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## Original Research Article

# Therapeutic efficacy of low dose (Dhaka regimen) versus high dose (Pritchard regimen) magnesium sulphate for management of eclampsia and impending eclampsia

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### ABSTRACT

**Background:** To compare the efficacy of low dose (Dhaka regimen) vis-a vis high dose (Pritchard regimen) magnesium sulphate in management of eclampsia and impending eclampsia.

**Methods:** The open-label, comparative study was conducted on 90 pregnant patients. They were admitted to emergency Department of Obstetrics and Gynaecology, Government Medical College, Amritsar with eclampsia or impending eclampsia. 10 patients dropped out at various stages of study and finally, 80 were enrolled and randomized (1:1 ratio) into two groups. Group-1, N=40 were given low dose MgSO<sub>4</sub> (Dhaka regime) and Group-2, N=40 were given high dose MgSO<sub>4</sub> (Pritchard). Termination of pregnancy was done as per Bishop's score, gestation age, maternal and fetal status. Primary outcome measure was therapeutic efficacy of equivalence for control of seizures whereas secondary outcome was adverse side-effects of both the regimens.

**Results:** Mean age in Group-1 was 24.90±4.02 years and that of Group-2 was 25.67±3.79 years. Antepartum eclampsia was the most common diagnosis among groups i.e., 47.5% and 55% respectively. After treatment, the seizure control was 97.5% in Group-1 and 100% in Group-2 with comparable results ( $\chi^2=1.013$ ;  $p=0.314$ ). However, highly significant difference was observed among dosage of MgSO<sub>4</sub> that was required for control of seizure (23.75±2.71 gm versus 41.35±4.76 gm;  $p<0.001$ ). Group-1 showed lower incidence of side-effects that is, loss of deep tendon reflex as compared to Group-2, but neonatal outcomes were comparable in both groups.

**Conclusions:** Low dose (Dhaka regimen) was equally effective in control of seizures as compared to high dose (Pritchard regimen) with lower incidence of side-effects.

**Keywords:** Dhaka regimen, Eclampsia, Magnesium sulphate (MgSO<sub>4</sub>), Pritchard regimen

### INTRODUCTION

Eclampsia is derived from the Greek word meaning flash of lightning, to shine forth. It is defined as the occurrence of generalized tonic-clonic convulsion in women with pre-eclampsia not caused by any other neurological or medical disorders. It is one of the most common obstetrical emergencies in developing countries causing significant maternal and perinatal morbidity and mortality. Incidence of eclampsia is 1 in 2000 deliveries

in developed countries and 1 in 50 to 500 deliveries in developing countries.<sup>1</sup> In India, the incidence of eclampsia ranges from 6 to 100 per 10,000 live births.<sup>2</sup> It accounts to 12% of maternal deaths worldwide as compared to 8% in India.<sup>3</sup> The worldwide estimated eclampsia deaths per year is 50,000.<sup>4</sup>

The principle management for eclampsia is control of convulsions along with supportive life measures and termination of pregnancy. Magnesium sulphate (MgSO<sub>4</sub>)

is the first-line drug for eclampsia, which acts by reducing presynaptic release of glutamate neurotransmitter, by blocking glutaminergic N-methyl-D-aspartate (NMDA) receptors and calcium entry via voltage gated ionic channels.<sup>5</sup> Various regimens are followed for management but Pritchard regimen is the most commonly used. The efficacy of MgSO<sub>4</sub> in severe preeclampsia and eclampsia is time tested in various studies. However, because of its narrow therapeutic index, toxic side-effects are the major area of concern in clinical use. Its safety and toxicity was recently reviewed by Smith and coworker; more than 9500 women were treated, overall rate of absent patellar reflexes was 1.6%, respiratory depression 1.3% and calcium gluconate administration 0.2%.<sup>6</sup>

Pritchard et al suggested that the dose of MgSO<sub>4</sub> should be limited in women who are known to be or appear to be small.<sup>7</sup> Women in India, especially from rural areas or from low socio-economic strata tend to have smaller body weight. Administering Pritchard regime might prove to be hazardous in these low weight women and there is possibility of most dreadful respiratory failure.<sup>8</sup> Reducing MgSO<sub>4</sub> toxicity without compromising its efficacy in controlling seizures and lowering mortality rates remains a major challenge.<sup>9</sup> A study conducted by Begum et al on women with low Body mass index (BMI) in Dhaka explains the efficacy of low dose regimen in controlling fits.<sup>10</sup>

Therefore, the present study aimed to measure efficacy of low dose MgSO<sub>4</sub> (Dhaka regimen) as compared to high dose MgSO<sub>4</sub> (Pritchard regimen) in control of convulsion in preeclampsia and eclampsia patients.

## METHODS

It was a comparative, randomized study conducted in emergency Department of Obstetrics and Gynaecology of Government Medical College, Amritsar, Punjab on patients with eclampsia or features of impending eclampsia. Cases who had already received either magnesium sulphate or any other anticonvulsant treatment before admission, other causes of convulsions like epilepsy, meningitis, encephalitis, cerebral tumors, metabolic abnormalities, and those who presented with complications like cerebro-vascular accidents, renal failure, aspiration pneumonitis and hemolysis elevated liver enzymes low platelet count (HELLP) syndrome were excluded from the study. A total of 90 patients were initially recruited in the study, after taking written informed consent, out of which 10 dropped out in due course of time who didn't meet inclusion criteria. Subsequently, the patients were divided into two groups assigning alternate patient in each group (1:1 ratio). Group-1 received low dose while Group-2 received high dose MgSO<sub>4</sub> as described further.

### History

Patients' detailed history was taken including age, parity, gestation age, number of convulsions and enquired

regarding symptoms of impending eclampsia i.e., headache, blurring of vision, epigastric pain, dizziness. Any past history of hypertension or eclampsia in previous pregnancy was elicited.

### Clinical examination

Included general physical and obstetric examination to assess anemia, degree of oedema and level of consciousness. BMI was calculated along with cardiovascular and respiratory system examination. All relevant investigations were done which included routine antenatal tests, liver function tests, renal function tests, coagulation profile, complete urine examination and fundus examination.

An intravenous access using a wide bore cannula was established and either of the two regimens started. Hourly urine output was measured by indwelling urinary catheter along with half hourly monitoring of pulse, BP, temperature, respiration and fetal heart sounds. In addition, recommended supportive measures were provided to eclamptic patients' i.e., lateral decubitus, protective mouth gag, oxygen inhalation at the rate of 6l/min, suctioning and avoidance of external stimulus.

### Antihypertensive measures

Injection Labetalol slow intravenous over 10-15 minutes was given in recommended doses when BP readings were > 160/110 mm of Hg. Tab Nifedipine at 10-30 mg was added when BP was not controlled by Labetalol alone.

### Anticonvulsant measures

Dhaka regimen and Pritchard regimen was given in Group-1 and Group-2 respectively as follows:

*Group 1:* Loading dose 4gm of 20% MgSO<sub>4</sub> was given slowly intravenous over 10 minutes with 3gm of 50% MgSO<sub>4</sub> intramuscularly in both buttocks making a full-loading dose of 10 gm.

*Maintenance dose:* 2.5gm of 50% MgSO<sub>4</sub> was given intramuscular on alternate buttock every 4 hours till 24 hours after last fit or delivery whichever was later.

*Group 2:* Received high dose MgSO<sub>4</sub> at loading dose of 14 gm which included 4 gm of 20% slow intravenous over 10 minutes and 5 gm of 50% MgSO<sub>4</sub> intramuscular in both buttocks followed by maintenance dose of 5 gm of 50% MgSO<sub>4</sub> intramuscular on alternate buttock every 4 hours till 24 hours after the last fit or delivery whichever occurred later.

Parameters to be monitored in both regimens before next dose of MgSO<sub>4</sub> were:

1. Deep tendon reflexes should be present
2. Respiratory rate >16/min
3. Urine output >30 ml/hour

If convulsions recur after initial loading dose, a repeat dose of 2 gm intravenously was given and on further recurrence, it was considered to be a failure.

**Obstetric examination and management**

Per abdomen was done to assess fetal lie, presentation, fetal heart sounds, to rule out intrauterine growth retardation (IUGR) and per vaginal examination was conducted to know Bishop’s score. Termination of pregnancy was done in all patients and mode of termination was planned according to gestational age, fetal status and Bishop’s scoring. For vaginal delivery, induction with prostaglandins followed by augmentation with injection (Oxytocin) was done in poor Bishop’s score of less than 6. In patients with good Bishop’s score of more than 6, only augmentation of labor was done. Lower section caesarian section (LSCS) was done for all relevant obstetric indications.

**Outcome measures**

Primary outcome was to measure effectiveness of both regimens for control and prevention of convulsions. Secondary outcome measure was maternal and neonatal

morbidity/mortality as depicted by side-effects and Apgar score at 1 and 5 minutes respectively.

**Statistical analysis**

Data thus obtained were entered in Microsoft excel sheet and then transferred to SPSS version 21. Discrete data was expressed as frequency and percentages. Continuous data were summarized as numbers, mean with standard deviation. The data in both the groups were compared using chi-square test and P value of less than 0.05 was taken to be statistically significant.

**RESULTS**

Out of 90 patients initially recruited in the study, 80 were finally enrolled with a response rate of 88.8%. Mean age of Group-1 was 24.90±4.02 years and that of Group-2 was 25.67±3.79 years. Most of the patients were primigravida in both groups (70% versus 52.5%). Mean gestation age of Group-1 was 36.40±3.42 weeks whereas of Group-2 was 37.00±2.97 weeks. The difference was statistically non-significant (Table 1).

There were unbooked 75% cases in Group-1 and 65% cases in Group-2. The baseline systolic and diastolic BP and urinary albumin is shown in Table 2.

**Table 1: Patient’s characteristics in both groups.**

Age (in years)	Dhaka n (%)	Pritchard n (%)	Chi-square	P value
<20	2 (5.0)	2 (5.0)	0.654	0.884
20-25	17 (42.5)	14 (35)		
25-30	16 (40.0)	17 (42.5)		
≥30	5 (12.5)	7 (17.5)		
Total	40 (100.0)	40 (100.0)		
Mean±S.D.	24.90± 4.02	25.67 ± 3.79		
<b>Parity</b>				
Primigravida	28 (70)	21 (52.5)		
Multigravida	12 (30)	19 (47.5)		
Total	40 (100)	40 (100.0)		
<b>Gestational age (in weeks)</b>				
<32	4 (10.0)	2 (5)	1.193	0.551
32-36	9 (22.5)	7 (5)		
>36	27 (67.5)	31 (90)		
Total	40 (100.0)	40 (100)		
Mean±S.D.	36.40 ± 3.42	37.00±2.97		
<b>BMI (kg/m<sup>2</sup>)</b>				
<19.8	24 (60)	19 (47.5)	3.981	0.137
19.8-26	14 (35)	21 (52.5)		
26-29	2 (5)	0.0		
>29	0	0.0		
Total	40 (100)	40 (100.0)		
Mean±S.D.	19.58 ± 2.48	19.93 ± 1.40		

**Table 2: Baseline blood pressure and urinary albumin.**

Systolic BP(mm of Hg)	Dhaka n (%)	Pritchard n (%)	Chi-square	P value
<160	15 (37.5)	14 (35)	2.218	0.330
160-180	23 (57.5)	26 (65)		
>180	2 (5)	0		
Total	40 (100)	40 (100)		
Mean±S.D.	160.37 ± 14.12	159.80 ± 9.40		
Diastolic BP(mm of Hg)				
<90	1 (2.5)	0	3.879	0.144
90-110	15 (37.5)	23 (57.5)		
>110	24 (60)	17 (42.5)		
Total	40 (100)	40 (100)		
Mean± S.D.	110.05 ± 9.53	109.55 ± 8.80		
Urinary albumin				
Nil	4 (10)	5 (12.5)	1.537	0.674
Trace	6 (15)	6 (15)		
1+	14 (35)	18 (45)		
≥2+	16 (40)	11 (27.5)		
Total	40 (100)	40 (100)		

Trace: 0.15-0.3 g/l; 1+: 0.3-1 g/l; ≥2+: >1 g/l

**Table 3: Type of eclampsia and frequency of convulsions.**

Type of eclampsia	Dhaka n (%)	Pritchard n (%)	Chi-square	P value
IE	14	35.0	0.580	0.748
APE	19	47.5		
PPE	7	17.5		
Total	40	100.0		
No. of convulsions				
<2	19 (47.5)	14 (35)	2.958	0.228
2-5	21 (52.5)	24 (60)		
>5	0	2 (5)		
Total	40 (100)	4 (100)		

IE: Impending eclampsia; APE: Antepartum eclampsia; PPE: Postpartum eclampsia.

Antepartum eclampsia was the most common type of eclampsia among groups accounting to 47.5% and 55% respectively. Most patients had 2-5 convulsions at the time of presentation (52.5% versus 60%) (Table 3).

**Table 4: Dose of magnesium sulphate.**

Group	Mean	S.D	P value	Significance
Dhaka	23.75gm	2.71	<0.001	HS
Pritchard	41.35gm	4.76		

There was a statistically significant difference in the doses of MgSO<sub>4</sub> required for control of fits (p<0.001) as shown in (Table 4). Convulsions were controlled in 97.5% (n=39) in Group-1 and 100% (n=40) in Group-2 and results were comparable (x<sup>2</sup>=1.013; p= 0.314).

There was one case of recurrence in Group 1 which was shifted to Group-2 while no patient had recurrence in Group-2. LSCS was the most common mode of delivery in both groups (62.5% versus 57.5%).

One patient in Group-1 had caesarian hysterectomy due to associated placenta accreta. 4(10%) patients in Group-1 had loss of deep tendon reflexes as compared to 11(27.5%) in Group 2 and the difference was statistically significant (p=0.045).

One patient in Group-2 had severe MgSO<sub>4</sub> toxicity, as evidenced by respiratory depression and timely ventilator support saved her. There was no maternal mortality in Group 1 but one patient in Group 2 died due to HELLP syndrome and pulmonary oedema. All other side-effects were comparable in both the groups (Table 5).

**Table 5: Maternal outcome.**

Mode of delivery	Dhaka n (%)	Pritchard n (%)	Chi-square	P value
VD	11 (27.5)	14 (35)	0.586	0.746
Forceps delivery	4 (10)	3 (7.5)		
LSCS	25 (62.5)	23 (57.5)		
Total	40 (100)	40 (100)		
<b>Convulsions</b>				
Controlled	39 (97.5)	40 (100)	1.013	0.314
Recurrent	1 (2.5)	0		
Total	40 (100)	40 (100)		
<b>Side-effects</b>				
Loss of knee jerk	4 (10)	11 (27.5)	4.021	0.045
Oliguria	3 (7.5)	4 (10)	0.157	0.692
PPH	3 (7.5)	5 (12.5)	0.556	0.456
Resp. depression	0	2 (5)	2.051	0.152
Pulmonary edema	0	1 (2.5)	1.013	0.314
Cerebral edema	0	2 (5)	2.051	0.152
HELLP	1 (2.5)	1 (2.5)	0.00	1.00
<b>BP on first post-delivery day</b>				
Mean diastolic BP	90.20±9.80	86.90±9.27	-	0.126
Maternal mortality	0	1(2.5)	1.013	0.314

VD: Vaginal delivery, LSCS: Lower segment caesarian section, HELLP: Hemolysis elevated liver enzymes low platelet count

**Table 6: Neonatal outcome.**

Baby weight (in kg)	Dhaka n (%)	Pritchard n (%)	Chi-square	P value
<2	7 (17.5)	7 (17.5)	1.668	0.434
2-2.5	14 (35)	9 (22.5)		
>2.5	19 (47.5)	24 (60)		
Total	40 (100)	40 (100)		
Mean±S.D.	2.45±0.789	2.47±0.821		
<b>Apgar (at 1 minute)</b>				
8-10	22 (55)	18 (45)	1.540	0.673
6-7	13 (32.5)	18 (45)		
4-5	2 (5)	1 (2.5)		
0-3	3 (7.5)	3 (7.5)		
Total	40 (100)	40 (100)		
Mean±S.D.	7.00±2.23	6.75±2.17		
<b>Apgar (5 minutes)</b>				
8-10	34 (85)	35 (87.5)	0.214	0.898
6-7	3 (7.5)	2 (5)		
4-5	0	0		
0-3	3 (7.5)	3 (7.5)		
Total	40 (100)	40 (100)		
Mean±S.D.	7.92±2.35	7.83±2.35		

It was observed that patient receiving Dhaka regimen had poor control of post-delivery diastolic BP as compared to Pritchard regimen. Neonatal outcome in terms of Apgar score at 1 minute and 5 minute was also comparable in both groups. There was one perinatal death among Group 1 (Table 6).

## DISCUSSION

MgSO<sub>4</sub> is used as different regimens in different parts of the world. Pritchard regimen is the most widely used regimen all over the world. Despite its efficacy, narrow therapeutic index is always a cause of concern due to its



toxicity. The present study and others by Begum et al and Seth et al reported more side-effects with high dose MgSO<sub>4</sub> in Pritchard regimen i.e., absence of deep tendon reflexes more as compared to Dhaka regimen. In our study, the mean total dose of MgSO<sub>4</sub> for Dhaka regimen was 23.75±2.71gm, which is significantly lower as compared to Pritchard regimen (41.35±4.76gm) with p value <0.001. Similarly, Sharma et al also reported statistically lower incidence of loss of deep tendon reflexes with Dhaka regimen and Jana et al, found total dose of MgSO<sub>4</sub> to be 23.9±4.3gm during collaborative eclampsia trial (P≤0.001).<sup>11,12</sup> Sahu et al, in her study found that the number of doses given in Dhaka regimen and Pritchard regimen were 9.6±1.97 gm and 9.04±1.69gm, respectively. Total cumulative dose was 31.5±4.94gm in Dhaka regimen and 54.2±8.47 (39-64) in Pritchard regimen.<sup>13</sup> In the study conducted by Begum et al, Seth et al and Chaudhary et al mortality with Pritchard regimen was higher (5.02%, 7.7% and 5% respectively) than those on Dhaka regimen (0%, 4.45% and 3.3%, respectively).<sup>1,9,14</sup> However, in our study no mortality was seen among those treated with Pritchard regimen but one death was reported with second regimen. It was observed that patients treated with Dhaka regimen had poor control of diastolic BP as compared to Pritchard regimen although the difference was not statistically significant. This observation was not elaborated in any previous studies to the best of our knowledge. Indian women have low weight and height as well as body mass index (BMI) than women from western countries. Low body weight decreases the volume distribution of magnesium and is recommended to decrease the standard dose for Indian population and overall cost of treatment, which is an important hindrance in achieving the universal health for all, where the availability and cost of injectable MgSO<sub>4</sub> is scarce and expensive.

## CONCLUSION

The study concludes that Dhaka regimen is as effective as Pritchard regimen in control of fits and should be incorporated as an alternative in patients of low BMI in population of developing countries and low income groups where there is deficient staff for monitoring. Thus, Dhaka regimen virtually eliminates the risk of MgSO<sub>4</sub> toxicity.

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