

Is Magnesium Sulphate more Effective than Placebo in Prevention of Seizure in Mild Preeclampsia? A Randomized Placebo-Controlled Clinical Trial

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Abstract

Aim: To evaluate the comparison between magnesium sulfate (MgSO₄) and placebo for prevention of seizures in mild pre-eclamptic patients. (Clinical trial code: 2016052111020).

Methods and material: This double blind randomized clinical trial study was conducted on 500 patients with mild Pre-eclampsia admitted in Arash Hospital in during 2014-2016. The patients entered to equal two groups, 250 patients in group A, received MgSO₄ and 250 patients in group Breceived Placebo. Primary outcome was occurrence of convulsion in mild pre-eclamptic patients. Secondary outcomes were 1 and 5 min Apgar scores in infants and number of caesarean section in each group.

Results: Mild pre-eclamptic patients in group A did not experience any convulsion; however 3 patients (1.2%) had experienced convulsion in group B. There were no significant differences in convulsion rate (p=0.08), one-min (p=0.43) and five-min Apgar score (p=0.34) between two groups but there was significant differences in numbers of caesarean section, 123 in group A (49.2%) versus 92 in group B (36.8%) between two groups (P=0.005).

Conclusion: Our results suggest that the magnesium sulfate and placebo groups are not statistically differ for prevention of seizure.

Keywords: Seizure; Convulsion; Mild pre-eclampsia; Magnesium sulphate

Introduction

Gestational hypertension and mild preeclampsia represent the most common medical complications of pregnancy [1]. Preeclampsia is characterized by the new onset of hypertension and proteinuria. Severe pre-eclampsia can involve several organs such as liver, kidneys, clotting system and brain [2-6]. Eclampsia refers to the occurrence of new-onset generalized tonic-clonic seizures in women with preeclampsia [7]. Pre-eclampsia and eclampsia are the second leading direct cause of maternal morbidity [8]. Eclampsia occurs in 2-3 percent of women with severe feature of preeclampsia that does not receive anti-seizure prophylaxis [4]. Many obstetricians administer intrapartum and postpartum seizure prophylaxis to all women with preeclampsia, based on randomized trials that demonstrated that magnesium sulfate reduced the risk of convulsion in preeclampsia [9,10]. The mechanisms that MgSO₄ is effective in prevention of convulsion in eclampsia are probably vasodilation and lowering of systemic blood pressure, protecting the blood-brain barrier (BBB) from cerebral edema [11-13]. Magnesium also may act by stimulating production of prostacyclin by endothelial cells causing vasodilation [7]. Several reports have suggested that gestation may influence vascular reactivity to MgSO₄ and that sensitivity varies with vascular bed [14,15]. In a meta-analysis of randomized trials of women with preeclampsia (any severity), magnesium sulfate was more effective for prevention of seizure than placebo or no treatment, and also was better than Phenytoin or an antihypertensive drug alone [16].

However, Because of seizure is an infrequent outcome in women with mild preeclampsia who do not receive seizure prophylaxis, American College of Obstetricians and Gynecologists [5] recommendations is that MgSO₄ not be administered universally in preeclamptic women with blood pressure of less than 160/110 mm Hg and with no maternal symptoms for the prevention of convulsion [5]. Our objective was to

compare the frequency of seizure in mild preeclamptic women who received MgSO₄ or placebo.

Materials and Method

After approval from ethics committee, present double blind randomized clinical trial study was conducted on pregnant women who admitted in Arash Hospital, Tehran, Iran during 2013-2016. Term primi-parous singleton mild preeclamptic women in ≥ 37 week gestational age were entered. Patients with the symptoms and signs of severe pre eclampsia such as organ damage and systolic blood pressure ≥ 160 mm Hg and/or diastolic blood pressure ≥ 110 mm Hg, heart disease, hypersensitivity to MgSO₄ and smoker patients, multi fetal patients, drug user's patients were excluded. According to inclusion criteria, patients were randomly entered into two groups. Group A received loading dose, 4 g, of 20% MgSO₄ in 100 ml of serum Ringer intravenously over 20-30 min followed by 2 g/h IV infusion. group B received 4 g of placebo included distilled water in the same shape in 100 ml of ringer intravenously over 20-30 min followed by 2 g/h IV infusion. Therapy was continued for 24 h post-partum or after last convulsion whichever was later. They were monitored every 4 h for

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presentation of patellar reflex, normal urine output and respiratory rate, systolic and diastolic blood pressure, laboratory data. Occurrence of convulsions, Apgar score at one and five minutes of fetus and the type of delivery were recorded as outcomes.

All data analyses were conducted using SPSS version 16.0 for windows (SPSS Inc., Chicago, IL, USA). Descriptive statistics for continuous variables were presented as mean \pm SD and for categorical variables as numbers (percentage). The baseline characteristics of the two groups were compared using independent t-test for continuous variables and the Chi-square test for categorical variables. Moreover, the convulsions between groups were compared using Chi-square test. The level of statistical significance was set at 0.05. All analyses were performed on an intent-to-treat basis. The conduct and analysis of the trial adhered to the 2010 CONSORT guidelines.

Results

Baseline and demographic characteristics are shown in Table 1. The mean age of group A was 22.32 ± 6.51 and the mean age of group B was 22.54 ± 5.58 . The mean gestational age of group A was 38.21 ± 1.10 and the mean gestational age of group B was 38.32 ± 1.41 . There were no statistically significant differences between two groups in maternal age and gestational age.

None of patients allocated in group A experienced convulsion. However among those treated with placebo, 3 patients (1.2%) progressed to eclampsia and experienced convulsion. There were not statistically significant differences between two groups (Table 1). The incidence of caesarean section was significantly greater in group A, 123 patients (49.2%) compared with group B, 92 patients (36.8%) ($P=0.005$) (Table 1). Neonates born to women in MgSO₄ group had similar mean Apgar scores at 1 minute (7.2 ± 1.2 versus 7.3 ± 1.1) ($p=0.43$) and 5 minutes (8.7 ± 0.5 versus 8.8 ± 0.4) ($p=0.34$) to those born to women assigned placebo (Table 1).

Discussion

In the present study, 3 (1.2%) seizures were happened in group B that received placebo. We found that the rate of caesarean section in group A was higher significantly than group B. One and five min Apgar scores were not different significantly between two groups. Although seizure is an infrequent outcome in women without severe features of preeclampsia, several studies demonstrated that magnesium sulfate treatment reduced the risk of convulsion in all women with preeclampsia [9].

Indeed one study has reported that a significant number of eclamptic women had either normal blood pressure or mild-to-moderate hypertension immediately before seizure and the findings are apparently in support of initiating MgSO₄ prophylaxis to all women with mild pre-eclampsia [17]. But Baha et al. represent that there are not acceptable benefit-to-risk ratio of administration of MgSO₄ for

prophylaxis in mild preeclampsia and routine use is not recommended [18]. Also Livingston and et al suggest that MgSO₄ did not prevent disease progression to severe preeclampsia and seizure in women with mild preeclampsia [19].

Roy et al. [8] considered to tocolytic effects of MgSO₄, reported that caesarean section rate increased significantly in administration of MgSO₄. In our study the rate of caesarean section in MgSO₄ group was higher significantly than placebo group. Similar to our study in Livingston study neonates born from women assigned MgSO₄ had similar mean Apgar scores at 1 and 5 min as those born to women assigned placebo [19].

Conclusion

There are not statistically significant different between MgSO₄ and placebo for prevention of seizure in mild preeclampsia, but in practice may be included many variables for making decision. We recommend further studies with larger sample size and more accurate methods.

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	Group A (n=250)	Group B (n=250)	P-value
Age (years)	22.32 \pm 6.51	22.54 \pm 5.58	0.62
BMI	24.38 \pm 2.72	24.68 \pm 2.74	0.27
Gestational age (Week)	38.21 \pm 1.10	38.32 \pm 1.41	0.31
Apgar 1min	7.2 \pm 1.2	7.3 \pm 1.1	0.43
Apgar 5min	8.7 \pm 0.5	8.8 \pm 0.4	0.34
convulsion	0 (0%)	3 (1.2%)	0.08
Cesarean section	123 (49.2%)	92 (36.8%)	0.005

Values given as mean \pm SD or number (percentage) unless otherwise indicated

Table 1: Baseline demographics and outcomes.

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