IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 17, Issue 12 Ver. 2 (December. 2018), PP 24-32
www.iosrjournals.org

Correlation of Blood Pressure with Serum Magnesium Levels during Treatment of Preeclampsia with Magnesium Sulphate: A Cross Sectional Study

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Abstract: *Magnesium sulphate is effective in the prevention and treatment of seizures of preeclampsia. Although postulated to have antihypertensive effects; its use as an antihypertensive in preeclampsia management is however yet to be established. Our study aimed to determine the relationship between serum magnesium and blood pressure levels during treatment of preeclampsia with magnesium sulphate. It is a secondary analysis of data obtained from a prospective cross sectional study, on the clinical and biochemical correlates of preeclampsia among 75 patients who were administered magnesium sulphate (MgS04) using the Pritchard protocol. The results of serum magnesium assay obtained before each dose of MgS04, were correlated with the mean arterial blood pressure (MABP), using Pearson correlation statistics. The participants were mostly admitted in the antepartum period 67/75 (89.3%), with mean gestational age of 36.4±3.0 weeks. The mean loading dose (LD)-delivery interval was 5.94±4.2hrs. Significant proteinuria was predictive of severe hypertension (95%CI 0.003-0.006, p=0.005) while significantly lower rates of severe hypertension occurred among patients who had convulsed before admission (95%CI 0.073-0.564, p=0.002, OR=0.203). No significant correlation was found between MABP and serum magnesium level before (r=0.223, p=0.054) and during treatment with magnesium sulphate [4hrs (r=0.120, p=0.321), 8hrs (r=0.064, p=0.602), 12hrs (r=0.078, p=0.526), 16hrs (r=-0.026, p=0.834), 20hrs (r=-0.027, p=0.833), 24hrs (r=-0.151, p=0.238)] respectively. Also, severe hypertension (MABP≥125mmHg) had no statistically significant relationship with serum magnesium levels throughout treatment; 4hrs (p=0.462), 8hrs (p=0.208), 12hrs (p=0.346), 16hrs (p=0.925), 20hrs (p=0.376) and 24hrs (p=0.887) respectively. While MABP demonstrated a progressive decline in slope until completion, serum magnesium levels had a sinusoidal pattern with a peak at 8hrs.*
The MABP was not significantly affected by magnesium sulphate administered for seizure treatment. Thus, antihypertensive drugs should be administered for blood pressure control during treatment of preeclampsia with magnesium sulphate.

Date of Submission: 26-11-2018 Date of acceptance: 07-12-2018

I. Introduction

Preeclampsia is a disease condition that is common both in the developing countries and the developed world, the complications , morbidity and mortality from preeclampsia however disproportionately affect low and middle income countries.[1]This condition is largely unpreventable as several remedies have been tried with none proven to prevent its occurrence it has been shown however to be a predictable condition.[2] The complications of preeclampsia are also predictable and preventable, this ability to pre-empt this condition has made a big difference in adverse maternal outcome between the developed world and the low resource countries.[3,4]

Preeclampsia has been described as a 'disease of theories' with postulates evolving over time; from the 'toxaemia' era, through the vascular reactivity, the nitrous oxide, immunological, free radical injury, micronutrient deficiency and today; the abnormal trophoblast invasion theory.[5,6]These theories have determined the management of preeclampsia especially the treatment which has been based at these different times on the prevalent theory. Women with preeclampsia have been made to undergo gastric lavage, ovariectomy, renal decapsulation, phlebotomy and bloodletting, chloral hydrate treatment and treatment with drugs like sedation with morphine and 'the lytic cocktail', phenytoin and diazepam.[7,8] Hypertension became associated with preeclampsia after proteinuria and antihypertensive treatment has also evolved over time.[9] Delivery appears to be the ultimate goal in treatment based on the current thinking of the condition being a disease of the placenta,

preeclampsia has however been shown to develop for the first time after delivery.[10] The treatment of hypertension in preeclampsia is also important as the sequela of hypertension such as stroke, intracerebral haemorrhage, placental abruption, renal failure, liver damage, acute pulmonary oedema and congestive cardiac failure may result in serious adverse maternal and perinatal outcomes.[7] Hydralazine and labetalol are the most commonly used antihypertensive drugs in the management of severe pre-eclampsia.[11]Nifedipine and sodium nitroprusside are potential alternatives, but their use has been associated with significant risks.[12] Angiotensin-converting enzyme(ACE) inhibitors are contraindicated in pregnant women because of the risk of foetal oliguria, anuria, renal abnormalities and oligohydramnios.[10]

Magnesium sulphate has been shown in studies to be more effective than placebo and other anticonvulsants ever used in preeclampsia for the treatment and prevention of seizures.[8] The WHO recommended magnesium sulphate as the anticonvulsant of choice in its publication in 2011on evidence-based interventions for the prevention and treatment of preeclampsia and eclampsia.[13]

The exact mechanism of action of magnesium sulphate is not known, but its properties such as calcium channel blocking, relief of cerebral vascular spasm and intracellular inhibition of nitrous oxide (NO) synthase in endothelial cells, have suggested a role for this drug as an antihypertensive agent.[14] While a strong causal relationship exists between low serum magnesium levels and occurrence of convulsions and hence administration of magnesium sulphate for seizure prophylaxis and treatment; [14,15] the same may not be said about its relationship with the occurrence of severe hypertension or its role in blood pressure control.

Although magnesium sulphate has been reported in some studies to exert antihypertensive properties during treatment of severe preeclampsia, the treatment of hypertension with conventional antihypertensive drugs still continues.[11,13] Studies have linked low levels of magnesium with occurrence of hypertension in experimental animals, in children and in the non-pregnant adults, reports linking blood pressure levels with serum magnesium in patients with preeclampsia are however conflicting.[16-19]

This study therefore aimed to establish the trends in blood pressure levels during MgS04 treatment and determine its correlation with the levels of serum magnesium and thus the effect of the administered magnesium sulphate on the severity of hypertension in preeclampsia.

II. Material And Methods

The data for this study were obtained from the prospective cross sectional magnesium for preeclapmpsia and eclampsia project correlating clinical and biochemical findings of women administered magnesium sulphate for seizure prophylaxis and treatment at the ObafemiAwolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, in south western Nigeria, from March to October 2012.[20].

Study Design: Prospective cross sectional study

Study Location: This was done at the maternity units of the ObafemiAwolowo University Teaching Hospitals Complex, a tertiary level centre in Ile-Ife, South western Nigeria.

Study Duration: March to October 2012.

Sample size: 75 patients.

Sample size calculation: The serum magnesium levels (2.3 ± 0.30mg/dl)obtained by Phuapradit et al in 1993 among women with severe pre-eclampsia who had not commenced magnesium sulphate [21]and the4.90 ± 1.90 mg/dl obtained by Preedatham et al in 2009 among women with severe pre-eclampsia treated with magnesium sulphate [22]were applied to the formula $[n=(u+v)^2 (\sigma_1^2+\sigma_0^2)/ (\mu_1-\mu_0)]$,[23]for comparison of mean total serum magnesium levels before and after commencing magnesium sulphate. The typeI error was set at 0.05 while the type II error was set at 0.1. A minimum sample size of 67 participants was obtained after adding 10% for attrition.

Subjects & selection method: Participants included all consecutive patients admitted for severe pre-eclampsia and eclampsia at OAUTHC, within the duration of the study. There were a total of 88 cases of severe pre-eclampsia and eclampsia within this period. Of this, 2 were admitted moribund; 1 with HELLP syndrome and the other with acute renal failure, they never recovered from unconsciousness and did not have magnesium sulphate. Nine were involved in another study at the Wesley Guild Hospital (Ilesha) arm of the OAUTHC involving a different regimen for magnesium sulphate. Two patients received magnesium sulphate but did not consent to the study, thus 75 participants were available for recruitment.

Inclusion criteria:

1. Pregnant women admitted for severe preeclampsia or eclampsia,
2. Aged ≥ 18 years,
3. Gestational age between 28 and 41 weeks,
4. Postpartum eclampsia or preeclampsia

Exclusion criteria:

1. Gestational age less than 28 weeks or more than 41 weeks,
2. Mild pre-eclampsia

3. Personal or family history of myasthenia gravis
4. Diabetes mellitus
5. Renal disease,
6. Cardiac disease,
7. History of allergy to magnesium sulphate
8. Use of other anticonvulsants

Procedure methodology

The participants were educated about the study and informed consent obtained from them or from adult relatives (when patient was unable to do so). Ethical approval was obtained from the research and ethics committee of the OAUTHC (Protocol number ERC/2012/06/05).All the participants received the standard Pritchard regimen of magnesium sulphate administration thus: a loading dose of 4g (of 20% solution) intravenous magnesium sulphate over 10-15 minutes, followed immediately by 10g (of 50% solution) of deep intramuscular magnesium sulphate (5g on each buttock), in the upper outer quadrant of each buttock. A maintenance dose of 5g was then administered by the intramuscular route every 4 hours on alternate buttocks until 24 hours after the loading dose. The blood pressure was checked before and after every dose of magnesium sulphate, this was measured with the mercury sphygmomanometer in all the patients and the 5thKorotkoff sound was taken as the marking for the diastolic blood pressure. [12] Urine protein was measured by dipstick and graded on a scale of 0 to 4+, thus: 0 (negative), trace (15-30 mg/dl), 1+ (30-100 mg/dl), 2+ (100-300 mg/dl), 3+ (300-1000 mg/dl) and 4+ (>1000 mg/dl). Serum magnesium assay was done on 5 ml of venous blood obtained from each patient before each dose of MgSO4 i.e before the loading dose and at the; 4th, 8th, 12th, 16th, 20th and 24th hour maintenance doses, respectively. Serum Magnesium estimation was done using the Atomic Absorption Spectrophotometry technology (AAS 100 machine, Varian Technologies, Inc. Australia).

Severe preeclampsia was defined as the occurrence of severe hypertension and significant proteinuria occurring after 20 weeks of gestation up to 7 days postpartum. Hypertension was defined as a blood pressure reading of ≥110mmHg diastolic or ≥160mmHg systolic on any one occasion or a blood pressure of ≥90mmHg diastolic or ≥140mmHg systolic on two or more occasions 4 hours apart.[24]Severe hypertension was defined as blood pressure ≥160 mm Hg systolic, ≥110 mm Hg diastolic or both or a mean arterial blood pressure (MABP) ≥125mmHg.[21] All participants with hypertensive urgency (diastolic BP ≥110mmHg or systolic BP≥160mmHg) were administered 10mg intravenous hydralazine slowly over 10-15 minutes and blood pressure rechecked in 5, 15 and 30 minutes, until normal. Participants who were on Alpha-methyl dopa and Nifedipine continued these oral medications until commencement of magnesium sulphate. Significant proteinuria was considered as one 24 hour collection with total protein excretion of ≥300 mg or two 'clean-catch – midstream' or catheter specimens of urine collected ≥4 hour apart with ≥2 + on reagent strip.[10]

Statistical analysis

Data was analyzed using SPSS version 15.0 (SPSS Inc., Chicago, IL). Numerical data were expressed as mean ± standard deviation (SD). Bivariate analysis was done and the independent T-test used for comparison of means of groups studied, while the Chi-square test was used to compare categorical variables. The Pearson's correlation statistics was used to investigate the relationship between the mean arterial blood pressure and the serum magnesium levels. The level of statistical significance was set at p-value of <0.05.

III. Result

The participants were mainly young with median age of 27.0 years (range 18-42) and primigravida 42/75 (56%). Most of them had completed secondary school 43/75 (57.3%) but a majority were of low socio-economic class 40/75 (53.3%). They were also observed to be mostly unbooked 55/75 (73.3%) and admitted in the antepartum period 67/75 (89.3%), the mean gestational age was 36.4±3.0 weeks. Although most 39/75 (52%) of the participants met the Blood pressure (BP) criterion (MABP≥ 125mmHg) for severe preeclampsia, a significant proportion 20/75 (26.7%), had normal blood pressures at admission. Most 59/75 (78.7%) of the participants had significant proteinuria [2+ 14/75 (18.7%), 3+ 44/75(58.7%) and 4+ 1/75 (1.3%)] at admission. A cumulative 8/75 (10.7%) had a complication at the time of admission. Most 66/75 (88%) of the participants had the 14g loading dose (LD) before delivery. The mean LD-delivery interval was 5.94±4.2 hours. [table 1].

Table no 1 : Biodata of participants

Biodata	Frequency (n=75)	Percentage (%)
Median age (range)	27.0 years (18-42)	
Parity		
Primigravida	42	56%
Multipara	33	44%
Social class		

Low	40	53.3%
Middle	34	45.3%
High	1	1.3%
Educational level		
Primary	35	46.7%
Secondary	43	57.3%
Tertiary	7	9.3%
Booking status		
Unbooked	55	73.3%
Booked	20	26.7%
Admission diagnosis		
Severe preeclampsia	47	62.7%
Eclampsia	28	37.3%
Timing of admission		
Antepartum	67	89.3%
Postpartum	8	10.7%
Mean gestational age (n=67)	36.4±3.0 weeks	
Mean maternal BMI	27.4±3.5 Kg/m^2	
[a]Timing of LD		
Antepartum	66	88%
Postpartum	9	12%
Mean LD-Delivery interval (n=66)	5.9±4.2 hours	
[b]Blood Pressure (MABP, mmHg)		
Normal (60-110)	20	26.7%
Mild hypertension (110-124)	16	21.3%
Severe hypertension (≥125)	39	52%
Degree of Proteinuria		
1+	16	21.3%
2+	14	18.7%
3+	44	58.7%
4+	1	1.3%
[c]Complications (n=75)		
[d]None	67	89.3%
Placental abruption	4	5.3%
Aspiration	2	2.6%
Pulmonary oedema	1	1.3%
Stroke	1	1.3%

[a]LD=Loading dose of magnesium sulphate in the Pritchard protocol.
[b]MABP=Mean Arterial Blood Pressure, [c]Occurrence of more than one variable in an individual was possible
[d]Eclampsia not included as a complication of preeclampsia

Table 2 reveals that a statistically significant relationship existed between increasing degrees of proteinuria and occurrence of severe hypertension (95%CI 0.003-0.006, p=0.005), it also showed that patients who had convulsed before admission had significantly lower incidence and risk for severe hypertension (95%CI 0.073-0.564, p=0.002, OR=0.203). The maternal age (p=0.593), parity (p=0.164), BMI (p=0.850) and gestational age at admission (p=0.082) were however not significant determinants of occurrence of severe hypertension. Participants with severe hypertension had significantly higher mean serum magnesium level (2.02±0.26mg/dl) than those with mild hypertension (1.86±0.32mg/dl, 95%CI 0.027-0.301, p=0.020), before commencing magnesium sulphate. This was however not the case during MgS04 therapy as no statistically significant relationship was found throughout treatment; 4 hour maintenance 4M (p=0.462), 8M (p=0.208), 12M (p=0.346), 16M (p=0.925), 20M (p=0.376) and 24M (p=0.887) respectively. On further analysis, it was observed that patients admitted for eclampsia had significantly lower blood pressures, than severe preeclamptics before commencing magnesium sulphate (124.52±16.08 mmHg, p=0.037), they also had significantly lower serum magnesium levels at this time (4.04±0.51mg/dl, p=0.045). The serum magnesium levels were then found to be comparable between severe preeclamptics who had severe hypertension and those who did not (95% CI -0.088 to 0.238, p=0.362).

Table no2: Factors associated with occurrence of severe hypertension

The determinants of severe hypertension					
Factor	**Hypertension (MABP)**		**95% CI**		**P-value**
	Milld (<125mmHg)	Severe (≥125mmHg)	Lower	Upper	
Mean age (years)	27.6±6.8	26.8±5.6	-2.11	3.67	0.593
Parity					
Primigravida (n=42)	17 (48.6%)	25 (62.5%)			0.164
Multipara (n=33)	18 (51.4%)	15 (37.5%)			OR=1.77

Gestational age(weeks)	35.6±3.2	36.9±2.8	-2.86	0.17	0.082
BMI (Kg/m^2)	27.39±2.43	27.19±4.32	-2.31	1.91	0.850
Proteinuria					
1+ (n=16)	13 (81.3%)	3 (28.7%)	0.003	0.006	0.005
2+ (n=14)	6 (42.91%)	8 (57.1%)			
3+ (n=44)	15 (34.1%)	29 (65.9)			
4+ (n=1)	1 (100%)	0 (0)			
Diagnosis					
Eclampsia (n=28)	16 (61.5%)	12 (24.5%)	0.073	0.564	0.002
Severe preeclampsia (n=47)	10 (38.5%)	37 (75.5%)			OR=0.203
Serum Magnesium levels					
Before LD	1.86±0.32	2.02±0.26	0.027	0.301	0.020
4M	4.56±0.46	4.65±0.56	-0.152	0.331	0.462
8M	5.60±0.77	6.24±0.62	-0.138	0.622	0.208
12M	5.73±0.79	5.95±0.80	-0.237	0.666	0.346
16M	5.54±0.71	5.51±1.02	-0.022	0.228	0.925
20M	5.27±0.86	5.49±0.93	-0.279	0.727	0.376
24M	5.02±0.84	4.97±0.95	-0.690	0.598	0.887
Comparison of MABP and serum magnesium levels between eclampsia and severe preeclampsia					
	Diagnosis		95% CI		p-value
Parameter	Eclampsia	SPE	Lower	Upper	
MABP (mmHg)	124.52±16.08	131.14±10.80	-12.798	-0.042	0.037
Serum Mg levels before LD	1.81±0.33	2.05±0.23	-0.369	-0.110	<0.001
MABP 4M	128.89±7.69	122.27±12.94	-8.46	-21.69	0.384
Serum Mg levels 4M	4.04±0.51	4.63±0.49	-1.155	-0.012	0.045
Serum magnesium level versus severity of hypertension among severe preeclamptics					
	Hypertension		95% CI		
Parameter	Mild (<125mmHg)	Severe (≥125mmHg)	Lower	Upper	p-value
Before MgS04 (mg/dl)	1.98±0.21	2.06±0.24	-0.088	0.238	0.362
4M (mg/dl)	4.66±0.56	4.59±0.43	-0.166	0.304	0.560

Table no3: Shows that there was no significant correlation between the MABP and the mean serum magnesium level before (r=0.223, p=0.054) and during treatment with magnesium sulphate [4M (r=0.120, p=0.321), 8M (r=0.064, p=0.602), 12M (r=0.078, p=0.526), 16M (r=-0.026, p=0.834), 20M (r=-0.027, p=0.833), 24M (r=-0.151, p=0.238)] respectively.

Table no3: Correlation of Mean arterial blood pressure with serum magnesium levels

Serum magnesium levels	[a]r	p-value
Before MgS04	0.225	0.054
4 hours after LD	0.120	0.321
8 hours after LD	0.064	0.602
12 hours after LD	0.078	0.526
16 hours after LD	-0.026	0.834
20 hours after LD	-0.027	0.833
24 hours after LD	-0.151	0.238

[a]r=Pearson correlation coefficient

Figure no 1(bar chart) highlights the trends in MABP and the mean serum magnesium levels. The MABP demonstrates a progressive decline from the 128.8mmHg just before commencement of MgS04 to the lowest level of 107.5mmHg observed at the completion of the Pritchard protocol for MgS04 administration. A different trend was however observed for the mean serum magnesium level; a sinusoidal pattern with the lowest mean serum magnesium level (19.62g/l) occurring at commencement of MgS04, rising to a peak (60.67g/l), just before the 8 hour maintenance dose and then falling progressively to reach 50.14g/l at the 24-hour maintenance dose.

Figure no 1: Bar Chart showing the trends in serum magnesium levels and the MABP

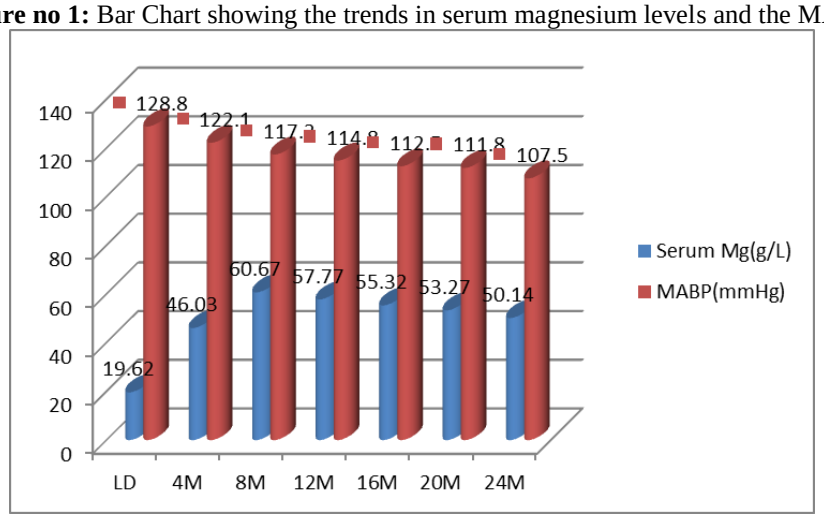

Table no4 reveals that;although significantly more participants with complications of preeclampsia (p<0.001) had severe hypertension at admission, the MABP was not statistically different between those who had complications (122.50±29.80mmHg) and those who did not (123.38±17.50, 95%CI -15.068 to 13.302, p=0.902). All fits during treatment occurred in the interval between the loading dose and the 4 hour maintenance dose of MgS04. Severe hypertension was not a significant determinant of occurrence of fits before (p=0.098) and during (p=0.0562) magnesium sulphate treatment. In contrast, the mean serum magnesium level was significantly lower in participants who convulsed before commencing (1.61±0.33 < 2.01±0.25mg/dl, 95%CI of 0.21 to 0.59, p<0.001), and during treatment with MgS04 (4.04±0.51 < 4.63±0.49mg/dl, 95%CI of 0.01-1.15, p=0.04). Unlike severe hypertension, there was no statistically significant difference in the mean serum magnesium level between the participants who had other complications of preeclampsia and those who did not (95% CI -0.28 to 0.16, p=0.59).

Table no 4: Comparing between hypertension and serum magnesium levels as predictors of seizures and complications of preeclampsia

[a]Occurrence of Convulsion					
Factor and interval	**Convulsion**		**95%CI**		**p-value**
	Yes	**No**	**Lower**	**Upper**	
MABP ≥125mmHg before LD					
Yes	3	46	0.092	0.104	0.098
No	6	19			
MABP before LD (mmHg)	122.14±18.26	123.97±19.43	-10.87	7.21	0.688
MABP≥125mmHg 4M					
Yes	2	28			0.562
No	1	43			
MABP at 4M	121.07±11.90	123.49±13.39	-8.60	3.78	0.439
Serum Mg level [b]LD (mg/dl)	1.61±0.33	2.01±0.25	0.21	0.59	<0.001
Serum Mg level [c]4M (mg/dl)	4.04±0.51	4.63±0.49	0.01	1.15	0.045
[d]Presence of complications of preeclampsia at admission					
Factor	Complications		95% CI		p-value
	Yes (n=8)	No (n=67)	Lower	Upper	
MABP≥125mmHg before MgS04					
Yes (n=40)	5	35	0.000	0.000	<0.001
No (n=35)	3	32			
Serum Mg level LD (mg/dl)	1.91±0.36	1.99±0.28	-0.278	0.159	0.591

[a]All convulsions during magnesium sulphate treatment occurred in the interval LD-4M
[b]LD- the loading dose of magnesium sulphate
[c]4M- the 4 hour maintenance dose of magnesium sulphate
[d]No complication of severe preeclampsia (apart from convulsion) occurred during MgS04 therapy.

IV. Discussion

The observed higher rate of severe preeclampsia and eclampsia among primigravidae in this study corroborates reports from other parts of Nigeria.[25] It is not surprising that most of the participants in this study were unbooked and of low socio-economic status. Lack of skilled care in pregnancy has earlier been reported as constituting the major risk factor for adverse maternal and perinatal outcome in Nigeria.[26]A majority (89.3%) of

the participants were admitted in the antepartum period, this is similar to the 73.9% reported from eastern Nigeria.[27] These hospital based reports may not be true reflections of the incidence of antepartum severe preeclampsia as most pregnant women in Nigeria go to the hospital only when disease conditions become symptomatic or complicated. Indeed 10.7% of the participants had a complication at the time of presentation. The lower rates of postpartum preeclampsia and eclampsia observed above may also be supported by a report that only 48% of women in developing countries like Nigeria have skilled attendance at delivery.[3] The uptake of postnatal services in third world countries are reportedly very low.[4] In fact reports from analysis of the Demographic and Health Survey (DHS) data from 23 sub-Saharan African countries show that only 13% of women that delivered at home received postnatal care within 2 days of childbirth.[28]

Significant proteinuria was the most consistently occurring feature that defined severe preeclampsia in this study as it was found in over 78.7% of the participants, a similar finding was earlier reported from a study in Turkey, where proteinuria was also associated with more severe preeclampsia and higher rates of preterm delivery.[29] Severe hypertension however occurred less frequently (52%) as definition for severe preeclampsia. Over ¼ of the participants had normal blood pressures at the time of admission, which is consistent with earlier reports from eastern Nigeria where 20% of eclamptic patients and 15% of those with HELLP syndrome were normotensive at the time of admission.24 Proteinuria was also found to be an important determinant of occurrence of severe hypertension as higher degrees were found among the participants with severe hypertension, this finding supports earlier reports.[29,30] However, the participants that were admitted for eclampsia had significantly lower MABP than those who had not convulsed, an earlier similar study reported that 23.9% of the eclamptics involved in their study had mild hypertension while20% were normotensive.[27] The eclamptics in our study were also observed to have significantly and consistently lower levels of serum magnesium before and after commencing magnesium sulphate treatment; low serum magnesium levels have been linked to the occurrence of fits in preeclampsia.[14,15] Maternal age and BMI were not significant determinants of the occurrence of severe hypertension in this study, which is in contrast to earlier reports.[31]

The observed serum magnesium levels had no significant relationship to the incidence of severe hypertension during magnesium sulphate treatment. This finding contrasts earlier reports of a direct relationship between low serum magnesium levels and severe hypertension.[17,19] While a meta-analysis of 20 clinical trials revealed a dose-dependent blood pressure reduction with magnesium supplementation, results from a more recent one involving 105 trials and 6805 patients showed that magnesium use has no significant effect on blood pressure.[17,18] A report from a study on orally administered magnesium supplements outside pregnancy, also showed that there was no association between baseline serum magnesium and the development of hypertension.[32]

The trends in serum magnesium levels during MgS04 observed in this study, shows a sinusoidal pattern with an initial increase reaching a peak at the 8-hour maintenance, followed by reduction in levels until the completion of the Pritchard protocol of MgS04 administration. The levels observed after the peak however remained within the therapeutic range (4.8 to 8.4mg/dl) for magnesium sulphate.[33] All convulsions in this study occurred either before commencing treatment with MgS04 or in the interval (n=3) between the loading dose and the 4-hour maintenance dose, when the serum magnesium levels were lower and mostly in sub-therapeutic ranges. The trends in MABP levels is however different as progressive reduction in blood pressures were noted until completion of the MgS04 regimen. The observed mean loading dose-delivery interval of 5.9 ± 4.2 hours suggests that most of the participants had delivered before the attainment of the 8-hour serum magnesium peak. Thus delivery, especially placental expulsion may be the most important reason for the continued fall in the blood pressure despite the changes in magnesium levels. This supports the present widely held theory of preeclampsia as a disease of the trophoblast and delivery the- ultimate-cure.[10]Orally administered magnesium supplements have however been associated with increased urinary magnesium excretion (up to 50% higher) in a non-pregnant population.[19]

The Pearson correlation statistics was used to determine the correlation of MABP with serum magnesium levels and no significant correlation was found. Although the serum magnesium levels increased; these levels did not produce a concomitant change in the blood pressures observed. One of the studies that found a role for magnesium supplementation as being effective in preventing hypertension, also reported that the observed blood pressure response was independent of baseline magnesium levels.[19] That study was however done among a non-pregnant population using orally administered supplements (which was subject to first pass metabolism and increased excretion needed to maintain a tight control) whereas this one involved pregnant women. It is established that magnesium levels are lower in pregnancy and hypomagnasemia may prevail; these changes are however reversed within 24 hours of delivery, with serum magnesium levels returning to pre-pregnant levels.[14] Our study also involved the use of parenterally administered magnesium (The Pritchard protocol) which produced a net increase in serum magnesium levels, despite the changes in pregnancy and delivery. These increments where however not associated with changes in blood pressures as reported above. It has been reported in earlier studies that intramuscularly administered MgS04 has an onset of action in 1 hour

and a duration of action of about 4 hours while intravenous administration has immediate effect which lasts for 30 minutes.[33] The administration of oral magnesium in the earlier study above,[19] may not be easily appreciated in the serum, as earlier studies have shown that oral magnesium cannot cause a significant rise in total serum magnesium level, because of its rapid excretion in the urine.[34] The action of oral magnesium as a cathartic is based on its ability to absorb water locally and distend the intestinal lumen, thus causing peristalsis and this explains why magnesium is not administered orally in the management of preeclampsia.[34]

The MABP and serum magnesium levels were compared as predictors of complications of preeclampsia. Hypertension was found to have a significant association while serum magnesium had no relationship to them. A comparison of these two as predictors of convulsion however highlights low serum magnesium level as being consistently related to the occurrence of fits before and during treatment with magnesium sulphate, a finding which is in support of earlier studies.[14,15] The MABP did not demonstrate any relationship with occurrence of seizures. This suggests that although magnesium sulphate is effective as an anticonvulsant in the management of preeclampsia, it may not be useful as an antihypertensive agent. Thus the use of magnesium sulphate in the treatment of preeclampsia should be restricted to the prevention and treatment of seizures.).

V. Conclusion

The MABP was not significantly affected by magnesium sulphate administered for seizure treatment. Thus, antihypertensive drugs should be administered for blood pressure control during treatment of preeclampsia with magnesium sulphate.

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John Osaigbovoh IMARALU, "Correlation of Blood Pressure with Serum Magnesium Levels during Treatment of Preeclampsia with Magnesium Sulphate: A Cross Sectional Study". " IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 12, 2018, pp 24-32.