

Maternal and perinatal outcome of patients with severe pre-eclampsia in a tertiary health centre in south-western Nigeria: a cohort study

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Original Article

ABSTRACT

Objective: To determine the effect of introducing MgSO₄ on the maternal and perinatal outcomes of severe pre-eclampsia in Sagamu, south-western Nigeria.

Methods: A retrospective cohort study of all cases of severe pre-eclampsia managed at Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Nigeria from 1 January 2001 to 31 December 2012 – 6 years before and 6 years after the introduction of MgSO₄ was carried out.

Results: The prevalence of severe pre-eclampsia within the study period was 4.2%. The mean age of study participants was 31.2 ± 6.7 years. Seventy-four women received MgSO₄ while 123 received diazepam. Eclampsia occurred in 3 members of the diazepam group and none in the MgSO₄ group. There were no maternal deaths. Babies from the diazepam group were more likely to have low Apgar score at 5 minutes (though the association was not statistically significant [OR=1.47, 95% CI 0.76, 2.82]). Babies from the diazepam group were significantly more likely to have prolonged hospital stay [OR= 6.09, CI 2.25, 17.40; p< 0.001] and suffer early neonatal deaths than babies from the MgSO₄ group [OR= 5.26, CI 1.35, 23.92; p=0.005]. Perinatal mortality did not differ between the groups.

Conclusion: MgSO₄ is more effective than diazepam in the management of severe pre-eclampsia at OOUTH, Sagamu, Nigeria. Therefore, its accessibility and wider use should be promoted to improve fetomaternal outcome.

Key words: Severe pre-eclampsia, seizure prophylaxis, perinatal mortality, magnesium sulfate.

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La santé maternelle et périnatale des patients atteints de pré-éclampsie sévère dans un centre de santé tertiaires dans le sud-ouest du Nigeria: une étude de cohorte

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Article Original

RÉSUMÉ

Objectif : Cette étude vise à déterminer l'impact de l'introduction de MgSO₄ sur les résultats maternels et périnataux de pré-éclampsie graves à Sagamu, au sud-ouest du Nigeria.

Méthode : Nous avons effectué une étude rétrospective de tous les cas de pré-éclampsie graves soignées au Centre Hospitalier Universitaire de l'Université Olabisi Onabanjo (OOUTH), Sagamu au Nigeria du 1er janvier 2001 au 31 décembre 2012 – 6 ans avant et 6 après l'introduction du MgSO₄.

Résultats majeurs : la prévalence de pré-éclampsie grave au cours de la période d'étude était de 4,2%. La moyenne d'âge des participants à cette étude était de 31,2±6,7 ans. Soixante-quatorze femmes ont reçu du MgSO₄ tandis que 123 ont reçu du diazépam. L'éclampsie s'est signalée chez 3 membres du groupe de 4diazépam et chez personne dans le groupe de MgSO₄. Il n'y a eu aucune mort maternelle. Les enfants issus du groupe de diazépam présentaient plus de chance d'avoir un indice d'Apgar bas à 5 minutes (quoique le rapport n'était pas statistiquement important [OR=1,47 ; 95% CI 0,76 ; 2,82]). Les enfants issus du groupe de diazépam présentaient plus de chances d'avoir un séjour hospitalier prolongé [OR=6,09 ; CI 2,25 ; 17,40 ; p=0,001] et souffrent de morts néonatales précoces plus que les enfants issus du groupe de MgSO₄ [OR=5,26 ; CI 1,35 ; 23,92 ; p=0,005]. La mortalité périnatale était la même dans les groupes.

Conclusion : le MgSO₄ est plus efficace que le Diazépam dans les soins administrés pour le traitement de pré-éclampsie grave à OOUTH, Sagamu au Nigeria. Par conséquent, nous devons encourager son accessibilité et son grand usage dans le but d'améliorer les résultats foeto-maternels.

Mots-clés : Pré-éclampsie grave, crise prophylaxie, mortalité périnatale, sulfate de magnésium, Nigeria.

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INTRODUCTION

Hypertension is one of the most common medical complications of pregnancy and affects both maternal and fetal health. Hypertensive disorders during pregnancy remain one of the leading causes of maternal death worldwide, accounting for 10 to 20 per cent of maternal deaths (1).

Hypertensive disease complicates 5-7 percent of all pregnancies. It can be categorized into pre-existing hypertension, pregnancy-induced hypertension and pre-eclampsia. Pre-eclampsia is a syndrome occurring only in pregnancy and puerperium and defined by new onset of hypertension after the 20 weeks of pregnancy accompanied by a new onset (significant) proteinuria (2). Pre-eclampsia complicates about 5 – 10% of pregnancies (2). Together with its major complications- eclampsia and HELLP syndrome, it is an important cause of maternal and perinatal morbidity and mortality both in Nigeria and globally (3,4). Its effective management and/or prevention of eclampsia would therefore contribute significantly to reduction in maternal and perinatal morbidity and mortality (5).

Though the exact etiology of pre-eclampsia is not known, some of the potential etiologies include abnormal placentation, immunological intolerance between fetoplacental and maternal tissues, dietary deficiencies and genetic predisposition. Although the exact etiology remains elusive, two basic abnormalities are consistently seen in pre-eclampsia- abnormal trophoblastic invasion of uterine blood vessels and endothelial cell dysfunction (6), which may explain why significant improvement in the maternal clinical condition is not achieved until the placenta is delivered.

Pre-eclampsia is a multisystem disorder. It can be divided further into mild and severe types. Severe pre-eclampsia is characterized by severe hypertension and significant proteinuria (1,2). The management of severe pre-eclampsia entails the use of antihypertensive drugs to control

the blood pressure, anticonvulsants for seizure prophylaxis and delivering the fetus as soon as it is viable. Seizure prophylaxis employs the use of drugs such as diazepam, phenytoin and magnesium sulfate ($MgSO_4$) (6). There is overwhelming evidence to suggest that $MgSO_4$ is superior to other anticonvulsants in the management of severe pre-eclampsia/eclampsia (8). In line with this, there has been increasing use of $MgSO_4$ in health institutions in Nigeria (9,10). From the year 2007, the use of intramuscular $MgSO_4$ regimen replaced diazepam in the protocol for the management of pre-eclampsia/eclampsia at the Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Nigeria.

MATERIALS AND METHODS

This was a retrospective study of 2 cohorts of women managed for severe pre-eclampsia at the Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Nigeria from 2001 to 2012. The first (Diazepam) cohort consisted of those managed from January 2001 to December 2006 and received Roche brand of Diazepam as infusion of 20mg in 500mls of intravenous fluid over 6 hours, and continued for 24 hours after delivery as seizure prophylaxis. The second ($MgSO_4$) cohort was made of those managed from January 2007 (to December 2012) when $MgSO_4$ was introduced as seizure prophylaxis. The modified form of Sibai regimen (11,12) consisting of a starting dose of 4 grams of $MgSO_4$ given intravenously, followed by 2 grams of $MgSO_4$ intravenously every 4 hours was adopted by the Department of Obstetrics and Gynaecology of the hospital. Those women with history of seizure prior to admission and chronic hypertension were excluded from the study.

The case notes of the patients were retrieved from the Medical Information Department of the hospital. Patients' biodata and relevant outcome variables were sought for and recorded in a data sheet prepared for the study. Maternal outcome variables were

the occurrence of seizure (eclampsia) after initiation of seizure prophylaxis, duration of hospital stay, and maternal deaths. Perinatal outcome variables were Apgar score at 1 and 5 minutes, perinatal deaths, and early neonatal deaths. The ethical approval to conduct this study was given by Research Ethics Review Committee of the Hospital.

Data were analyzed by both descriptive and inferential statistics at 95% confidence level using SPSS software for Windows version 17.0. Frequency tables were generated for relevant variables. Proportions were compared using the Pearson chi-square test. Relationships were expressed using odds ratio and confidence intervals.

The diagnosis of severe pre-eclampsia was made in a woman with pre-eclampsia in line with standard protocols which include a diastolic blood pressure equal to or greater than () 110 mmHg and or systolic blood pressure 160 mmHg or urine protein is 5g/24 hours (8). A low Apgar score at 1 and/or 5 minutes was defined as a score less than 7. Prolonged hospital stay was defined as a hospital stay of more than 7 days following caesarean section or more than 2 days following vaginal delivery.

The Olabisi Onabanjo University Teaching Hospital (OOUTH), Sagamu, Nigeria is a teaching hospital which offers both primary and specialist care to pregnant women in Ogun State of Nigeria and its environment. It provides emergency obstetric services to women referred from other centers in addition to providing antenatal care and delivery services for low and high risk pregnant women from Sagamu community and neighboring towns. However, the proportion of booked pregnant patients that eventually deliver at OOUTH is less than 50%. In a study carried out in this hospital by Lamina et. al (13), it was found out that 28% of pregnant patients who booked at the center eventually delivered there. Attitude of hospital staff, cost of services and distance of the hospital from patient's homes were some of the reasons

given for not wanting to deliver at the Teaching Hospital and hence, the low delivery rate.

RESULT

During the 12 year study period, there were 197 cases of severe pre-eclampsia and 4682 deliveries which gave a prevalence rate of 4.2%. The mean age of the participants were 31.2 ± 6.7 years with a range of 19 – 48 years. The modal age group was 30 – 39 years and it consisted of 91 (46.2%) women. Sixty-five (33%) women registered and received antenatal care at the study center while the remaining (132; 67%) women were referred. A sizeable proportion of participants (81; 41.1%) were primigravidae, and the commonest gestational age at presentation was 34 – 36 weeks. Details of the socio-demographic data and other characteristics are shown in Table 1.

The diazepam cohort consisted of 123 women while the MgSO₄ cohort had 74 women. None of the patients in the MgSO₄ group had seizures after the commencement of the drug. Three women in the diazepam group had 2 to 4 episodes of tonic clonic seizures each. There were no maternal deaths in either of the groups.

Fifty-seven neonates from the diazepam group had low Apgar score at 1 minute as against 35 neonates from the MgSO₄ group. There was no statistical significant difference in terms of propensity of babies from either group to low Apgar score at 1 minute [OR= 0.84, CI 0.45 1.56]. On the other hand, 32 and 14 neonates from the diazepam and MgSO₄ groups respectively had low Apgar score at 5 minutes. Babies from diazepam group were more likely to have low Apgar score at 5 minutes but the association was not statistically significant [OR= 1.47, CI 0.76, 2.82]. Table 2 shows the details of the relationships between the MgSO₄ and diazepam groups with respect to Apgar scores.

Furthermore, out of the 197 women studied, 169 (85.8%) had a prolonged

hospital stay: 53 (71.6%) women in the MgSO₄ group and 116 (94.3%) in the diazepam group. The observed difference was statistically significant [OR= 6.09, CI 2.25, 17.40, p<0.001]

One hundred and ninety-seven pre-eclamptic women delivered 201 babies (4 were twin deliveries): 73 babies died within the perinatal period giving a perinatal case fatality rate of 36.3%. There were 23 perinatal deaths (21 stillbirths and 2 early neonatal deaths) in the MgSO₄ group which did not vary significantly with the 50 perinatal deaths (32 stillbirths and 18 early neonatal deaths) in the diazepam group (Tables 3 and 4). However, there was statistical significant difference between the two groups in terms of early neonatal deaths, babies in the diazepam group had more propensity to suffer early neonatal death than babies in the MgSO₄ group [OR= 5.26, CI 1.35, 23.92, p<0.05]. Forty-nine stillbirths occurred in 132 mothers who were referred while 4 stillbirths occurred in 65 mothers who were booked. Babies who were born by mothers who were referred were more likely to suffer stillbirth than babies who were born by mothers who were booked (OR=9.20, CI 3.45, 25.89, p<0.05). The perinatal mortality rates were 48.5% and 13.9% for babies born by referred and booked mothers respectively (OR=5.67, CI 2.72, 11.99, p<0.05).

DISCUSSION

Pre-eclampsia is a common and potential serious complication of pregnancy. The severe type occurs in about 25% of all cases of pre-eclampsia (8). The prevalence of severe pre-eclampsia of 4.2% observed in this study is similar to 5% in United Kingdom population (14) but higher than 0.3% reported from Nepal, South Asia (15). About two-thirds (67%) of all cases identified in this study were referred and they contributed significantly to the perinatal mortality. This underscores the importance of antenatal care and early recognition and prompt referral to hospitals where specialist care can be provided so as to prevent its complications

and improve fetomaternal outcome. The participants' mean age, parity and gestational age distribution of the cases were similar to those from related report (16-18).

The superior efficacy of MgSO₄ in the management of pre-eclampsia/eclampsia has been confirmed (19). This modified regimen is prescribed at the study center in preference to Pritchard (18) and other regimens because of low cost, ease of administration and unavailability (lack) of infusion pumps (20). The use of MgSO₄ as seizure prophylaxis in cases of severe pre-eclampsia reduces the risk of progression to eclampsia by more than half (8). This was evident in this study where eclampsia was observed only in the diazepam group. Furthermore, it may not be surprising that no maternal death was recorded in this study irrespective of the type of seizure prophylaxis because prompt commencement of seizure prophylaxis and prompt delivery in severe pre-eclampsia is associated with lower incidence of maternal death (8).

In this study, a newborn with a low 5-minute Apgar score was 1.47 times more likely to belong to a woman who received diazepam as seizure prophylaxis, when compared to the MgSO₄ group, though the association was not statistically significant. Low Apgar score has been associated with use of diazepam as seizure prophylaxis in pre-eclampsia. It has been suggested that diazepam crosses the placenta at a substantial dose to affect the fetus, causing depression of respiration in the newborn from cumulative effect of diazepam (8). Therefore, it is pertinent to ensure the availability of basic skills and equipment for newborn resuscitation not only in centers where diazepam is still being used for management of severe pre-eclampsia but also in centers where the use of MgSO₄ has been instituted because a substantial number of babies from the women in the latter group also suffered low Apgar score (birth asphyxia). The reason for the observed significant increase in hospital stay among the diazepam group was not clear and calls for further studies.

Severe pre-eclampsia is also

injurious to the fetus and this was reflected in the study by the high proportion (56.9%) of low birth weight babies and high perinatal case fatality of 36.3%. Nevertheless, the likelihood of perinatal death did not vary significantly between the MgSO₄ and diazepam groups.

Limitations: The study is limited by its retrospective nature and dependence on patient's records. It is likely that substantial measurement bias might have occurred especially with Apgar scoring but it was probably non-directional and therefore, would not have affected the study in any direction. It was also assumed that patients' management in either group was strictly in line with the hospital's protocol but that might not have been the case in our environment where payment for health care is essentially out of pocket. Furthermore, a larger number of participants could have produced more precise significant study results. Despite these limitations, the study has initiated the process of filling the existing gap on severe pre-eclampsia and the use of MgSO₄ in our environment.

CONCLUSION

This study has shown reduced perinatal morbidity (low Apgar score) and maternal morbidity (eclampsia and longer hospital stay) among severe pre-eclamptic women who received MgSO₄ when compared to those who receive diazepam. These findings support the superiority of MgSO₄ in the management of severe pre-eclampsia. It is pertinent to improve the accessibility and wider use of MgSO₄ as part of our nation's struggle to achieve the much desired reduction in maternal and perinatal mortality.

Acknowledgement: We acknowledge the contribution of the members of staff of Medical Information Department of the hospital in retrieval of patients' case files and records.

Conflict of Interest: No conflicts of interest declared.

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Table 1: Characteristics of study participants

Age (years)	Number	Percentage
< 20	7	3.6
20–29	82	41.6
30–39	91	46.2
>39	17	8.6
Total	197	100.0
Parity		
Para 0	81	41.1
Para 1-4	95	48.2
Para 5 and above	21	10.7
Total	197	100.0
Educational level		
No formal education	21	10.7
Primary	35	17.8
Secondary	74	37.6
Tertiary	67	34.0
Total	197	100.0
Gestational age range (weeks)		
Less than 29	11	5.6
29–33	41	20.8
34–36	43	21.8
37–42	99	50.3
Greater than 42	3	1.5
Total	197	100.0
Route of delivery		
Spontaneous vertex delivery	85	43.2
Assisted breech delivery	2	1.0
Vacuum delivery	5	2.5
Caesarean section	105	53.3
Total	197	100.0
Birth weight		
Less than 1.5kg	35	17.4
1.5–2.49kg	79	39.3
2.5–4.0	85	42.3
Greater than 4.0kg	2	1.0
Total	201	100.0

Table 2: Relationship between diazepam and MgSO₄ versus Apgar score⁴

Anticonvulsant	Low Apgar score at 1 minute		P value	OR (CI 95%)
	Yes (%)	No (%)		
Diazepam	57 (60.6)	37 (39.4)	0.5579877	0.84 (0.46, 1.56)
MgSO ₄	35 (64.8)	19 (35.2)		
Total	92 (62.2)	56 (37.8)		

Anticonvulsant	Low Apgar score at 5 minute		P value	OR (CI 95%)
	Yes (%)	No (%)		
Diazepam	32 (34.0)	62 (66.0)	0.2170439	1.47 (0.76, 2.82)
MgSO ₄	14 (25.9)	40 (74.1)		
Total	46 (31.1)	102 (68.9)		

Table 3: Perinatal mortality associated with diazepam and MgSO₄ prophylaxis

Seizure prophylaxis	Perinatal mortality		Total
	No (%)	Yes (%)	
Diazepam	76 (60.3)	50 (39.7)	126
MgSO ₄	52 (69.3)	23 (30.7)	75
Total	128	73	201

Table 4: Perinatal mortality type associated with diazepam and MgSO₄ prophylaxis⁴

Seizure prophylaxis	Stillbirth No. (%)	Early-neonatal death No. (%)	Total	P value	OR, CI 95%
Diazepam	32 (25.4)	18 (14.3)	50	0.0052861 23.92	5.26 1.35,
MgSO ₄	21 (28.0)	2 (2.7)	23		
Total	53	20	73		