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Study of the role of low dose magnesium Sulphate in Hypertensive Disorders of Pregnancy

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Abstract :

Objectives : To study the efficacy and safety of low dose magnesium sulphate in prevention and treatment of eclamptic convulsions and to compare it with the standard regimen.

Methodology : This is a prospective observational study conducted in St.Martha's hospital, Bangalore. Patients with eclampsia, impending eclampsia and severe preeclampsia were administered low dose magnesium sulphate. Comparative analysis with standard regimen was done to assess the maternal & perinatal outcomes.

Results : Total number of deliveries during the study period was 1622, out of which 9 patients had eclampsia, 32 patients had impending eclampsia and 48 patients had severe preeclampsia. 50% of eclampsia patients received < 6 doses of magnesium sulphate, while none received > 24 doses. 77.4% of impending eclampsia cases received < 12 doses and 9.7% received > 24 doses. 71.4% of severe preeclampsia cases received <12 doses and none received > 24 doses. Only 7 patients lost knee jerk and serum magnesium was checked in 2 cases, and was found to be within therapeutic range. None had convulsion or recurrence.

Conclusion : Low dose magnesium sulphate is effective in preventing the onset and recurrence of convulsion in hypertensive disorders of pregnancy. Clinical monitoring for magnesium toxicity is sufficient. Hence low dose magnesium sulphate regimen is safe, which suits Indian women who have relatively low body mass index as compared to their western counter parts.

Key Words : Low dose magnesium sulphate, convulsion, eclampsia. impending eclampsia and severe preeclampsia.

Introduction :

Hypertensive disorders complicating pregnancies is one of the leading causes of maternal and perinatal morbidity and mortality[1].The incidence of eclampsia in developing countries ranges from 1:100 to 1:1700 pregnancies which contributes to 8% of maternal death and 33.98% perinatal deaths. This is much higher compared to developed countries[2].The incidence of eclampsia is often viewed as index of civilization[3]. The main objective of management of eclampsia is to control the convulsions and termination of pregnancy[4].

CET[5] (Collabarative Eclampsia Trial), a large multicentre trial done in 25 developing countries found magnesium sulphate to be a better drug for controlling and preventing convulsion. Indian women are smaller in built. Indian women from lower socioeconomic groups weigh much less than their counterparts in western world[6]. Hence low dose magnesium sulphate may be equally effective in with significant reduction in toxicity of the drug as well. Clinical monitoring appears to be sufficient which can reassure health professionals at primary and secondary level hospital about the safety of this drug.

WHO has recommended that both the intramuscular and intravenous regimens can be used. Intramuscular administration is associated with greater fluctuation in serum magnesium levels than intravenous route. Intramuscular route may be associated with pain and infection at the site. Intravenous route is associated with less side effects.

Methodology :

This prospective observational study was conducted in the department of Obstetrics and Gynecology, Bangalore for a period of one year from June 2011 to May 2012. Total of 50 patients who satisfied the criteria for severe preeclampsia, imminent eclampsia and eclampsia were selected. Magnesium sulphate was administered according to Suman Sardesai (low dose) regimen[7].

Detailed history of patient was taken. In case of eclampsia, the level of consciousness, orientation, pallor, pulse and blood pressure was checked. Loading

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dose of 4 grams of magnesium sulphate was given over 3-5 minutes. Patients were catheterized and albuminuria was checked. Rest of the clinical examination was done. Maintenance dose of intravenous magnesium sulphate 2 grams was given if

1. Patellar reflex were present
2. Respiratory rate was normal
3. Urine output was at least 100 ml in preceding 4 hours.

This maintenance dose was continued for 48 hours and was stopped if patients remained undelivered or continued for 24 hours after delivery

Patients were started on antihypertensive therapy depending on the blood pressure. 2 Intramuscular doses of 12 mg of Betamethasone (24 hours apart) was given if gestational age was less than 34 weeks. Blood, urine investigations and fundoscopy were done. Cardiotocography and ultrasonography were done whenever found necessary.

Induction of labor was done and labor was monitored. Decision for cesarean delivery was taken as per the maternal and fetal indications. All neonates were attended by pediatricians.

Magnesium sulphate was continued upto 24 hours after delivery. In case of postpartum eclampsia, the low dose regimen was started and continued for 24 hours after the convulsions.

Observation & Results :

During the study period of one year from June 2011 to May 2012, total number of deliveries in the hospital was 1622. The number of eclampsia, impending eclampsia and severe preeclampsia were 9, 32 and 48 respectively, with incidence of 5.5%, 19.7% and 29.6% respectively. The study group included 50 patients, out of whom 7(14%) cases had eclampsia, 32(64%) cases had impending eclampsia and 11(22%) cases had severe preeclampsia.

Table 1: Total dose of magnesium sulphate before delivery

		EIESE			
		E	IE	SE	Total
Magnesium Sulpate Treatment (dose) 1 maintainence Dose=2g 1loading dose=4g	1- 6 times	3 50.0%	12 38.7%	1 14.3%	16 36.4%
	7-12 times	2 33.3%	12 38.7%	4 57.1%	18 40.9%
	13-18 times	1 16.7%	4 12.9%	2 28.6%	7 15.9%
	>24 times	0 .0%	3 9.7%	0 .0%	3 6.8%
Total		6 100.0%	31 100.0%	7 100.0%	44 100.0%

50% (3 patients) of eclampsia group, 38.7% (12 patients) of impending eclampsia group and 14.3% (1 patient) of severe preeclampsia group received < 6 doses of magnesium sulphate before delivery.

33.3% (2 patients) of eclampsia group, 38.7% (12 patients) of impending eclampsia group and 57.1% (4 patients) of severe preeclampsia group received between 7-12 doses of magnesium sulphate before delivery.

16.7% (1 patient) of eclampsia group, 12.9% (4patients) of impending eclampsia group and 28.6% (2 patients) of severe preeclampsia group received between 13-18 doses of magnesium sulphate before delivery.

Only 9.7% (3 patients) of impending eclamptic cases received >24 doses of magnesium sulphate before delivery.

Table 2: Mode of onset of Labour

		EIESE			
		E	IE	SE	Total
Labour	Induced	3 75.0%	24 85.7%	7 87.5%	34 85.0%
	Spontaneous	1 25.0%	4 14.3%	1 12.5%	6 15.0%
Total		4 100.0%	28 100.0%	8 100.0%	40 100.0%

75% (3) of eclampsia patients, 85.7% (24) of impending eclampsia patients and 87.5% (7) of severe preeclampsia patients were induced for delivery.

25% (1) of eclampsia, 14.3% (4) of impending eclampsia and 12.5% (1) of severe preeclampsia patients had a spontaneous onset of labor. Labor was induced with oral or vaginal misoprostal and cerviprime gel.

Table 3: Induction Delivery Interval

		EIESE			
		E	IE	SE	Total
Induction Delivery Interval	<12 hrs	2	5	3	10
		40.0%	22.7%	37.5%	28.6%
	12-24 hrs	2	9	2	13
		40.0%	40.9%	25.0%	37.1%
	24-72 hrs	0	5	3	8
		.0%	22.7%	37.5%	22.9%
	>72 hrs	1	3	0	4
		20.0%	13.6%	.0%	11.4%
Total		5	22	8	35
		100.0%	100.0%	100.0%	100.0%

40% (2) of patients in eclampsia group, 22.7% (5) patients of impending eclampsia group and 37.5% (3) patients of severe pre eclampsia group delivered within 12hrs of induction. 40% (2) patients of eclampsia group, 40.9% (9) patients of impending eclampsia group and 25% (2) patients of severe preeclampsia group delivered between 12- 24 hrs of induction. 22.7% (5) patients of impending eclampsia group and 37.5% (3) patients of severe preeclampsia group delivered between 24-72hrs of induction.

20% (1) patients of eclampsia group and 13.6% (3) patients of impending eclampsia group delivered after 72hrs of induction.

Table 4: Indications for caesarean section

Indication	E	IE	SE
NRCTG	2	5	2
Failure to progress	-	2	-
Failed induction	-	3	1
Breech presentation/ Transverse lie	-	2+1	-
Previous lscs not willing for VBAC	-	2	-

The most common indication for LSCS was non reactive CTG.

Table 5: Mode of Delivery

		EIESE			
		E	IE	SE	Total
Mode of Delivery	Term Vaginal Delivery Two vacuum delivery	0	5	0	5
		.0%	15.6%	.0%	10.2%
	Preterm Vaginal Delivery One outlet forceps delivery	3	11	8	22
		50.0%	34.4%	72.7%	44.9%
	Term caesarena section	1	7	1	9
		16.7%	21.9%	9.1%	18.4%
	Preterm caesarean section	1	6	2	9
		16.7%	18.8%	18.2%	18.4%
	abortion	1	3	0	4
		16.7%	9.4%	.0%	8.2%
Total		6	32	11	49
		100.0%	100.0%	100.0%	100.0%

50% (3) patients of eclampsia, 34.4% (11) patients of impending eclampsia and 72.7% (8) patients of severe preeclampsia ended up with preterm vaginal delivery.

16.7% (1) patients of eclampsia, 18.8% (6) patients of impending eclampsia and 18.2% (2) patients of severe preeclampsia required preterm caesarean section.

15.6% (5) patients of impending eclampsia had term vaginal delivery and 9.4% (3 patients) aborted.

16.7% (1) patients with eclampsia, 21.9% (7) patients with impending eclampsia and 9.1% (1) patients of severe preeclampsia had term caesarean section.

16.7% (1) patients in eclampsia group and 9.4% (3) patients in impending eclampsia group had abortion between 24-25weeks.

Table 6: First Convulsion-delivery Interval

< 6 HOURS	2
6-24 HOURS	2
24-48 HOURS	1
> 48HOURS	1

In only 1 patient of eclampsia group delivery was prolonged for more than 48 hrs from the onset of first convulsions.

Table 7: Third Stage Complication

		EIESE			
		E	IE	SE	Total
III stage Complication	No complication	6	30	9	45
		100.0%	93.8%	81.8%	91.8%
	Atonic PH	0	2	2	4
		.0%	6.3%	18.2%	8.2%
Total		6	32	11	49
		100.0%	100.0%	100.0%	100.0%

6.3% (2) patients in impending eclampsia group and 18.2% (2) patients in severe pre-eclampsia group had atonic postpartum hemorrhage.

Table 8: Maternal Outcome

		EIESE			Total
		E	IE	SE	
Maternal Outcome	Good	4	29	8	41
		57.1%	90.6%	72.7%	82.0%
	Anemia	1	2	2	5
		14.3%	6.3%	18.2%	10.0%
	Recurrrent Convulsion	1	0	0	1
		14.3%	.0%	.0%	2.0%
	Pres Syndrome	1	0	0	1
		14.3%	.0%	.0%	2.0%
	UTI	0	1	1	2
		.0%	3.1%	9.1%	4.0%
Total		7	32	11	50
		100.0%	100.0%	100.0%	100.0%

There was no maternal mortality. Only 1 patient (14.3%) of eclampsia group had recurrent convulsion (1episode) within 10mins of giving magnesium sulphate loading dose. 1 patient (14.3%) in eclampsia group had posterior reversible encephalopathy syndrome. 1 each from impending eclampsia (3.1%) group and severe preeclampsia group (9.1%) had urinary tract infection.

1 patient (14.3%) of eclampsia group, 2 patients (6.3%) of impending eclampsia group and 2 patients (18.2%) of severe preeclampsia group had anemia.

Table 9: Neonatal Complication

		EIESE			Total
		E	IE	SE	
Neonatal Outcome	Jaundice	1	4	1	6
		16.7%	13.3%	9.1%	12.8%
	Flabby+Hypocalcemia	0	1	0	1
		.0%	3.3%	.0%	2.1%
	FSB	0	3	3	6
		.0%	10.0%	27.3%	12.8%
	Good	2	14	3	19
		33.3%	46.7%	27.3%	40.4%
	LBW	1	0	0	1
		16.7%	.0%	.0%	2.1%
	MSB	0	1	1	2
		.0%	3.3%	9.1%	4.3%
	Respiratory Distress	0	4	1	5
		.0%	13.3%	9.1%	10.6%
	Sepsis	2	1	1	4
		33.3%	3.3%	9.1%	8.5%
	NND	0	1	0	1
		.0%	3.3%	.0%	2.1%
	NEC	0	0	1	1
		.0%	.0%	9.1%	2.1%
	Birth Asphyxia	0	1	0	1
		.0%	3.3%	.0%	2.1%
Total		6	30	11	47
		100.0%	100.0%	100.0%	100.0%

Jaundice was seen in 12.8% (6) of babies, hypocalcaemia in 2.1% (1), respiratory distress in 10.6% (5), sepsis in 8.5% (4), necrotizing enterocolitis in 2.1% (1) and birth asphyxia in 2.1% (1). Of all 2.1% of babies (1) died in the neonatal period.

Discussion :

This study was conducted in St. Martha's Hospital on 50 cases of severe preeclampsia, impending eclampsia and eclampsia

The total number of deliveries during study period was 1622, out of which 9 patients had eclampsia, 32 patients had impending eclampsia and 48 patients had severe preeclampsia. The incidence (per 1000) of eclampsia, impending eclampsia and severe preeclampsia was 5.5%, 19.7% and 29.59% respectively.

The study group included 7 cases of eclampsia, 32 cases of impending eclampsia and 11cases of severe preeclampsia.

Low dose magnesium sulphate therapy was started according to Suman Sardesai regimen. The dose is less than half of standard Pritchard regimen[8] in which loading dose of 4 grams of 20% magnesium sulphate is administered intravenous followed by maintenance dose of 50% magnesium sulphate intramuscular every fourth hourly after checking for magnesium toxicity.

50% of eclampsia patients received less than 6 (2grams) doses of magnesium sulphate following loading dose of 4 grams intravenous 50% magnesium sulphate and none required more than 18 doses. 38.7% and 9.7% of impending eclampsia patients received less than 6doses and more than 24 doses of magnesium sulphate respectively and 14.3% of severe preeclampsia patients received less than 6 doses of intravenous 20% magnesium sulphate. However none required more than 18 doses.

One patient in eclampsia group received magnesium sulphate second time (one day later), as she developed symptoms of impending eclampsia again with persistent headache and high blood pressure. She was diagnosed with posterior reversible encephalopathy syndrome. CT scan was done which confirmed the diagnosis.

Knee jerk was lost in 7 patients including all groups of patients during therapy and magnesium sulphate was given on and off.

Serum magnesium level was checked only in 2 patients who lost knee jerk during therapy and was found to be within normal limits. Serum magnesium level was not checked in other patients due to financial constraints.

In our study, perinatal mortality observed was 14.9%, out of which only 1 was neonatal death while others were stillbirths.

In a study conducted by Bangal V et al[9] only eclampsia patients were included. Perinatal mortality rate was 33%.

In a study conducted by Suman Sardesai et al[7] perinatal mortality in impending eclampsia group and eclampsia group was 20.22% and 33.9% respectively. There is statistically significant increase in perinatal mortality in eclampsia as compared to imminent eclampsia.

Eclamptic convulsions cause severe hypoxia and acidosis in fetus. Hence seizure prophylaxis should be given to all patients of imminent eclampsia to improve the perinatal outcome.

Table 10: Comparision with other studies

	Sujata et al[10]	Sadhananagar et al[11]	Eclampsia trial collaborative group[12]	SMH (our study)
Perinatal mortality rate	34.5%	9.57%	26.1%	14.9%

In above compared studies, high dose magnesium sulphate regime was used. In our study common cause for perinatal mortality were prematurity, IUGR and abruption. The delivery was more than 4hours after the last dose in 3.1% of impending eclampsia patients. Other patients delivered within 4 hours of last dose of magnesium sulphate.

Low dose magnesium sulphate regimen was started irrespective of weight of the patient and none of them had recurrent convulsions. Serum magnesium levels were checked when knee jerk was lost only in 2 patients out of total 7 patients who lost the knee jerk because of financial constrains. In both the patients serum magnesium level was within therapeutic range

In the eclampsia group, 50% had preterm vaginal delivery, 16.7% was preterm emergency caesarean delivery and 16.7% had full term emergency caesarean delivery. In the impending eclampsia group, 34.4% had preterm vaginal delivery, 15.6% had term vaginal delivery, 18.8% had preterm emergency caesarean delivery and 21.9% had term emergency caesarean delivery. The commonest indication for caesarean was non-reactive CTG. In the severe preeclampsia group, 72.7% had preterm vaginal delivery, 18.2% had preterm emergency caesarean delivery and 9.1% had term emergency caesarean delivery.

The perinatal mortality in general was 41.1 per 1000 live births in our hospital. 20% of perinatal mortality was found to be due to preeclampsia. Impending eclampsia contributed to 10% of all perinatal mortality. Eclampsia contributed to 6.3% of all perinatal deaths. In study group the perinatal mortality in our hospital was 14.9%.

There was no maternal mortality or significant maternal morbidity in either of the groups. Our study result regarding maternal mortality was compared with other studies in the below table.

Table 11: Comparison of Maternal & Pe Rinatal Outcome in Different Studies

Particulars	Suman Sardesai et al[7]	Joydeb Roy et al[13]	Bangal V et al[9]	Single dose Suyajna Joshi etal[14]	Sokoto regimen (Brisallah A Ekele) et al[15]	Padhar regimen Niraj N mahajan et al[16]	SMH (our study)
Recurrence rate of convulsion	7.89%	2%	8 %	9.14%	7.4%	1.003%	0%
Treatment failure rate	0.18%	--	6%	--	--	--	0%
Occurrence of convulsion in IE	1.25%	--	--	--	--	--	0%
Maternal mortality	2.63%	3.3%	0%	3.3%	9.9%	--	0%
Perinatal mortality (in E)	33.98%	--	24%	23.6%	--	--	14.9%

Conclusion :

1. Low dose magnesium sulphate regime is effective to prevent the occurrence of eclampsia in impending eclampsia, severe preeclampsia patients and effective in preventing recurrence of convulsions in eclampsia patients.
2. Dose required to control convulsions and to prevent convulsions with low dose magnesium sulphate regime was less than half of standard Pritchard regimen.
3. Clinical monitoring appears to be sufficient. Serum magnesium levels need not be monitored in all patients.
4. Low dose magnesium sulphate regime is safe, which suits the Indian women, having relatively low body mass index as compared to their western counterparts.
5. None of the patients in study group developed magnesium related toxicity with low dose magnesium sulphate regime.

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