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Blood Serum Magnesium Values in Chronic Stable Asthmatic Patients: A Case - Control Study

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ABSTRACT

***Background**: Bronchial asthma is characterized by airways inflammation and hyperreactivity of tracheobronchial tree. Magnesium (Mg) deficiency leads to increased airways hyperreactivity. This study was performed on patients with chronic stable asthma to determine their blood serum magnesium values and compare them with general healthy population to assess whether there is a difference between them.*

***Materials and Methods**: This was a prospective, case-control study which was performed on patients with chronic stable asthma in Loghman Hakim Hospital. Forty-two consecutive volunteer patients with chronic stable asthma according to the definite criteria and healthy sex and age-matched subjects were chosen. Secondary causes of hypomagnesemia were found out by the questionnaire and were ruled out. Serum blood sample for measuring magnesium value was obtained. Normal values were 1.8 mg/dl in males and 1.9 mg/dl in females.*

***Results:** In the final exam, significant difference between two groups was noted (P<0.001). Hypomagnesemia was detected in 40.5% of the chronic stable asthmatic patients. Overall mean age was 40.16±12.8 yrs. and the mean Mg value was 1.85±0.28. Male to female ratio was 23/19.*

Conclusion**: Hypomagnesemia was confirmed in chronic stable asthma in Iranian patients. It may be due to the quality and quantity of using therapeutic agents and type of diets which are low in magnesium supply. However, further evaluation is needed. **(Tanaffos 2005; 4(13): 27- 32)

***Key Words**: chronic asthma, Hypomgnesemia, Magnesium*

INTRODUCTION

Bronchial asthma is characterized by airways inflammation and hyperreactivity of tracheobronchial tree. Magnesium (Mg) deficiency leads to increased airways hyperreactivity (1, 2, 3, 4). Medications used in the treatment of asthma cause decreased magnesium value in total body stores (4), especially in acute asthma management (5) . Diet is important in Mg homeostasis and effective in bronchial hyperresponsiveness (6, 7, 8).

Magnesium is an essential element of human body. Only 0.3% of total body Mg exists in serum

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(9). Recently, its role in asthma and effect on respiratory airways has been recognized. It is a relaxing factor of airway smooth muscles (9,10), regulates bronchial tone, competes with Ca influx by blocking voltage dependent calcium channels, inhibits intracellular Ca release from sarcoplasmic reticulum (9,10), and is associated with airways hypersensivity (11), stabilization of mast cells (12), and manifestation of wheeze and impairment of lung function (7). Also, it has some influence (at least in part) inhibits cholinergic transmission, stimulates synthesis of nitric oxide and prostacyclin (9). MgSO4 improves lung function and causes bronchodilatation (9,11).

However, despite the considerable studies conducted magnesium deficiency in acute asthma, little is known about the prevalence and serum magnesium level in chronic stable asthma particularly in comparison with general population. There was no study in this regard in Iran and only one report had shown significant difference in serum Mg values of asthmatic patients and general population (13). However, other studies on acute and chronic asthma have revealed no significant difference between Mg levels of asthmatic and non-asthmatic control groups (14).

Previous studies suggested a 40% magnesium deficiency in total body stores of asthmatic patients (15).

The purpose of this study was to compare serum magnesium values in chronic asthmatic patients and healthy subjects, and assessing the difference between them.

MATERIALS AND METHODS

This was a case-control study which was conducted from May through August 2001 at Loghman Hakim Hospital, Shaheed Beheshti University of Medical Sciences and Health Services. Forty-two (n=42) consecutive stable patients with moderate asthma on regular follow-up were recruited as volunteers. The patients were diagnosed according to American thoracic Society Criteria (16). Diagnosis was based on clinical history, physical examination, spirometric pulmonary testing, reversibility of FEV1, or peak expiratory flow >15%, diurnal variation of peak expiratory flow rate >20%, and chest x-ray. Patients were under observation and regular examination. Information was obtained by a questionnaire including the patient's age, sex, duration of asthma, nocturnal symptoms, history of hospitalization in recent six months of study, type and number of medications used (in three months before the study), smoking, alcohol abuser, and symptoms of primary Mg deficiency.

Moderate asthma was defined as: nocturnal asthma symptoms> twice per month, PEF> 60-80%, PEF variability> 30% and exacerbation> 1-2times per week (17).

Patients with any of the criteria were excluded. Inclusion criteria were made up of any causes of secondary magnesium deficiency such as pregnancy, breast-feeding, gastrointestinal, cardiovascular or metabolic diseases (diabetes mellitus), recent convalescence history, drugs history such as contraceptive pills, vitamin D, diuretics, calcium antagonists, digoxin, laxative, and/or signs and symptoms of primary magnesium deficiency such as history of cramp, anorexia, and palpitation (12).

None of the subjects showed any evidence of acute respiratory infection within one month prior to present study.

Asthmatic volunteers received inhaled glucocorticoid steroids including fluticasone (47.6%) and beclomethasone (52.4%). Inhaled salbutamol (52.4%) and salmeterol (50.0%) were used when needed. 61.6% of patients received oral theophylline associated with other regimens.

Healthy subjects from the same population served as control group. Forty-two (n=42) age and

sex–matched subjects (control group) were healthy with no allergic disorders, pulmonary diseases, asthma, drug use, and secondary symptoms of Mg deficiency.

Normal magnesium values in our laboratory were 1.8-2.6mg/dl in males and 1.9-2.5mg/dl in females.

Heparinized blood samples were used for analysis of serum Mg. After overnight fasting , venous blood sample was obtained from individuals in sitting position without using tourniquet .After transferring the aspirated blood to a metal-free test tube containing sodium heparin , plasma was separated within 30 minutes (rpm=3500). Mg concentration in plasma is determined by colorimetric assay (Pars Azemon Co. Ltd). However, Mg value in plasma is equal to its serum concentration. All assays were performed in one laboratory.

PEF measurements were performed by Wright's peak flow meter (Ferraris Medical Pocket peak, Made in England).

Informed consent was obtained from all subjects. Data were entered into database file and statistical analysis was performed by using SPSS software. Descriptive analyses were carried out on all variables. Independent sample t-test was used for comparison of mean Mg values between asthmatic and normal groups. Level of significance was considered to be < 0.05 throughout the analysis.

RESULTS

A total of 42 consecutive patients with chronic stable asthma were compared with healthy subjects. Results of the analysis are presented in table 1. Overall mean age was 40.16±12.80.Overall Mg deficiency was 40.5% and the mean Mg value was 1.85±0.28. Mean duration of asthma was 5.61±1.32 .

Twenty three (54.8%) patients were male with the mean age of 44.91±12.74. Hypomagnesemia was found in 8 (34.7%). Also, 19 (45.2%) were female with mean age of 38.05±12.97. Mg deficiency was found in 9 (47.3%).

The mean whole blood Mg level in our healthy population was 2.5±0.0.

We compared overall results between the two groups and found statistically significant differences (P<0.001).

Table 1. Characteristic features of Mg values in chronic stable asthma relative to control group.

	p value	Asthmatic group	Control group
Patients number		42	42
Serum Mg value (mg/dl)	<0.001	1.85±0.28	2.04±0.25
Age (yrs)		40.16±12.80	40.16±12.80
M/F		23/19	23/19
Male N (%)		23 (54.8%)	23
Mean age (yrs)		44.91±12.74	-
Serum Mg value (mg/dl)	<0.001	1.81±0.34	2.5±0.0
Female N (%)		19(45.2%)	-
Mean age (yrs)		38.05±12.97	-
Serum Mg Value (mg/dl)	<0.001	1.9±0.2	2.5±0.0
PEF		448.09±52.78	0
Duration of asthma (yrs)		5.61±1.32	

DISCUSSION

The purpose of the present study was to compare serum magnesium values in chronic stable asthmatic patients and healthy subjects. According to the results of the study, Mg serum values in chronic stable asthmatic group were significantly different from the control group.

Hypomagnesemia in this study was found in 40.5% of the subjects. Epidemiology and prevalence of hypomagnesemia in chronic asthma are not known (4, 12). Although magnesium deficiency is the most common undiagnosed electrolyte abnormality in clinical states (4), its prevalence in hospitalized patients was reported variable (4.6- 47 %) (12); but highest prevalence of hypomagnesemia in critically

ill patients has been reported in intensive care units to be over 65 % (12), and lowest value (11.5%)was shown in severe chronic obstructive lung disease (17). The present study reveals highest Mg deficiency rate which is similar to the results of Alamoudi et al. studies (4,12).

Mg deficiency has several effects on asthma and its clinical presentations. Low serum Mg level causes increased hospitalization (40%) (12).It is mast cell stabilizer results in bronchoconstriction due to increasing airway hyperreactivity and hyperresponsiveness through increased acetylcholine production at cholinergic nerve ending and improves pulmonary functions.

Serum Mg level comprises only 1% of total body content (5). Recent study discloses no correlation between serum and intracellular content of Mg and signs of hypomagnesemia may be occur in normal or minimally low serum Mg concentration (5). This finding is important from the therapeutic point of view and suggests adding Mg supplements to asthmatic patients' diet. It is supported by earlier studies as well (6,8).

Medications that are prescribed in asthma divided into two broad groups, anti-inflammatory agents as glucocorticoid and bronchodilator agents as beta-2 agonists and theophilline. Receiving these drugs for long times especially its over use by the patients in acute states may cause depletion of Mg in human through intracellular shift and urinary excretion (4). Also, recent studies have shown no effect of the regular daily controller asthmatic therapy in Mg status (inhaled beta-2 agonists, glucocorticoid steroids) (4, 5). Patients in this study underwent precised control only for six months. Duration of asthma and use of older drug regimens by the patients may be effective on Mg status.

The potential role of dietary intake of Mg has been recognized in Mg level. Low dietary intake of Mg is associated with impaired lung function, bronchial hyperreactivity and wheezing (7). Chlorophyll is the Mg chelate of porphyrin , green leafy vegetables ,legumes, and nuts are the excellent and richest dietary sources of Mg. Vitamin D and metabolites enhance Mg absorbtion by the distal bowel .Although fish , meat , milk, starches and fruits are generally poor sources of Mg (9). Evidences indicated that Iranian diets are rich in starch and meat, and it may affect Mg homeostasis.

Low Mg value was found in 47.3% of female which is higher than in male. The results are in agreement with the results of Alamoudi (4,12). Childbearing age in female patients and influence of estrogen and progesterone may be effective in Mg status (9).

Results of this study reveal that hypomagnesemia in asthmatic Iranian patients is higher as compared to general population. Improvement of Mg deficiency through Mg supplement may be effective in asthma symptoms, reducing risk of hospitalization, and achieving better therapeutic results, but further investigation is needed to complete this hypothesis.

We have a number of limitations. First of all, six months control of asthmatic patients for drug usage is not sufficient and needs more time. Secondly, dietary Iranian regimens play an important role in this type of study, and we are unable to control it.

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