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ABSTRACT

Objective: **To determine the plasma magnesium levels in adult asthmatics.**
Design: **Case control study.**
Setting: **Lagos University Teaching Hospital, Lagos, Nigeria.**
Subjects: **Forty stable asthmatics and thirty five apparently healthy controls.**
Methods: **Detailed history including drug history was obtained from patients and controls. Fasting venous blood was collected into heparinized tubes from both patients and controls. Plasma magnesium, albumin, calcium and phosphorus were measured using spectrophotometric end point methods.**
Results: **Mean (SD) plasma magnesium concentration of 0.93(0.24) mmol/L in the asthmatics was significantly lower compared to the controls which was 1.15(0.28) mmol/L, $p<0.001$. There was no significant difference in the plasma albumin, calcium and phosphorus levels between the patients and controls. Plasma magnesium levels correlated with the plasma albumin level ($r=0.62$) but did not correlate with the duration of disease, peak flow rate and age of patients. There was no gender difference in plasma magnesium levels in the asthmatics.**
Conclusion: **Adult Nigerian asthmatics have lower plasma magnesium concentrations compared to healthy controls. This may be of use in future therapeutic management of asthma. A large scale multi-centre study needs to be carried out since this study was done in one hospital.**

INTRODUCTION

Asthma is a disease characterised by increased responsiveness of the tracheobronchial tree to a multiplicity of stimuli (1). The exact prevalence in Nigeria is unknown. Recently there has been considerable interest generated in the possible importance of magnesium ions in the regulation of bronchial smooth muscle tone directly and indirectly (2). New concepts suggest that magnesium influences lung functions. Intracellular magnesium is thought to modulate smooth muscle contractions and it is known to have a direct effect on calcium uptake resulting in smooth muscle relaxation (3).

Diverse clinical manifestation has been reported in conjunction with magnesium deficiencies of which asthma is one of them (4). These factors have aroused the possible utilisation of magnesium salts in the management of asthma and magnesium sulfate in particular has been found to play an adjunctive role to the traditional asthma therapy in acute and chronic cases (5,6).

In a case control study to investigate the relationship between allergic and dietary antioxidants, it was found that decreased intake of magnesium was significantly associated with increased risk of hyperactivity (7). In another study by Harari *et al,* a significant improvement of asthmatic attack was recorded after a four-week stay at the dead-sea which has a high magnesium content. It was suggested that this improvement may be due to absorption of magnesium through the skin and in the lungs and due to it's involvement in anti-inflammatory and vasodilatory processes (8).

Decreased magnesium intake has been implicated in type 1 brittle asthma (9), a prospective study of replacement therapy has been proposed to confirm this hypothesis. Epidemiological evidence suggests that a low dietary magnesium intake is associated with impaired lung function, bronchial hyperactivity and wheezing (10); A high dietary magnesium intake is also associated with better lung function and a reduced risk of airway hyperactivity and wheezing (11). It has been suggested that a low magnesium intake could be involved in the aetiology of asthma and other chronic obstructive airway disease or that it constitutes a decompensatory factor for asthma (12).

It was therefore necessary to ascertain the range of plasma magnesium concentration in Nigerian asthmatics and also to determine if magnesium deficiency occurs in them. This will serve as a baseline for future intervention studies on the possible therapeutic effects of magnesium in Nigerian asthmatics.

MATERIALS AND METHODS

Forty stable patients with asthma and thirty five apparently healthy controls of both sexes were recruited into the study. The stable asthmatic patients were those that had been free from any symptoms of asthma for at least two weeks prior to the blood collection, they had no exacerbations requiring hospital admissions or bronchodilation by nebulisers or intravenous theophylline. Patients on steroids, long acting ß agonists or leukotriene antagonists were not included.

The patients were on oral salbutamol, oral theophylline, vitamins and antibiotics (erythromycin). The age range was 17-54 years for the patients and 18-56 years for the controls. The age, duration of asthma disorder and a detailed drug history was obtained from each patient. Patients and controls on any form of magnesium supplements were excluded from the study. Consent was obtained from each patient for the study. The patients were recruited from the adult respiratory unit of the Lagos University Teaching Hospital. The control group comprised blood donors, hospital workers and medical students who were found to be in good health and not on magnesium supplements.

The peak expiratory flow rate was measured in the patients. Five ml of venous blood was obtained from the anticubital-fossa of both patients and controls into heparinized tubes after an overnight fast. The plasma was separated after centrifugation at 3000rpm for five minutes and stored at -20°C. Analysis was carried out within one week of collection.

Magnesium analysis was carried out in acid washed tubes using an end point spectrophotometric method with calmigite as the dye reagent (13). Albumin, calcium and phosphorus were also analysed using bromocresol green O-cresolphthalein complexone and ammonium molybdate dye methods respectively: the later two in acid washed tubes.

Statistical analysis: Data are expressed as means (SD). The distribution of the variables was gaussian. The students "t" test was used for comparison of means while Pearson's correlation test was used for the correlation between variables. This was done using the EPI-INFO (version 6.04) statistical package. $P<0.05$ was accepted as significant.

RESULTS

There were forty patients (20 females and 20 males) and thirty five controls (18 females and 17 males). The mean duration of the disease in the patients studied was 9.2 years. The mean(SD) plasma magnesium concentration in patients was 0.93(0.24)mmol/L and this was significantly lower than that obtained in the controls which was 1.15(0.28) mmol/L, p=0.00045. There was no statistical difference in the magnesium concentration between the male and female asthmatics. There was a positive correlation of 0.62(p=0.000019) between the plasma albumin and plasma magnesium levels.

The mean (SD) plasma albumin in the patients was 40.2(5.2) g/L, this was not significantly different from that obtained in the controls which was 41.9(6.2)g/L.

The mean (SD) plasma calcium and phosphorus in the patients were 2.41(0.3) mmol/L and 0.99(0.2) mmol/L respectively. These were not significantly different from the values obtained in the controls (Table 1).

Table 1

Mean (SD) values of plasma magnesium, albumin, calcium and phosphorus in asthmatic patients and controls

	Control n=35 Mean (SD)	Patients n=40 Mean (SD)	p-value
Age	33.9(10.68)	32.3(8.22)	0.484
Plasma magnesium	1.15(0.28)	0.93(0.24)	0.0004
Plasma albumin	41.9(6.2)	40.2(5.2)	0.223
Plasma calcium	2.4(0.28)	2.41(0.3)	0.834
Plasma phosphorus	0.98(0.2)	0.99(0.2)	0.842

* Significant, $p<0.001$

The mean peak flow rate in the male patients was 346.0(88.8) and this was significantly higher than that in the female patients 275.8(71.1), p=0.007. There was no correlation between plasma magnesium and plasma calcium, phosphorus, duration of disease, peak flow rate and age. There was no correlation between peak flow rate and the duration of asthma.

DISCUSSION

Magnesium has been found to play a role in the pathomechanism of allergic reactions especially asthma (14) and several clinical reports point to the salutary actions of magnesium in asthma and asthma-like conditions (2). This study shows that the asthmatic patients studied had a significantly lower mean plasma magnesium level of 0.93(0.24) mmol/L when compared to controls with a mean plasma magnesium level of 1.15(0.28) mmol/L. The extent to which albumin binds magnesium has not been reported in Nigerians but it is generally accepted that magnesium binding to protein is weaker than that of calcium (15). Although statistically significant, the clinical significance of the lower serum magnesium in our study will be looked into in further intervention studies which will include patients with severe asthma.

Fedoseev *et al.* (16) reported hypomagnesaemia in patients with bronchial asthma but differed to this study in that he found hypercalcaemia in such patients. It was suggested that this abnormal homeostasis of the divalent cations in bronchial asthma patients may be due to hyperactivation of free radical oxidation of cell membrane lipids.

In a study by de Valk *et al*(17), mean plasma magnesium in 20 stable asthmatics and 20 controls were 0.81(0.05) mmol/L and 0.79(0.06) mmol/L respectively, there was no significant difference between the two groups. The values obtained in our study are however higher than those obtained by de Valk *et al.* (17). Assessment of magnesium status of asthmatics in Japan (18) reported serum magnesium in the asthmatics as 0.99(0.1) mmol/L and 0.99(0.2) mmol/L in the controls with no significant difference between them. The Japan study also revealed a significantly lower erythrocyte magnesium levels in the asthmatics compared to the controls; It was therefore inferred that the low red blood cell magnesium indicates decreased magnesium stores in the asthmatics. Another study by Zervas *et al.* (19) revealed a decreased red blood cell magnesium after histamine challenge to mildly asthmatic patients while there was no significant change in plasma magnesium post challenge. Fantidis *et al*. (20) however reported a low magnesium level in polymorphonuclear cells and normal magnesium levels in serum and erythrocytes of patients with bronchial asthma. There is need to carry out the intracellular magnesium concentrations in Nigerian asthmatics to verify this claim. Magnesium levels in serum and erythrocytes decreased during attacks as the histamine levels increased in atopic asthma. This relationship was less marked in patients with non-atopic asthma (14).

A study carried out in Turkey by Vural *et al.* (21) revealed a significantly reduced serum albumin and zinc and a significant increase in serum calcium and copper in patients with bronchial asthma when compared to controls. However, there was no significant difference in the serum magnesium levels in the two groups. This contrasts with findings in this study of decreased plasma magnesium with normal plasma calcium and albumin. Petrov *et al.* (22) reported hyper-magnesaemia and hypocalcaemia in patients with allergic bronchial asthma with statistical significance, this alteration depended on the stage and severity of the bronchial asthma.

Diet is a newly recognised risk factor for asthma occurrence and dietary cations especially magnesium and sodium have been implicated (23). Current literature concerning magnesium supplementation recommends that on a national basis, magnesium should be added to the water supplies of large areas (4). In the United States it is reported that the intake of magnesium has reduced since the beginning of the last century (15). Magnesium supplementation has been shown to be of a large preventive advantage especially for disorders such as asthma, artherosclerosis, neurologic and psychiatric clinical entities (4). It is however rather premature to make this conclusion based on this study until therapeutic aspects are studied.

The significant correlation between albumin and plasma magnesium in asthmatics may support the fact that plasma magnesium binds to albumin to a considerable extent. The lack of correlation between the plasma magnesium, peak flow rate and the duration of the disease might be a pointer to a multi-factorial cause for the lower magnesium levels in asthmatics. The effect of anti-asthmatic drugs on plasma magnesium is yet to be reported as this might have an influence on their magnesium state because all the patients studied were already placed on anti-asthmatics.

There is paucity of information regarding plasma magnesium concentrations in asthmatics in this region. The findings in this study suggest a need for an expanded multi-center investigation as to the role of magnesium in the patho-physiology of asthma and its role in determining management strategies.

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