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Original Research Article

A prospective randomised study comparing intermittent intramuscular regimen and intravenous infusion regimen of magnesium sulfate in the treatment of severe preclampsia and eclampsia

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ABSTRACT

Background: Eclampsia and preeclampsia are important causes of mortality during childbirth and puerperium. Commonly used regimens of magnesium sulfate are i.m. Pritchard regimen and i.v. zuspan regimen. This study was done with aim to compare the efficacy of i.m. regimen with i.v. regimen for prevention and recurrence of seizures.
Methods: This study was carried out in the department of obstetrics and gynaecology, in a medical college in north India. 88 patients presenting with pre-eclampsia and eclampsia were included. Duration of the study was 18 months (from 1st October 2017-31st March 2019). The patients enrolled were classified randomly into two groups, group A and group B. Our target was to include 50 patients in both groups but few patients left against medical advice and not all patients met inclusion criteria group A was given the following regimen- loading dose of magnesium sulfate 4 gm $MgSO_4$ in 12 ml normal saline slow intravenous infusion in 10-15 minutes and 5 gm $MgSO_4$ deep intramuscular route each buttock, then maintenance dose of magnesium sulfate 5 gm alternate buttock group B was given- loading dose of magnesium sulfate 4 gm $MgSO_4$ in 12 ml normal saline slow i.v. infusion in 10-15 minutes then maintainence dose of magnesium sulfate i.v infusion 1 gm/hr.
Results: There was no significant difference between serum Mg^{2+} levels measure at 0 hours (baseline), 2 hours, 4 hours, 6 hours and 8 hours after administration of loading dose in both groups.
Conclusions: The intermittent i.m. regimen and i.v. infusion regimen are comparable in terms of recurrence and prevention of seizure, maternal and neonatal outcome.

Keywords: Eclampsia, Magnesium sulfate, Preeclampsia, Pritchard, Zuspan

INTRODUCTION

Magnesium Sulfate is the mainstay of prevention and recurrence of convulsions in preeclampsia and eclampsia respectively.[1]

Hypertensive disorders complicate 5 to 10 percent of all pregnancies and together they are one member of the deadly triad along with hemorrhage and infection that contribute greatly to maternal morbidity and mortality.[2]

According to WHO high blood pressure during pregnancy was one of the major direct causes of maternal deaths globally and its contribution in 2014 was 14 %.[3]

A major breakthrough happened when J. A. Pritchard introduced his standardized treatment protocol in 1984. His protocol for management is popularly known as the Pritchard regimen.[3]

Owing to the experience of its uses and its relative safety for both the mother and her infant.

Our primary objective was to assess and compare the efficacy of i.m. regimen and i.v. regimen of magnesium sulfate in prevention and control of convulsions by following parameters: Prevention of convulsions in severe preeclampsia and recurrence in eclampsia, serum magnesium levels in two groups (group A and group B). Our secondary objective was to report maternal outcome in the form of mode of delivery and perinatal outcome in the form of incidence of neonatal outcome and admissions to NICU.

METHODS

This prospective randomised study was carried out in department of obstetrics and Gynaecology, Mata Gujri Memorial Medical College and Lions Seva Kendra, Kishanganj.

It was a tertiary referral centre and serves people of poor socio-economic status.

Duration of the study was 18 months (from 1st October 2017-March 31st 2019).

The patients enrolled were classified randomly into two groups, group A and group B. Initially our target was to include 50 patients in both groups but few patients left against medical advice and not all patients met our inclusion criteria therefore in our study a number of 44 patients were enrolled.

Group A- loading dose of magnesium sulfate 4 gm $MgSO_4$ in 12 ml normal saline slow intravenous infusion in 10-15 minutes and 5 gm $MgSO_4$ deep intramuscular route each buttock, then maintenance dose of magnesium sulfate 5 gm $MgSo_4$.

Group B- loading dose of magnesium sulfate 4 gm $MgSO_4$ in 12 ml normal saline slow i.v. infusion in 10-15 minutes then maintainence dose of magnesium sulfate 1 gm/hr.

Statistical analysis

Z test was used for comparison of sample means of group A and group B for parametric data with sample size 44 (n>30) and Z test for comparison of sample proportions. Chi square test was used for test of association. P value <0.05 will taken as a level of statistically significant difference.

RESULTS

Age, weight and BMI of patients in group A (i.m. group) and B (i.m. group)

In our study the mean study the age in group A (i.m. group) and group B (i.v. group) were 22.95±1.97 years and 23.36±2.14 years respectively (p value 0.3524), mean BMI in i.m. group and i.v. group was 26.32±1.26 and 26.2±1.2 years respectively (p value 0.6241).

Table 1: Age, weight and BMI of patients in group A (i.m. group) and B (i.m. group).

Parameters	Group A	Group B	P value
	Mean±SD	Mean±SD	
Age	22.95±1.97	23.36±2.14	0.3524
Weight	56.006±2.76	56.775±2.12	0.1441
BMI	26.32±1.26	26.2±1.21	0.6241

Blood pressure in group A and group B

According to our study mean systolic blood pressure (SBP) in group A (i.m. group) and group B (i.v. group) was 172.045±14.876 and 170.954±14.273 mmHg respectively (p value 0.7696), the mean diastolic blood pressure (DBP) in i.m. and i.v. group was 110.45±8.61 mmHg and 109.09±8.01 respectively (p value=0.443).

Table 2: Blood pressure in group A and group B.

Parameters	Group A	Group B	P value
	Mean±SD	Mean±SD	
SBP	172.04±14.87	172.95±14.27	0.7697
DBP	110.45±8.61	109.09±8.01	0.443

Gestational age in group A and group B

According to study, the mean gestational age in group A (i.m. group) and group B (i.v. group) was 36.63±1.76 weeks and 36.89±1.68 and weeks respectively (p value =0.4776).

Table 3: Gestational age in group A and group B.

Parameters	Group A	Group B	P value
	Mean±SD	Mean±SD	
Gestational age	36.63±1.76 weeks	36.89±1.61 weeks	0.4776

Serum magnesium levels in group A and group B

Drug concentration levels of magnesium sulphate in our study serum levels did not reach toxicity levels, signs of impending magnesium toxicity were not seen.

Table 4: Serum magnesium levels in group A and group B.

Parameters	Group A	Group B	P value
	Mean±SD	Mean±SD	
S. Mg 0 hours	1.91±0.28	2.0±0.20	0.1175
S. Mg 2 hours	3.09±0.81	2.83±0.45	0.0697
S. Mg 4 hours	2.94±0.46	3.11±0.38	0.0718
S. Mg 6 hours	3.17±0.65	3.30±0.54	0.3238
S. Mg 8 hours	3.20±0.51	3.34±0.49	0.1762

In our study there was no significant difference between serum Mg^{2+} levels measured at 0 hours (baseline) p value

value 0.1175, 2 hours p value 0.0697, 4 hours p value 0.718, 6 hours p value 0.3283 and 8 hours p value 0.1762.

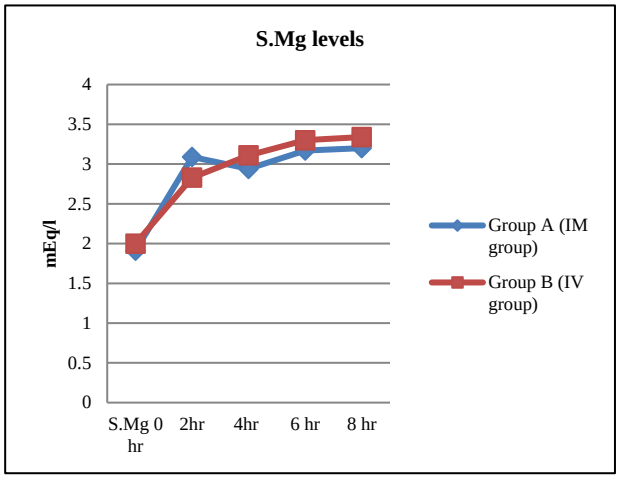

Figure 1: Graph depicting serum magnesium levels.

Serum creatinine levels in group A and group B

Serum creatinine in group A (i.m. group) was 1.0±0.17 and in group B (i.v. Group) was 0.99±0.19 mg/dl, p value 0.7947.

Table 5: Serum creatinine levels in group A and group B.

Parameters	Group A	Group B	P value
	Mean±SD	Mean±SD	
Serum creatinine	1.0±0.17	0.99±0.19	0.7947

Booking status in group A and group B

In i.m. group booked and unbooked patients 6 and 38 respectively in group A (IM group) and 7 and 37 in and group B (i.v. group), p value 0.763851.

Table 6: Booking status in group A and group B.

Group	Booked	Unbooked	P value
A	6	38	0.763851
B	7	37	

Mode of delivery in group A and group B

The number of vaginal deliveries in i.m. and i.v group were 36 and 38 respectively and lower segment caesarean section were 8 and 6 respectively (p value 0.3780).

Table 7: Mode of delivery in group A and group B.

Group	LSCS	VD	P value
A	8	36	0.378
B	6	38	

NICU admission in group A and group B

In our study the no. of NICU admissions in i.m. and i.v. group were 37 and 39 respectively (p value =0.5352) and number of early neonatal deaths were 06 and 05 respectively (p value =0.74896) and 01 still birth was seen in patient in i.m. group (p value =0.3125).

Table 8: NICU admission in group A and group B.

	Group A	Group B	Z value	P value
NICU admissions	37	39	0.6213	0.53526
Early neonatal death	06	05	0.3223	0.74896
Still birth	01	00	1.0057	0.3125

Maternal morbidity in group A and group B

Maternal morbidity in our study, postpartum occurred in 3 patients in i.m. group and 4 patietns of i.v. group p value 0.6965, obstructed labour was seen in 1 patient of i.m. and i.v. group each (p value =1). ICU admission was seen in 1 patient of i.m. group (p value 0.3125), recurrence of seizure in eclampsia was seen in 2 patients of i.m. group and 1 patient of i.v. group, pulmonary edema was seen in 1 patient of i.m. group (p value 0.3125).

Table 9: Maternal morbidity in group A and group B.

	Group A	Group B	Z value	P value
PPH	3	4	-0.394	0.69654
Obstructed labour	1	1	0	1
ICU admissions	1	0	1.0057	0.3125
Recurrence	2	1	0.5875	0.5552
Pulmonary edema	1	0	1.0057	0.3125

Table 10: Number of patients included in the study.

	I.M. group	I.V. group
Total no. of patients	60	60
Leave against medical advice	6	7
Did not give consent	5	5
Did not meet inclusion criteria	5	4
Net sample of patients	44	44

DISCUSSION

We compared our findings with similar studies done previously and made the following observations.

In a study done by Kanti et al, the mean age in i.m. group and i.v. group was 25.7±4.24 years and 25.8±3.72 years respectively (p value=0.934). Mean BMI in i.m. group and i.v. group was 22.5±1.74 and 23.2±3.38 respectively (p value 0.209) and mean weight in i.m. and i.v. group was 51.4±4.46 and 52.4±5.81 kg respectively (p value =0.397).[3]

In a study done by Singh et al, the mean age in i.m. group and i.v. group was 20.38±2.02 years and 20.16±1.43 years respectively (p value =0.533). Mean BMI in i.m. group and i.v. group was 22.5±3.09 and 22.49±3.09 respectively (p value =0.99) and mean weight in i.m. and i.v. group was 46.84±4.84 and 45.66±4.88 kgrespectively (p value =0.228).[4]

In a study done by Singh et al, the mean age in control group, i.m. group and i.v. group (Sibai i.v. regimen) was 24.17±4.04 years, 23.65±3.94 and 23.51±4.04 years respectively.[5]

In our study the mean study the age in group A (i.m. group) and group B (i.v. group) were 22.95±1.97 years and 23.36±2.14 years respectively (p value 0.3524), mean BMI in i.m. group and i.v. group was 26.32±1.26 and 26.2±1.2 years respectively (p value 0.6241).

In a study done by Kanti et al, the mean SBP in i.m. group and i.v. group was 174.44±12.97 and 173.22±14.81 respectively, (p value =0.693). Mean DBP in i.m. group and i.v. group was 110.98±10.48 and 110.24±7.58 respectively (p value =0.718).[3]

In a study done by Singh et al, the mean SBP in i.m. group and i.v. group was 174.00±11.2 and 170.68±9.83 respectively (p value =0.751), mean DBP in i.m. group and i.v. group was 108.84±6.68 and 110.28±6.59 respectively. (p value =0.281).[4]

In a study done by Singh et al, the mean DBP in control group, i.m. group and i.v. group (Sibai i.v. regimen) was 74.17±4.04 years, SBP was 112.17±12.66 and 111.48±12.29 years respectively.[5]

In our study mean systolic blood pressure (SBP) in group A (i.m. group) and group B (i.v. group) was 172.045±14.876 and 170.954±14.273 mmHg respectively (p value 0.7696), the mean diastolic blood pressure (DBP) in i.m. and i.v. group was 110.45±8.61 mmHg and 109.09±8.01 respectively (p value=0.443).

In a study done by Kanti et al, the mean gestational age in i.m. group and i.v. group was 35.5±3.07 weeks and 36.0±3.00 weeks respectively (p value =0.383).[3]

In a study done by Singh et al, the mean gestational age in i.m. group and i.v. group was 35.92±1.65 weeks and 36.18±1.73 weeks respectively.[4]

In a study done by Verma et al, the mean gestational age in i.m. group and i.v. group was 35 weeks and 36 weeks respectively.[6]

In our study, the mean gestational age in i.m. group and i.v. group was 36.63±1.76 weeks and 36.89±1.68 weeks respectively (p value =0.4776).

As per study done by Kanti et al, number of unbooked patients in i.m. and i.v. group were 5 and 7 respectively and number of booked patients were 36 and 34 respectively (p value =0.532).[3]

As per study done by Singh et al no. of unbooked patients in i.m. and i.v. group were 2 in each group, and number of unbooked patients were 48 each (p value =1.0).[4]

As per study done by Verma et al number of unbooked patients in i.m. and i.v. group were 3 in and 2 respectively, and number of booked patients were 47 and 48 respectively.[6]

As per study i.m. group booked and unbooked patients 6 and 38 respectively and in i.v. group 7 and 37 respectively, p value 0.763851.

As per study done by Kanti et al number of vaginal deliveries in i.m. and i.v. groups were 31 and 28 respectively and LSCS were 10 and 13 respectively (p value 0.461).[3]

As per study done by Singh et al number of vaginal deliveries in i.m. and i.v. groups were 25 and 21 respectively and LSCS were 25 and 29 respectively (p value 0.422).[4]

As per study done by Verma et al number of vaginal deliveries in i.m. and i.v. groups were 25 and 20 respectively and LSCS were 25 and 30 respectively.[6]

In our study number of vaginal deliveries in i.m. and i.v. groups were 36 and 38 respectively and LSCS were 8 and 6 respectively (p value =3780).

As per study done by Kanti et al, number of NICU Admissions in i.m. and i.v. group were 9 and 10 respectively (p value =0.951).[3]

As per study done by Singh et al number of NICU admissions in i.m. and i.v. group were 10 and 14 (p value =0.603) respectively, and number of early neonatal deaths were 8 and 10 respectively (p value =0.603) and stillbirth +IUD were 18 and 17 (p value =0.834).[4]

As per study done by Verma et al number of NICU admissions in i.m. and i.v. group were 12 and 16 respectively and number of early neonatal deaths were 24 and 29 respectively.[6]

In our study number of NICU admissions in i.m. and i.v. group were 37 and 39 respectively and number of early neonatal deaths were 06 and 05 respectively and still birth was seen in 1 patient in i.m. group.

As per study done by Kanti et al the number of patients that developed loss of patellar reflex in i.m. and i.v. group were 10 and 3 respectively (p value =0.034) decrease in urine output was seen in 4 and 2 patients respectively (p value =0.396). Respiratory rate <16/minute was seen in 1 patient of i.m. group (p value =0.314). Local site complication was seen in 1 patient of i.m. group (p value =0.314).[3]

As per study done by Singh et al loss of knee jerk in i.m. and i.v. group was seen in 7 and 1 patients respectively (p value =0.027), oliguria in 5 and 2 patients respectively (p value =0.240) and respiratory rate <12/minute was seen in 2 patients of i.m. group only (p value =0.153).[4]

As per study done by Verma et al loss of knee jerk in i.m. and i.v. group was seen in 5 and 1 patients respectively, oliguria was seen in 6 and 1 parents respectively and respiratory depression was seen in 2 patients of i.m. group.[6]

In our study, serum magnesium levels did not reach toxicity level, signs of impending of magnesium sulfate toxicity were not seen.

According to a study done by Kanti et al complications during delivery (PPH and Abruption) in i.m. and i.v. group were 7 and 6 respectively (p value =0.762), other complications (ARF, PE) were 7 and 4 respectively (p value = 0.331), ICU admissions occurred in 1 patient in i.m. group (p value =0.314) and mortality was seen in 1 patient of i.m. group (p value =0.314), recurrence of seizure was seen in 1 patient each of i.m. and i.v. group (p value =1.0).[3]

According to a study done by Singh et al hemorrhage in i.m. and i.v. group was seen in 3 and 4 patients respectively (p value =0.695), pulmonary edema in 8 and 3 patients respectively (p value =0.110), renal failure in 3 and 2 patients (p value =0.646), DIC was seen in 2 and 1 patients respectively (p value =0.558), HELLP syndrome was seen in 2 and 1 patients respectively (p value =0.558).[4]

According to study by Verma et al hemorrhage in i.m. and i.v. group was seen in 4 patients in each group, pulmonary edema in 2 patients in each group, renal failure in 6 and 2 patients respectively, HELLP syndrome was seen in 1 patient in each group.[6]

In our study, PPH occurred in 3 patients of i.m. group and 4 patients of i.v. group (p value 0.6965), obstructed labour was seen in 1 patient of i.m. and i.v. group each (p value =1). ICU admission was seen in 1 patient of i.m. group (p value =0.3125), recurrence of seizures in eclampsia patients was seen in 2 patients of i.m. group and 1 patient of i.v. group, pulmonary edema was seen in 1 patient of i.m. group (p value =0.3125).

In another study in i.m. regimen and i.v. regimen (Sibai) there was statistically significant difference in the mean serum Mg^{2+} at 4 hours (p value <0.001) after magnesium sulfate therapy, however after 8, 12, 16, 24 and 32 hours of therapy, the difference between mean serum magnesium levels in the group were statistically insignificant (p value >0.05).[5]

In our study there was no significant difference between serum Mg^{2+} levels measured at 0 hours (baseline) (p value =0.1175), 2 hours (p value 0.0697), 4 hours (p value 0.718), 6 hours (p value 0.3283) and 8 hours (p value 0.1762) after administration of loading dose (group A- i.m. regimen and group B- i.v. regimen).

In our study sample size is limited, duration is one and half years. The incidence of severe preeclampsia and eclampsia is low. So establish statistical significance in serum magnesium levels and maternal and neonatal outcomes a larger sample size is required

CONCLUSION

In our study there was no significant difference in serum magnesium levels measured at 0 hours, 2 hours, 4 hours, 6 hours, 8 hours after administration of loading dose. In our study signs of impending magnesium toxicity were not seen. The total dose given in 24 hours in i.m. group was 38 gm magnesium sulfate and in i.v. group was 24 gm magnesium sulfate. There was no significant difference in neonatal outcome and maternal morbidity in i.m. and i.v groups.

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