

A Lower Dose of Magnesium Sulphate for Control of Convulsion in Eclamptic Women of Bangladesh

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Abstract:

Eclampsia, a life threatening complication of pregnancy. It is one of the important cause of maternal mortality of Bangladesh. Eclamptic seizure can effectively controlled by use of magnesium sulphate. A prospective randomized case control study was conducted at eclampsia ward of Dhaka Medical College Hospital for one year from June 2007 to May 2008.

Objective: *To find out whether only 8gm of magnesium sulphate heptahydrate (Nalepsin) as a single loading dose is sufficient to control eclamptic convulsion and also to compare the efficacy between 8gm & 10gm of MgSO₄ used to control convulsion.*

Methodology: *A random selection was done by lottery of those antepartum and intrapartum cases who fulfill the selection criteria. Hundred patient were selected and grouped them into case & control. 8gm Nalepsin (Magnesium sulphate heptahydrate) as a single I.V dose was selected for case and 10gm MgSO₄ (4gm I.V + 3gm I.M in each buttock) was for control group. Different variables were compaired and results were analyzed by unpaired 't' test and chi-square test (X₂) by SPSS programme.*

Result: *Statistically there was no significant difference of any finding between two groups after comparing all variables individually.*

Conclusion: *8gm Nalepsin intravenously as a single loading dose is sufficient to control eclamptic convulsion and prevention of its recurrence.*

Introduction:

Eclampsia, a life threatening complication of pregnancy, result when a pregnant women previously diagnosed with pre- eclampsia (high blood pressure and protein in urine) developed seizures or coma.¹ In some cases, seizures or coma may be the first recognizable sign that a pregnant women has pre- eclampsia². A sudden increase in blood pressure or occurrence of proteinuria may precipitate the disease in a patient of pre- eclampsia³. So, it is quite a preventable disease if adequate antenatal care is taken by the pregnant mother⁴. About 31% of pre- eclampsia are not preventable despite taking adequate prenatal care^{4,5}.

Eclampsia accounts for approximately 50,000 maternal death world wide annually.⁶ It is relatively uncommon in developed countries where it complicates about one in every 2000 deliveries⁷. It is 20times more common in developing countries and leading to 3rd cause of

maternal mortality in Bangladesh and account 16% of maternal death^{7,8,9}. It is also a major cause of neonatal morbidity and mortality both directly and indirectly with intrauterine growth restriction and preterm delivery for abruption of placenta^{9,10}. Death from eclampsia is difficult to prevent. So standard practice in eclampsia is urgent control of convulsion and prevention of its recurrence with the help of a suitable anti convulsion, prompt initiation of general and obstetrics management & control of hypertension if needed.^{11,12} Among the many anticonvulsants, magnesium sulphate MgSO₄ topped the list of all in terms of controlling convulsion & improving other secondary outcome¹³. It is the abnormally low level of ionized magnesium in serum, which is responsible for eclamptic convulsion.^{6,14,15}. In DMCH, from begining magnesium sulphate (MgSO₄) being used as a routine anticonvulsant (The dose schedule is 4g intravenous(IV) & 3g intramascular in

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each buttock, a total of 10g as a loading dose followed by 2.5g I.M every 4 hours in alternate buttock until 24 hours after delivery or last fit). Now, only the loading dose of $MgSO_4$ is being routinely used for controlling convulsion in eclampsia & the dose is 4g IV & 3g IM in each buttock (total 10g) for all patients. This study was planned to find out whether 8g Magnesium sulphate heptahydrate (2 bags of nalepsin) is sufficient to control convulsion & to prevent recurrence in Bangladeshi women as they were lighter in their body weight. As the Bangladeshi women is light in their body weight this reduced dose appears to control convulsion effectively.

So, this small dose may control convulsion effectively & to compare its efficacy with 10g $MgSO_4$ (intravenous plus intramuscular) used as a loading dose. As Dhaka Medical College Hospital is a tertiary referral center and there is a separate eclampsia unit with improved facilities and intensive care, having a large number of critically ill patient and about 800-1100 were admitted in every year. So, DMCH was selected for this study. According to the hospital statistics in year 2002, admission of eclampsia patient were 865 and maternal mortality of this group was 38⁶. In subsequent years upto 2006, statistical analysis shows death rate reduces not significantly. Lastly in 2007, among 10,242 of total obstetric patient, eclampsia cases were 713 and death due to eclampsia was 34 (Total death of that year was 111) ,if 8g magnesium sulphate heptahydrate ($MgSO_4 \cdot 7H_2O$) is used , we can avoid painful intramuscular injection, toxicity of drug also can be minimize, no need of calculating the dose & administration is easy which require minimum medical personnel.

Justification of the study

The justification of this study is to reduce the eclampsia related maternal mortality by giving minimum dose of $MgSO_4$ by prompt. I.V route without elapsing any time for calculating the dose and also to minimise the dose related side effect and toxicity as because the therapeutic and toxic dose of $MgSO_4$ is very close. This method needs minimum man power to manage the case.

Aim and Objective

Specific

To find out whether only 8g of magnesium sulphate as a single loading dose is sufficient to control eclamptic convulsion.

General

- To compare the efficacy between 8g and 10g of $MgSO_4$ used to control the convulsion.
- To compare the recurrence of convulsion and other side effect between two groups.
- To find out maternal and fetal outcome between two groups during study period.

Material and Method

Study design

Prospective randomized Case – Control study.

Study Place

Eclampsia unit, Department of Obstetrics and Gynaecology, Dhaka Medical College Hospital. Dhaka , Bangladesh.

Study Period

1 (one) year. From June '07 to May 08'

Study Population

Eclamptic patients fulfilling the criteria for study

Inclusion Criteria

Women with either ante partum or intrapartum eclampsia

Exclusion Criteria

- Eclampsia with severe complication, such as CVA, HELLP Syndrome, DIC, renal failure, pulmonary oedema & shock. Women having known Medical diseases like diabetes mellitus, heart disease, Jaundice, blood dyscrasia etc.
- Contraindication of magnesium therapy (eg oligurea, renal failure, absent knee- jerk)
- Patient who received magnesium sulphate outside the hospital.

Sample size

100 case will be grouped by lottery into group A and group B.

- Group –A** : For 8g of magnesium sulphate heptahydrate (Nalepsin) intravenous (IV) route.
- Group - B** : For 10g magnesium sulphate, (4gm I.V slowly than 3g I.M in each buttock) conventional treatment.

Methodology

This study was conducted at DMCH for 1 (one) year from June 2007 to May 2008. Patient fulfilling the above mentioned criteria were selected for study and divided them randomly by lottery into two groups after taking detailed history from attendant, a preformed questionnaire was filled by investigator herself and a written consent for including them for study were taken. After thorough evaluation of cases, all necessary investigations like CBC, estimation of total urinary protein, blood urea, serum creatinine, uric acid, FDP, fibrinogen level, serum electrolyte, platelet count, liver function test were done. But due to lack of facilities and inadequate funding serum magnesium level before and after the treatment with $MgSO_4$ was not possible. Weight measurement was not also possible due to convulsive state. So weight should be recorded from previous ANC record. Among two groups, the patients under group A were selected as a case and treated by 8g of magnesium sulphate intravenously (4g @ of 70-75d/m and another 4g (20-25d/m) and group B were selected as a control 10g $MgSO_4$ as per schedule if their respiratory rate >16/min, urine output > 30ml / hour, knee jerk present. All patients were monitored hourly by pulse, BP, respiratory rate, level of consciousness, knee jerk, auscultation of lungs, urine output with its colour, abnormal bleeding from any site. Continuous catheterization and I.V fluid was given very cautiously. Injection hydralazine 20mg in 200ml of 5% dextrose in aqua was given in continuous I.V drip when indicated for controlling of blood pressure. If recurrence of convulsion occur within 24 hours, then maintenance dose was given and if recurrence occur after 24 hours of initial dose than again loading dose was given with maintenance dose.

Complication if occurred any, such as HELLP syndrome, renal failure, cardiac arrest, pulmonary oedema were treated accordingly. After control of convulsion irrespective of gestational age, termination of pregnancy was done according to obstetric indication and Bishop scoring within limited time for eclamptic patient. Treatment was recorded in a clinical data sheet selected for case & control group with proper & systemic input; data was compiled, edited and analyzed by using SPSS programme. Because of the nature of analysis, chi-square (X^2) test and unpaired 't' was performed and collected data were analyzed

to decide upon the significance of finding. A 'P' value of < 0.05 was considered as significant.

Result:

During study period from June 2007 to May 2008 total number of eclamptic patients were 710 (ante partum, intrapartum and postpartum). Among them, only 100 of the ante partum and intrapartum patient who fulfilled the inclusion criteria were including in this study. Different variable were studied between case and control group and results were analyzed by unpaired 't' test and chi-square test (X^2).

The number of patient in group A = 48 and group B =52

The result of different parameters of patient profile of both group such as age, gravidity, socioeconomic condition, status of antenatal care, gestational age, type of eclampsia were found not significant statistically.

All parameters of this study shown below.

Table-I
Age distribution

Age (Years)	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
≤20	22 (42.3)	19 (39.6)	>0.50 ^{ns}
>20	30 (57.7)	29 (60.4)	
(Meant ± SD)	22.44±4.11	22.92±3.83	>0.50 ^{ns}
Range	18-35	18-36	

Table – I Shows age distribution of case & control group & result is statistically not significant. Chi-square / unpaired Student's 't' test ns= Not significant.

Table-II
Socioeconomic status

Status	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
Low	45 (86.5)	34 (70.8)	>0.05 ^{ns}
Middle	7 (13.5)	14 (29.2)	

Table-II Shows the socioeconomic status of both group & result shows no statistical significance between two group.

Chi-square test
ns= Not significant.

Table-III
Gravidity of the patients.

Gravidity	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
Primi	37 (71.2)	36 (75.0)	
Multi	12 (23.1)	10 (20.8)	>0.50 ^{ns}
Grandmulti	3 (5.8)	2 (4.2)	

Table-III Shows gravidity between case & control group & shows no significance between two group statistically. Chi- square test
ns= Not significant.

Table-IV
Status of antenatal care

ANC	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
Regular	11 (21.2)	13 (27.1)	
Irregular	20 (38.5)	19 (39.5)	>0.50 ^{ns}
None	21 (40.0)	16 (33.3)	

Table-IV Shows status of antenatal care in two group & statistical analysis of result proves no significance between two group
Chi- square test
ns= Not significant.

Table-V
Gestational age

Gestational (weeks)	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
≤32	14 (26.9)	14 (29.2)	
33-36	17 (32.7)	22 (45.8)	>0.10 ^{ns}
≥37	21 (40.0)	12 (25.0)	

Table- V. Shows gestational age of the patient between two group on admission & result is statistically not significant.
Chi- square / unpaired Student's 't' test
ns= Not significant.

Table-VI
Type of eclampsia

Type	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
Antepartum	43 (83.7)	34 (70.8)	
Intrapartum	9 (17.3)	14 (29.2)	>0.10 ^{ns}

Table-VI Shows type of eclampsia of both groups & after statistical analysis, shows not significant between two groups.
Chi- square test
ns= Not significant.

Table-VII
Number of convulsion before hospital admission

Number of convulsion	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
1-2	11 (21.2)	15(31.3)	
3-5	25 (48.1)	17(35.4)	>0.10 ^{ns}
>5	16 (30)	16(33.3)	

Table -VII display the number of convulsion before hospital admission and after statistical analysis of both group by chi-square test, result shows no significance difference between two groups.

Table-VIII
Recurrence of convulsion after initiation of treatment.

Recurrence	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
Yes	9(17.3)	6(12.5)	>0.50 ^{ns}
No	43(82.7)	42 (87.5)	

This table also shows no significant result after analysis by chi-square test.

Table IX
Level of consciousness on admission to the Hospital.

Level of consciousness	Control (n-52) No. (%)	Case (n-48) No. (%)	P value
Conscious	30(57.7)	25(52.1)	
Unconscious	9(17.3)	14(29.2)	>0.10 ^{ns}
Semi conscious	13(25.0)	9(18.8)	

Table of this parameter of both group after analysis by chi-square test shows not significant.

Table X
Time required to regain consciousness after initiation of treatment.

Time (Hours)	Control n-22 No(%)	Case (n-23) No(%)	P value
<4	11(50.0)	12 (52.2)	
4-24	8 (36.4)	12 (30.4)	>0.50 ^{ns}
>24	3(13.6)	4 (17.4)	

This table shows time required to regain consciousness after initiation of treatment and result shows not significant statistically after analysis by chi-square test.

Table-XI
Status of blood pressure on admission and at discharge from Hospital.

Blood Pressure (mm of Hg)	Control (Meant ± SD)	Case (Meant ± SD)	P value
SBP On Admission	148.56 ± 21.24(n=52)	152.92 ± 23.58(n=48)	>0.10 ^{ns}
At discharge	123.47 ± 13.35(n=49)	124.67 ± 11.66(n=46)	>0.50 ^{ns}
DBP On Admission	104.12±16.97(n=52)	102.29±12.84(n=48)	

Table-XI. States of blood pressure on admission and at discharge between two group & result is not significant statistically.

Unpaired Student's 't' test and Chi-square test
ns= Not significant.

Table XII
Maternal complication

Complication	Control (n-52)	Case (n-48)	P value
	No. (%)	No. (%)	
Present	6(11.5)	4 (8.3)	>0.05 ^{ns}
Absent	46 (88.5)	44 (91.7)	
Type of complication			
Pulmonary oedema	2(33.3)	1(25.0)	
Renal Failure	2(33.3)	1(25.0)	
PPH	2(33.2)	2(50.0)	

Table – XII Shows maternal complications of both group and after statistical analysis result shows no significant difference between two groups.

Chi-square test
ns= Not significant.

Discussion:

Eclampsia is one of the main cause of maternal mortality in developing country. It is a very serious & relatively frequent life threatening obstetrics emergency. In developing country like Bangladesh among other causes of maternal death eclampsia account one third.^{7,16,17} Magnesium level <0.7mmol/L indicative of magnesium deficiency. Symptoms appears when level fall <.5mmol/L Magnesium has independent attributes in cellular function. This low Mg⁺² level causes disruption of cellular function⁶. Magnesium sulphate (MgSO₄) which is the most commonly used medication for the treatment & prevention of convulsion in patient with severe pre-eclampsia & eclampsia as because it is superior to all other anticonvulsant in term of controlling & preventing convulsion¹⁸. Its efficacy for preventing a second convulsion in eclampsia has been proven conclusively by prospective randomized trails & its prophylactic role is currently being assured

Table-XIII
Maternal death & cause of death

Death	Control (n-52)	Case (n-48)	P value
	No. (%)	No. (%)	
Yes	3 (5.8)	2 (4.2)	>0.05 ^{ns}
No	49 (94.2)	46 (95.8)	
Cause of death			
Respiratory Failure	1 (33.3)	1 (50.0)	
Renal Failure	2 (66.7)	1 (50.0)	

Table.XIII Shows number of maternal death and their causes, after analysis of the result it shows no significance difference

chi-square test.
ns= Not significant.

prospectively in several studies.¹⁹ Use of magnesium sulphate has been found to be associated with significant reduction of maternal mortality primarily by its action on relieving cerebral vasospasm^{20,21}.

This prospective case control study was designed to find out the lowest single dose of MgSO₄ which effectively control the eclamptic seizures & also prevent the recurrence of convulsion. The idea for this lowest dose is, as because the Bangladeshi women are lighter in their body weight which may reduce the MgSO₄ related toxicities. By this study we also compare the treatment outcome with the existing regimen of MgSO₄ 4gm I.V (over 15 minute along with 3gm in each buttock intramuscularly as a loading dose. There was another study done by (Dr. Nilufar et al' 2003) they proved that only 10 gm loading dose of magnesium sulphate was sufficient to control convulsion in eclamptic patient & also to prevent recurrence with the previous regimen (4gm I.V +6gm I.m +2.5gm I.m 4 hours for 24 hour). By this study we

also proved 8 gm of $MgSO_4$ if given intravenously in a single dose is sufficient to control eclamptic convulsion which is not statistically significant with the 10gm used for control group. Though there was some limitations even than we found that fetal hypotonia & neonatal hypermagnesemia also reduced due to minimum dose.

Limitation of the study

1. Different type of essential investigation were difficult to do in emergency basis due to lack of facilities and as well as lack of ability of the patient.
2. This study confined to a limited number of patient was probably statistically not much significant and too difficult to find out the exact epidemiological importance.
3. Most of the patient was unable to respond to the questionnaire. The attendant in many instances were helpful, but were less informative. So they were also unable to answer correctly to the questionnaires.

Conclusion

As because the Bangladeshi women were lighter in their body weight & if any pregnant patient developed eclampsia and fulfilling the inclusion criteria only 8gm $MgSO_4$ heptahydrate (2bags Nalepsin) can be used effectively to control convulsion in eclamptic patient and it is also cost effective and easy to use.

Recommendation

Unless any serious complication occurred with eclamptic patient it is the 8gm of $MgSO_4$ heptahydrate which is sufficient to control the convulsion in eclamptic patient. It also minimize the dose related toxicity and mode of administration is easy and avoid intramuscular painful injection. But further study with a big series is needed.

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