SERUM MAGNESIUM LEVELS IN WOMEN WITH BREAST CANCER IN BENIN CITY, NIGERIA

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ABSTRACT

Aim: The aim of this study was to compare the serum magnesium levels of patients with breast cancer and apparently healthy people without the disease.

Study Design: This is a cross-sectional prospective study.

Place and Duration of Study: The study was carried out at the Department of Surgery, Central Hospital, Benin City and Department of Chemical Pathology, University of Benin Teaching Hospital Benin city, Nigeria, between July, 2011 and October 2012.

Methodology: A total of 60 female participants from Central Hospital, Benin City, Nigeria were recruited for this study. 30 of the women (50%) had breast cancer and 30 women (50%) without the disease served as control. Venous blood was obtained from participants and serum magnesium level was determined using standardized laboratory methods.

Results: The results showed a statistically significant reduction in serum magnesium level of patients with breast cancer compared with those without the disease.

Conclusion: We demonstrated from this present study that the participants with breast cancer have reduced serum magnesium level compared to those without the disease (control) and it is advisable to cautiously add magnesium as an adjuvant therapy in the management of breast cancer.

Key words: Serum magnesium, breast cancer, hypomagnesaemia, metabolism, adjuvant therapy.

Introduction

Breast cancer is the commonest malignancy among females worldwide[1]. The exact cause of breast cancer is unknown, however some risk factors include age, family history, life style (alcohol consumption, hormone use), obesity, post menopausal women with hypercholesterolemia. Researchers at the University of North Dakota in the United States suggested that analysis may be ignoring the role of magnesium as an important risk factor in breast cancer[2]. Aleksandrowicz et al also reported in Poland that inadequacy of magnesium and antioxidants are important risk factor in predisposing to leukamia[3].

Studies have shown that 46% of all critically ill cancer patients admitted to an ICU (intensive care unit) in a tertiary cancer center presented with hypomagnesemia and they concluded that the incidence of hypomagnesemia in critically ill cancer patients is high[4]. The incidence rises to 60 to 65% in all patients admitted into the intensive care units in which nutrition, diuretics, hypoalbuminemia, and aminoglycosides may play important roles[5,6,7].

Over 300 enzymes systems that influence the metabolism of carbohydrate, amino acids, nucleic acid, protein and ion transport, require magnesium[8,9]. The role of magnesium in fatty acid and phospholipid metabolism, that affect permeability and stability of membrane, were elucidated[10,11].It has been proposed that magnesium is central in the cell cycle, and that its deficiency is an important condition in pre-cancerous cell transformation[12,13,14]. Magnesium deficiency would therefore lead to physiological decline in cells setting the stage for cancer.

It is known that carcinogenesis induces magnesium distribution disturbance, which causes magnesium mobilization through blood cells and magnesium depletion in non-neoplastic tissue. Magnesium deficiency seems to be carcinogenic and in case of solid tumours a high level of supplemented magnesium inhibits carcinogenesis[15].Studies carried out at the University of Ibadan, Nigeria showed an increased serum magnesium level in breast cancer patients compared with controls and it was suggested that this increase may be an indication of its protective effect against cancer.[16]

The objective of this study is to evaluate and compare serum magnesium levels of patients with breast cancer with apparently healthy controls without the disease.

Patients and methods

A total of 60 female participants from Central Hospital Benin City, Nigeria were recruited for this study between 1st July 2011 through 31st October 2012 (15 months). 30 of these women (50%) had breast cancer and 30 women (50%) without the disease served as control. Informed consent was obtained from the participants and participation was voluntary. Biochemical analysis was done at the Department of Chemical Pathology, University of Benin Teaching Hospital.

Sample collection and preparation

Venous blood was obtained from participants with breast cancer immediately diagnosis was made prior to the commencement of chemotherapy, venous blood was also obtained from age matched female control subjects. The samples were allowed to clot, retracted and centrifuged at 3000 RPM for 15mins. The sera were harvested and stored frozen at -20^{0}C until analysis was carried out.

Data analysis

Data analysis was conducted using the general linear model of SAS, 2004 model. The result of the study was expressed as mean ± standard error of mean. Analysis of variance was used to test for difference in the group. Duncan's multiple range tests was employed to express the mean that show significant differences.

Assay method

Serum magnesium level~~s~~ was assayed using direct spectrophotometric method. In the reaction, magnesium forms a coloured complex with calmagite in alkaline medium to produce a red complex which was measured spectrophotometrically at 539 nm. EGTA (ethylene glycol tetra acetic acid) was added to prevent calcium interference, and a surfactant which eliminated the effect of protein. The colour produced was proportional to the magnesium concentration[17].

The concentration of magnesium is obtained from the equation

$$\frac{\text{Absorbance of sample}}{\text{Absorbance of standard}} \times \text{concentration of standard}$$

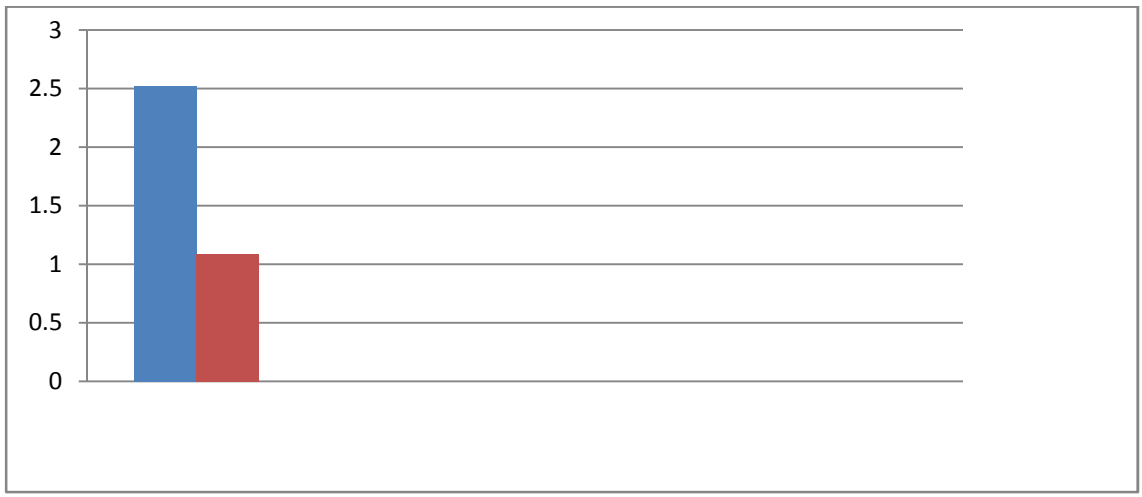
Result

Participants were both pre-menopausal and post-menopausal women. The mean age of breast cancer patients was 55±1.6 (range 45 to 65) years while that of the control was 51±1.4 (range 42 to 66) as shown in table 1.

Table1 also shows statistically significant difference between the mean serum magnesium levels of breast cancer patients compared with control; 1.095±0.007 Vs 2.520±0.053 with P-value 0.03.

Table1: The mean age and magnesium level of breast cancer patients compared with controls.

SUBJECTS	N	AGE (YEARS)	MAGNESIUM (mmol/L)
Controls	30	51	2.520
Breast cancer patients	30	55	1.095
p-value			0.03



This is a histogram showing serum magnesium level of breast cancer patient Vs control

Key

Control

Breast Cancer Patient

Discussion

The findings from this study showed reduced serum magnesium level in breast cancer patient compared to the control, this is in agreement with earlier studies by Aleksandrowicz in Poland who reported hypomagnesaemia in leukemic patients[3] and this contradicts the findings by Arinola et al in Ibadan, Nigeria who reported slight hypermagnesaemia in breast cancer patients.[16]

Studies have shown that 4% of breast cancer women in the United Kingdom are due to alcoholic consumption[18]. It was shown that women who had one or two drinks a day had increased risk of developing breast cancer by 10%, while those that had more than three drinks a day raised their risk by 30%. This probably may be due to the fact that alcohol causes a reduction in magnesium level. Studies have shown that low magnesium level is associated with dramatic increase in free radical generation as well as glutathione depletion and this is implicated in infection and cancer[19].

Studies have shown an increased cancer rate in regions with low magnesium level in soil and drinking water[20]. School of public health at the Kaohsiuny Medical College in Taiwan, found that magnesium also exerts a protective effect against gastric cancer[21]. Pretreatment hypomagnesaemia has been reported in young leukaemic children, 78% of whom have history of anorexia, and have excessive gut and urinary loss of magnesium.

Study from Sweden reported that women with the highest magnesium intake had a 40% lower risk of developing cancer than those with the lowest intake of mineral[22]. Studies from Russia showed that stomach cancer is four time more common in the Ukraine where the magnesium content of soil and drinking water is low, than it is in America where the magnesium is more than twice as high[20].

It has also been reported that cancer patient receiving chemotherapy may be at high risk for developing hypomagnesaemia due to side effects such as diarrhea that can deplete magnesium stores[23].

Conclusion

We have demonstrated from this present study that breast cancer patients have reduced serum magnesium level. It is advisable to add magnesium as an adjuvant therapy in the management of breast cancer patients but this should be done with caution. Magnesium may be routinely assayed for in patients with breast cancer as a baseline investigation and during the course of chemotherapy.

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Competing Interest: there was no competing interest.

Author's Contribution: There were equal contributions by all the authors to this study. All the authors read and approved the final manuscript. Dr Eboreime recruited the subjects while Dr Atoe and Dr Idemudia carried out the laboratory and statistical analyses. All the authors were involved in the design of the study.

Consent: *All the participants were* properly briefed about the study and an informed consent was obtained from them before venous blood was collected.

Ethical Approval: The study was approved by the Management of Central Hospital, Benin city, Nigeria

REFERENCES

1) Parkeh D.M., Piscani P. and Ferlay J. Estimates of the worldwide incidence of 25 cancers ch 1990. *Intl. J. Cancer, 80, 1999, 827 – 841*
2) Sahmoun AE, Singh BB, "Does a higher ratio of serum calcium to magnesium increase the risk for post menopausal breast cancer". *Medical hypotheses; Sept 2010;315-318*
3) Aleksandrowicz J., Blicharski, J., Dzigowska, A., Leuko – and Oncogenesis in the light of studies on metabolism of magnesium and its turnover in biocenosis. *Acta Med. Pol. 1970; 11 : 289 – 302*
4) D. Dchenzelin E.M. Negra 1, M.R. Tucci, M.Z. saleu 1, V.M. da cruz, R.M Oliveira, I.N. Nishimoto and C. Hoelz. Hypomagnesenia in critically ill cancer patients; a prospective study of predictive factors. *Braz J. Med. Bio Res, December 2000, Volume 33 (12) 1443 – 1448*
5) Chernow, B, Bambeger, S, Stoiko, N, et al, Hypomagnesemia in patients in post operative intensive care, *Chest 1989: 95 : 391.*
6) Desai, TK, Cartson, Run, Geheb, NA, Prevalence and Clinical implications of hypocalcemia in acutely ill patients in a Medical Intensive Care setting. *ANJ Med 1988; 84: 209.*
7) Ryzen E. Magnesium homeostasis in critically ill patients, *Magnesium 1989; 8: 201.*
8) Wacker, W.E.C, Magnesium and Man. *Harvard Uni. Press, Cambridge, M.A, 1980;160-184*
9) Aikawa, J.R. Magnesium; Its Biologic significance CRC press, *Boca Raton, FL, 1981;21-38*
10) Fleaton F.W., Tongyai, S., Rayssiguver, Y. Membrane function in magnesium deficiency. In magnesium in Health and Disease. (from 5th Intl Mg sympos, Kyoto, Japan, 1988) Itokawa, Y. and Durlach J., *Eds., John Libbrey Fress, London, Pairs, 1989; 27 – 33*
11) Gventher, T., Avendulk, R. Membrane of magnesium deficiency induced neoplastic cells. *Magnesium Bull, 1985; 7: 146 – 151.*
12) Walker, G.M. Magnesium as the fundamental regulator of the cell cycle. *Magnesium 1982; 2:1 – 160*
13) Walker, G.N. Magnesium and cell cycle control; an update. *Magnesium. 1986; 5: 9 – 23.*
14) Duffos, J.H., Walker G.M. Magnesium in Mitosis and the cell cycle, In Magnesium. *Medical Hypothesis 1980; 6: 863 – 871.*
15) Blondell, J.W. The anti cancer effect of magnesium. *Medical hypothesis 1980;6:863-871*
16) Arinola,O.G, Charles-Davies M.A. Micronutrient levels in the plasma of Nigerian females with breast cancer. *Afri J Biotech. 2008:7(11):1620-1623.*

17) Henry JB. Clinical Diagnosis and management, 17th ed., W.B Saunder Co., Philadelphia, pg 157(1984).
18) Anghileri, L.J., Collery, P., Duriach, J. Experimental relationship between magnesium and cancer. *Magnesium Bull. 1981;3:1-5*
19) Paunier L. Radde. I.C; Normal and abnormal magnesium metabolism. *Bull of Hosp. for sick children. (Toronto), 1965:14;16-23*
20) Bazikian, K.L. The significance of magnesium salts in oncology. Proc of First Intl Mg Sympos. Vittel, France, *Ed J Durlach 1971;593-606*
21) Yang CY, Cheng MF, Tsai SS, Hsieh YL. Calcium, magnesium, and nitrate in drinking water and gastric cancer mortality. *Jpn J Cancer Res. 1998;89(2):124–130.*
22) Armstrong RW. Is there a particular kind of soil or geologic environment that predispose to cancer? Ann. N.Y. Acad Sci. 1972;199:239-248
23) Mohammed WS. Management of hypomagnesemia in cancer patients receiving chemotherapy. Supportive oncology 2008;6:243-248