SERUM MAGNESIUM LEVEL IN CHILDREN WITH BRONCHIAL ASTHMA IN DUHOK CITY

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ABSTRACT

Background

Asthma is an increasingly common disease over the last century. It is caused by chronic inflammation of lung airways with increased airway responsiveness and airflow obstruction. Magnesium is the fourth most common cation in the body and the major intracellular divalent cation. Mg^{+2} in extracellular fluid is crucial for normal neuromuscular activities. Magnesium deficiency is associated with increased contractility of smooth muscle cells including bronchiolar resulting in bronchospasm.

Objectives

To detect the prevalence of hypomagnesemia among asthmatic children and to find out any significant correlation of hypomagnesemia with asthma in children.

Patients and Methods

A case control study conducted in Duhok, North of Iraq in the period between January the 1st 2014 and January the 1st 2015. One hundred asthmatic patients aged between 1 and 15 years were examined. All patients had acute asthmatic attacks with features of respiratory distress for which they were admitted to Heevi Pediatric Teaching Hospital. Those with fever, dehydration, localized wheezing, pneumonia, cardiac, renal, or hepatic dysfunction were excluded. They were all studied in terms of age, gender, duration of asthma, drugs used for treatment, severity of asthma and the patients' growth as measured by Body Mass index. Control group included 100 children who were healthy non asthmatic and visited the hospital with their parents. Samples of blood were taken to measure serum magnesium level.Statistical analysis were performed by using the SPSS 19 where $P<0.05$ is significant.

Results

The mean serum magnesium in patients group was 1.91± 0.33 mg/dl while in the control group it was 2.03± 0.33 mg/dl. Serum magnesium levels were lower in the asthmatic patients than controls P= 0.01. Male gender predominated in both groups (68% , 61%) and the most common age among cases was 1- < 3 years and controls 5- <10 years. Serum magnesium level indirectly correlated with duration of asthma but not significantly (P=0.1). Serum magnesium level was not significantly related to body mass index P=0.3.Serum magnesium level decreased with increasing severity of asthma symptoms P= 0.05. Serum level is slightly lower in asthmatics on steroids and bronchodilators than those who were not P=0.7, P=0.9 respectively.

Conclusion

Serum magnesium level is significantly lower in asthmatic children as compared to the control group. Serum Mg^{+2} level decreases as the duration of asthma is longer but not significantly. There is an inverse relation between serum Mg^{+2} and the severity of asthma. No significant change in serum Mg^{+2} develops when steroids and bronchodilators are used.

Keywords: *Serum magnesium, Childhood Asthma, Duhok City.*

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INTRODUCTION

Asthma is an increasingly common disease over the last century. It is caused by chronic inflammation of lung airways with increased airway responsiveness and airflow obstruction. In the last decades, its prevalence has been markedly increased especially in western countries.

The rise in asthma and allergic disease among children is a matter of worldwide concern [1, 2].Many authors have argued that the changes in diet may have been an important determinant of increased susceptibility to asthma [3, 4].

Magnesium (Mg^{++}) is the fourth most common cation in the body and the major intracellular divalent cation. Mg^{++} in extracellular fluid is crucial for normal neuromuscular activities; intracellular Mg^{++} forms a key complex with ATP and is an important cofactor for a wide range of enzymes, transporters, and nucleic acids needed for normal cellular function, replication, and energy metabolism.

Total body Mg^{++} is about 25 g (1000 mmol). About 50% of it is in the bones, just 1% of body Mg is present in the fluid outside cells, and the rest is within the cells. Albumin binds around 30% of Mg^{++}in the serum. Mg^{++} has several actions on rabbit bronchial airways including relaxation of airway smooth muscle, bronchodilation, anticholinergic effects, and stabilization of mast cells[5].

Since magnesium intervenes in calcium transport mechanisms and intracellular phosphorylation reactions, it constitutes an important determinant of the contraction and relaxation state of bronchial smooth muscle [6]. Deficiency of Magnesium is associated with increased contractility of smooth muscle cells. Since contractility of bronchial smooth muscle is important in patients with asthma, magnesium deficiency could lead to bronchial smooth muscle contraction or lack of bronchial muscle relaxation [7].

There are lower levels of serum magnesium in asthmatic children than normal children according to some studies. While in other case-control studies showed no significant difference in serum magnesium between patients with asthma and controls. Intravenous infusion of magnesium sulfate has been found to have a beneficial response in lung function tests while treating acute exacerbation of asthma in several studies [8, 9].

Although clinical trials using magnesium as an adjunct to treating asthma exacerbation have been conducted in children, no work has yet been done to determine whether serum magnesium levels in asthmatic children differ from those of controls and whether asthma exacerbation in children is associated with low serum magnesium levels [10, 11].

Aim of the study

We conducted this study to detect the prevalence of hypomagnesemia among asthmatic children and to find out any significant correlation of hypomagnesemia with asthma in children**.**

MATERIALS AND METHODS

A case control study conducted in Duhok, North of Iraq in the period between January1st 2014 and January1st 2015. One hundred asthmatic patients aged between 1 and 15 years were studied. The participants were asthmatic patients who suffered acute attacks for which they were admitted to Heevi Pediatric Teaching Hospital to receive treatment.

They had positive history of asthma. Some had history of treatment with controller long acting inhaled bronchodilators and some were treated with controller inhaled steroids. Some of them were not on none of these medications and were treated for the acute attacks only. They had features of respiratory distress. Diagnosis of asthma and severity of disease were identified based on the Global Initiative for Asthma (GINA) guideline criteria [12] .We excluded from the study any patient with localized wheezing, dehydration, fever, pneumonia, renal, hepatic or cardiac dysfunction.

They were all studied in terms of age, gender,duration of asthma, drugs used for treatment, severity of asthma and the patients' growth as measured by Body Mass index.

Control group included 100 children who were healthy non asthmatic and visited the hospital with their parents.

A written consent was taken from parents of patients and controls. The study was approved by Ethical Committee in Directorate of Health in Duhok.

Before administration of any medication, venous blood samples were obtained under standard conditions for the measurement of serum Mg^{+2} levels. and immediately sent to laboratory. Samples were centrifuged and serum samples were analyzed with atomic absorption spectrophotometry to measure serum magnesium level. Serum level of <1.5 mg/dl was considered hypomagnesemia.

Statistical analysis was performed by using the SPSS. Mean، standard deviation and p values of two groups were obtained for comparison of serum magnesium

levels between patients and controls and to assess the significance of the variables above in affecting serum magnesium level among patients.

RESULTS

Hypomagnesemia was found in 9 (9%) patients and in 1 (1%) controls.

Serum magnesium levels were lower in the asthmatic patients as compared to the control and this was statistically significant since P value was 0.01 as shown in Tables 1 and 2.

Male gender predominated in both case and control groups (68 % and 61% respectively) and the most common age among cases was 1- 3 years representing 40% while among controls, age group 5-10 years was the most common representing 36% as shown in Table 3.

Table 1. Comparison between mean Serum Magnesium levels in Asthmatic and control group .

Groups	No.(%)	Serum Mg level(mg/dl) Mean(±SD.)	P-value
Asthmatic patient	100	1.91± 0.33	0.01
Controls	100	2.03± 0.33	

Table 2. Comparison between Serum Magnesium levels in Asthmatic and control group .

Serum Magnesium	Asthmatic patients	Control group	Total
Low S.Mg(<1.5 µg/dl)	9(9%)	1(1%)	10(5%)
Normal S.Mg (1.5-2.3 mg/dL)	91(91%)	99(99%)	190(95%)
Total	100(100%)	100(100%)	200(100%)

X2=8.36, df=2, P=0.01

Table 3. Age and gender distribution of asthmatic patients and controls.

Age (years)	Asthmatic patients			Control Group		
	No.(%)	Male	Female	No.	Male	Female
1 - <3	40(40%)	27(27%)	13(13%)	25(25%)	18(18%)	7(7%)
3 - <5	22(22%)	16(16%)	6(6%)	14(14%)	9(9%)	5(5%)
5 - <10	29(29%)	19(19%)	10(10%)	36(36%)	19(19%)	17(17%)
10-15	9(9%)	6(6%)	3(3%)	25(25%)	15(15%)	10(10%)
Total	100(100%)	68(68%)	32(32%)	100(100%)	61(61%)	39(39%)

Serum magnesium level decreased by the increased duration of asthma but this was not statistically significant as shown in Table 4.

Serum magnesium level was not found to be significantly related to body mass index of asthmatic patients though the overweight patients had the lowest level as shown in Table 5

Serum magnesium level decreased with increasing severity of asthma symptoms with 0.05 P value as shown in Table 6.

Serum magnesium level was slightly higher in those asthmatic patients who were on inhaled steroids than those who were not. Also those who used long acting inhaled bronchodilators had a bit higher serum magnesium level than those who did not with no clinical significance as shown in Table 7.

Table 4. Relation between mean Serum Magnesium levels and duration of asthma.

Duration of Asthma	No.(%)	Serum Mg level(mg/dl) Mean(±SD.)	P-value
< 1 year	28 (28%)	1.97±0.27	
1 - <3 years	48 (48%)	1.91±0.33	
3- <5 years	11 (11%)	1.87±0.36	0.1
>5 years	13 (13%)	1.72±0.44	
Total	100 (100%)	1.91±0.33	

Table 5. The relation between mean Serum Magnesium and BMI of Asthmatic patients.

BMI	No.(%)	Serum Mg level(mg/dl) Mean(±SD.)	P-value
Under weight <5%	21(21%)	1.97±0.25	
Normal 5% to 85%	57 (57%)	1.90±0.36	
Overweight 85% to 95%	13 (13%)	1.78±0.30	0.3
Obese >95%	9 (9%)	2.00±0.32	
Total	100 (100%)	1.91±0.33	

Table 6. Comparison between mean Serum Magnesium levels & severity of Asthma.

Severity of Asthma	No. (%)	Serum Mg level(mg/dl) Mean(±SD.)	P-value
Intermittent	67(67%)	1.96±0.33	
Mild persistent	20 (20%)	1.85±0.26	
Moderate persistent	10 (10%)	1.79±0.42	0.05
Severe persistent	3(3%)	1.50±0.10	
Total	100 (100%)	1.91±0.33	

Table 7.Comparison between mean Serum Magnesium levels & use of medications (controller) in Asthmatics.

Drugs	No. (%)	Serum Mg level (mg/dl) Mean(±SD.)	P-value
Steroid as controller medications			
Used steroid	20 (20%)	1.92±0.37	0.7
Not used steroid	80 (80%)	1.90±0.30	
Bronchodilators as controller medications			
Use	31 (31%)	1.91±0.34	0.9
Not used	59 (59%)	1.90±0.31	
Total	100 (100%)	1.91±0.33	

DISCUSSION

In the present study serum magnesium level was found to be significantly lower in asthmatic children as compared to the control group. The mean serum magnesium was 1.91± 0.33 mg/dl while in the control group it was 2.03± 0.33 mg/dl.

This shows that serum Mg^{+2} values in asthmatic group were significantly lower than the controls.

Hypomagnesemia in this study was present in 9% of the subjects. This is much lower than the study that reported hypomagnesemia in 40.5% of asthmatic patients [13] and another study that found it in 26.9% of cases [14]. Prevalence of hypomagnesemia in asthmatics is otherwise unknown [15]. Despite being the commonest undiagnosed abnormality of electrolytes in clinical conditions, its prevalence is variable (4.6- 47 %) [14].

Magnesium deficiency exerts significant effects on asthma and its clinical presentations so that hypomagnesemia increases hospitalization [15]. Since Mg^{+2} stabilizes mast cell so its deficiency results in bronchoconstriction as a result of increasing airway hyper responsiveness by increasing acetylcholine production at cholinergic nerve ending thereby improving pulmonary functions [13]. Although the cause of hypomagnesemia in patients with chronic asthma was unknown, [14] it may be related to either low magnesium intake in asthmatics or increased urinary loss of magnesium, as a side effect of therapy with b2-

agonist, corticosteroid, and theophylline [16,17].

Other studies have found no significant difference in serum level between asthmatics and controls but found the intracellular Mg^{+2} in erythrocytes to be lower in asthmatics [18-22].

This finding may have a therapeutic benefit. It suggests that Mg^{+2} supplementation for asthmatics may improve the clinical condition as suggested by earlier studies as well [23, 24].

Medications used in treatment of asthma include, anti-inflammatory agents as glucocorticoid and bronchodilator agents as beta-2 agonists. Long term use of these drugs by the patients may cause depletion of Mg^{+2} through urinary excretion and intracellular shift [14]. Studies have shown no effect of the regular daily controller inhaled beta-2 agonists and glucocorticoid steroids asthmatic therapy on Mg^{+2} status [14, 25]. Similar result was found in our study where the use of controller medication do not lower Mg^{+2} level in the serum of asthmatics but rather the level was found eventually higher in those on controller therapy while many other studies have shown significant lowering of serum Mg with the use of such medications [5, 16, 21, 26-28]. This is possibly explained by the poor compliance of our patients with use of these controller medications.

In our study the serum Mg^{+2} inversely correlates with the duration of asthma but this is not statistically significant.Similar result was found in a Nigerian study. [29] This may be a pointer to multifactorial cause of hypomagnesemia in asthma.

Neither body weight nor body mass index is significantly related to serum Mg^{+2}. Similar results were found in other studies [20, 21, 27] and this precludes any direct role of nutritional status as a determinant of body Mg^{+2}.

The inverse correlation between serum Mg^{+2} and severity of asthma is clearly shown in this study. Such results were also seen in other studies [5, 19, 30-31] which proves the role of Mg^{+2} deficiency in potentiating contractility of bronchial smooth muscles. Unlike that, two other studies could not find such a correlation [21, 32].

Conclusion

Serum magnesium level is significantly lower in asthmatic children as compared to the control group**.** Serum Mg^{+2} level inversely correlates with the duration of asthma but not significantly. There is an inverse relation between serum Mg^{+2} and the severity of asthma. No significant change in serum Mg^{+2} develops with the use of steroids and bronchodilators in treatment.

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