Research Article

Comparison of serum levels of calcium and magnesium among preeclamptic and normotensive pregnant women at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria

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ABSTRACT

Background: Despite numerous studies, the exact aetiology of pre-eclampsia remains unknown. Some studies have shown that supplementation of calcium and magnesium could ameliorate the effects of pre-eclampsia. The objective of this study was to compare the calcium and magnesium levels in the serum of Nigerian women with or without pre-eclampsia.
Methods: In this study, serum calcium and magnesium levels were determined using atomic absorption spectrometry in 54 patients and 48 healthy normotensive pregnant women. The mean, standard deviation, Student's 't' test and Pearson correlation were employed.
Results: Serum calcium was significantly lower in patients than controls (9.17 ± 0.6 vs. 7.22 ± 0.5 mg/dl. P <0.001) (t test). Plasma Magnesium was significantly lower in patients than controls 13.19 ± 1.1 vs. 9.81 ± 0.7 mg/dl. P <0.001). The systolic and diastolic blood pressure showed significant inverse correlation with both calcium and magnesium (P<0.01).
Conclusion: There was significant reduction in the levels of calcium and magnesium in patients with pre-eclampsia. Dietary supplementation of these trace elements may help to prevent pre-eclampsia.

Keywords: Preeclampsia, Atomic absorption spectrometry, Calcium, Magnesium

INTRODUCTION

Pre-eclampsia refers to a syndrome of new onset of hypertension and proteinuria after 20 weeks of gestation in a previously normotensive woman.[1] Hypertension associated with pregnancy is the most common medical risk for maternal morbidity and mortality.[2] Pre-eclampsia has been dubbed the "disease of theories" because of the

multiple hypothesis have been proposed to explain its occurrence.[3] Despite its prevalence and severity, the pathophysiology of this multisystemic disorder is still poorly understood. Some studies have shown that changes in the levels of trace elements in pre-eclamptic patients may implicate its pathogenesis,[4] while others have failed to show any association of blood levels of trace elements and prevalence of pre-eclampsia.[5] High rate of preeclampsia in developing countries have forced

some authors to conclude that malnutrition is a risk factor in the aetiology of preeclampsia and implicate it by deficit of calcium and zinc.[6] Modern management of preeclampsia focuses on prevention rather than treatment.[7] Among the advocated modalities of prevention is calcium and magnesium supplementation.[8] This is based on the physiology of these trace elements in cellular and neuronal metabolism and functions.

The objective of this study was to assess the calcium and magnesium levels in the blood of Nigerian women with or without pre-eclampsia. The roles of magnesium and calcium ions have been noted in the pathogenesis of seizure disorder, which often complicate pre-eclampsia. It is therefore very crucial to evaluate the levels of these trace elements in pregnant women with a view to providing a preliminary data regarding calcium and magnesium supplementation in pregnancy in our area.

METHODS

Study design

This was a cross-sectional study designed to evaluate the levels of calcium and magnesium in pregnant women with pre-eclampsia.

Study population

The study population involved pregnant women that were managed at Nnamdi Azikiwe University Teaching Hospital (NAUTH) Nnewi (Eastern Nigeria). The patients were selected based on pre-set criteria by the researchers.

Inclusion criteria for the patients were age: 18-45 years, women diagnosed with pre-eclampsia, as defined in accordance with (US) national High Blood Pressure Education Program working group.[9] The controls were selected from pregnant women also after 20 weeks of gestation, but not diagnosed with pre-eclampsia, in the same age range.

Exclusion criteria included patients on magnesium sulphate and calcium lactate drugs, patients with medical complications like diabetes mellitus, renal failure, heart diseases (diseases that alter vascular response). The patients and controls were sampled with a well-designed questionnaire, administered by the researchers.

Blood sample collection

Blood was drawn from the cubital vein using a sterile needle and syringe into an appropriate tube. The samples in plain tubes were allowed to clot undisturbed and serum were separated by centrifugation for 10 min at 4000 rpm into plain tubes and stored at -20°C until time of analysis.

Biochemical analysis

Calcium and magnesium were determined by flame atomic absorption Spectrophotometry as described by Kaneko.[10]

Principle

Serum levels of the selected trace elements were estimated by Atomic absorption spectrophotometer. The principle is based on the dissociation of the elements (from the flame) from its chemical bonds. This is then placed in unexcited or ground state (neutral atom). Thus the neutral atom is at a low energy level in which it is capable of absorbing radiation at a very narrow bandwidth corresponding to its own line spectrum. The amount of radiant energy absorbed is proportional to the concentration of trace elements in the serum.

Statistical analysis

The statistical package for social sciences (SPSS) software package was used for analysis. Values obtained from this study were expressed as mean and standard deviation when compared using Independent 't' test. Pearson correlation coefficient was used to measure the degree of association between variables. The level of significance was set at $P < 0.005$.

RESULTS

Fifty four patients and forty eight controls were studied.

Table 1: Sociodemographic characteristics of subjects.

Variables	Non pre-eclamptic (%)	Pre-eclamptic (%)
Age		
<20	2 (4.2)	15 (27.8)
20-25	12 (25.0)	8 (14.8)
26-30	17 (35.4)	13 (24.1)
31-35	11 (22.9)	11 (20.4)
36-40	6 (12.5)	6 (11.1)
>40	0 (0.0)	1 (1.9)
Total	48 (100.0)	54 (100.0)
Parity		
Nullipara	18 (37.5)	33 (61.1)
Para 1	19 (39.6)	7 (13.6)
Multipara	8 (16.7)	9 (16.7)
Grand multipara	3 (6.3)	5 (9.3)
Total	48 (100.0)	54 (100.0)
Obesity		
<18.9	1 (2.1)	0 (0.0)
18.9-24.9	12 (25.0)	12 (22.2)
25-29.9	22 (45.8)	19 (35.2)
≥30	13 (27.1)	23 (42.6)
Total	48 (100.0)	54 (100.0)

Table 1: The mean age of the patients was 27 ± 7.02 years and that of the control was 29 ± 5.35 years .Most of the patients and controls were of parity 0 and 1. Most of the patients who had pre-eclampsia were of age <20 years and a greater percentage of patients who had pre-eclampsia also had obesity. The mean systolic blood pressure was 174.62 ± 27.45 mmHg for patients and 113.3 ± for controls, P <0.0001 (t-test). The mean diastolic blood pressure for patients was 111.48 ± 13.65 mmHg and 76.66 ± 9.07 mmHg controls, P <0.001 (t-test).

Table 2: Plasma calcium was significantly higher in controls than patents. (9.17 ± 0.6 vs. 7.22 ± 0.5 mg/dl. P<0.001) (t test). There was significant difference between serum magnesium levels of controls and patients (13.19 ± 1.1 vs. 9.81 ± 0.7 mg/dl. P <0.001) respectively.

Table 2: The characteristics of the study population.

Parametres	Patients (n=54) Mean ± SD	Control (n=48) Mean ± SD	't' value	P value
Age (years)	27 ± 7.02	29 ± 5.35	1.326	0.188
BMI(kg/m^2)	29.29 ± 6.01	27.80 ± 4.34	-1.415	0.160
SBP (mmHg)	174.63 ± 27.45	113.33 ± 19.17	-13.19	<0.0001
DBP (mmHg)	111.48 ± 13.65	71.67 ± 9.07	-17.52	<0.0001
Calcium (mg/dl)	7.22 ± 0.5	9.17 ± 0.6	12.88	<0.0001
Magnesium (mg/dl)	9.81 ± 0.7	13.19 ± 1.1	18.18	<0.0001
SD = Standard deviation; mg/dl= milligram per deciliter; KG/m^2 = Kilogram per meter square; BMI = Body mass index, SBP = systolic blood pressure; DBP= Diastolic blood pressure; mmHg = Millimeter mercury.				

There was an inverse relationship between calcium, magnesium and diastolic blood pressure (r = -0.819, P <0.01, r = -0.783, P <0.01) respectively. There was also inverse correlation between systolic blood pressure and levels calcium and magnesium (r = -0.719, P <0.01, r = -0.740, P <0.01).

DISCUSSION

Our study showed no statistically significant difference between maternal age and pre-eclampsia (P=0.188). This was similar to the findings of Shamsi et al.[11] and Ganesh et al.[12] It was however different from the findings of Macdonald-Wallis et al.[13] Such difference may be due to specificity of each population and hospital of the attendant patients. Furthermore, some studies have shown that high body mass index (BMI) before pregnancy increases the risk of a woman developing pre-eclampsia[14,15] however our study noted no significant difference between BMI and pre-eclampsia (P = 0.15).

Moreover, our study showed a significant difference between nulliparity and pre-eclampsia (P = 0.02), this corroborated the findings by Odegard et al.[16] who noted that nulliparity and hypertension increased pre-eclampsia risk. This may be explained by the immunologic theory of pre-eclampsia which was of the view that increase incidence of pre-eclampsia in nullipara is due to inadequate blocking antibodies to the paternal antigens.

Calcium and magnesium are two intracellular ions that are very important for cellular metabolism such as muscle contractility, secretions, neuronal activity as well as cellular death.

Our result showed significant reduction in the levels of calcium and magnesium in pre-eclamptic women compared to normotensive women. This is consistent with the findings by other workers.[17] While the cause of pre-eclampsia remains elusive to scientific knowledge, magnesium and calcium ions are thought to be implicated.

Although, calcium alone might play a role in the rise of blood pressure, a proper balance of calcium and magnesium is of vital importance to control blood pressure because blood vessels need calcium to contract, but they also require sufficient magnesium to relax and open up. Thus, magnesium acts as calcium channel blocker by opposing calcium dependent arterial constriction and by antagonizing the increase in intracellular calcium concentration leading to vasodilatation.[18] Magnesium competes for a prejuctional site with calcium ions. High magnesium concentrations inhibit the release of acetylcholine and high calcium concentrations increases release of acetylcholine from pre-synaptic nerve terminal.[8]

The process of cellular injury entails influx of calcium ions into the cell leading to increased intracellular ions and loss of calcium homeostasis[8]. This mechanism is involved in cell death and reperfusion injuries.[19] In pre-eclampsia and eclampsia, there is initial vasospasm, ischaemia and cellular hypoxia; this may culminate in reperfusion injury following treatment. To mitigate the

effect of reperfusion injury, magnesium which is a physiological antagonist to calcium will also flow into the cell[8]. This explains the reduction in the levels of calcium and magnesium in our patients.

Hypomagnesaemia may lead to a reduction in cerebral blood flow, cerebral vasospasm and increase in neuronal burst. Macdonald et al have demonstrated the vasoprotective effects of magnesium[20]. Lu and Nightingale found a reduced incidence of maternal mortality from 16% to 8% in Bangladesh following the introduction of low dose of magnesium sulphate for pre-eclamptic women[21], thus the success of magnesium therapy as a treatment of eclamptic seizures and the known effect of magnesium on vascular responses in vitro suggest that magnesium might be deficient in women with pre-eclampsia.

The systemic effects of magnesium include vasodilatation, and increase in blood flow, this prevent eclampsia by selectively dilating cerebral vasculature and relieving the cerebral vasospasm associated with preeclampsia. In eclampsia, it will prevent recurrent seizure which is beneficial in reducing mortality and morbidity in both the mother and the foetus.

CONCLUSION

Our study showed significant reduction in the levels of calcium and magnesium in pre-eclamptic women when compared with normotensive pregnant women. In the light of the reduction in the concentration of these elements, dietary supplementation or direct replacement therapy of these trace elements is suggested for women with pre-eclampsia.

ACKNOWLEDGEMENTS

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