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The use of magnesium sulphate ($MgSO_4$) for seizure prophylaxis: clinical correlates in a Nigerian tertiary hospital

Imaralu JO[1*], Olaleye AO[1], Badejoko OO[2], Loto OM[2], Ogunniyi SO[2]

[1]Department of Obstetrics and Gynaecology, Babcock University Teaching Hospital, Ilishan-Remo, Nigeria.
[2]Department of Obstetrics and Gynaecology, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria.

[*]Corresponding author: imaralujohn@yahoo.co.uk, imaraluj@babcock.edu.ng

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ABSTRACT

Background: Magnesium sulphate use in the prevention of seizures resulting from pre-eclampsia and eclampsia is widely accepted. However, several protocols exist worldwide. **Aim:** To determine serum magnesium levels and associated clinical outcomes in severe pre-eclamptic and eclamptic women treated with magnesium sulphate. **Methods**: Women, 28-41weeks pregnant or in the puerperium with severe pre-eclampsia or eclampsia, participated in this cross sectional study and their serum magnesium levels were measured using the Atomic Absorption Spectrophotometer (AAS) machine. All participants received the standard Pritchard regimen, including monitoring. **Results:** Seventy five patients participated in the study. They were mostly overweight (mean BMI 26.38 ± 3.40kg/m^2). Mean pre-treatment serum magnesium level was 1.96 ± 0.29 mg/dL; eclamptics had significantly lower levels ($p<0.001$). Mean treatment serum magnesium level attained was 5.41 ± 0.58 mg/dL. No evidence of magnesium toxicity was observed. Therapeutic range of serum magnesium was required to prevent seizures, and was attained ≥4-hours after loading dose in most of the eclamptics (74%). All convulsions occurred in the interval between the loading dose and the first maintenance dose; eclamptics had greater risk of convulsing while on treatment (RR=11.56, 95%CI= 0.62-216.36, *P*=0.049). **Conclusion:** Low serum magnesium level before or during treatment with magnesium sulphate is a risk factor for convulsion in OAUTHC. The Pritchard regimen has a low risk for toxicity thus administration of magnesium sulphate at peripheral centres before referral may be beneficial in preventing repeat convulsions. Modifications involving additions to the loading dose in eclamptics and fewer number of maintenance doses may be beneficial.

Key words: Pre-eclampsia, eclampsia, magnesium, convulsion, puerperium, Nigeria

INTRODUCTION

Pre-eclampsia is a disorder of widespread vascular endothelial dysfunction that occurs after 20 weeks gestation.[1] This condition is characterized by hypertension and proteinuria, with or without oedema in a previously normotensive non-proteinuric patient and which resolves after the 6th week of delivery.[2,3] It may become complicated with eclampsia, which is the occurrence of new onset generalised tonic-clonic seizures in a woman with pre-eclampsia that cannot be attributed to other causes.[2-4]

The global incidence of pre-eclampsia has been estimated at 5-14% of all pregnancies while in developing nations, the incidence of the disease

ranges from 4-18%.[5] Hypertensive disorders are the second most common obstetric cause of stillbirth and early neonatal deaths in these developing countries, where about 10% of the cases of pre-eclampsia occur at less than 34 weeks of gestation.[4] The incidence of eclamptic convulsions reported in developed countries is 1/2000 while in developing countries; the incidence varies from 1/500 to 1/50 deliveries.[6,7]

Annually, approximately 63,000 women worldwide die of pre-eclampsia and eclampsia, with 99% of these deaths occurring in low-income countries.[8] The reported maternal mortality rates from eclampsia range from 1.8% in some centres in high-income countries, to as high as 15% in Nigeria and Bangladesh.[9,10] However, unlike pre-eclampsia, eclampsia can be considered a preventable condition.[11]

Magnesium sulphate ($MgSO_4$) has been in use for more than 80 years in the management of pre-eclampsia and eclampsia. Currently, it is the first choice in the prevention and treatment of eclamptic convulsions.[12] Research reveals that it is superior to phenytoin and diazepam in preventing the recurrence of seizures and maternal death in patients with eclampsia.[13-15]

$MgSO_4$ may be administered by various routes as depicted in different protocols; the Pritchard regimen combines intravenous and intramuscular routes while the Zuspan and Sibai regimens are entirely intravenous.[16] Maintenance doses for the intravenous routes can be safely administered with the use of infusion pumps. The intravenous regimens have the advantage of being less painful as patients do not require repeated intramuscular injections which may also be associated with a risk of abscess development. These intravenous protocols however pose a risk of toxic serum magnesium levels especially in low resource settings where gravity-fed drip sets are used to administer drugs due to paucity of infusion pumps. Magnesium toxicity can lead to respiratory paralysis, central nervous system depression and cardiac arrest.[17]

The Pritchard regimen is thus becoming more popular in low-resource settings. In Nigeria, the Federal Ministry of Health (FMOH) recommends use of this regimen.[18] This protocol was modified in a North-western Nigerian teaching hospital by limiting the maintenance doses to 12 hours instead of 24 hours and good results have been reported.[19]

Monitoring forms the keystone in the prevention of magnesium toxicity and the use of tendon reflexes, respiratory rate and urine output are currently well recognised.[16] Calcium gluconate (10%) is currently recommended as an effective antidote which should be made available in all hospitals where $MgSO_4$ is used.[16] Existing literature reports that serum levels of magnesium ranges between 2.0 and 3.5 mmol/l (4.8 -8.4 mg/dL) after any of the standard protocols.[10,17]

Studies on the levels of serum magnesium and clinical outcomes among low resource populations are few, especially in Nigeria where eclampsia mortality is unarguably high. Some studies suggest a direct relationship between serum magnesium levels and adverse clinical outcomes associated with $MgSO_4$ use.[16,18] A study questioned the routine measurement of serum magnesium levels among patients administered magnesium sulphate for pre-eclampsia and eclampsia.[20] Serum magnesium assay is currently not routinely done in OAUTHC Ile-Ife, one of the leading tertiary care centres in Nigeria.

There is a need to determine the serum levels of magnesium in patients who receive the full course of the standard Pritchard regimen, since this therapy is what the Federal Ministry of Health recommends and is indeed the regimen that is commonly used. Can this drug be used in lower cadres of health facilities like primary health centres, where facilities for monitoring magnesium dosing and toxicity levels are lacking? Which regimen, route or dose should be given before referral to a higher level facility?

It is also imperative to observe the serum magnesium levels before, during and after treatment to note the trends among our pre-eclamptic population and relate these with clinical manifestations. Studies in developed countries have suggested an association between low serum magnesium levels and occurrence of eclampsia; some of these reports have attempted to use this relationship to explain the mechanism of action of $MgSO_4$ in the management of pre-eclampsia.[21]

To this end, this study was conducted to determine serum magnesium levels and associated clinical outcomes in severe pre-eclamptic and eclamptic women treated with magnesium sulphate at the Obafemi Awolowo University Teaching Hospital, Ile-Ife, Nigeria.

METHODOLOGY

This prospective cross sectional study was conducted over a six month period in the Department of Obstetrics, Gynaecology and Perinatology of the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Osun state South-west Nigeria, where an average of 2,500 deliveries occur annually.

Participants were consecutive pregnant women aged 18 years or more, whose pregnancies were between 28 and 41 weeks, or in the puerperium; admitted for severe pre-eclampsia or eclampsia in whom informed consent had been obtained (or from relatives if unable to consent because of clinical state).

The primary outcome variable of this study was the mean serum magnesium level among severe pre-eclamptic patients before and after commencing treatment with magnesium sulphate. In a study on the maternal serum total magnesium levels in patients treated with magnesium sulphate, Preedatham *et al.* reported a mean serum total magnesium level of 4.90 ± 1.90 mg/dl among women with severe pre-eclampsia treated with magnesium sulphate.[22] An earlier study by Phuapradit *et al.* observed a mean serum total magnesium level of 2.3 ± 0.30mg/dl among women with severe pre-eclampsia who had not received magnesium sulphate.[23]

This formula were applied in the calculation of sample size using the formula:[24]

$$n = (u+v)^2 (\square_1^2+\square_0^2)/ (\mu_1-\mu_0)$$

n = Minimum sample size
u= Determined from a statistical table based on the level of significance, the type I error margin of 0.05 was set for this study corresponding to 1.96.
v= Determined from a statistical table based on the acceptable power of comparison between the 2 groups, the type II error margin for this study was set at 0.1 corresponding to 1.28. This implies a power of 90%.
$\square_1$= This is the standard deviation of the mean serum total magnesium level in the treated group (that is after administering magnesium sulphate). The value obtained by Preedatham *et al.* (1.90mg/dl)[22] was adopted.
$\square_0$= This is the standard deviation of the mean serum total magnesium in the untreated group. The value observed by Phuapradit *et al.* (0.30mg/dL)[23] was also used.
$\mu_1-\mu_0$= This stands for the minimum difference in maternal serum total magnesium levels attributable to the Magnesium sulphate. Akther and Maliha observed a difference of 0.66mg/dl in ionized fraction of serum magnesium.[25] A minimum difference of 0.8mg/dl was assumed for the serum total magnesium levels observed in this study to be attributable to the Magnesium sulphate administered.

Thus: $n = (1.96+1.28)^2 (1.90^2 +0.30^2)/ (0.80)^2$
$n = 60.68$
10% was added for attrition, giving minimum sample size of 67 patients.

Consecutive patients aged between 18 and 45 years, with singleton pregnancies, gestational ages 28 and 41 weeks, or in the puerperium; admitted for severe pre-eclampsia or eclampsia were included in the study while patients with pregnancies less than 28 weeks or more than 41 weeks, mild pre-eclampsia, personal or family history of myasthenia gravis, diabetes mellitus, renal disease, cardiac disease and those with allergy to magnesium sulphate, or who had previously received other anticonvulsants were excluded from the study.

Urine analysis for presence and level of albuminuria was done at admission and repeated routinely. All participants received standard care for severe pre-eclampsia and its complications. The Pritchard regimen of $MgSO_4$ administration was used for all participants.

On admission, 5ml of venous blood was collected into a plain vacuum tube with the patients in supine position prior to commencement of any intravenous therapy; when patients were already on intravenous infusion, the sample was collected from the contra-lateral upper limb. At the time of blood collection, urine output, dipstick urine protein assay, respiratory rate and deep tendon reflexes were assessed. Blood samples were further obtained at the 4th, 8th, 12th, 16th, 20th and 24th hour after the loading dose of MgSO4.

The blood samples obtained were allowed to clot at room temperature and then centrifuged at 2,000 rpm for 5-8 minutes.[26,27] Serum aliquots were then stored at 2-8ºC until analysis in the Central Science laboratory of the Obafemi Awolowo University (OAU).Ile-Ife. Serum magnesium assay was done by the Atomic Absorption Spectrophotometric (AAS) method using the Techtron AA100 absorption spectrophotometer by Varian technologies Inc. Australia.[26,27]

Blood pressure measurements were obtained with manually operated mercury powered sphygmomanometers with all patients in supine position, using Korotkoff sound V for diastolic blood pressure. Monitoring of some vital parameters such as respiratory rate, urinary output and tendon reflexes was ensured before each maintenance dose. Absent tendon reflexes, oliguria (urine output <25ml/hour) and/or respiratory rate < 16/minute were considered as clinical evidence of toxicity. Calcium gluconate (10ml of 1%) was made available for management of overdose or toxicity.

Severe pre-eclampsia was considered as the presence of one or more of the following criteria: blood pressure of at least 160/110 mmHg measured on two occasions each 4 hours apart, proteinuria of at least 5g per 24 hours, or at least 3+ on dipstick testing, oliguria with urine output of less than 500 ml per 24 hours, cerebral or visual disturbances, pulmonary edema or cyanosis, epigastric or right upper quadrant pain, impaired liver function, thrombocytopenia and fetal growth restriction.[28]

Human rights and informed consent

Ethical approval of the research from the ethics committee of OAUTHC was obtained prior to the commencement of the study. The antenatal records of all participants were reviewed when available, after obtaining written informed consent from them by signature or thumb print. This was also obtained from relatives of participants who were too ill to do so. The research was conducted in accordance with the ethical standards of the Helsinki Declaration.

Statistical analysis

The collected data was analysed using the Statistical Software Package for Social Sciences (SPSS) version 17.0 (Chicago, Illinois). Results were displayed on frequency tables using comparative percentages. Comparison of results among groups was done using the student's t- test for continuous variables and chi-square for categorical variables. Statistical significance was set at a *P*-value of less than 0.05.

RESULTS

A total of 75 patients participated in the study over a period of six months giving an expected count of 525 blood samples (7 per patient). Twenty three samples were excluded from analysis due to processing errors. Thus a total of 502 serum magnesium samples were analysed (95.6%).

The mean age, parity and body mass index (BMI) were; 27.19± 6.23 years, 0.93± 1.4, and 26.34± 3.4 kg/m^2 respectively with eclamptics being significantly younger (23.46± 5.17 years), of lower parity (0.54± 0.79) and having lower BMI (24.97± 3.46 kg/m^2) (table 1).

The mean pre-treatment serum magnesium level for the study population was 1.96 ± 0.29 mg/dL while the mean serum magnesium level obtained during the 24- hour treatment with the Pritchard regimen was 5.41 ± 0.58 mg/dL. Again the patients with eclampsia were observed to have lower values (table 2).

The highest mean serum magnesium levels during treatment (6.07 ± 0.73mg/dL) was observed 8 hours after the loading dose and magnesium levels were noted to decrease progressively afterwards, before each subsequent maintenance dose. It however did not return to pre-treatment levels during the 24hr Pritchard Protocol (figure 1). This trend was observed both in patients presenting antepartum and postpartum.

All convulsions while on magnesium sulphate in this study occurred among eclamptics, and were in the interval between the loading dose and the 4-hr maintenance (table 3). Most of the eclamptics (74%) were yet to attain therapeutic range magnesium levels, 4 hours after the loading dose (table 4).

No clinical feature of magnesium toxicity was observed and no toxic serum magnesium level was obtained in any participant throughout the duration of the study. Postpartum haemorrhage was the commonest complication observed among patients with severe pre-eclampsia while on the Pritchard regimen, while among eclamptics repeat convulsions was the main complication. No maternal death occurred among participants during the period of study. There was no statistically significant difference in the mean 1-minute and 5-minute APGAR scores between the eclamptics and patients with severe pre-eclampsia; more perinatal deaths were however recorded in the latter group (17.3%, *P*-value<0.05), mostly occurring in the early neonatal period. Low birth weight (mean birth weight 2.40± 0.74kg) was a major problem; babies of severe pre-eclamptics were also noted to be delivered at higher mean gestational age (36.43± 3.34 weeks) (table 5).

Table 1: Obstetric biodata of patients receiving $MgSO_4$

	Indication for magnesium sulphate		
Variable	**Eclampsia N=28**	**Severe Pre-eclampsia N=47**	**p-value (95% CI)**
Mean Age [years] Population: 27.19 ± 6.23	23.46 ± 5.17	29.40 ± 5.76	< 0.0001 (-8.58 to -3.29)
Mean parity Population:0.93 ± 1.4	0.54± 0.79	1.17± 1.58	0.053 (-1.269 to 0.009)
Mean BMI (kg/m^2) Population: 26.34± 3.4, N=69	24.97± 3.46, N=22	26.98 ± 3.21, N=47	0.021 (-3.706 to -0.313)
Booking status: Booked Unbooked	3 (10.7%) 25 (89.3%)	18 (38.4%) 29 (61.7%)	0.025 (0.022 to 0.028)
Stage of Pregnancy: Antepartum Intra-partum Postpartum	15 (53.6%) 5 (17.9%) 8 (28.5%)	36 (76.6%) 11 (23.4%) • (0.0%)	0.002 (0.001 to 0.003)
Mean loading dose-delivery interv (hours) N=64 Population: 5.82 ± 4.22	N=20 4.57 ± 2.92	N=44 6.40 ± 4.61	0.108 (-0.408 to 0.416)

CI= confidence interval

Table 2: Serum magnesium levels of participants before and during treatment with $MgS0_4$

Serum magnesium levels (mg/dL)	**Values**	**N**	**Mean (mg/dL)**
Pre-treatment	Total population	74	1.96 ± 0.29
	Eclampsia	27	1.81 ± 0.33
	Severe pre-eclampsia	47	2.05 ± 0.23
Intra-treatment	Total population	55	5.41± 0.58
	Eclampsia	19	5.34 ± 0.59
	Severe pre-eclampsia	36	5.43 ± 0.58

Mean serum magnesium levels were lower among eclamptics

Table 3: Relationship between indication for magnesium sulphate and occurrence of convulsion at OAUTHC

Variable	**Convulsion**	**No convulsion**	**TOTAL**
Eclampsia	3 (11%)	25 (89%)	28
Severe pre-eclampsia	0 (0%)	47 (100%)	47
TOTAL	3	72	75

Fisher's exact test; p-value=0.049, Relative Risk (RR) = 11.586, 95% Confidence interval: 0.620 to 216.36.

Table 4: Relationship between the indication for magnesium sulphate and the 4-hour serum magnesium level

Indication	**≤ 4.79mg/dL**	**≥ 4.80 mg/dL**	**TOTAL**
Eclampsia	20 (74%)	7 (26%)	27
Severe pre-eclampsia	24 (60%)	16 (40%)	40
TOTAL	44	23	67

P -value = 0.298, Odds ratio (OR) =1.905, 95% Confidence interval (CI): 0.65 to 5.54
[Therapeutic range for serum magnesium is 4.8-8.4mg/dl[17]]

Table 5: Maternal and fetal outcomes during magnesium sulphate therapy

Variable	Indication for magnesium sulphate (%) Eclampsia	Severe pre-eclampsia	*P*-value (95% Confidence interval)
Maternal Complications	N=4	N=3	
Postpartum haemorrhage	1 (25.0%)	3 (100.0%)	
Convulsion	3 (75.0%)	0 (0.0%)	0.047
Mean APGAR score:	N=21	N=44	
1 minute	7.1 ± 2.4	7.2 ± 3.0	0.894 (-1.596 to 1.396)
5 minute	9.1 ± 1.4	8.4 ± 2.9	0.299 (-0.637 to 1.046)
Perinatal Outcome:	N=34	N=52	
Alive	31 (91.2)	43 (82.7)	
Dead	3 (8.8)	9 (17.3)	0.067 (0.062 to 0.072)
Time of perinatal mortality:	N=3	N=9	
IUFD	1 (33.3)	4 (44.4)	
END	2 (66.7)	5 (55.6)	0.320
Mean Birth Weight [kg] N=73	N=26	N=47	
Total population= 2.40 ± 0.74	2.37 ± 0.59	2.50 ± 0.82	0.479 (-0.494 to 0.234)
Mean GA (weeks) N=75	N=28	N=47	
Total population =36.35±3.03	36.21 ± 2.49	36.43± 3.34	0.766 (-1.673 to 1.233)
Mode of delivery			
Caesarean section	18 (64.3)	32 (68.1)	
SVD	10 (35.7)	14 (29.8)	
Vacuum extraction	0 (0)	1 (2.1)	0.872 (0.865 to 0.878)

IUFD=Intrauterine Fetal Death, END= Early Neonatal Death, SVD= Spontaneous Vaginal Delivery

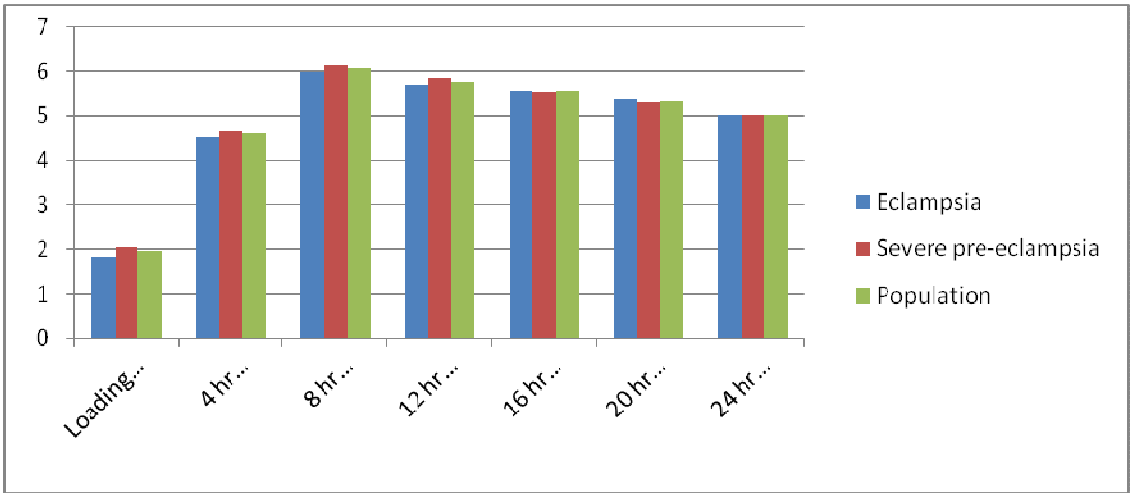

Figure 1: Bar chart showing the trend in mean serum magnesium levels during treatment with magnesium sulphate
NB: Values were taken just before each dose of magnesium sulphate.
Magnesium levels (y-axis) are in mg/dL
Population = mean magnesium level of total study population

DISCUSSION

Pre-eclampsia and eclampsia are still significant threats to maternal and foetal survival globally. Magnesium sulphate ($MgS0_4$) is the agent most commonly used for treatment of eclampsia and prophylaxis against convulsions in severe pre-eclampsia.[17] This study was done to assess the effect of $MgSO_4$ on women receiving it and its impact in preventing convulsions and repeat convulsions.

The participants observed were mainly young women, with eclamptics (mean age 23.46 ± 5.17 years) being significantly younger (*P*<0.005) and mostly nulliparous (64.3%) with a mean parity of 0.54 + 0.79 which is similar to findings in Nnewi, Eastern Nigeria where the mean age of eclamptics was 23.55 years and 65% were nulliparae.[29] Low socio-economic status and non-booking for antenatal care are recognised risk factors for the development of complications of pre-eclampsia.[30] Most of the participants were unbooked (89.3% and 61.7% for eclampsia and severe pre-eclampsia respectively).

The mean pre-treatment maternal serum magnesium level was significantly lower in eclamptics than in patients with severe pre-eclampsia (*P*<0.001) but within normal reference range (1.5-2.5mg/dl).[32] This value of 1.81 ± 0.33mg/dL (i.e 0.74 ± 0.14 mmol/L) is similar to 0.72 ± 0.10mmo/L observed among eclamptics in Sokoto, north-western Nigeria.[20] Low serum magnesium levels have been linked with occurrence of seizures in pre-eclampsia and this has been suggested as the reason for the efficacy of magnesium sulphate in prevention of convulsions.[19,32-34]

The mean treatment magnesium level observed in this study is comparable between eclamptics and severe pre-eclamptics (*P*-value =0.62) even though the eclamptics had lower BMI. The entire study population's treatment serum magnesium level (5.43 ± 0.58mg/dL) is greater than the value observed by Preedatham *et al.* (4.90 ± 1.90mg/dL) among women with greater body mass indices.[22] This finding is in keeping with observations by Dayicioglu *et al.*, who found an inverse relationship between serum magnesium level and body mass index among patients receiving $MgSO_4$ for pre-eclampsia.[35] Among eclamptics, the mean treatment serum magnesium level of 5.34 ± 0.59 mg/dL (i.e 2.2 ± 0.24 mmol/L) is comparable to the 2.1 mmol/L observed in Sokoto, among eclamptic women who had lower body mass indices.[20]

The mean treatment magnesium level observed in this study is in the lower border of the therapeutic range for magnesium sulphate, which agrees with similar observations in Sokoto, Northern Nigeria[20] and Istanbul in Turkey,[35] where most of the patients were in the lower 50% of the therapeutic range. Similarly, a report from a study in South Africa revealed that no seizures occurred, despite treatment magnesium levels mostly below 2.0mmol/L.[36] Although the mean serum magnesium level of 4.60 ± 0.49 mg/dL (i.e 1.89 mmol/L) obtained 4 hours after the loading dose is sub-therapeutic, no further convulsions occurred after this time in Ile-Ife. A similar finding (4.7 ± 0.3mg/dL), was obtained among Asian women of comparable BMI.[23]

It is quite pertinent to mention that no clinical features of magnesium toxicity were observed in any of the participants, and serum analysis also did not reveal any toxic range magnesium level throughout the duration of this study.

Although most (62.5%) of the eclamptics in this study had BMI within normal ranges, a large proportion of them (74%, table1), had sub-therapeutic magnesium levels during treatment and in fact, all seizures observed were among this group. This suggests that low serum levels from other mechanisms, rather than just the BMI-dependent drug bioavailability, may be associated with the occurrence of fits while on $MgSO_4$ therapy.

There were three repeat convulsions, all in the interval between the loading dose and the 4 hour maintenance dose and no further seizures afterwards. Eclamptics were more likely to convulse while on treatment with $MgSO_4$ (RR=11.56, CI=0.62-216.36, *P*=0.049), possibly because they had lower magnesium levels before and during treatment. This further confirms a link between low serum magnesium level and occurrence of seizures before and during treatment with $MgSO_4$.[21,32-34,37] Interventions involving administration of $MgSO_4$ at community level may thus be beneficial in eclamptics to help them attain therapeutic range (or near therapeutic) serum magnesium levels needed to prevent further fits, before arriving at centres where definitive specialist care is available.

The highest mean treatment magnesium level was observed 8 hours after the loading dose for both eclampsia (5.98 ± 0.69mg/dL) and severe pre-

eclampsia (6.12 ± 0.76mg/dL). This value progressively reduced with subsequent doses, but did not return to pre-treatment levels. The finding that most women delivered before the 8- hour maintenance (mean loading dose-delivery interval was 5.82 ± 4.22 hours), suggests that circulatory and renal postpartum changes may be responsible for elevated magnesium levels at this time. Serum magnesium levels decline progressively in pregnancy with hypomagnesaemia predominating in the 2nd and 3rd trimesters with associated hypo-osmolality. These changes are reversed at delivery, such that in the first 24 hours, serum magnesium returns to pre-pregnancy levels.[38] A similar trend was however observed among patients with postpartum eclampsia, suggesting that another mechanism or a combination of factors may be responsible for this 8- hour peak levels.

The attainment of peak treatment magnesium levels 8 hours after the loading dose, coupled with the subsequent maintenance of therapeutic levels and the absence of further convulsions after the 4- hour dose, can be the basis for modifications of the Pritchard regimen into protocols involving smaller number of doses and shorter duration of treatment, to reduce cost, repeated intramuscular injections and the risk of toxicity. Some studies have shown similar maternal and perinatal outcomes between these modifications and the standard Pritchard regimen.[38-40] An example in Nigeria, is the ultra-short regimen practiced in Sokoto where the drug is stopped after the 12-hour maintenance dose.[20]

It is difficult to say whether the four cases of primary postpartum haemorrhage observed were due to side effects of magnesium sulphate or a complication of pre-eclampsia. Magnesium sulphate is a recognised tocolytic and in doses similar to that used in pre-eclampsia, aborts contractions in preterm labour. It may thus predispose to postpartum uterine atony.[41] Pre-eclampsia on the other hand, is associated with increased risk for coagulopathy and uterine atony.[42] Further research would be required for such an inference to be confidently made.

Low birth weight and prematurity are still major threats to survival of foetuses in pregnancies complicated by pre-eclampsia. Although normal mean values of 1- and 5-minute APGAR scores were observed, some perinatal deaths were recorded. This is most likely a complication of pre-eclampsia, rather than an effect of magnesium sulphate, since no toxic manifestation or toxic serum magnesium level was observed. Significantly, more perinatal deaths occurred among babies of severe pre-eclamptics (17.3%, *P*-value<0.05), although babies of eclamptics had lower mean birth weight (2.37 ± 0.59 kg). These deaths probably occurred as a result of attempts at preventing prematurity, with longer exposure of the babies to the effects of progressive disease. It is also likely that these babies were growth restricted ab initio. A balance in timing of delivery is thus very important to ensure foetal survival without compromising maternal safety.

CONCLUSION

Low serum magnesium level is a risk factor for convulsion in OAUTHC. Convulsion while on $MgSO_4$ is more likely among eclamptics due to delay in attaining therapeutic serum magnesium levels. The attainment of a threshold, close to or probably therapeutic range serum magnesium level is essential to prevent convulsions in the Pritchard regimen. Administration of magnesium sulphate to eclamptics at community level before referral is thus recommended to boost their serum magnesium levels and prevent further fits.

The Pritchard regimen appears to be effective and has very low risk for toxicity. However, modifications involving a greater loading dose or an additional dose in the interval between the loading dose and the 4-hour maintenance with monitoring may be beneficial. Protocols involving less maintenance doses especially after the 8-houir maintenance may be justified.

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REFERENCES

1. Akhigbe RE. The role of low-dose aspirin in the prevention of pre-eclampsia. Niger Med J 2014. 55: 86.
2. Sibai BM. Diagnosis and management of gestational hypertension and preeclampsia. Obstet Gynecol 2003;102:181-192.
3. Abudu OO, Afolabi BB. Pregnancy induced hypertension, Pre-eclampsia and chronic hypertension. In: Agboola A (ed), Textbook of Obstetrics and Gynaecology for Medical Students,

2nd edition. Heinemann Educational Books, Ibadan, 2006. Pp 348-355.
4. Ngoc NT, Merialdi M, Abdel-Aleem H, Carroli G, Purwar M, Zavaleta N, Campodonico L, Ali MM, Hofmeyr GJ, Mathal M, Lincetto O, Villar J. Causes of stillbirths and early neonatal deaths: data from 7993 pregnancies in six developing countries. Bull World Health Organ 2006;84:699-705.
5. Villar J, Betran AP, Gulmezoglu M. Epidemiological basis for the planning of maternal health services. WHO/RHR. 2001.
6. Andersgaard AB, Herbst A, Johansen M. Eclampsia in Scandinavia: incidence, substandard care, and potentially preventable cases. Acta Obstet Gynecol Scand 2006; 85:929-936.
7. Douglas KA, Redman CW. Eclampsia in the United Kingdom. BMJ. 1994;309:1395–1400.
8. Langer A, Villar J, Tell K, Kim T and Kennedy S .Reducing eclampsia-related deaths, a call to action. Lancet 2008; 371:705–706.
9. Katz V, Farmer R and Kuller JA. Preeclampsia into eclampsia: Toward a new paradigm. Am J Obstet Gynecol 2000;182:1389–1396.
10. Igberase GO, Ebeigbe PN. Eclampsia: ten-years of experience in a rural tertiary hospital in the Niger delta, Nigeria. J Obstet Gynecol 2006;26:414–417.
11. Duley L. The global impact of pre-eclampsia and eclampsia. Semin Perinatol 2009;33:130-137.
12. Saver JL, Kidwell C, Eckstein M and FAST-MAG Pilot Investigators. Prehospital neuroprotective therapy for acute stroke results of the field administration of stroke therapy—magnesium (FASTMAG) pilot trial. Stroke 2004;35:106–108.
13. Lucas MJ, Leveno KJ and Cunningham FGA comparison of magnesium sulfate with phenytoin for the prevention of eclampsia. N Engl J Med 1995;333:201–205.
14. Eclampsia Trial Collaborative Group. Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. Lancet 1995; 346:258.
15. Khan KS. Magnesium sulphate and other anticonvulsants for the treatment for severe preeclampsia. (Cochrane Review). In: The Reproductive Health Library, Issue 10, 2007. Oxford.
16. Pritchard JA ,Cunningham FG and Prichard SA: The Parklands Memorial Hospital protocol for treatment of eclampsia :evaluation of 245 cases. Am J obstet Gynecol 1984;84:607-610.
17. Lu J, Nightingale CH. Magnesium sulfate in eclampsia and preeclampsia: pharmacokinetic principles. Clin Pharmacokinet 2000;38:305-314.
18. FMOH. National Clinical Service Protocol for Obstetrics and Neonatal Care, 2006.
19. Ekele BA, Ahmed Y. Magnesium sulfate regimens for eclampsia. Int J Gynecol Obstet 2004;87:149-150.
20. Ekele BA, Badung SL. Is serum magnesium estimate necessary in patients with eclampsia on magnesium sulphate? Afr J Reprod Health 2005;9:128-132.
21. Sanders R, Konijnenberg A, Huijgen HJ, Wolf H, Boer K,Sanders GT. Intracellular and Extracellular ionized and total magnesium in pre-eclampsia and uncomplicated pregnancy. Clin Chem Lab Med 1999;37:55-59.
22. Preedatham K, Tansupswatdikul P. Serum Magnesium Level in Severe preeclampsia and eclampsia patients undergoing Magnesium Sulfate Therapy at Chonburi Hospital. Thai Journal of Obstetrics and Gynaecology 2009;17:190-195.
23. Phuapradit W, Saropala N, Haruvasin S, Thuvasethakul P. Serum level of magnesium attained in magnesium sulfate therapy for severe preeclampsia. Asia Oceania J Obstet Gynaecol 1993;19:387-390.
24. Kirkwood BR, Sterne JAC (Eds). Essential Medical Statistics, 2nd ed, Blackwell Science Ltd. Massachusetts, 2003. Pp 420.
25. Akther R, Maliha R. Is Low Level of Serum Ionized Magnesium Responsible for Eclampsia? J Bangladesh Coll Phys Surg 2009;27: 76-81.
26. Rhagavamma ST, Sri AM, Nadendla RR. Antimicrobial activity of mucilage isolated from Coccinia grandis (L) J. Voigts fruits. IJAPR 2013;4: 2497-2502.
27. Glaser LM. Directory of Geoscience research facilities in Australian tertiary education institutions. Bureau of mineral resources, Geology and Geophysics Report 272. 1985. Pp 6-8.
28. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol 2000;183:S1–S22.
29. Ikechebelu JI, Okoli CC. Review of eclampsia at the Nnamdi Azikiwe University Teaching Hospital Nnewi (January 1996- December 2000). J Obstet Gynaecol 2002;22:287-290.
30. Owolabi AT, Fatusi AO, Kuti O, Adeyemi AB, Faturoti SO, Obiajunwa PO. Maternal complications and outcomes in booked and unbooked Nigerian mothers. Singapore Med J 2008; 49:526-531.
31. Taber EB, Tan L, Chao CR, Beall MH, Ross MG. Pharmacokinetics of ionized versus total

magnesium in subjects with preterm labor and preeclampsia. Am J Obstet Gynecol 2002;186:1017–1021.
32. Tong GM, Rude RK. Magnesium deficiency in critical illness. J Intensive Care Med 2005;20:3-17.
33. Touyz RM. Role of magnesium in the pathogenesis of hypertension. Mol Aspects Med 2003;24:107-136.
34. Idogun ES, Imarengiaye CO, Momoh SM. Extracellular calcium and magnesium in preeclampsia and eclampsia. Afr J Reprod Health 2007;11:89-94.
35. Dayicioglu V, Sahinoglu Z,Kol E, Kucukbas M. The use of standard dose of magn esium sulphate in prophylaxis of eclamptic seizures; do BMI alterations have any effect on success? Hypertens Pregnancy 2003;22:237-265.
36. Chissel S, Botha JH, Moodley J, McFayden L. Intravenous and intramuscular magnesium sulphate regimens in severe pre-eclampsia S Afr Med J 1994;84:607-610.
37. Abbade JF, Costa RA, Martins AM, Borges VT, Ridge MV, Perocalli JC. Zuspans' scheme versus an alternative magnesium sulphate scheme; randomized clinical trial of magnesium serum concentrations. Hypertens Pregnancy 2010;29:82-92.
38. Shoiab T, Khan S, Javed I, Bhutta SZ. Loading dose of magnesium sulphate versus standard regime for prophylaxis of pre-eclampsia. J Coll Physicians Surg Pak 2009;19:30-33.
39. Sardesai S, Maira S, Patil A, Patil U. Low dose magnesium sulphate for eclampsia and imminent eclampsia: regimen tailored for tropical women. J Obstet Gynaecol Ind. 2003;53:546-550.
40. Mahajan NN, Thomas A, Soni RN Gaikwad NL, Jain SM. 'Padhar Regime' – A low dose magnesium sulphate treatment for eclampsia. Gynecol Obstet Invest 2008;67:20-24.
41. Witlin AG, Sibai BM. Magnesium sulfate therapy in preeclampsia and eclampsia. Obstet Gynecol 1998;92:883–889.
42. Metz J, Cincotta R, Francis M, derosa L, Balloch A. Screening for consumptive coagulopathy in preeclampsia. Int J Gynecol Obstet 1994;46:3-9.

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