

original ARTICLE

A Shortened versus Standard Matched Postpartum Magnesium Sulphate Regimen in the Treatment of Eclampsia: a Randomised Controlled trial.

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Abstract

Magnesium sulphate is currently the most ideal drug for the treatment of eclampsia but its use in Nigeria is still limited due its cost and clinicians inexperience with the drug. The purpose of this study was to determine whether a shortened postpartum course of magnesium sulphate is as effective as the standard Pritchard regimen in controlling fits in eclampsia. Between January and June 2011, 98 eclamptic mothers presenting at the labour ward of the University of Maiduguri Teaching Hospital were randomised to receive either the standard Pritchard regimen of magnesium sulphate or a shortened postpartum course in which only two doses of intramuscular magnesium sulphate is given four hours apart. The maternal and fetal outcomes were compared. The primary outcome measure was recurrence of fits. The recurrence of fits and other maternal complications were similar in the two groups. The total dosage of magnesium sulphate in the shortened group was reduced by 40% in 66% of patients. The shortened postpartum course of magnesium sulphate is as effective as the standard Pritchard regimen in the management of eclampsia. (*Afr J Reprod Health* 2013; 17[3]: 131-136).

Résumé

Le sulfate de magnésium est actuellement le médicament le plus idéal pour le traitement de l'éclampsie, mais son utilisation au Nigeria est encore limitée en raison de son coût et des cliniciens inexpérience avec la drogue. Le but de cette étude était de déterminer si un cours du post-partum raccourci de sulfate de magnésium est aussi efficace que le traitement standard de Pritchard dans le contrôle unique de l'éclampsie. Entre janvier et juin 2011 98 mères éclampsie qui se présentent à la salle de travail du Centre Hospitalier de l'Université de Maiduguri ont été randomisés pour recevoir soit le traitement de Pritchard standard de sulfate de magnésium ou d'un cours du post-partum raccourci dans lequel seulement deux doses de sulfate de magnésium par voie intramusculaire sont données quatre heures d'intervalle. Les résultats maternels et fœtaux ont été comparés. Le critère de jugement principal était la récurrence de crises. La récurrence des crises et autres complications maternelles étaient similaires dans les deux groupes. La dose totale de sulfate de magnésium dans le groupe raccourci a été réduite de 40% à 66% des patients. Le cours du post-partum abrégée du sulfate de magnésium est aussi efficace que le traitement standard de Pritchard dans la gestion de l'éclampsie. (*Afr J Reprod Health* 2013; 17[3]: 131-136).

Keywords: Eclampsia, postpartum magnesium sulphate, shortened regimen

Introduction

Eclampsia remains an important cause of maternal and fetal morbidity and mortality worldwide¹. It accounts for 9% and 26% of maternal deaths in Africa and Latin America respectively^{2,3}. Available statistics indicate that eclampsia is the second leading cause of maternal mortality in Nigeria^{4,5,6}. In northern Nigeria, eclampsia

accounts for only 4% of all obstetric emergencies but responsible for up to 45% of maternal mortality^{7,8}. Over the past decade or so, eclampsia has consistently remained the leading cause of maternal deaths in our centre^{9,10}.

Since the publication of the collaborative multicentre study on eclampsia in 1995,

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magnesium sulphate has remained the most ideal anticonvulsant drug for the treatment of eclampsia, with a maternal death rate of 4%^{11,12}. Although its mode of action is not well understood, magnesium sulphate probably acts peripherally at the neuromuscular junction and does not cross the intact blood brain barrier. Although magnesium sulphate was included in the essential drug list in Nigeria since 2009, its use is still limited because of its cost, relative non-availability and clinicians' inexperience on its use^{13,14,15}.

The dosage of magnesium sulphate recommended by Pritchard is a loading dose of 4g IV plus 10g IM; 5g on each buttock. This is followed by a maintenance dose of 5g IM on alternate buttocks every 4 hours for up to 24 hours after delivery or the last fit¹⁶. The rationale for continuing magnesium sulphate for 24 hours after delivery was because 25% of eclamptic seizures occur during the first 12 to 24 hours postpartum¹⁷. Although life threatening toxicity is rare with the use of magnesium sulphate when continuously monitored during treatment, many researchers have tried to reduce both the dose and duration of treatment in order to reduce adverse effects, cut costs and decrease patient discomfort^{18,19}. Additionally, due to non-availability and cost of the drug, a lot of our patients are unable to receive the full course of the Pritchard's regimen. This study prospectively compares the effectiveness of a shortened course of magnesium sulphate after delivery or the last fit to the standard Pritchard regimen.

Methods

All patients admitted with eclampsia into the labour ward of the university of Maiduguri teaching hospital from January to June 2011 were assessed for enrolment into the study. Eclamptic patients who had received any anticonvulsant elsewhere before referral to our centre were excluded from the study as were those with added complications like stroke, renal failure and heart failure. Patients were divided into two groups, A and B, using a computer generated randomization protocol. The allocation was concealed in sealed sequentially numbered brown envelopes, which had been prepared by one of the researchers and

handed over to the matron in-charge of labour ward. On admission of an eclamptic into the labour ward, the matron allocated the next available number on entry into the study and gives the corresponding envelope to the attending resident doctor. The envelope was opened and the regimen of magnesium sulphate administered as per the code inside the envelope. Because of the nature of drug administration, the doctors and nurses responsible for drug administration were not blinded to the randomization allocation.

In study group A, the standard Pritchard regimen was used: a loading dose of magnesium sulphate 4g slow IV bolus plus 10g IM (5g in each buttock), followed by a maintenance dose of 5g magnesium sulphate IM 4 hourly in alternate buttocks for 24 hours after delivery or the last fit. In study group B, the same loading dose was used but the maintenance dose was limited to two doses of 5g magnesium sulphate IM 4 hours apart after delivery or the last fit. In both regimens, 2g magnesium sulphate was given IV if there was recurrence of fit.

The sample size calculation was based on an equivalence trial. In the collaborative multicentre study on eclampsia¹¹, recurrence rate of fits in eclamptics on magnesium sulphate was 5.7%. We accepted equivalence as long as the recurrence of fits did not exceed 10% in the shortened postpartum regimen. Thus with type I and type II errors of 5% and 20% respectively, the sample size needed was approximately 39 participants in each group (a total of 78 patients).

All patients were monitored for development of magnesium sulphate toxicity by hourly blood pressure, respiratory rate, patellar reflexes and urinary output through an indwelling Foley's catheter. Slow IV infusion of normal saline and oxygen by face mask were given. Whenever the diastolic blood pressure was 110mmHg or more IV hydralazine 10mg IV slowly was given. This could be repeated 4 hourly till the diastolic BP was less than 110mmHg. After stabilization, early delivery was ensured by emergency caesarean section if labour was not established and augmentation of labour if labour was established. Both maternal and perinatal outcomes were recorded. The primary outcome measure was recurrence of fits. All patients had their complete

blood count, serum electrolytes, urea and creatinine as well as liver function tests performed on admission.

All data entries were double checked by one of the investigators. The data were analysed using SPSS statistical software and the outcomes between the two groups were compared using χ^2 test. A p value of <0.05 was considered statistically significant at 95% confidence interval. The study was approved by the ethical committee of the university of Maiduguri teaching hospital.

Results

From January to June 2011, about 2,201 mothers were delivered at the university of Maiduguri teaching hospital, Maiduguri, out of which 141(6.41%) had eclampsia. Of these, 21 had received anticonvulsants (mainly diazepam) from the referring health facilities, while 8 had one or more complications. The remaining 112 were recruited into the study (56 in each group). At the end of data collection, 14 patients had incomplete information and were excluded from analysis. The remaining 98 were analysed (50 in group A and 48 in group B).

Table 1 shows the socio-demographic characteristics of the patients with no significant

differences in their age, parity and booking status. Majority of them were teenage, primigravidas who did not book for antenatal care. More than 80% did not receive any formal education.

Table 2 shows the clinical features of the patients at presentation. The clinical features in the two groups were also similar. About 50% of them presented in established labour after about 2 to 3 fits at home. About 40% of them had systolic blood pressure of 162 to 200mmHg and a diastolic blood pressure of 102 to 110mmHg at presentation. About 10% of them presented with a blood pressure of $<140/90$ mmHg.

Table 3 shows the treatment outcomes. The recurrence of fits was not significantly different among the two groups ($p=0.684$). There was a significant reduction in the total dose of magnesium sulphate needed in the two groups with 67% of those in group B requiring only 24g of magnesium sulphate versus 4% in group A ($p=0.001$). Similarly, 64% of those in group A needed 39-44g of magnesium sulphate versus 2% in group B ($p=0.000$).

The mode of delivery and duration of labour were not significantly different in the two groups. The maternal and perinatal outcomes were also similar.

Table 1: Socio-demographic characteristics of patients

Characteristic	group A: n=50	%	group B: n=48	%	χ^2	p value
Age (years)						
15-19	36	72.0	32	66.67		
20-24	10	20.0	8	16.66		
25-29	2	4.0	4	8.33		
30-34	2	4.0	2	4.17		
35+	0	0.0	2	4.17	2.010	0.366
Parity						
0	32	64.0	28	58.33		
1-4	16	32.0	18	37.50		
5+	2	4.0	2	4.17	3.044	0.218
Antenatal care						
Booked	5	10.0	2	4.17		
Unbooked	45	90.0	46	95.83	0.153	0.927
Educational status						
No formal education	42	84.0	40	83.33		
Primary	3	6.0	5	10.45		
Secondary	5	10.0	2	4.17		
Tertiary	0	0.0	1	2.08	0.926	0.393

Table 2: Clinical features of patients

Characteristics	group A: n=50	%	group B: n=48	%	χ^2	p value
type of eclampsia						
Antepartum	16	32.0	15	31.25		
Intrapartum	26	52.0	26	54.17		
Postpartum	8	16.0	7	14.58	1.861	0.180
number of fits pre-admission						
1	6	12.0	5	10.42		
2	14	28.0	8	16.67		
3	10	20.0	11	22.91		
4	9	18.0	4	8.33		
5+	7	14.0	12	25.0	2.132	0.434
BP on admission (mmHg)						
systolic <140	8	16.0	10	20.83		
systolic 140-160	16	32.0	14	29.17		
systolic 162-200	20	40.0	18	37.50		
systolic >200	6	12.0	6	12.50		
diastolic <90	6	12.0	8	16.67		
diastolic 90-100	18	36.0	16	33.33		
diastolic 102-110	22	44.0	20	41.67		
diastolic >110	4	8.0	4	8.33	0.152	0.894
proteinuria (dip stick)						
1+	8	16.0	8	16.67		
2+	28	56.0	24	50.0		
3+	14	28.0	16	33.33	0.912	0.411

Table 3: Treatment outcome of patients

Characteristics	group A: n=50	%	group B: n=48	%	p value	95% CI
fit recurrence						
Recurrence	2	4.0	3	6.25	0.984	-11.23 to 15.24
no recurrence	48	96.0	45	93.75	0.918	-7.36 to 11.25
total dose of MgSO ₄ used						
24g	2	4.0	32	66.67	0.001	23.42 to 26.11
29-34g	14	28.0	15	31.25	0.840	-15.68 to 15.89
39-44g	32	64.0	1	2.08	0.000	20.12 to 22.34
>44g	2	4.0	0	0.00	0.004	11.31 to 12.44
mode of delivery						
vaginal delivery	41	82.0	35	72.92	0.618	-15.34 to 17.11
caesarean delivery	9	18.0	13	27.08	0.391	-13.04 to 15.14
duration of labour	n=42*		n=41*			
0-6 hours	17	40.48	20	48.78	0.334	-10.92 to 16.10
7-12 hours	20	47.62	17	41.46	0.101	-11.94 to 15.64
13-18 hours	3	7.14	4	9.75	0.834	-8.84 to 10.92
19-24 hours	2	4.76	0	0.00	0.089	-14.31 to 18.14
perinatal outcome						
alive (normal)	33	66.0	34	70.83	0.211	-15.51 to 15.86
birth asphyxia	12	24.0	10	20.83	0.188	-6.71 to 21.32
fresh stillbirth	2	4.0	2	4.17	0.918	-14.51 to 16.99
macerated stillbirth	3	6.0	2	4.17	0.762	-9.32 to 12.13
maternal outcome						
Alive	42	84.0	41	85.42	0.911	-0.93 to 10.14
acute renal failure	2	4.0	1	2.08	0.683	-2.67 to 14.21
Stroke	1	2.0	2	4.17	0.454	-8.16 to 13.56
PPH	4	8.0	4	8.33	0.898	-7.37 to 11.25
cortical blindness	1	2.0	0	0.00	0.667	-6.71 to 10.57
Death	1	2.0	1	2.08	0.982	-11.45 to 13.21

*those who delivered at home were not included

Discussion

This prospective, randomised study compared the outcome of short course intramuscular (IM) magnesium sulphate with the standard Pritchard regimen in treating eclampsia¹⁶. Despite the proven efficacy of magnesium sulphate in the treatment of eclampsia and the participation of some ten centres in Nigeria in the 1995 multicentre collaborative eclampsia trial¹¹, the use of magnesium sulphate is still limited in our environment. This is largely due to cost and lack of adequate manpower. The rationale for the use of the short course regimen is to see if the cost and the demand on manpower can be minimised without compromising the quality of care given to eclamptic patients in low resource areas like Nigeria. It may also have the added advantage of reducing the chances of drug toxicity.

The socio-demographic characteristics of the patients in the two groups were similar. Previous studies in this environment had shown that eclamptic patients were mainly nulliparous teenagers from low socio-economic class^{18,19,20}. In this study, about 60% of the patients were nulliparous. 70% were teenagers and over 90% of them received no antenatal care. Majority of them had no formal education.

The clinical presentations of the patients were also typical. About half the number of patients presented in established labour. About 31-32% presented antepartum and the remaining few (14-16%) presented postpartum. Although 40-50% of them presented after 2 to 3 fits, quite a number had more than 5 fits before presentation. This is because the patients go through a tortuous journey from the traditional birth attendant to pharmaceutical chemists and clinics before reaching the hospital. A number of them also did not require antihypertensive on admission because the diastolic blood pressure was below 100mmHg. The primary outcome measure, recurrence of fits, occurred in 6.25% in the short course magnesium sulphate group which was not significantly different from the 4.0% recurrence fits in the standard Pritchard regimen group. The 1995 multicentre collaborative eclampsia study group observed a 5.7% recurrence of fits in the IM magnesium sulphate group¹¹.

By using the short course magnesium sulphate, the total dose of magnesium sulphate required was

reduced to 24g in 67% of the patients. This is more than 40% reduction in the total dose of magnesium sulphate of 39-44g required in 64% of the patients in the standard Pritchard regimen. With similar perinatal and maternal outcomes in the two groups, the short course regimen confers the benefit of low cost, reduced demand on manpower and probably less chance of drug toxicity without compromising quality of care. A similar study using a low dose intravenous infusion of magnesium sulphate has been shown to be as effective as the standard Pritchard regimen²³. Maternal death occurred in 2% of cases in both the study groups. The eclampsia collaborative trial reported maternal deaths ranging from 2.6-3.8% among eclamptic women treated with magnesium sulphate¹⁰. Pritchard et al and Nagar et al showed an incidence of maternal death of about 4% in eclamptic women treated with magnesium sulphate^{16,24}.

Previous studies have shown that magnesium sulphate does not inhibit myometrial contractility and therefore does not affect the course of labour. In our study, 70-80% of our patients had vaginal delivery. This is comparable to Pritchard and Lucas' series^{16,25}. In a similar recent study, Bhattacharjee et al recorded a caesarean section rate of 73-76% due to an institutional policy of early delivery in eclamptic patients²³. In our centre, once labour is established, vaginal delivery is the preferred mode of delivery in eclamptic patients provided there is no other obstetric contraindication.

This comparative study shows that the short course magnesium sulphate is as effective as the standard Pritchard regimen in the management of eclampsia. The maternal and perinatal outcomes were similar and the total dose of magnesium sulphate required was reduced by more than 40%. We recommend that the trial be conducted on a larger population sample.

Contribution of authors

This study was conceived by Dr. Ado Geidam who shared it with members of the fetomaternal unit during a regular unit meeting. The study was then designed by Dr. Calvin Chama who also prepared this manuscript. Dr. Adamu Atterwahmie

supervised the patient randomisation in the labour ward and also followed-up the patients after delivery to ensure complete data collection. The data analysis was carried out by Dr Abdulkarim Mairiga and Dr Babagana Bako. The authors have no conflict of interest

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