Niger J Paediatr 2020; 47 (2):91 – 95

ORIGINAL

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Magnesium levels in stable children with asthma: It's relationship with asthma control

DOI:http://dx.doi.org/10.4314/njp.v47i2.7

Accepted: 8th April 2020

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Abstract*: Background:* Asthma prevalence is rising worldwide. Amongst the various factors influencing asthma control, the magnesium level of the affected individuals seems to make a major contribution to achieving asthma control through its anti-inflammatory and bronchodilation effects.This study therefore was aimed at determining the magnesium level of stable asthmatic children and its relationship, if any, with their levels of asthma control.

Methods: A cross-sectional study where the serum magnesium levels of 30 stable asthmatic children attending Asthma clinic and those of 30 children without asthma attending Children Out-patient clinic (CHOP) both at the University of Nigeria Teaching Hospital (UNTH), Enugu, were assessed using atomic absorption spectrophotometer. The levels of asthma control of children with asthma were assessed using asthma therapy assessment questionnaire (ATAQ). Mean serum magnesium levels of the different asthma control levels were compared using the analysis of variance (ANOVA).

Results: The mean ages of children with asthma and those without asthma were 10.4 ± 2.98 years and 10.5 ±3.00 years respectively. The mean serum magnesium level of stable children with asthma (1.13 ±1.04 mmol/L) was found to be significantly lower than those of the non-asthmatic controls (1.46 ±1.01 mmol/L), p= 0.004.A significant association was also found between the serum magnesium levels and the levels of asthma control (p = 0.015).

Conclusion: This study shows that the serum magnesium level of stable asthmatic children is significantly lower than that of children without asthma and there is a significant association between the mean serum magnesium levels and their levels of asthma control.

Keywords: Serum magnesium, asthma control, stable asthma

Introduction

Asthma is a chronic inflammatory airway disorder characterized by variable air flow obstruction and bronchial hyperresponsiveness.[1] It is a global disease with rising prevalence rates especially among children[1] and in communities with the increasing levels of urbanization and industrialization.[2]Attainment of total asthma control remains the goal of asthma management.[1] Asthma control refers to the degree to which manifestations of asthma are minimized by therapeutic interventions and the goals of therapy are met.[3] Amongst the various factors influencing asthma control, the magnesium status of the affected individuals seems to make a major contribution towards achieving optimal asthma control. Magnesium, an essential trace element largely derivable from dietary intake, is involved in numerous biochemical and physiological processes that directly influence lung function and indirectly influence respiratory symptoms.[4] The mechanisms of action of magnesium on respiratory airways are multiple and include relaxation of airway smooth muscle[5] and stabilization of the mast cells.[6]

Asthma presents with recurrent episodes of cough, difficult breathing, chest tightness and wheezing. Magnesium is known to cause bronchial smooth muscle relaxation which helps to relieve asthma symptoms and consequently enhance asthma control. Hypomagnaesemia therefore predisposes the airways to increased smooth muscle excitability and bronchoconstriction[6] resulting in frequent exacerbations and poor asthma control. Magnesium levels of children with asthma may therefore have some relationship with their level of asthma control. Previous studies on asthma in Nigerian children have essentially been focused on the epidemiology and clinical manifestations. None sought to determine the role of magnesium on the pathogenesis of asthma and/or its relationship with asthma control in children.

This study therefore aimed to determine the magnesium level and its relationship, if any, with the levels of asthma control of stable asthmatic children

Methods

This was a cross-sectional comparative study where 30 stable children with asthma attending asthma clinic and those of 30 children without asthma whose parents gave written consent, attending Children Out-patient clinic (CHOP), were consecutively recruited over a five month period from 8th September, 2013 through 31st January, 2014. The inclusion criteria were: Children aged 6 – 16 years attending asthma clinic with stable asthma. Stable asthma was defined as absence of asthma exacerbations for four weeks preceding presentation.[7] The inclusion criteria for the control group were: (a) Children aged 6 – 16 years, without asthma and other respiratory diseases such as pneumonia, pulmonary tuberculosis (b) Children not on any medication that can affect magnesium level e.g diuretic therapy, calcium blockers. (c) Children without chronic illnesses such as renal diseases, malignancy, sickle cell disease, determined through historical information and physical examination. Ethical clearance was obtained from Health Research and Ethics Committee.

Sample size determination

The mean serum magnesium(Mg) levels determined from a previous study[8] in Lagos, were 0.93 ± 0.24 mmol/L in asthmatics and 1.15 ± 0.28 mmol/L in non-asthmatics. Using the formula[9] for comparison of two means:

$$n = \frac{(u+v)^2 (\sigma 1^2 + \sigma 0^2)}{(\mu 1 - \mu 0)^2}$$

Where n = minimum sample size for each group
u = minimum power at 90% = 1.28
v = significant level required at 5 % = 1.96
σ1 = standard deviation of mean serum Mg in control = 0.28
σ0 = standard deviation of mean serum Mg in asthmatics = 0.24
μ1 – μ0 = size of difference of clinical importance between the two means = 0.22 mmol/L

Thus substituting in the formula,[9]

$$n = \frac{(1.28 + 1.96)^2 (0.28^2 + 0.24^2)}{0.22^2}$$

$$= \frac{3.24^2 . (0.28^2 + 0.24^2)}{0.0484}$$

$$= \frac{10.5 \times 0.136}{0.0484}$$

$$= 29.5.$$

The sample size calculated for each group was 30.

Structured questionnaires were self-administered by parents of selected subjects. The study variables were recorded into the relevant sections of the questionnaire. In the first section, predictor variables which included socio-demographic features of participants were obtained and categorized as follows: (i) respondent's age (ii) gender (iii) occupation (iv)highest educational attainment of respondents and their spouses. Social classification was done using the socioeconomic index scores designed by Olusanya.[10]

The second section of the questionnaire obtained information on variables that assessed whether symptoms occurred during the previous seven days in order to exclude the subjects with current asthma symptoms. The symptoms assessed were breathlessness, fast breathing, wheezing and /or limitation of activity (categorized as yes or no). Systemic examination was done, and findings recorded.

The third section of the questionnaire obtained information on outcome variables that measured serum magnesium levels (in mmol/L) of the participants and the levels of asthma control were assessed using Asthma Therapy Assessment Questionnaire (ATAQ). ATAQ is a brief 4-item parent-completed questionnaire designed and validated for children and adolescent aged 5 – 17 years to assess the level of their asthma control in the prior 4 weeks.[11] The selected children with asthma were graded as either having or not having a control problem in each one of the 4 questions contained in the questionnaire; the item scores were then summed to provide a total, which ranges from 0 (no asthma control problems) to 4 (4 asthma control problems). The levels of asthma control were then classified as well controlled if score was 0, not-well controlled if score was 1 – 2 and very poorly controlled if score was 3 – 4.

Sample collection

Venous blood sample, 2 – 3ml, was collected with plain specimen bottles and allowed to coagulate for 30minutes but not more than 1 hour before centrifugation. The supernatant fraction, the serum of about 0.8 – 1ml, was immediately separated and then stored in plain bottles in a refrigerator, with regular power supply, at 2 - 8ºC. Serum ionized magnesium analysis was done using atomic absorption spectrophotometer (AAS) (Buck Scientific Model 210 VGP, USA) within seven days of blood collection.

Data handling and statistical analysis

Descriptive characteristics such as means and standard deviations were calculated for continuous variables while frequency and percentages were calculated for categorical variables. The socioeconomic class of the study participants was analysed using chi square test. Mean serum magnesium levels of stable asthmatics and non-asthmatic controls were compared using Student t-test. Mean serum magnesium levels of the different asthma control levels were compared using analysis of variance (ANOVA). The data obtained and recorded on the study proforma was analysed using Statistical Package for Social Sciences (SPSS) software for windows ® version19.0 (IBM Inc Chicago Illinois USA 2011).

Results

Of the 50 children with asthma on follow-up visit at asthma clinic, 30 of these children met the inclusion criteria and were enrolled. The 20 children that were

excluded had asthma exacerbation 4 week preceding their presentation for the study. Majority of the study participants,9 (30%)were under the age group 8-9 years. The male to female ratio of the study population was 1.5: 1. The mean ages of the asthmatics and non-asthmatics were 10.4 ± 2.98 years and 10.5 ±3.00 years respectively. Table 1 below shows the age and sex distribution of children with asthma and the non-asthmatic controls.

Table 1: Age and sex distribution of the study groups

	Groups			
	Asthmatics		Non Asthmatics	
Age (years)	Male n (%)	Female n (%)	Male n (%)	Female n (%)
6 – 7	3 (16.7)	2 (16.7)	3 (16.7)	2 (16.7)
8 – 9	7 (23.3)	2 (6.7)	7 (23.3)	2 (6.7)
10 – 11	3 (10.0)	3 (10.0)	3 (10.0)	3 (10.0)
12 – 13	2 (6.7)	2 (6.7)	2 (6.7)	2 (6.7)
14 – 15	2 (6.7)	2 (6.7)	2 (6.7)	2 (6.7)
16	1 (3.4)	1 (3.4)	1 (3.4)	1 (3.4)
Total	18 (100.0)	12 (100.0)	18(100.0)	12 (100.0)

Serum magnesium levels of the children with asthma and those without asthma

Comparison of the mean serum magnesium levels of the asthmatics and non-asthmatics in their different age groups did not show significant statistical difference (Table 2). However, when the mean serum magnesium levels of stable asthmatic group (1.13 ± 1.04 mmol/L) was compared with those of the non-asthmatic group (1.46± 1.01 mmol/L, a significant statistical difference was noted (p = 0.004)

Table 2: Serum magnesium levels of the subjects and controls

Age groups (years)	Asthmatics (n =30) Mean ± SD (mmol/L)	Non-asthmatics (n = 30) Mean ± SD (mmol/L)	t	p value
6- 7	1.19 ± 0.92	1.49 ± 0.52	1.536	0.163
8 – 9	1.12 ± 1.10	1.36 ± 1.19	1.103	0.286
10 – 11	1.29 ± 1.37	1.40 ± 1.21	0.351	0.733
12 – 13	1.15 ± 0.99	1.70 ± 0.85	2.049	0.086
14 – 15	0.96± 0.98	1.46 ± 1.29	1.516	0.180
16	0.93 ± 0.78	1.48 ± 0.85	1.658	0.239
All	1.13 ± 1.04	1.46 ± 1.01	2.969	0.004

Levels of asthma control

Most of the children with stable asthma 17 (57%) had well controlled asthma while 11(36%) of the subjects had not-well controlled asthma. Only 2 (7%) had very poorly controlled asthma as shown in fig 1 below

Serum magnesium and asthma control

The mean serum magnesium levels of each of the three levels of asthma control: well controlled, not-well controlled and very poorly controlled asthma were 1.28 ± 1.00, 0.95 ± 0.93 and 0.86 ± 1.19mmol/L, respectively. Although the mean serum magnesium of the well-controlled group was much higher than any of the other two groups, the difference in their mean values was not statistically significant (p = 0.09) as shown in table 3 below.

Fig 1: Levels of asthma control

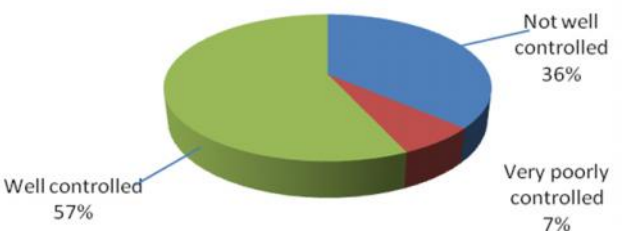

Table 3: Serum magnesium across the levels of asthma control

	Well controlled (n = 17) Mean±SD (mmol/L)	Not well controlled (n = 11) Mean±SD (mmol/L)	Very poorly controlled (n = 2) Mean±SD (mmol/L)	F	p value
Serum magnesium (mmol/L)	1.28 ± 1.00	0.95 ± 0.93	0.86 ± 1.19	2.636	0.090

However when the mean serum magnesium of the well-controlled asthmatics was compared with the serum magnesium of the not-well controlled and very poorly controlled asthmatics combined, now termed poorly controlled group (Table 4), a significant difference was noted (t = 2.313; p = 0.028).

Spearman correlation analysis that determined the degree of the association, showed a significant positive association between the mean serum magnesium and levels of asthma control (r = 0.438, p = 0.015)

Table 4: Comparison of serum magnesium of well controlled asthmatics and poorly controlled group

	Asthma control					
	Well controlled (n = 17) Mean±SD (mmol/L)	Poorly controlled group (n = 13) Mean ± SD (mmol/L)	Mean difference	95% C.I of the difference	t	p value
Serum magnesium (mmol/L)	1.28±1.00	0.53± 0.92	-0.82	-1.56 to 0.09	2.313	0.028

Discussion

This study has shown that an association exists between asthma control and serum magnesium levels in children with asthma. Children with very poorly controlled asthma in this study were noted to have the lowest serum magnesium while those with well controlled asthma had the highest mean serum magnesium. This shows that the relatively high magnesium levels in the well-controlled group may have contributed to bronchial smooth muscle relaxation and consequently good asthma control. Alamoudi[12] in Saudi Arabia found an

indirect relationship between hypomagnesaemia and asthma severity, frequent exacerbation, increased incidence of hospitalization and consequently poor asthma control among adult patients with stable asthma. Similarly, Kazaks and co-workers[13] in United States of America (USA) reported a significant improvement in subjective measures of asthma control and quality of life among asthmatic patients who received oral magnesium supplementation. These findings give credence to the fact that hypomagnesaemia predisposes to airway hyperreactivity and hyperresponsiveness leading to bronchoconstriction and that restoration of normal serum magnesium may reverse the deleterious effects of hypomagnesaemia on the respiratory system via relaxation of airway smooth muscle[5] and stabilization of the mast cells.[6]

This study has further demonstrated that the serum magnesium levels of children with asthma were significantly lower than that of the children without asthma. This finding is in keeping with similar study by Somashekar and colleagues[14] in India who compared the serum magnesium levels of 44 children with asthma and their controls and found a lower serum magnesium levels in the affected children than their controls. Several other studies by Alamoudi,[12] Das and co-workers[15] and Oladipo and colleagues,[8] although done amongst adult population, independently documented lower serum magnesium levels among the asthmatic patients compared to the non-asthmatic controls. Alamoudi study further showed a strong association between hypomagnesemia and higher incidence of hospitalization and increasing asthma severity amongst asthmatic patients. This finding of lower magnesium level in children with asthma may therefore partly explain the challenge of achieving total asthma control in the affected children. It is therefore pertinent to consider the magnesium status of children with asthma especially when they have poorly controlled asthma while managing them in the hospital setting.

Studies by De Valk*et al.*[16] and Amin and colleagues[17] found no difference between the serum magnesium level of the asthmatics and that of non-asthmatic controls in contrast to the findings of this present study. However, Amin and colleagues further observed that the erythrocytic magnesium levels of the asthmatic patients were significantly lower than the non-asthmatic controls. This observation was further corroborated by the findings of Emelyanov*et al,*[18] Zervas and colleagues[19] and Hassane and co-workers[20] who independently found a lower erythrocytic magnesium levels in asthmatic patients. This shows that the magnesium level of asthmatic children is lower than that of the normal subjects and this may explain the pathophysiology of asthma in the affected children. Furthermore, this observation shows that intracellular magnesium estimation may give a better reflection of body magnesium stores than the serum magnesium measurement. However, recognizing that intracellular magnesium measurement tests are expensive and the capacity to do the tests in a resource-poor country such as Nigeria, not readily available, serum magnesium estimation, as used in this present study, may be a reliable alternative in determining magnesium status of children with asthma in our environment.

Recognizing the fact that magnesium is largely derived from dietary intake, our failure to assess and document the regular dietary intake of the study participants over a certain period to adequately determine the magnesium status of the study participants is a limitation of this study. This study documented lower magnesium levels in children with asthma even when majority of the affected children (76.7%) were of normal nutritional status. Estimation of the dietary intake of magnesium of the study population, which we were not able to do in this study, would have helped to explain this finding more appropriately.

Conclusion

In conclusion, this study has shown that the serum magnesium level of stable asthmatic children is significantly lower than that of children without asthma and there is a significant association between the mean serum magnesium levels and their levels of asthma control.

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