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MATERNAL-FETAL MEDICINE

Low-dose magnesium sulphate in the control of eclamptic fits: a randomized controlled trial

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Abstract
Context Magnesium sulphate is now the gold standard for the control of eclamptic fits. The place of low-dose magnesium sulphate for the control of eclamptic seizures is yet to be determined.
Objectives To determine the effectiveness of low-dose magnesium sulphate in controlling eclamptic fits.
Study design Randomized controlled trial comparing low-dose with standardized dosing regimen.
Setting Labour Unit of the department of Obstetrics and Gynecology Federal Medical Centre Azare, north-eastern Nigeria.
Protocol Thirty-nine patients randomized into the low-dose regimen group received 9 g loading dose (4 g iv and 5 g im) and im maintenance of 2.5 g four hourly for 24 h post-delivery or post last fit, while the 33 patients in the standard dose regimen group received loading dose of 14 g followed by im maintenance dose of 5 g four hourly. In both study groups, 2 g iv of magnesium sulphate is given for breakthrough fits and 10 ml of 10 % calcium gluconate (slowly iv) was administered in the event of toxicity. Outcome measures include recurrent fits, mode of delivery, mean Apgar Score at 5 min, perinatal death, maternal complications including death.
Result The mean age of the 72 patients was 22.3 ± 5.4 years and 60 % were primigravidas. Intrapartum eclampsia was encountered in 44 % of the patients followed by antepartum eclampsia (26 %). Overall 4.2 % recurrent convulsion rate was documented and it is not different among the study groups. There were also no differences in both foetal and maternal outcomes in the two study groups.
Conclusion The effectiveness of low-dose regimen of magnesium sulphate appeared comparable to the 'standard dose regimen'. Low-dose regimen may guarantee more safety and in an environment (such as ours) where cost is an important determinant of accessibility to qualitative health services, it is certainly attractive. More studies are needed to establish the place of low-dose regimen of magnesium sulphate in the management of eclampsia.

Keywords Eclampsia · Low dose · Recurrent fits · Magnesium sulphate · Maternal complications

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Introduction

Eclampsia remained a major cause of maternal and perinatal morbidity and mortality. It accounts for 10–12 % of maternal deaths globally of which 97 % of these deaths occur in the developing countries particularly sub-Saharan Africa [1–3]. In Nigeria, the prevalence of eclampsia ranges between 0.7 and 9 % [4–7] and maternal deaths from eclampsia ranged from 8 to 43 % [4, 5, 8–10].

The superiority of magnesium sulphate over diazepam and other anti-convulsants in the management of eclampsia has been established [11, 12]. The drug is now considered as one of the cost effective medical interventions in the reduction of maternal mortality [13] and included in the essential drug list [1].

The dosing regimen of magnesium sulphate in eclampsia appeared to vary from centre to centre although the

dosing used in the Collaborative Eclamptic Trial is widely used and recommended by WHO [1].

Recurrent convulsion is perhaps one of the most important prognostic factor in eclampsia [14]. Other prognostic factors include presence of complications such as malignant hyperpyrexia, HELLP syndrome, pulmonary odema, renal failure and intracranial haemorrhage [15].

In this submission, we investigate the effectiveness of using lower dosing regimen of magnesium sulphate in controlling eclamptic fits. Low dosing of magnesium sulphate has the potential for reducing cost and reducing the likelihood of toxicity of the drug.

Materials and methods

The study design for this research was a randomized controlled trial. The Federal Medical Centre Azare is a public referral centre serving the northern part of Bauchi state and the neighbouring Yobe State, in north-eastern Nigeria. The dosing regimen of magnesium sulphate used in this centre is same as that used in the Collaborative Eclamptic Trial using the Pritchard Method. For the purpose of this study this will be regarded as the 'standard dose regimen' and will serve as the control group. The low-dose regimen used in this study was a modified version of the 'Dhakar regimen' [16].

The study population was eclamptic women who presented to the hospital for management. Pre-treatment randomization was done (into two groups: standard and the low-dose groups) using computer-generated numbers for all eclamptics that fulfilled the inclusion criteria and delivered by sealed opaque envelope as the patients were admitted into the labour/eclamptic ward from January to August 2008. Inclusion criteria include patients with ante, intra and post-partum (within 1 week of delivery) eclampsia including eminent eclampsia. Exclusion criteria include eclamptic patients in critical condition with hypotension and low respiratory rate (<14 breaths/min) in which magnesium sulphate therapy is contraindicated.

Protocol

Patients randomized into the standard dose regimen received 14 g loading dose of magnesuim sulphate (4 g of 20 % iv + 10 g im) followed by im maintenance dose of 5 g four hourly for 24 h post-delivery or post last fit if further convulsions occurred within 24 h of delivery. Those in the low-dose group received 9 g loading dose (4 g of 20 % iv and 5 g im) then im maintenance of 2.5 g four hourly for 24 h post-delivery or post last fit whichever was earlier. In both study groups, 2 g iv of magnesium sulphate is given for breakthrough convulsions and 10 ml of 10 % calcium gluconate (slowly iv) was administered in the event of toxicity.

Outcome measures include recurrent fits as primary outcome while secondary outcome measures include mode of delivery, mean Apgar Score at 5 min, perinatal death, maternal complications including death.

Data entry was done using a data form which also includes age and parity of patients, gestational age on admission and type of eclampsia. The data were analysed using SPSS Statistical software version 11.0. Mean values were compared using student *t* test and rates/proportions using Chi-square test and where appropriate Fisher exact test or coefficient of correlation.

Informed consent was obtained from close relations of patients and ethical approval for the study was obtained from the hospital's ethical committee.

Results

Seventy-two patients were recruited into the study. Of these, 39 were randomized into low-dose magnesium sulphate group while 33 were in the standard regimen group. During the study period, 1,720 deliveries were conducted hence the prevalence rate of eclampsia was 4.2 %. The overall mean age of the patients was 22.3 ± 5.4 years; range 14–41 years. Primigravidas constituted 57 % of the patients while grandmultiparas accounted for 8 % of subjects. The mean gestational age of the patients was 35.5 ± 2.7 weeks. Thirty-two patients (44 %) were admitted in labour (intrapartum eclampsia) while 26 and 15 % of the patients were antepartum and postpartum eclampsia, respectively.

Table 1 revealed the outcome measures including the recurrent convulsion rate, Cesarean section rate and mean Apgar Score at 5 min in the study groups. The outcomes did not differ significantly between the two groups.

Table 2 showed the maternal complications in the study groups. These complications appeared not to differ significantly.

Discussion

The incidence of 4.2 % for eclampsia in this study is comparable to that of 5 % for Sokoto northern Nigeria [7], but higher than the rates quoted for south-west [4, 17], south-east [18] and south-south Nigeria [19]. Our figure is less than the 9 % for Birnin Kudu—a suburb in north-western Nigeria [5].

Nearly 60 % of our patients were primigravidas and this is consistent with established data [1, 2, 7]. Majority of the patients recruited into the study were admitted in labour.

Table 1 Outcome measures in the study groups

Outcome	Study group		*P* value
	Low dose	Std. dose	
Mean Apgar score (5 min)	5.2 ± 3.3	6.7 ± 2.4	0.186
Perinatal death	9	5	0.129
Recurrent convulsion	2	1	0.587
C/S rate	13	9	0.590
Maternal death	1	3	0.270

Table 2 Maternal complications in the study groups

Maternal complications	Study group		Total
	Low dose	Std. dose	
Nil	35	29	64
Abruptio placenta	1	0	1
Resp. disorder	1	2	3
Renal failure	1	1	2
Others	1	1	2
Total	39	33	72

P value = 0.339

This is consistent with most data in Nigeria but differ to the situation in India where majority were antepartum eclampsia [20].

The recurrent convulsion rate did not differ significantly between the two study groups. Furthermore, our overall recurrent convulsion rate of 4.2 % is comparable to reports from Nigeria [14, 21] and that of Collaborative Eclamptic Trial [22]. However, our figure for recurrent convulsion rate is higher than the 2 % reported by Begum and co-workers [23] and 1.1 % by Mahajan and colleagues [16] in their experiences of low-dose regimen. Our study design differs from the two studies referred to above (non-randomized trials) and this among other factors such as the environment may account for the differences.

Although there were more cesarean deliveries and perinatal deaths in the low-dose study group, the differences was not statistically significant. This finding is similar to the observations made by Chowdhury and colleagues [24], in which low-dose intravenous infusion of magnesium sulphate was compared with the Pritchard regimen.

Maternal complications including mortality do not differ significantly between our study groups. This is in agreement with the observation of Chowdhury and co-workers [23] among India women. Our case fatality rate for eclampsia of 5.5 % observed in this study is almost half of the 9.9 % reported by Ekele and colleagues [25] working in a similar environment in Nigeria. However, our dosing regimen differs from that utilized by Ekele [25]. In the ultra-short regimen in the non-randomized trial of Ekele and co-workers [25], their patients only receive a loading dose of 14 g magnesium sulphate and no maintenance doses.

The total dose of magnesium sulphate in the low-dose regime is about half of that in the standard regimen group thus reducing significantly the cost of anticonvulsant therapy (15 vs. 29 USD) and by extension the total cost of care. This is certainly an important observation in an environment where the payment system for health care is largely out of pocket expenses. Although no toxicity was recorded in the study groups, the low dosing regimen may guarantees more safety particularly in the lower levels of care where routine monitoring of eclamptics may not be optimal owing to fewer personnel.

Given the limitations of this study which include our sample size and the fact that our trial was not blinded, it may be concluded that the effectiveness of low-dose regimen of magnesium sulphate appeared comparable to the 'standard dose regimen'. Low-dose regimen may guarantee more safety and in an environment (such as ours) where cost is an important determinant of accessibility to qualitative health services, it is certainly attractive. More studies are needed to establish the place of low-dose regimen of magnesium sulphate in the management of eclampsia.

Conflict of interest We declare that there is no conflict of interest in this study.

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