BMI in group A and group B was 28.51$\pm$1.6 kg/m^2 and 28.40$\pm$1.5 kg/m^2 respectively. Majority of the participants in group A were nulliparous 22(33.33%) and multiparous 28(42.42%) in group B. Postpartum eclampsia was observed in 49(37.1%), followed by antepartum 44(33%) and intrapartum 39(29.5%). Most of the women 87(65.9%) presented with less than 3 episodes of fits and the median of fits of the patients was 2(IQR=1, range: 1-5). Demographic profile of patients is presented in table 1.

Efficacy of loading dose of magnesium sulphate verses standard pritchard regime for controlling of fits in eclampsia is shown in table 2. Women who were treated with standard Pritchard regimen, fits was controlled in 62(93.94%) only 4(6.06%) had recurrence of convulsions while in loading dose group 8(12.12%) had recurrence of convulsions and 58(87.87%) women remained fits free.

Table No.1: Demographic characteristics of participants n=132

Variable Age (Years)	Group A n=66	Group B n=66	Mean+-SD
<25	17 (25.75%)	26 (39.39%)	28.28+4.44
26-30	27 (40.9%)	36 (54.65%)	
31-35	22 (33.33%)	4 (6.05%)	
BMI (Kg/m2)			
<28	22 (33.33%)	22 (33.33%)	28.45+-1.60
28-30	32 (48.48%)	33 (50.0%)	
>30	12 (18.18%)	11 (16.66%)	
Parity			
Nulliparous	22 (33.33%)	18 (27.27%)	-
Primiparous	17 (25.76%)	16 (24.24%)	
Multiparous	18 (27.27%)	28 (42.42%)	
Grandmultiparous	09 (13.64%)	04 (6.05%)	
Type of Eclampsia			-
Antepartum	18 (27.27%)	26 (39.39%)	
Intrapartum	22 (33.33%)	17 (25.76%)	
Postpartum	26 (39.39%)	23 (34.85%)	
No of fits			
<3	44 (66.67%)	43 (65.15%)	-
>3	22 (33.33%)	23 (34.85%)	

Table No.2: Efficacy of standard Pritchard regimen versus loading dose n=132

Efficacy	Group A n=66	Group B n=66	P Value
No Convulsions	62 (93.94%)	58 (87.87%)	0.36
Recurrence Of convulsions	4 (6.06%)	8 (12.12%)	

DISCUSSION

Preeclampsia and eclampsia are main concern for obstetricians due to its associated complications. Worldwide, it is responsible for majority of maternal, fetal and neonatal death.[16]Preeclamptic women are receiving anticonvulsant drugs for centuries in the belief that they decrease the risk of convulsions and ultimately improve fetomaternal outcome.[17] In 1998 a systemic review of anticonvulsants[18] for women with pre-eclampsia identified four trials, comparing an anticonvulsant with placebo. The review concluded that the magnesium sulphate is the most preferable drug for women with eclampsia and better than diazepam[19], phenytoin or lytic cocktail. Routine use of Magnesium sulphate as an anticonvulsant in them management of pre-eclampsia started in 2002 after publication of Magpie trial[20]. In our study the average age of the patients was 28.28±4.44 years. We observed that the occurrence rates were highest in age group of 20-30 years in both the groups. Studies conducted by L Myatt[21] and S Latika[22] found that peak incidence of eclampsia in the same age group. Eclampsia is a disease of Primigravida. In our study 33.33% of the participants in group A and 27.27% in group B were nulliparous. In the study by Bangalet al[23] and Serdesai[24] et al in their studies observed eclampsia in Primigravida 80% and 79% respectively. Postpartum, antepartum and intrapartum eclampsia was observed in 37.1%, 33% and 29.5% respectively in our study. The study conducted by Bhattacharjee F et[25] al observed 43.74% cases of postpartum, 46.73% cases of intrapartum and 109.5% cases of antepartum eclampsia.

The average BMI in our study was 28.45kg/m^2. The risk of side effects or toxicity of MgSO4 depends on the Body mass index (BMI) as shown in the Tudela et al[26] and Jana et al[27] study and observed that women with having low BMI low dose MgSO4 (8g loading- 3g IV and 5g IM; followed by 2.5g IM 4 hourly) was effective regimen. They also observed that in comparison to Collaborative Eclampsia Trial the risk of recurrence convulsions and maternal mortality was also lower with low dose regimen.[27]

In our study efficacy of loading dose of magnesium sulphate verses standard pritchard regime for controlling of fits in eclampsia was nearly equal. We observed that in women with standard Pritchard regimen 93.94% women had control of convulsions only 6.06% had recurrence of convulsions while in women with only loading dose 87.87% had control of convulsions and recurrence of fits occurred in 12.12%. The study conducted by Talukdar RK et al[28] observed that out of 100 patients treated with Pritchard regimen, 3 patients had recurrence of convulsions, while patients treated with only loading dose of magnesium sulphate, not even a single patient had convulsion. Another study conducted by El-Khayatetal[29] in Egypt on postpartum preeclamptic women and reported that I/V loading dose might be a promising alternative regime. Another study conducted by Shoaib et al[30] reported that single loading dose of MgSO4 was preferred in terms of control of convulsions, efficacy, cost and ease of monitoring as compared to standard Pritchard regimen.

There are several studies have been done in favor of MgSO4 despite of this majority of eclamptic women in Primary health center do not receive MgSO4 as a first line drug for the control of convulsions. Most of the eclamptic women either receive no immediate treatment or health personnel administer other anticonvulsants like diazepam and then referred the patient to tertiary care centers for further management. The transportation of these highly irritable women in the third world countries, including Pakistan is not an easy task.[31] To improve fetomaternal outcome it is necessary that seizures should be controlled as soon as possible especially in Primary health care settings. There is a risk of 10% patients may develop further convulsions after receiving the loading dose. This recurrence may be acceptable. There is a need to trained midwives and nursing staff for monitoring and administration of MgSO4 as this achievement has definite implications

for care, especially in the low and middle-income countries[31].

CONCLUSION

Magnesium sulphate is the most preferable drug for prevention and treatment of eclamptic patients. The single loading dose of magnesium sulphate is equally effective as standard Pritchard regimen in prevention of convulsions with the added advantage of reduced toxicity, fewer side effects and ease of monitoring.

Author's Contribution:

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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