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ORIGINAL ARTICLE

STUDY OF EFFICACY OF LOW DOSE MAGNESIUM SULPHATE REGIMEN (DHAKA REGIMEN) AS COMPARED TO STANDARD REGIMEN (PRITCHARD) IN THE MANAGEMENT OF ECLAMPSIA

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ABSTRACT: BACKGROUND: Eclampsia is one of the most important cause of maternal mortality and morbidity worldwide Dr. J. A. Pritchard in 1955, introduced magnesium sulphate for control of convulsions in eclampsia and now magnesium sulfate is the anticonvulsant drug of choice for both prevention and treatment of eclampsia, but due to its narrow therapeutic window its dose-related toxicity is a major concern. Considering the lower body weight of Indian women than western counter part, different low dose magnesium sulphate regime has been formulated in different parts of India and Bangladesh and these modifications appeared to reduce drug toxicity. The Objective was to compare the efficacy of low dose magnesium sulphate regimen (Dhaka regimen) with standard Pritchard's regimen for management of eclampsia. **METHODS:** This was a hospital based prospective study conducted in the Dept. of O & G of VSSMCH, Burla from Oct. 2012 to Sept. 2014. Total 300 patients with eclampsia were included in study and randomly distributed into two groups containing 150 patients each in both Dhaka & Pritchard groups. The statistical software SPSS version 20 has been used for the analysis. An alpha error of 5% has been taken as significant. **RESULTS:** In the present study, there is no recurrence of convulsion among both the groups. The Dhaka regimen was associated with significantly lower deep tendon reflex loss (2.67% vs 8. 0%; P=0. 040), significantly lower total amount of Mgso4 requirement, and lower maternal mortality (3.33% vs 6. 67%; P=0. 185) as compared with the standerd Pritchard regimen. **CONCLUSIONS**: The maternal morbidity and mortality in the present study were comparable to those of standard Pritchard's regimen. The Dhaka regimen was equally effective and moresafe for the management of eclampsia in a region where most women are of low body weight

KEYWORDS: Antepartum Eclampsia; Magnesium Sulphate; Dhaka Regimen; Pritchard Regimen.

INTRODUCTION: Eclampsia is derived from the Greek word meaning flash of lightening, to shine forth. Eclampsia is defined as the occurrence of generalized tonic-clonic convulsion in women with pre-eclampsia not caused by any other neurological or medical disorders. Eclampsia remains an important cause of maternal mortality and morbidity worldwide. Studies have indicated that it accounts for more than 50,000 maternal deaths globally. Magnesium sulphate has a narrow therapeutic index leading to concerns related to its toxicity. Experience with Pritchard's magnesium sulphate regimen for eclampsia showed multiple toxicity and needed dose omission. Hence studies have been carried out in developing countries to determine the lowest effective dose. Reducing magnesium sulfate toxicity without compromising its efficacy in controlling seizures and lowering mortality rates remains a major challenge. The Collaborative Eclampsia Trial Group,[1] which remains the largest trial of magnesium sulfate for the management of eclampsia, included women from 27

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centers from 10 countries. No dose adjustments were made for maternal weight in this trial, even though maternal weight is much higher in high- than in low-income countries (65kg vs 45kg). A smaller study carried out at Dhaka Medical College by Begum et al at the same time as the Collaborative Eclampsia Trial Group[1,2] came to exactly the same conclusions. The main difference between these 2 studies was the dosage regimen of magnesium sulphate.

This study aimed to study the efficacy of low dose Magnesium sulphate Regimen -Dhaka Regimen in Antepartum Eclampsia and to compare the effects of Magnesium sulphate regimens – Dhaka regimen with Pritchard regimen in terms of preventing recurrent convulsions.

This was a randomized controlled trial conducted in VSS Medical College & Hospital, Burla, Sambalpur during the period of October 2012–September 2014. All cases of eclamptic patients attending the labour room of VSS Medical College and Hospital were considered for study. First 300 cases of antepartum eclampsia, admitted to VSS MCH, irrespective of parity and gestational age were included in the study after taking informed consent from patients or attendees. Intrapartum and postpartum cases, lady who received magnesium sulphate loading dose before admission, who had convulsions due to other causes, those with cardiac failure, and renal failure, were excluded from study. The cases were divided randomly into 2 groups; Gr A received the standard Pritchard regimen and Gr B the low dose (DHAKA) regimen. All the data were analyzed using spss 20 version.

In PRITCHARD REGIMEN OF MAGNESIUM SULPHATE Loading dose was given as 4gm of magnesium sulfate (20% solution) intravenously at a rate not to exceed 1g/min, Follow promptly with 10g of 50% magnesium sulfate solution, one half (5gm) injected deeply in the upper outer quadrant of each buttock through a 3-inch-long 20-gauge needle mixed with 1.0ml of 2% lidocaine. If convulsions persisted after 15min, additional 2gm mgso4 (20% solution) given intravenously at a rate not to exceed 1g/min. Every 4hr thereafter, 5gm of a 50% solution of magnesium sulfate injected deeply in the upper outer quadrant of alternate buttocks, but only after ensuring that: The patellar reflex is present, Respirations not depressed, and Urine output during the previous 4hr exceeded 100 ml Magnesium sulfate is discontinued 24hr after delivery.

Loading Dose in DHAKA REGIMEN consists of 4gm of magnesium sulphate as 20% w/v solution given intravenously slowly over 15 minutes & 3gm mgso4 50% w/v solution given intramuscularly in each buttock.[3] The concentration was maintained by giving 2.5gm mgso 4 every 4 hourly intramuscularly in alternate buttocks, Monitoring urine output, knee jerks, and respiratory rate until 24 hrs after delivery.

Primary outcome measures were recurrence of convulsions after starting the treatment in both the regimens, dose omission due to toxicity.

Age	Group		Total
	Pritchrd Regimen	Dhaka Regimen	
< 20yrs	9(6%)	15(10%)	24(8%)
21-25 yrs	113(75.33%)	103(68.67%)	216(72%)
26-30 yrs	18(12%)	25(16.67%)	43(14.33%)
>30 yrs	10(6.67%)	7(4.67%)	17(5.67%)
Total	**150(100%)**	**150(100%)**	**300(100%)**

Table 1: Distribution of Age

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	Group		Total
	Pritchard Regimen	Dhaka Regimen	
High	12(8%)	15(10%)	27(9%)
Middle	29(19. 33%)	30(20%)	59(19. 67%)
Low	109(72. 67%)	105(70%)	214(71. 33%)
Total	**150(100%)**	**150(100%)**	**300(100%)**

Table 2: Distribution of Socioeconomic Status

The difference is nonsignificant among both the groups.

	Group		P Value	Significance
	Pritchard regimen	Dhaka regimen		
	Mean±Std. Deviation	Mean±Std. Deviation		
Age(years)	23.45±3.47	23.43±3.26	0.973	Not Significant
Weight(kg)	56.73±5.61	56.79±5.56	0.926	Not Significant
Height(cms)	150.71±4.22	151.58±4.48	0.084	Not Significant
BMI	24.93±1.67	24.72±2.11	0.332	Not Significant

Table 3: Distribution of Demographic Parameters

		Group		Total		
		Pritchard Regimen	Dhaka Regimen		P Value	Significance
Liver Function Test	Abnormal	35(23.33%)	32(21.33%)	67(22.33%)	0.677	Not Significant
	Normal	115(76.67%)	118(78.67%)	233(77.67%)		
Renal Function Test	Abnormal	18(12%)	25(16.67%)	43(14.33%)	0.249	Not Significant
	Normal	132(88%)	125(83.33%)	257(85.67%)		
Platelet Count	<1lac	18(12%)	17(11.33%)	35(11.67%)	0.857	Not Significant
	Normal	132(88%)	133(88.67%)	265(88.33%)		

Table 5: Laboratory Parameters

No significant difference is observed among the both groups. These findings are correlated with other Indian studies.

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	Group		Total	P Value	Significance
	Pritchard Regimen	Dhaka Regimen			
Forceps assisted	53(35.33%)	53(35.33%)	106(35.33%)	0.449	Not Significant
LSCS	46(30.67%)	35(23.33%)	81(27%)		
Vaginal delivery unaided	43(28.67%)	51(34%)	94(31.33%)		
Ventouse application	8(5.33%)	11(7.33%)	19(6.33%)		
Total	**150(100%)**	**150(100%)**	**300(100%)**		

Table 6: Mode of Delivery

	Group			
	Pritchard Regimen	Dhaka Regimen		
	Mean±Std. Deviation	Mean±Std. Deviation	P Value	Significance
No. of Convulsion Before Admission	5.1±2.85	4.99±2.7	0.739	Not Significant
Convulsion To Admission Interval(In Hours)	7.63±3.44	7.67±3.27	0.918	Not Significant
Total Time of Mgso4 Therapy(In Hour)	35.05±6.03	34.99±5.78	0.922	Not Significant
No Of Mgso4 Doses	9.13±1.56	9.27±1.41	0.438	Not Significant
No. of Mgso4 Dose Omitted	0.25±0.66	0.12±0.4	0.035	Significant
Total Amount Of Mgso4 Given(In Gms)	54.67±7.81	30.83±3.64	<0.001	Significant
Hospital Sta (In Days)	5.15±1.42	4.23±1.42	<0.001	Significant

Table 7: Number of Convulsion & Treatment

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		Group		P Value	Significance
		Pritchard Regimen	Dhaka Regimen		
Recurrence of convulsion	No	150 (100%)	150 (100%)	NA	NA
Need of additional anticonvulsant	No	150 (100%)	150 (100%)	NA	NA
Oliguria	Absent	135 (90%)	132 (88%)	0.580	Not Significant
	Present	15 (10%)	18 (12%)		
Loss of knee jerk reflex	Absent	138 (92%)	146 (97.33%)	0.040	Significant
	Present	12 (8%)	4 (2. 67%)		
Respiratory depression	Absent	150 (100%)	150 (100%)	NA	NA
Pulmonary edema	Absent	135 (90%)	142 (94.67%)	0.129	Not Significant
	Present	15 (10%)	8 (5.33%)		
Atonic PPH	Absent	129 (86%)	137 (91.33%)	0.145	Not Significant
	Present	21 (14%)	13 (8. 67%)		

Table 8: Distribution of Efficacy & Side effects

		Group		Total		
		Pritchard Regimen	Dhaka Regimen		P Value	Significance
Maternal mortality	Absent	140 (93. 33%)	145 (96. 67%)	285 (95%)	0.185	Not Significant
	Present	10 (6. 67%)	5 (3. 33%)	15 (5%)		
Birth	Live Birth	127 (84. 67%)	132 (88%)	259 (86. 33%)	0.401	Not Significant
	Still Birth	23 (15. 33%)	18 (12%)	41 (13. 67%)		
Total		**150 (100%)**	**150 (100%)**	**300 (100%)**		

Table 9: Maternal mortality and still birth

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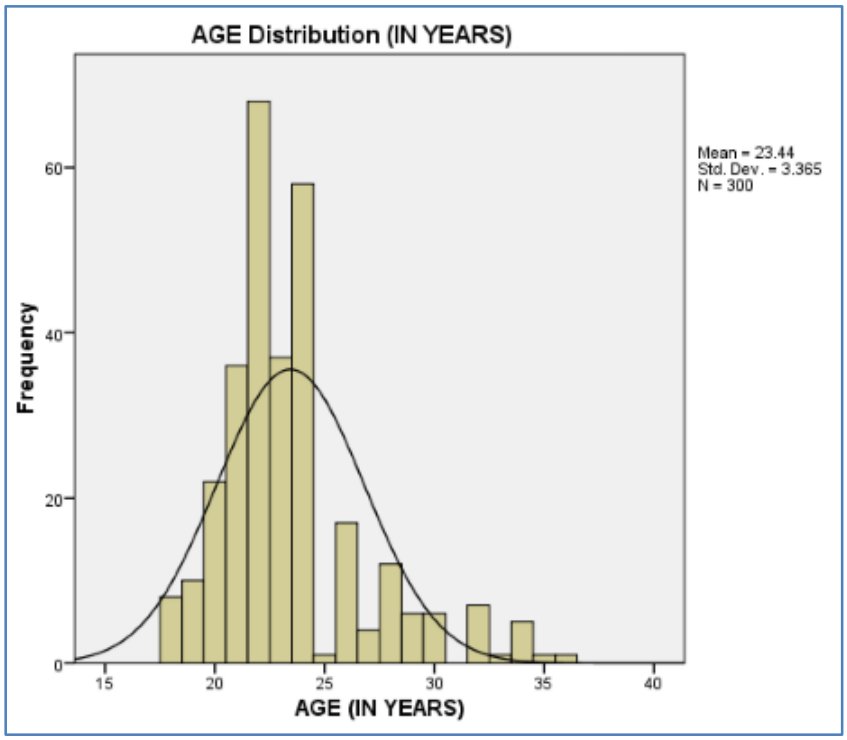

Fig. 1: Showing age distribution

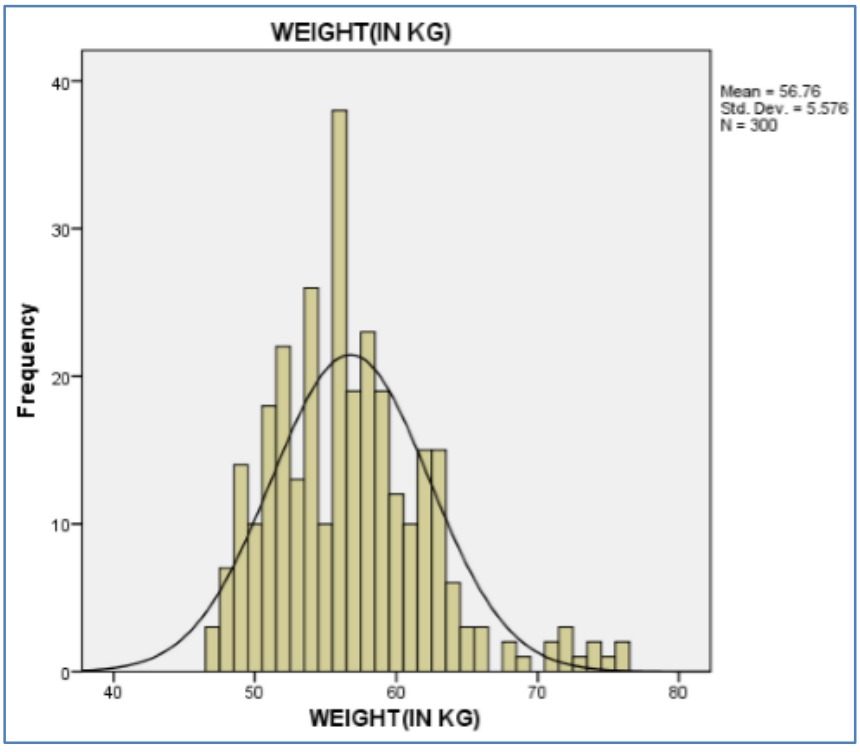

Fig. 2: Showing weight

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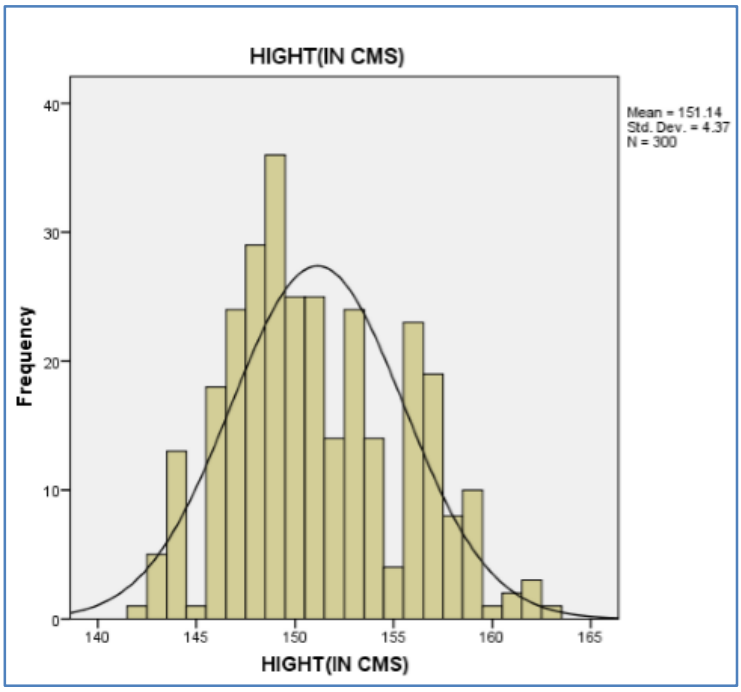

Fig. 3: Showing height distribution

RESULTS & DISCUSSION: Most of the patients received little or no antenatal care (Table III). As a result pre-pregnancy weight of mother is not available in most of the cases. So we have to measure weight at the time of admission after stabilizing the patients. Eclampsia is associated with abnormal weight gain and is almost entirely due to abnormal fluid retention. Hallak et al, 1993, says magnesium administered parenterally promptly crosses the placenta to achieve equilibrium in fetal serum and less so in amnionic fluid.[4] Gortzak-Uzen et al, 2005 says levels of magnesium in amnionic fluid increase with duration of maternal infusion and has small but significant effects on the fetal heart rate pattern-specifically beat-to-beat variability[5]. So measuring the body weight before delivery also helps us in evaluating the perinatal outcome.

When body weight was taken before pregnancy and after delivery, it shows Indian women have lower body weight and BMI than western women. Narayan Jana et al (2012) measured weight after three to four days of delivery & when patient was ambulatory and showed most women were of small stature, with a mean height of 151±7.0cm, a mean weight of 41.7±5.3kg, and a mean body mass index of 19.3±2.1.[6] Also Latika Sahu et al (2013) had taken pre pregnancy maternal weight in her study and found mean BMI in Dhaka regimen 20. 75±1.33 and in Pritchard regimen is 20. 64±1.24.[7] Bangal et al (2009) observed that seventy percent of women had body weight less than 50 kilograms at the time of admission.[8]

Indian women have low weight and height as well as low BMI than women from western countries. Low body weight decreases the volume of distribution of magnesium. So it is needed to decrease the dose for Indian women. The total dose in Dhaka regimen was significantly lower than that administered in Pritchard regimen (P<0.001). The mean no of dose omitted in Pritchard regimen is 0.25±0.66 and in Dhaka regimen is 0.12±0.4. Significant difference is observed among both the

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groups (p value-0. 035). No of days spent in hospital is also significantly improved in Dhaka regimen than Pritchard regimen (4.23±1.42 days vs 5.15±1.42days, p value -<0. 001).

As shown in table VII there was no recurrence of convulsion in both the groups as well as there is no need for additional anticonvulsant in both the groups. Oliguria, Pulmonary edema and Atonic PPH showed no statistically significant difference among both the groups. No patient in either group had developed respiratory depression, however loss of knee jerk was significantly lower in Dhaka regimen (p value-0. 040).

This study is also well correlated with the study from Latika Sahu et al and Bangal V et al they observed 72% of cases had less than 3 convulsions before admission to hospital.[7,8] Narayan Jana et al observed in his study that the number of seizures before admission varied from 1 to more than 10.[6] Seizures on the way to the hospital were very common, but medical help was seldom available during transportation. The delay in seeking medical attention or hospital admission due to lack of transport & proper awareness among relatives which are responsible for high incidence of complications & mortality.

The mean total dose of magnesium sulphate administered in Dhaka regimen (30.83±3.64) is significantly lower than that administered for Pritchard regimen (54.67±7.81) (p value<0.001) [Table VII]. Narayan Jana et al observed in his study that total dose of magnesium sulfate administered 23.9±4.3gm was significantly lower than that administered during the Collaborative Eclampsia Trial (Pb 0.001).[1,6] Latika Sahu et al in her study found that the number of doses given in Dhaka regimen and Pritchard regimen were 9.6±1.97gms and 9.04±1.69 respectively.[7] Total cumulative dose was 31.5±4.94gms in Dhaka regimen and 54.2±8.47 (39-64) in Pritchard regimen. In the low dose magnesium sulphate regimen by Begum et al and Mahajan et al maintenance dose was omitted in 9 %and 41 % respectively due to loss of deep tendon reflex.[2, 9]

In our study in both Dhaka Group and Pritchard Group none of patients had recurrence of convulsion as well as no need for additional anticonvulsant. Narayan Jana et al observed recurrence of seizures in 34 patients (6.1%) after administration of the loading dose of magnesium sulphate. [6] Latika Sahu et al observed recurrence of convulsion in one patient (4%).[7] Pritchard et al and Sibai et al have reported recurrence rates of 12% and 14% respectively.[10] Begum et al using low dose regimen reported only one out of 65 cases had recurrent convulsion.[2] Recurrence of convulsion in various Indian studies using low dose regimen is reported in the range of 5 to 10%.

As there was no evidence of recurrence of convulsion in any of the patients, additional magnesium sulphate dose was not administered showing the efficacy of low dose mgso4 regimen.

As shown in table VI hospital stay was significantly less in Dhaka regimen 4.23±1.42 days vs 5.15±1.42 days in Pritchard group (p value <0. 001). Less no of cases suffered from loss of knee jerk in Dhaka regimen (p value-0.040). Thus, evidence consistent with magnesium toxicity was observed even with the low dose magnesium sulphate regimen and definitely with standard dose regimen, the results suggesting a need to lower the dose of magnesium sulphate. Smith et al showed that the overall rate of absent patellar tendon reflexes was 1.6 percent; respiratory depression 1.3 percent; and calcium gluconate administration 0.2 percent 11. Sibai et al described major maternal complications among 399 patients including placental abruption 10%, neurological deficits 7%, aspiration pneumonia 7%, pulmonary edema 5%, cardiopulmonary arrest 4%, and acute renal failure in 4% cases 10. Andersgaard and associates described a third of the women among 232 women with eclampsia experienced major complications that included HELLP syndrome, renal failure, pulmonary edema, pulmonary embolism, and stroke 12.

Maternal deaths & still birth rate showed statistically non-significant difference (Table VIII). The maternal mortality observed in this study in either group which was similar in other Indian studies. The multinational Eclampsia Trial Collaborative Group study1 involving 1687 women with eclampsia showed maternal mortality with mgso4 regimen is 3. 1%. Sibai et al described 1 percent of women died in their studies 10. Zwart et al, 2008 observed in Netherlands, there were three maternal deaths among 222 eclamptic women 13).

In such cases, advanced management could not be provided because there was no adequate ICU facility at VSS Medical College.

CONCLUSION:

The Study Results have 4 Major Implications:

1. Dhaka regimen is equivalent to Pritchard regimen in controlling convulsions and preventing recurrence of convulsions.
2. Following the regimen virtually eliminated the risk of magnesium toxicity and thus increased the safety of the drug.
3. As the regimen lowered the drug dose for each patient, it substantially lowered the overall cost of treatment-which is very important in low-resource countries, where injectable magnesium sulphate is scarce and expensive.
4. With a lesser toxicity, magnesium sulphate treatment is likely to become acceptable at peripheral health centres.

This study can add to the literature regarding the efficacy of low dose magnesium sulphate in low resource peripheral health services. It is vital to consider the body wt into account while prescribing any medicine. Taking into consideration the above results and low wt of majority pregnant lady the dose modification of magnesium sulphate in eclampsia/pre-eclampsia may be recommended in our set-up, without compromising the efficacy Some limitations of our study.

Only antepartum eclampsia patients were included in this study excluding intra partum & post-partum cases. We had to exclude those cases who had already received magnesium sulphate before reaching this tertiary Institution. Pre-pregnancy weight of mother is not available in most of the cases. So we have to measure weight on the time of admission after stabilizing the patients Serum magnesium level is not measured in this study. It is one of the major limitations in this study.

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