International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2020; 4(1): 213-217
Received: 04-11-2019
Accepted: 08-12-2019

Dr. Shaily Agarwal
Associate Professor, Department of Obstetrics and Gynaecology, G.S.V.M Medical College Kanpur, Uttar Pradesh, India

Dr. Renu Gupta
Associate Professor, Department of Obstetrics and Gynaecology, G.S.V.M Medical College Kanpur, Uttar Pradesh, India

Dr. Kiran Pandey
Professor and Head, Department of Obstetrics and Gynaecology, G.S.V.M medical college Kanpur, Uttar Pradesh, India

Dr. Neena Gupta
Professor, Department of Obstetrics and Gynaecology, G.S.V.M Medical College Kanpur, Uttar Pradesh, India

Dr. Pavika Lal
Assistant Professor, Department of Obstetrics and Gynaecology, G.S.V.M Medical College Kanpur, Uttar Pradesh, India

Dr. Madhavi Verma
Junior Resident, Department of Obstetrics and Gynaecology, G.S.V.M Medical College Kanpur, Uttar Pradesh, India

Corresponding Author:
Dr. Renu Gupta
Associate Professor, Department of Obstetrics and Gynaecology, G.S.V.M Medical College Kanpur, Uttar Pradesh, India

Is low dose magnesium sulfate regimen a better option for treatment of hypertensive disorders of pregnancy: Our experience at tertiary care centre

Dr. Shaily Agarwal, Dr. Renu Gupta, Dr. Kiran Pandey, Dr. Neena Gupta, Dr. Pavika Lal and Dr. Madhavi Verma

DOI: https://doi.org/10.33545/gynae.2020.v4.i1d.464

Abstract
Introduction: Hypertensive disorders of pregnancy is one of the leading causes of fetomaternal mortality and affecting 10% of all pregnancies.
Materials and Methods: A prospective interventional study was conducted on 140 patients from January 2017 to January 2019 and comparision was made among the three different magnesium sulfate regimens.78 patients with severe preeclampsia and 62 patients with eclampsia were randomly allocated in 3 groups and were followed up to delivery to evaluate the fetomaternal outcome. Then the results were compared and analysed.
Results: Statistically higher incidence of signs of impending toxicity such as loss of patellar reflex, oliguria, respiratory rate depression were more in group 1(Pritchard) as compared to other groups. There were no significant differences in other measures of feto-maternal complications.
Conclusion: As compared to Pritchard, Zuspan and Dhaka (Low dose regimens) have similar efficacy in controlling and prevention of convulsions & potentially have less side effects.

Keywords: Eclampsia, severe preeclampsia, magnesium sulphate, drug toxicity, fetomaternal outcome

Introduction
Hypertensive disorders of pregnancy (HDP) is still one of the most common medical disorders during pregnancy as well as the leading cause of maternal and perinatal morbidity and mortality, affecting 10% of all pregnancies [1, 2]. In India, maternal mortality due to hypertensive disorders ranges from 8 – 14% [3-5]. Among the various treatment interventions of this disease, magnesium sulfate has been proved to be a boon as an anticonvulsant and is the drug of choice for both prevention of seizures in severe pre-eclampsia and treatment of eclampsia but the major concern is its toxicity such as oliguria, loss of patellar reflex and respiratory depression which limits its use in many low middle income countries (LMIC) [6, 7]. Most of the patients being referred to our tertiary care centre do not receiveeven the loading dose, due to the apprehension caused by magnesium sulfate toxicity. Using low dose regimen will not only decrease the risk of maternal toxicity and fetal side effects as well asdecrease the cost of therapy and increase its safety for low resources settings where biochemical means of measurements of magnesium sulfate is not readily available and the physician totally relies on clinical findings of dose related toxicitiy [8]. The aim of our study was to compare the various regimens of magnesium sulfate in severe preeclampsia and eclampsia without compromising its efficacy in feto-maternal outcome.

Materials and Methods
This was a prospective interventional study carried out from January 2017 to January 2019 (2 years) in the department of Obstetrics and Gynaecology, Upper India Sugar Exchange maternity hospital at G.S.V.M. Medical College, Kanpur. All antenatal patients who presented with severe preeclampsia and eclampsia at a gestational age of ≥ 24 weeks, were enrolled for this study, after taking a proper written and informed consent and were followed up to delivery to evaluate the feto-maternal outcome. Patients with mild preeclampsia, gestational hypertension, chronic hypertension and neurological disorders were excluded. 140Patients were randomly allocated among three groups namely: Pritchard (group1), Zuspan (group2) and Dhaka (group3) by using random number tables.

Pritchard Regimen: Loading dose - 4 grams of magnesium sulfate intravenous (20% solution in 10 – 15 minutes) with 5 grams intramuscular (50% solution) in each buttock and maintenance dose - 5 gms intramuscular in alternative buttock 4 hourly for 24 hours after last fit or delivery, whichever was later.

Zuspan regimen: Loading dose - 4 grams of magnesium sulfate intravenous (20% solution in 10 – 15 minutes) and maintenance dose - 1 gram/ hour infusion for 24 hours after last fit or delivery whichever was later.

Dhaka regimen: Loading dose - 4 grams of magnesium sulfate intravenous (20% solution in 10-15min) with 3 grams (50% solution) intramuscular in each buttock along with maintenance dose of 2.5 grams intramuscular in alternate buttock every 4 hourly after last fit or delivery, whichever was later.
In case of repeat fits, 2 grams Magnesium sulphate (20% solution) was given as I.V. bolus. Total number of patients were 50, 44 and 46 in group I, group II and group III respectively.

Table 1: Reduction from standard dose

Regimen	Loading dose	Maintenance dose	Total dose in 24 hours	Reduction from standard dose
Pritchard	4grams IV+5+5grams IM	5 grams/4 hourly	44 grams	Standard dose
Zuspan	4 grams IV	1 gram / hour	28 grams	36.4%
Dhaka	4 grams IV+3+3 grams IM	2.5grams/4 hourly	25 grams	43.2%

A structured form was filled for each patient under the following headings:

(I) Maternal events
a. Recurrence of fits (number and times),
b. Spontaneous onset or induction along with progress of labour,
c. Mode of delivery.

(II) Perinatal events
a. mean birth weight,
b. frequency of neonatal depression i.e. apgar Score<7 at the time of birth.

(III) Complications - birth asphyxia, respiratory distress syndrome, sepsis, hyperbilirubinemia, neonatal mortality. Subjects with severe preeclampsia and eclampsia were admitted in the labour room and initial supportive treatment was given along with athorough and quick general, systemic and obstetrical examination was done along with bed side proteinuria. Antihypertensive agents were given and all the relevant feto-maternal data were recorded and analyzed.

Statistical analysis
The data was compiled and statistically analyzed by statistical software namely Graph pad Instat version 3.1 by using CHI SQUARE TEST. The following assumptions were made on data,
Suggestive significant (P value: 0.05<P<0.10)
Moderately significant (P value: 0.01<P≤0.05)
Strongly singnificant (P value: P<0.01).

Results
140 Patients of severe preeclampsia (78) and eclampsia (62) were randomly given magnesium sulfate by three regimens namely: Pritchard (group1), Zuspan (group 2) and Dhaka (group3) and were followed and assessed for feto-maternal outcome. The mean systolic blood pressure of eclampsia and severe preeclampsia patients was 164.03±11.38mmHg and 170.28±8.82mmHg respectively and mean diastolic blood pressure was 106.19±8.22mmHg and 108.70±6.56mmHg in eclampsia and severe preeclampsia respectively.
The socio-demographic and clinical profiles of the enrolled women were summarized in Table 1 and Table 2 respectively.

Table 1: Socio-demographic characteristics of the study population

Characteristics	Eclampsia(n=62)	Severe preeclampsia(n=78)
	No (%)	No. (%)
Booked/unbooked		
Booked	16 (25.81%)	33(42.31%)
Unbooked	46 (74.19%)	45 (57.69%)
Socio-economic status		
Low	30(48.39%)	38 (48.72%)
Medium	26 (41.94%)	33 (40.31%)
High	6 (9.58%)	7 (8.97%)
Age(years)		
<20(years)	4 (6.45%)	9 (11.34%)
20-35(years)	38 (61.29%)	49 (62.82%)
>35(years)	20 (32.26%)	20 (25.64%)
Parity		
Nulliparous	33 (53.23%)	43 (55.13%)
Multiparous	29 (46.77%)	35 (44.87%)
Family h/o HTN	22 (35.48%)	32 (41.03%)

h/o HTN=history of hypertension

Commonest gestational age when eclampsia occurred was at 32-37 weeks, most of the patients were 20-35 years of age group, unbooked and belonged to low socioeconomic status. The admission-delivery interval was approximately 12-24 hours as shown in Table 2. 71% cases of eclampsia and 75.65% cases of severe pre-eclampsia were delivered by vaginal route.

Table 2: Clinical Profile of the Study Population

Clinical profile	Eclampsia(n=62)				Severe preeclampsia(n=78)			
	I(Pritchard) (n=22)	II(Zuspan) (n=19)	III(Dhaka) (n=21)		I(Pritchard) (n=28)	II(Zuspan) (n=25)	III(Dhaka) (n=25)	
	No. (%)	No. (%)	No. (%)	P-value	No. (%)	No. (%)	No. (%)	P-value
Gestational Age								
<37 (weeks)	11 (50%)	9(47.37%)	11 (52.38%)	0.94	14 (50%)	13 (52%)	8 (32%)	0.48
37-40 (weeks)	7 (31.82%)	7(36.84%)	8 (38.10%)		17(28.67%)	9 (36%)	12 (48%)	
>40 (weeks)	4 (18.18%)	3(15.79%)	2 (9.52%)		6 (21.42%)	3 (12%)	5 (20%)	
Admission-delivery time interval								

<12 (hours)	7 (31.82%)	5 (26.32%)	3 (14.29%)	0.61	9 (32.14%)	6 (24%)	8 (32%)	0.61
12-24 (hours)	11 (50%)	10 (52.63%)	15 (71.43%)		11(39.29%)	10 (40%)	12 (48%)	
>24(hours)	4 (18.18%)	4 (21.05%)	3 (14.29%)		8 (28.57%)	9 (36%)	5 (20%)	
Mode of delivery								
Vaginal								
Spontaneous	9 (40.91%)	8(42.11%)	10 (47.62%)	0.98	12 (42.86%)	8 (32%)	10 (40%)	0.70
Induced	6 (27.27%)	6(31.58%)	5 (23.81%)		8 (28.57%)	12 (48%)	9 (36%)	
LSCS	7 (31.82%)	5(26.32%)	6 (28.57%)		8 (28.57%)	5 (20%)	6 (24%)	

LSCS=lower segment cesarean section

Signs of impending toxicity is shown in Table 3. Loss of patellar reflex was significant in group I as compared to other groups. Rest of the signs of toxicity like oliguria, decrease respiratory rate and local site complication (gluteal abcess) though more in group I were statistically insignificant as compared to other groups. Recurrence of fits were insignificantly found more with group I as compared to other groups.

Table 3: Signs of magnesium sulfate toxicity

Signs	Eclampsia(n=62)				Severe preeclampsia(n=78)			
	I(Pritchard) (n=22)	II(Zuspan) (n=19)	III(Dhaka) (n=21)		I(Pritchard) (n=28)	II(Zuspan) (n=25)	III(Dhaka) (n=25)	
	No. (%)	No. (%)	No. (%)	P value	No. (%)	No. (%)	No. (%)	P value
Loss of patellar reflex	7 (31.82%)	2 (10.53%)	1 (4.76%)	0.04	8 (28.57%)	3 (12%)	1 (4%)	0.01
Oliguria(<30ml/hour)	5 (22.72%)	1 (5.26%)	-	0.031	7 (25%)	2(8%)	1(4%)	0.05
RR(<16/min)	4 (18.18%)	1 (5.26%)	-	0.07	6 (21.43%)	2 (8%)	-	0.03
Local site complication (gluteal abcess)	4 (18.18%)	-	-	0.02	5 (17.86%)	-	1 (4%)	0.02
Recurrence of fits	1 (4.54%)	-	1 (4.76%)	0.63	-	-	-	-

RR=Respiratory rate

10/62(16.13%) and 5/78 (6.41%) patients of eclampsia and severe preeclampsia were required intensive care unit (ICU) respectively. 4 patients of eclampsia and 1 patient of severe preeclampsia were expired and caused 6.45% and 1.28% maternal mortality in cases of eclampsia and severe preeclampsia respectively as shown in table no-4. Very severe anemia and aspiration pneumonia followed by pulmonary edema were accounted for majority of these deaths.

Table 4: Maternal Complication and Outcome

Complication	Eclampsia (n=62)	Severe preeclampsia (n=78)
	No. (%)	No. (%)
Atonic PPH	5 (8.06%)	9 (11.54%)
Abruption	4 (6.45%)	7(8.97%)
HELLP (total/partial)	13 (20.91%)	10 (12.82%)
ARF	6 (9.68%)	10 (12.82%)
Pulmonary edema	8 (12.90%)	4 (5.43%)
Maternal ICU admission	10 (16.13%)	5 (6.41%)
Maternal mortality	4 (6.45%)	1 (1.28%)

PPH = Post partum hemorrhage, ARF = acute renal failure

Most common complication was HELLP syndrome (total or partial) in both of cases of severe preeclampsia and eclampsia as shown in table no-4.

Table 5: Neonatal Outcome

Neonatal Outcome	Eclampsia (n=62)	Severe preeclampsia (N=78)
	No. (%)	No. (%)
Live Birth	43 (69.35%)	58 (74.36%)
Perinatal mortality	19 (30.65%)	20 (25.64%)
APGAR score < 7	25 (40.32%)	27 (34.62%)
NICU admission	21 (33.37%)	25 (32.05%)
Severe-birth asphyxia	8 (12.90%)	13 (16.67%)
Hyperbilirubinemia	15(24.19%)	22 (28.21%)
Sepsis	8 (12.90%)	4 (5.13%)

Mean birth weight of neonates of eclampsia and severe preeclampsia patients were 2.23±0.46 and 2.38±0.69 respectively. 21(33.37%) and 25(32.05%) neonates in cases of eclampsia and severe preeclampsia required neonatal intensive care units (NICU) due to various complication. Perinatal mortality in cases of eclampsia was 30.65% and in severe pre-eclampsia it was 25.64% as shown in table 5. There were no significant difference in other measures of feto-maternal complication.

Discussion

Various regimens of magnesium sulfate like Zuspan and Dhaka (low dose regimens) are now being increasingly used as anticonvulsant regimens over Pritchard regimen, as low dose regimen were reported to have decrease incidence of side effects without significantly decreasing the therapeutic benefits. Dhaka regimen would be clinically relevant for obstetrician in low income countries, where maternal height and weight are almost always on the lower side.

Various studies reported the mean age of incidence of severe pre-eclampsia and eclampsia to be 26.5 years as this is the peak reproductive age group. In our study, majority of the patients were unbooked belonging to rural background and lower socioeconomic status. This reflects lack of proper antenatal coverage as well as ignorance and unawareness among the rural population about the importance of antenatal visits. Similar findings were observed by Agarwal [9] and Sahu [10] *et al*. Majority the patients of eclampsia (53.23%) and severe preeclampsia (55.13%) were nulliparous. Ekele [11] reported it to be 89% while Seth *et al*. [12] found incidence of eclampsia in primigravida to be 74.2%. Most of the patients of eclampsia (50%) and severe PET (44.87%) had gestational age <37 weeks and our findings was concordance with the study of Seth *et al*. [12].

4.54% cases of eclampsia had recurrence of fits in group1 (Pritchard regimen) and 4.76% cases had recurrence in Group 3(Dhaka regimen) and none of the case was found in group 2(Zuspan regimen) but it was statistically insignificant (p=0.63).Similar results were found in the study of Vaibhav

Kanti *et al*. [13]. In study of Begum R *et al*. [14] and Begum MR *et al.* [15] recurrence rate of fits with Dhaka regimen was 21.4%. which was higher as compared to the above mentioned study.

Chinayon P [16] and Ekele [11] *et al*. suggested that, clinical assessment of knee jerk, respiration and urine output was adequate to monitor maternal magnesium toxicity without the need to measure the magnesium serum levels. In our study, we observed the impending signs of magnesium sulfate toxicity as loss of deep tendon reflex in16.13% and 15.38% cases of eclampsia and severe preeclampsia respectively which were very significant (P-values 0.04 and 0.01 respectively) majority of cases were in group I (Pritchard), oliguria (<30ml/hour) in 9.68% and 12.82% cases of both eclampsia and severe preeclampsia respectively (P-values were significant 0.031 and 0.05 respectively) most of cases were found in group I (Pritchard). The local site complication i.e gluteal abcess was only found in patients who received Pritchard regimen which was in concordance with the study conducted by Vaibhav Kanti [13] and Anshu Sharma [17], this complication becomes important as it requires daily dressing and some time debridment and therefore prolongs the hospital stay thereby increasing the maternal morbidity. In a study conducted by ChissellS [18], who found that magnesium sulfate toxicity was in 12.5% cases of intravenous group and none in intramuscular group, contrast to our findings. Begun R *et al*. [14] and Seth S *et al*. [12] described that absent deep tendon reflexes were more among those on Pritchard regimen as compared to Dhaka regimen which was similar to our study. In our study, it was observed that HELLP syndrome was the most common complication in patients of eclampsia and severe preeclampsia. 16.13% of eclampsia patients and 6.41% of severe preeclampsia patients were admitted in intensive care unit, out of which 6.45% of eclampsia patients expired. Sardesai [19] *et al*. also reported that complications were more with intravenous regimen (Zuspan) than the intramuscular regimen (Pritchard) which was found to be contrast to our study.

4/62 (6.45%) patients of eclampsia and 1/78 (1.28%) of severe pre-eclampsia were expired despite of intensive management. Thus, maternal mortality rate was 3.57% in our study which was similar to study conducted by Chaudhary *et al*. [20] (3.3%).In the numerous studies conducted by Begum MR [15] *et al*, Seth S [12] *et al.* and Chaudhary JR *et al*. [20] maternal mortality with standard regimen was higher than those with low dose regimen which was similar to our study.

In our study significantly more patients of eclampsia and severe PET on Pritchard regimen (group 1) were undergone LSCS. The finding of our study was similar to the study of Chissell S [18] and collaborative eclampsia trial whereas Shikha Seth [12] found at 29.2% of patients on Dhaka regimen underwent caesarean section as compared to Pritchard regimen (10.9%) which was contrary to our study.

Sardesai [19] and Pritchard [21] had 20.22% and 3.83% perinatal mortality respectively. Collaborative Eclampsia trial using standard dose regimen found perinatal mortality rate to be 24-26% and birth asphyxia of 44 - 48% in eclampsia. Results of our study pertaining to perinatal mortality (35%) were similar to above mentioned studies.

Conclusion

Our study concludes that low dose magnesium sulfate regimens like Zuspan and Dhaka used in treatment of patients of severe preeclampsia and eclampsia had similar efficacy in controlling and prevention of convulsions, potentially have less toxicity with better perinatal outcome when compared to Pritchard regimen. Therefore it can be a better alternative to standard dose magnesium sulfate regimen and can be beneficial in the prevailing gloomy maternal mortality scenario in developing countries attributed to hypertensive disorders of pregnancy.

Our results can have three major implications

First: Low dose regimen virtually eliminated the risk of magnesium sulfate toxicity and thereby increasing the safety of drug.

Second: As the regimen lowered the drug dose for each patient, it decreases the frequency of biochemical monitoring of serum magnesium level which is feasible as well as cost effective and it becomes very important in low resource settings.

Third: With low dose Dhaka regimen and better safety profile, usage of magnesium sulfate at peripheral health centres, will be promoted that can markedly improve the outcome of reffered severe preeclampsia and eclampsia patients.

References

1. LoJo Mission, JF Caughey AB. Hypertensive Disease of pregnancy and maternal mortality CurrOpin Obstet. Gynaecol. (Epup ahead of print). 2013
2. Muti MT, Shimanga M, Motion GT, Bangore D, Chonzi P. Prevalence of pregnancy induced HTN and pregnancy outcomes among women seeking maternity services in harare Zimbabwe BMC cardiovascular disorders. 2015; 15:11.
3. Bhargawa A, Paul R, Chutani N, Singh SK. In search for accelerated recovery from eclampsia Obs. Gynaecology India. 2006; 56(5):402-05.
4. Usha K, Shrinar NK. OBG in prospective pregnancy induced hypertension. Orient Longman Publications. Endocr. Jr. 2009; 56(8):921-34.
5. Dutta DC. Text book of Obs 8th Edition Chapter 17; Hypertensive disorders on pregnancy central publishers 2016, 221-242.
6. Duley L, Matar HE, Almerie MQ, Hall DR. Alternative magnesium sulfate regimens for women with pre-eclampsia and eclampsia. Cochrane Database Syst Rev. 2010; (8): CD007388.
7. Begum R, Begum A, Bullough CH, Johanson RB: Reducing maternal mortility from eclampsia, using magnesium sulfate. Eur J Obstet Gynecol Reprod Biol. 2000; 92(2):223-4.
8. Within AG. Prevention and treatment of eclamptic convulsions. Clin Obstet Gynecol. 1999; 42(3):507-18.
9. Agarwal S, Dhall K, Bhatia K. Epidemiologic IV of eclampsia J Obstet. Gynaecol India. 1983; 33:83.
10. Latika Sahu, Shubhra Singh, Anjali Tempe BC, Koner. A randomized comparative study between low dose magnesium sulfate and standard dose regimen for management of eclampsia Int. J Reprod. Contracept Obstet Gynaecol. 2014; 3(1):79-86.
11. Ekele BA, Badung SL. Is serum magnesium estimate necessary in patients with elampsia on magnesium sulfate. Afr. J Reprod Health. 2005; 9(1):128-32.
12. Seth S, Nagrath A, Singh DK. Comparison of low dose single loading dose and standard Pritchard regimen of magnesium sulfate in ante partum eclampsia. Anatol. J Obstet Gynaecol. 2010; 1(1):1-4.
13. Kanti V, Gupta A, Seth S, Bajaj M, Kumar S, Singh M. Comparison between IM and IV regimen of Magnesium sulfate in management of severe preeclampsia and eclampsia Int. J. Reprod Contracept Ostet. Gynaecol. 2015;

4:195-201.
14. Begum R, Begum A, Johanson R, Ali MN, Akhtar SA. Low dose (Dhaka) magnesium sulfate regimen for eclampsia. Acta Obstet. Gynaecol. Scaned. 2001; 80:998- 1002.
15. Begum MR, Begum A, Quadir E. Loading dose versus standard regimen of Magnesium sulphate in the management of eclampsia: A randomized trial J Obstet Gynaecol. 2002; 28(3):154-9.
16. Chinayon P. Clinical management and outcome of eclampsia at rajavithi Hospital. J Med Assoc.thai 1998; 81(8):579-85.
17. Sharma A, Gupta KB, Nigam A, Pathania K. Comparison of low dose Dhaka regimen of Magnesium sulfate with standard Pritchard regimen in eclampsia. Int. Jreprod Contracept Obstet. Gynaecol 2016; 5:3954-8
18. Chissell S, Botha JH, Moodley J, Mcfadyen L. IV and IM magnesium sulfate regimen in severe pre-eclampsia. S Afr Med J.1994; 84(9):607-10.
19. Sardesai S, Maria S, Patil A. Low dose magnesium sulfate therapy for eclampsia and imminent eclampsia-Regimen tailored for Indian women J obstet Gynaecol. India. 2003; 53(6):546-50
20. Chowdhary JR, Chowdhary S, Bhattacharya N, Biswas PK. Comparision of intramuscular magnesium sulfate with low dose intravenous magnesium sulfate regimen for treatment of eclampsia. J. Obstet Gynaecol research. 2009; 35(1):119-25.
21. Pritchard JA, Cunningham FG, Pritchard SA. The Parkland memorial hospital protocol for treatment of eclampsia evaluation of 245 cases. Am J Obstet Gynaecol. 1984; 148(7):951-63.