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Original Research

Pritchard's Regimen: The Effect of 12-Hour Versus 24-Hour Magnesium Sulphate Maintenance Regimen on the Occurrence of Seizures and Maternal Outcome in Women with Severe Features of Preeclampsia: A Triple-Blind Randomized Controlled Trial

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Abstract

Background: Magnesium sulphate ($MgSO_4$) administered for twenty-four hours is the drug of choice for seizure prophylaxis in patients with preeclampsia with severe features. Due to its narrow therapeutic index, a reduction in the duration of $MgSO_4$ administered in the postpartum period may not only prevent the occurrence of seizures but also reduce the adverse effects associated with this drug. This study aimed to compare the efficacy of the 12-hour and 24-hour Pritchard's MgSO4 maintenance regimen on the occurrence of seizures and maternal outcomes in patients with preeclampsia with severe features.

Methodology: A triple-blind randomized controlled trial was conducted among women with preeclampsia with severe features between 1st June 2022 and January 31st, 2023. The primary outcome measure was the occurrence of seizure in either arm of the study. One hundred and forty-six women were randomized into two groups, those who received a 12-hour $MgSO_4$ regimen and placebo for the remaining twelve hours (Group I) and those who received a 24-hour $MgSO_4$ regimen in the postpartum period (Group II). The collected data was coded and analyzed using Statistical Product and Service Solutions (SPSS) version 26 and $p<0.05$ was considered significant.

Results: There was no statistically significant difference between the two groups concerning the occurrence of seizures, the need to recommence $MgSO_4$, clinical evidence of toxicity and adverse effects of MgSO4. There was also no statistically significant difference between the two groups in the total dose of MgSO4 administered, duration of urethral catheterization and duration of hospital admission. No maternal mortality was recorded in this study.

Conclusion: The results of this study suggest that the 12-hour $MgSO_4$ maintenance regimen is as efficacious as the traditional 24-hour regimen in preventing seizures without worsening maternal outcomes.

Keywords: Efficacy; Magnesium Sulphate; Preeclampsia with Severe Features; Randomized Controlled Trial, Seizures, Therapeutic Index.

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Quick Response Code:

Introduction

Preeclampsia is a pregnancy-specific disease characterized by hypertension and proteinuria arising after the 20th week of gestation in a previously normotensive and non-proteinuric woman.[1-3] It affects 5-10% of pregnancies worldwide and can occur in the antenatal, intrapartum or postpartum periods.[4-5] In a patient with preeclampsia the presence of one or more of the following indicates a diagnosis of preeclampsia with severe features; severe blood pressure elevation of ≥160/110, symptoms of CNS dysfunction, hepatic abnormality, thrombocytopenia (with platelet count < 100,000 platelets/microliter), renal impairment and pulmonary oedema.[2]

Prompt commencement of prophylactic anticonvulsant therapy to prevent seizures is one of the core principles of the management of severe preeclampsia. The other principles include control of hypertension, early detection, and correction of haematologic and electrolyte abnormalities, early detection and management of end-organ derangements such as acute kidney injury and delivery of the fetus by the most expedient route.[1]

Magnesium sulphate ($MgSO_4$) is the drug of choice for prophylactic anticonvulsant therapy and is more effective and safer than the use of other options like diazepam, phenytoin, and lytic cocktail.[6-7] Despite the benefits of $MgSO_4$ in seizure prophylaxis and treatment, its toxicity is still a major concern.[8] The risk of side effects which span from neurological, and cardio-respiratory depression amongst others could increase with the duration of treatment especially if there are challenges in clinical monitoring of the patient as this drug has a narrow therapeutic index. Hence the benefit of magnesium sulphate prescription should always outweigh its adverse effects.[8]

Traditionally, the use of $MgSO_4$ has been recommended for 24 hours following delivery, the period of greatest risk for the occurrence of eclampsia.[9-10] The method of administration, dosage and duration of $MgSO_4$ after delivery have been compared in different studies.[8,10]Some recent studies have suggested that anticonvulsant therapy may be continued for shorter periods of 8 or 12 hours rather than the traditional 24-hours postpartum with the same degree of effectiveness and without putting the mother at an increased risk of morbidity or mortality.[8-10]However, there is no consensus on replacing the 24-hour maintenance dose.[9]

This study aimed to compare the efficacy of the 12-hour or 24-hour Pritchard's MgSO4 maintenance regimen on the occurrence of seizures and maternal outcomes in women with preeclampsia with severe features using a triple-blind randomized controlled trial study design.

Methodology

Study Design: A triple-blind randomized controlled trial (parallel design) was used for this study. Also, the Consolidated Standards of Reporting Trials (CONSORT) were followed.[11]. The study was registered with RCT registration number: PACTR202206623958155

Participants: This included all consenting patients who presented with pre-eclampsia with severe features at the Federal Medical Centre Asaba between 1st June 2022 and 31st January 2023. FMC Asaba is a 350 bedded tertiary hospital located in Asaba the capital of the oil rich Delta State in Nigeria. It receives referrals from primary, secondary, and even tertiary hospitals in Delta state and neighboring Anambra and Edo states too.

Eligibility Criteria: All patients booked and unbooked above 20 weeks gestation with preeclampsia with severe features as indicated by any of the following: blood pressure elevation of ≥160/110, symptoms of CNS dysfunction, hepatic abnormality, thrombocytopenia (with platelet count < 100,000

platelets/microliter), renal impairment and pulmonary oedema. Patients without contraindication to the use of $MgSO_4$ such as drug hypersensitivity, myasthenia gravis, anuria, oliguria (<0.5ml/kg/hour of urine).

Outcome Measures: The primary outcome measure for this study was the occurrence of seizures within six weeks of delivery in either arm of the study while the secondary outcome measures included the total dose of magnesium sulphate received, duration of urethral catheterisation, duration of hospital stay, occurrence of maternal mortality, adverse effects, and evidence of toxicity in the mother clinically.

Sample Size Determination:

The sample size was calculated by the formula below.[12]

$n=2(P)\ (1-P)\ (Z_\beta + Z_{\alpha/2})^2 / (P_1-P_2)^2$

Where, n = Sample size in each group (assumes equal-sized groups), (P) (1-P) = A measure of variability (similar to standard deviation), Z_β= Represents the desired power (typically 0.84 for 80% power), $Z_{\alpha/2}$ = Represents the desired level of statistical significance (typically 1.96), P_1-P_2 = Effect size (difference in proportions)

P_1 = Seizure prevention rate among the study population in an earlier study [9] = 97.4% or 0.974, P_2 = Proportion of participants in the study group expected to exhibit the outcome of interest. This is usually set relative to P_1. $P = (P_1+P_2)/2$. A minimum detectable difference in seizure prevention rate of 15% using the 12-hour maintenance dose of $MgSO_4$ in patients with preeclampsia with severe features was determined.

This formula determined a sample size of 66 participants per study group. Allowance was made for 10 % loss to follow up giving a final sample size of 73 per group with a total of 146 for the study.

Data Collection and Analysis: A study proforma was used to obtain data from the patients recruited for this study after randomizing the study participants using computer-generated random numbers from the research randomizer application. The research randomizer application was used to generate two sets of numbers with 73 for each group; those who received a 12-hour $MgSO_4$ regimen and placebo which was sterile water for injection for the remaining twelve hours (Group I) and those who received a 24-hour $MgSO_4$ regimen in the postpartum period (Group II).

A Hospital Pharmacist who was not part of the study numbered each patient's drug with a masking tape in the sequence to be administered for each randomized number in each group with no form of identification and kept it in sealed opaque envelopes. This was to avoid administering the placebo before the main drug. The sealed envelopes were handed over to the appointed Nurse who administered the drugs in the sequence prepared by the Pharmacist. The numbers were only decoded to the researcher at the end of the study. The $MgSO_4$ and the sterile water for injection were procured from the same company with the same batch number. They also appeared in indistinguishable bottles with all forms of identifiers removed.

The study participants, the outcome measure assessors and the data analyst were blinded to which intervention each patient received. The patients were admitted and were all followed up till their discharge. At the end of their hospital stay, the proforma for each patient was checked for completion and entered a spreadsheet. Data was subsequently analyzed using the Statistical Product and Service Solutions (SPSS) IBM version 26. Categorical variables were expressed in frequencies and percentages while continuous variables were expressed as mean and standard deviation. The test of association

between the categorical variables was via the chi-square and Fisher exact test where necessary while the t-test was used for continuous variables with a p-value <0.05 considered statistically significant.

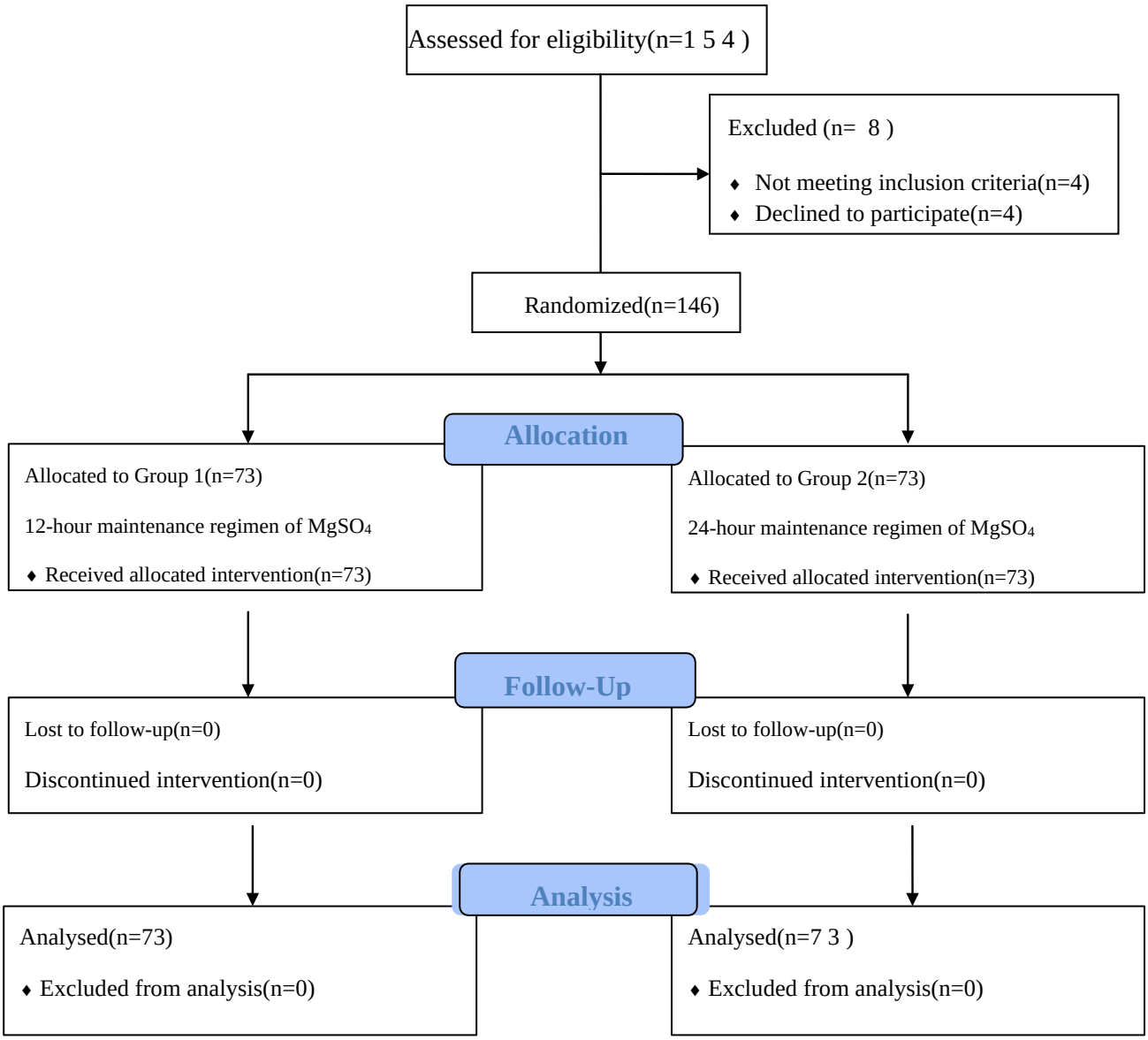
Ethical Consideration

Ethical approval was obtained from the Hospital Research and Ethics Committee (HREC) with approval number FMC/ASB/A81 VOL.XIII/241

Results

The study participants' randomization, allocation, follow-up, and analysis are displayed in the CONSORT flow chart.

Fig 1. CONSORT flow Diagram of Study Participants



The socio-demographic and obstetric characteristics of the participants are shown in Table 1. There were no statistically significant differences between either group regarding the socio-demographic and obstetric variables. The variables that showed no statistically significant difference between the two groups include the age distribution, marital status, level of education, occupation and parity as shown in Table 1.

Table 1. Sociodemographic features of the participants

Variables	12-hour(n=73)	24-hour(n=73)	χ^2	p-value
Age				
≤30	40 (54.8%)	37 (50.7%)	0.80	0.67
31-40	31 (42.5%)	32 (43.8%)		
>40	2 (2.7%)	4 (5.5%)		
Marital Status				
Single	4(5.5%)	4(5.5%)	0.00	1.00
Married	69(94.5%)	69(94.5%)		
Level of Education				
Primary	2(2.7%)	1(1.4%)	5.47	0.07
Secondary	27(37%)	41(56.2%)		
Tertiary	44(60.3%)	31(42.5%)		
Occupation				
Unskilled	61(83.6%)	59(80.8%)	0.19	0.67
Skilled	12(16.4%)	14(19.2%)		
Booking Status				
Unbooked	53(72.6%)	55(75.3%)	0.14	0.71

Booked	20(27.4%)	18(24.7%)		
Parity				
Nullipara	34(46.6%)	37(50.7%)	2.28	0.32
Para 1	17(23.3%)	10(13.7%)		
Multipara	22(30.1%)	26(35.6%)		

Table 2 below shows no statistically significant difference between the gestational ages of participants in the 12-hour and 24-hour groups. Also, there was no statistically significant difference in either the systolic or diastolic blood pressure of both groups at presentation.

Table 2. Comparison of differences in mean values of some characteristics

Variable	12-hour(n=73)	24-hour(n=73)	t-test	p-value
Gestational Age (In weeks)	34.53±5.72	34.49±4.41	0.16	0.87
Systolic BP on admission (mmHg)	177.88±21.89	177.53±21.78	0.10	0.93
Diastolic BP on admission (mmHg)	115.96±13.14	114.25±16.82	0.69	0.49

The 12-hour group recorded one incidence of seizure while none was recorded in the 24-hour group. This was however not significant (p=0.32). There was therefore a need to recommence $MgSO_4$ in this one patient who had seizures after completing therapy. This too was not statistically significant as seen in Table 3.

Table 3. Occurrence of seizures and maternal complications following 12-hour vs 24-hour regimen of $MgSO_4$

Variables	12-hour(n=73)	24-hour(n=73)	χ^2	p-value
Occurrence of seizures				
Yes	1(1.4%)	0	1.01	0.32
No	72(98.6%)	73(100%)		
Need to recommence $MgSO_4$				
Yes	1(1.4%)	0	1.01	0.32
No	72(98.6%)	73(100%)		
Adverse Effect				
Dizziness				
Yes	38(50.7%)	44(60.3%)	1.00	0.32
No	35(49.3%)	29(39.7%)		
Injection site redness/pains				
Yes	73(100%)	73(100%)	-	-
No	0	0		
Hot flushes				
Yes	73(100%)	73(100%)	-	-
No	0	0		
Weakness				
Yes	12(16.4%)	19(26.0%)	2.01	0.16

No	61(83.6%)	54(74.0%)		
Hyporeflexia				
Yes	2(2.7%)	1(1.4%)	0.34	0.56
No	71(97.3%)	72(98.6%)		
Reduced urinary output (<500ml in 24 hours)				
Yes	2(2.7%)	1(1.4%)	0.34	0.56
No	71(97.3%)	72(98.6%)		
Pulmonary oedema				
Yes	1(1.4%)	0	1.01	0.32
No	72(98.6%)	73(100%)		
Respiratory Depression (Respiratory rate<12cpm)				
Yes	0	0	-	-
No	73(100%)	73(100%)		

Table 3 showed that there was no statistically significant difference in the occurrence of adverse effects such as dizziness, injection site redness/pain, hot flushes, pulmonary oedema, and weakness between the two groups following $MgSO_4$ administration. All the women recruited for the study had hot flushes and injection site redness/pain. There was no statistically significant difference between groups I and 2 as seen in Table 3 concerning clinical evidence of toxicity.

Caesarean section was the major route of delivery for the patients enrolled in this study with more occurring in the 12-hour arm (84.9%) as against 69.9% in the 24-hour arm as seen in Table 4. This was statistically significant. (p=0.03). There was however no statistically significant difference for the total dose of $MgSO_4$ received, duration of urethral catheter, duration of hospital admission and admission into the intensive care unit (ICU). No maternal deaths were recorded in both groups.

Table 4. Postpartum clinical outcomes of participants

Variable	12-hour(n=73)	24-hour(n=73)	χ^2	p-value
Mode of delivery				
SVD	10(13.7%)	23(30.1%)	6.62	0.01*
CS	63(86.3%)	50(69.9%)		
Total dose of $MgSO_4$ (In grams)	51.79±10.59	50.23±7.67	t-test 1.02	0.31
Duration of Urethral Catheterization (In hours)	46.86±19.32	49.86±39.07	t-test -0.59	0.56
Duration of Hospital Stay (In days)	5.74±2.32	5.88±4.43	t-test -2.34	0.82
Admission into ICU				
Yes	1(1.4%)	1(1.4%)	0.00	1.00
No	72(98.6%)	72(98.6%)		
Maternal Mortality				
Yes	0	0	-	-
No	73	73		

*; statistically significant

Discussion

The study's results showed that there was no statistically significant difference in the socio-demographic variables between the two study groups. This suggests that the randomization process was effective in ensuring that both groups had a similar distribution of probable confounders. Proper randomization of participants into the comparison groups is considered the most effective way to eliminate the effects of confounders, which is critical to the validity of the study's findings. [13-14]

According to the findings of this study, there was no statistically significant difference in the occurrence of seizures among women who received a 12-hour or 24-hour maintenance regimen of magnesium sulphate for preeclampsia with severe features. This finding is consistent with the results of previous randomized controlled trials conducted by Unwaha et al in Ibadan,[15] Dixit et al and Anjum et al in India,[16,17] Orisabinone et al in Ile-Ife,[9] and Elkhayat et al in Egypt.[18] The clinical significance of this result is that the 12-hour maintenance regimen of magnesium sulphate is as effective as the 24-hour regimen in preventing seizures in women with preeclampsia with severe features.

In addition, the findings of this study did not show any statistically significant difference in the need to recommence magnesium sulphate in the two arms of the study. This is similar to the findings of Orisabinone et al in Ile Ife [9]and Darngawn et al in India [19] where there was no difference in the need to recommence magnesium sulphate among women who received either a 12-hour or 24-hour maintenance regimen of magnesium sulphate in the post-partum period. This further buttress the role of magnesium sulphate in both the prevention and treatment of seizures in eclampsia. [20, 21]

The study found no significant difference in the total dose of magnesium sulphate used between the two groups. This is consistent with the findings of previous studies by Orisabinone et al [19] and Anjum et al. [17] However, those studies reported a slightly lower amount of MgSO4 used in the 12-hour arm as they only calculated the dose given to patients in the postpartum period. In contrast, this study included all magnesium sulphate used from presentation, throughout the stabilization period, to the postpartum period. Furthermore, the study by Orisabinone et al [9] did not use a placebo to compensate for the remaining twelve hours for patients recruited under the 12-hour arm.

The study results indicate that there was no significant difference in the occurrence of adverse effects and toxicity features between the two groups. These adverse effects included hot flushes, injection site pain, weakness, dizziness, pulmonary oedema, loss of reflexes, urinary output, and respiratory depression. Similar findings were reported by Unwaha et al in Ibadan.[15] However, this finding differed from the study in Nepal conducted by Rimal et al [23] where 56.7% of cases experienced MgSO4 toxicity after receiving MgSO4 treatment for 24 hours. This could be due to the high number of eclampsia cases noted in the study, which required re-institution of MgSO4 treatment.

There was no significant difference in postpartum clinical outcomes such as the duration of hospital stay and urethral catheterization between the two study groups. However, these values were lower in the 12-hour group. The study recruited women with preeclampsia with severe features who received intramuscular injections to prevent seizures for 24 hours, whether they were in the study group (12 hours of magnesium sulfate and 12 hours of placebo-sterile water) or the control group (24 hours of magnesium sulfate). Typically, the urethral catheter of these patients is removed after 24 hours of magnesium sulfate unless there are other obstetric reasons to keep it. This could be why there was no significant difference in urethral catheterization and hospital stay between the two groups. Similar findings were observed in other randomized controlled trials conducted by Unwaha et al in Ibadan,[15] Dixit et al in India,[16] Anjum et al in India,[17] and Maia et al in Brazil [10]

Importantly, there was no maternal mortality recorded in either arm of this study. This was similar to the findings of previous authors. [9, 10, 15] This could be primarily attributed to the efficacy and safety of $MgSO_4$ whether used for twelve or twenty-four hours in the management of women with preeclampsia with severe features and the immediate commencement of resuscitation and standard emergency care given to each patient that presented with this condition in this study.

This study had a triple-blind randomized controlled trial design to minimize the possible effects of confounders and bias on the findings. The study participants, outcome measure assessors, and data analysts were unaware of the group allocation of each participant. The randomization ensured that all potential confounding factors were equally distributed between the two groups compared while the blinding minimized bias. [13,14] However, the intramuscular administration of MgSO4 is usually painful, while the administration of sterile water intramuscularly may not be as painful. This may raise suspicion among the patients that they are not receiving the appropriate drug or give them an idea of the study group they belong to when they are receiving the placebo. To minimize this perceived limitation, both active drugs and placebo were used in bottles that appeared similar, procured from a particular company with all forms of identifiers removed from the bottles, thereby making them indistinguishable.

The demonstrated effectiveness of the randomization process in this study, the triple blinding carried out and the measures instituted to minimize the effects of the anticipated limitation of this study make it most likely that the results and conclusions of this study are valid and generalizable to similar clinical settings in Nigeria and other countries where patients with preeclampsia with severe features are being managed.

Conclusion

This study found no statistically significant difference in the effectiveness of 12-hour and 24-hour maintenance regimens of MgSO4 in preventing seizures in women with preeclampsia with severe features. Additionally, there was no statistically significant difference in adverse maternal outcomes between those who received a 12-hour or 24-hour maintenance regimen of MgSO4. The 12-hour group had a lower incidence of side effects, a shorter duration of urethral catheterization, and a shorter hospital stay, but these differences were not statistically significant.

References

1. Kwawukume EY, Ekele BA. Hypertensive disorders in pregnancy. In Kwawukume EY, Ekele BA, Danso KA, Emuveyan EE, editors. Comprehensive Obstetrics in the tropics. 2nd Ed Accra, Ghana: Assemblies of God Literature Centre Limited; 2015:211-31
2. American College of Obstetricians and Gynaecologists (ACOG) Practice Bulletin No. 222: Gestational Hypertension and Preeclampsia. ObstetGynecol 2020;135: e237
3. Magee LA, Brown MA, Hall DR, Gupte S, Hennessy A, Karumanchi SA, et al. The 2021 International Society for the study of Hypertension in Pregnancy Classification, diagnosis and management recommendations for International Practice. Pregnancy Hypertens 2022;27148
4. Ebeigbe PN, Aziken ME. Early onset pregnancy-induced hypertension/eclampsia in Benin City, Nigeria. Niger J Clin Pract 2010;13(4):388-93.
5. Waugh JS, Smith MC. Hypertensive disorders. In: Edmonds DK, editor. Dewhurst's Textbook of Obstetrics and Gynaecology 9th Ed. West Sussex UK: John Wiley and Sons, Ltd; 2018:73-84.
6. Dasgupta S, Sarkhel A, Jain A. Single loading dose of magnesium sulphate in severe preeclampsia and eclampsia - Is it effective? A randomized prospective study. ObstetGynaecol Int J 2015;2(6):189-194.
7. Ekele BA, Muhammed D, Bello LN, Namadina IM. Magnesium sulphate therapy in eclampsia: The Sokoto (ultrashort) regimen. BMC Research Notes 2009; 2:165-168.
8. Kashanian M, Koshpayehzadeh J, Sheikhansan N, Bararpour F, Sahraian G, et al. A comparison between the two methods of magnesium sulphate administration for the duration of 12 versus 24

hours after delivery in patients with severe preeclampsia: A randomized clinical trial; J Mtern Fetal Neonatal Med 2016;29(14):2282-7.
9. Orisabinone IB, Onwudiegwu U, Adeyemi AB, Orji CP, Makinde OI. Shortened versus standard post-partum maintenance therapy of magnesium sulphate in severe preeclampsia: a randomized control trial. Int J Reprod Contracept Obstet Gynecol 2020;9(4):1646-1653.
10. Maia SB, Katz L, Neto CN, Caiadr BV, Azevedo AP, Amorim MM et al. Abbreviated (12-hour) versus traditional (24-hour) post-partum magnesium sulphate therapy in severe preeclampsia. Int J Gynaecol Obstet 2014;126:260-4.
11. Schulz KF, Altman DG, Moher D; CONSORT Group. CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomized trials. BMC Med. 2010;8:18.
12. Sathain B, Sreedharan J, Baboo NS, Sharan K, Abhilash ES, Rajesh E. Relevance of sample size determination in medical research. Nepal J Epidem 2010;1(1):4-10.
13. Kabisch M, Ruckes C, Seibert-Grafe M, Blettner M. Randomized controlled trials. Part 17 of a Series on Evaluation of Scientific Publications. Dtsch Arztebl Int 2011;108(39):663-8.
14. Monaghan TF, Agudelo CW, Rahman SN, Wein AJ, Lazar JM, Everaert K, Dmochowski RR. Blinding in clinical trials: seeing the big picture. Medicina 2021;57(7):64.https://doi:10.3390/medicina57070647
15. Unwaha EA, Bello OO, Bello FA, Oladokun A. Intravenous magnesium sulphate in the management of severe preeclampsia: A randomized study of 12-hour versus 24-hour maintenance dose. Int J Gynecol Obstet 2020; 149:37-42.
16. Dixit P, Thakur S, Singh K, Sharma J, Singh S. To compare abbreviated regimens of single dose and 12-hours magnesium sulphate administration with the conventional 24-hours post-partum in severe eclampsia: A randomized clinical trial. International Journal of Clinical Obstetrics and Gynaecology 2020;4(4):205-210.
17. Anjum S, Goel N, Sharma R, Mohsin Z, Garg N. Maternal outcomes after 12 hours and 24 hours of magnesium sulphate therapy for eclampsia. International Journal of Gynaecology and Obstetrics 2016; 132:68-71.
18. Elkhayat W, Atef A, Abdelatly S, El-semary A. A novel protocol for post-partum magnesium sulphate in severe preeclampsia: A randomized controlled trial. The Journal of Maternal-Fetal and Neonatal Medicine 2014:1-5.https://doi:10.3109/14767058.2014.991915.
19. Darngawn L, Jose R, Regi A, Bansal R, Jeyaseelan L. A shortened post-partum magnesium sulphate prophylaxis regimen in preeclamptic women at lowrisk of eclampsia. International Journal of Gynaecology and Obstetrics 2012;116(3):237-239.
20. The eclampsia trial collaborative group. Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. Lancet 1995;345(8963):1455-63.
21. The Magpie Trial Collaborative Group. Do women with preeclampsia and their babies benefit from magnesium sulphate? The Magpie Trial, a randomized placebo-controlled trial. Lancet 2002;359(9321):1877-1890.
22. Rimal SP, Rijal P, Bhatt R, Thapa K. Loading dose only versus standard dose magnesium sulphate seizure prophylaxis in severe preeclamsia. J Nepal Med Assoc 2017;56(208):388-94.