A study on serum magnesium level in bronchial asthma patients

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Abstract

Background: Bronchial Asthma is one of the most common respiratory diseases that we see in day to day practice and has been increasing in prevalence over the last few decades. Magnesium ion has an inhibitory action on smooth muscle contraction, histamine release from mast cells and acetylcholine release from cholinergic nerve terminals. Magnesium has been shown to dilate bronchial smooth muscles and influence the function of respiratory muscles. Hypomagnesaemia have been associated with diminished respiratory muscle power. Although magnesium is used through intravenous and inhalation route in the management of asthma, the exact prevalence of hypomagnesaemia in asthma is not known.

Materials and Methods: Forty patients attending outpatients department of respiratory medicine with stable asthma, were randomly selected. They were assessed clinically and their serum magnesium levels were measured. This was compared with the serum magnesium values of forty non-asthmatic healthy controls.

Results: In this study, serum magnesium value between 1.5 and 2.5mg/dl was considered normal and any value below 1.5 mg/dl was considered as hypomagnesaemia. Using this cut-off value, a total of 40 patients is compared with 40 healthy individuals. About 35(87.5%) patients were found to have hypomagnesaemia and their serum magnesium value ranged between 0.70 and 1.4 mg/dl. Rest 5(12.5%) patients had normal serum magnesium level.

Conclusions: It can be concluded from the present study that hypomagnesaemia is more prevalent in stable asthmatics than non-asthmatic control. There is statistically significant correlation of hypomagnesaemia with severity of asthma. We measured serum concentration of magnesium which may not be representative of actual body store. We did not consider the amount of dietary magnesium in the patients. Therefore, further studies are needed using large number of patients, and measuring Mg^{++} levels in RBC, WBC, or muscle cell in addition to serum $Mg^{++}$and this would be very helpful for assessing the effect of hypomagnesaemia in stable asthmatic patients.

Keywords: Bronchial muscle relaxation; Serum hypomagnesaemia; Stable asthmatics

Introduction

Magnesium is the fourth most abundant cation in our body and the second most common intracellular cation [1]. Magnesium intervenes in calcium transport mechanisms and intracellular phosphorylation reactions and so, it constitutes an important determinant of the contraction and relaxation state of bronchial smooth muscle. Magnesium deficiency is associated with increased contractility of smooth muscle cells [2]. Contractility of bronchial smooth muscle is important in patients with asthma and therefore, magnesium deficiency could lead to bronchial smooth muscle contraction or lack of bronchial muscle relaxation [3]. The present study was done to evaluate the serum magnesium level in patients with bronchial asthma.

Materials and Methods

Study design and setting: This case control study was conducted in subjects attending the outpatient department of Pulmonary Medicine, Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Pondicherry, India for a period of two months from October to November 2015.

Sample: Considering, the mean of magnesium level among asthmatics 1.85±0.28 and normal patients 2.04±0.25, 95% confidence interval the sample size was 62 (31 case and 31 control), calculated using Open Episoftware package (version 2.3). Considering 10% of non-response rate, the final sample size studied was 80 (40 cases and 40 controls).

Sampling

Case: Those patients who were diagnosed as to have bronchial asthma based on clinical history, physical examination and pulmonary spirometry testing were taken as subjects

Control: Normal healthy individuals with no asthma attack for atleast one week before the start of the study.

Inclusion criteria:

For cases: 40 individuals of age above 18 years with known bronchial asthma were included.

For control: 40 healthy individuals of age above 18 years with no asthma attack for at least one week before the start of the study.

Exclusion criteria:

- Patients who were above the age of 18 years
- Patients who were smokers
- Subjects in control group who are in the state of pregnancy, breast-feeding, menopause, metabolic disorders
- Asthmatics, who had taken bronchodilators within 24 hours prior to assessment

Patient`s name, age, sex and duration of the symptoms were noted, and a detailed history was taken

in each patients regarding the duration of asthma symptoms, frequency and severity of the exacerbation, smoking history and previous medical history.

Spirometry: Pulmonary function test was done before and twenty minutes after giving nebulized salbutamol 400 micro grams. Peak expiratory flow rate (PEFR), force expiratory volume in first second (FEV1) Forced vital capacity (FVC) and FEV1/FVC and FEV 25-75% was recorded. An improvement of 12% or more in FEV1 was considered as criteria for the diagnosis of asthma [4].

Serum magnesium analysis: After taking the necessary aseptic precautions from the median cubital vein, 2ml of venous blood was collected from each patient. After collecting the blood sample it was left undisturbed for about half an hour for complete clot formation. The sample was then centrifuged to separate the serum from the clot. After centrifugation the serum was stored at minus 20° C in Eppendorf tubes till the analysis was done. Serum magnesium was measured using ELISA kit [5].

Other investigations: Chest X-Ray, complete blood count, electrocardiography, Erythrocyte sedimentation rate [ESR] sputum for AFB and Gram`s stain was done for the study subjects.

Statistical analysis: Data was entered and analyzed with Epi-info software version 3.4.3, proportions were calculated and Chi-square test was used to find its association. Mean values of all patients were interpreted.

A written informed consent was obtained from all the patients participating in the study. Study was approved by institutional ethical committee.

Results

In this study, serum magnesium value between 1.5-2.5mg/dl was considered normal and any value below 1.5 mg/dl was considered as hypomagnesaemia. Using this cut-off value, a total of 40 patients is compared with 40 healthy individuals. About 35(87.5%) patients were found to have hypomagnesaemia and their serum magnesium value ranged between 0.70-1.4 mg/dl. Rest 5(12.5%) patients had normal serum magnesium level.

Table 1: Results of the analysis is presented in the following table

Variables	Cases n=40 Mean (SD)	Controls n=40 Mean (SD)	p-value
FEV1 (%)	46.49	95.42	<0.001
Serum magnesium(meq/lit)	1.76	2.31	<0.001

The mean (SD) serum magnesium concentration(Figure.1) in asthmatic patients was significantly lower than that obtained in the control with p<0.001 (Table 1).

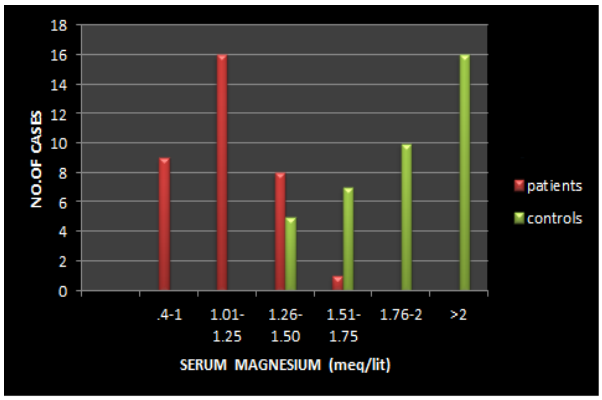

Figure 1: Comparison of serum magnesium level (meq/lit) between cases and controls

The mean (SD) Forced Expiratory Volume (FEV1 %) in asthmatic patients is significantly lower than in controls with p value <0.001 (Table 1).

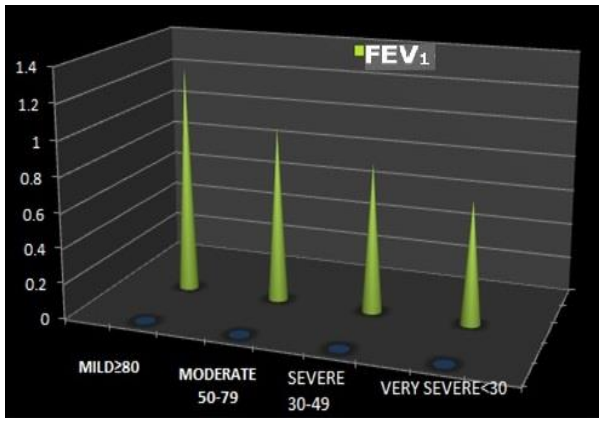

Figure 2: Change in serum magnesium level (meq/lit) with FEV1% in asthmatics

And also it was found that, there was a linear relationship between serum magnesium level and FEV1. As the FEV1 decreased, there was an associative decrease in serum magnesium levels (Figure 2).

Discussion

Magnesium has been found to play a role in the pathophysiology of allergic reactions especially in asthma [6] the contraction and relaxation of the myofibrillar proteins in bronchial smooth muscle cells are due to the phosphorylation and dephosphorylation reactions which include the enzymes myosin kinase, and myosin phosphatase. Myosin kinase is magnesium dependent and myosin phosphatase is calcium dependent enzyme [7]. Since magnesium is involved in calcium transport across the cellular membrane, both types of enzymes are directly or indirectly influenced by magnesium level [8]. Such effects of magnesium would be expected to result in relaxation of bronchial smooth muscle and reduction of the airway reactivity.

This study shows that the asthmatic patients had a significantly lower serum magnesium level when compared to the control. This study also shows high prevalence of hypomagnesaemia and association of hypomagnesaemia with asthma as proved by the correlation between FEV1 and serum magnesium level.

Fedoseev *et al*, reported hypomagnesaemia in patients with bronchial asthma and this abnormal homeostasis of magnesium in asthmatics may be due to hyper activation of free radical oxidation of cell membrane lipids [9]. The magnesium deficiency in asthma may favor the movement of calcium to inside the smooth muscle cell leading to a potentiation of myosin phosphorylation and rendering the cell more contractile and thus increasing bronchial hyper-reactivity. Other mechanisms by which magnesium deficiency increases bronchial hyper-reactivity include increased production of acetylcholine in cholinergic nerve endings, increased histamine release from mast cell, increased production of interleukin-1 & 6, degranulation of basophils, and enhanced production of IgE [10].

Causes of magnesium deficiency in asthma may be multi-factorial. It may be genetically determined. Though reports say hypomagnesaemia as side effect of bronchodilators, decreased magnesium level was reported in the patients who were not on treatment with bronchodilators, corticosteroids or even withdrawal of the drugs.

Diet is a newly recognized risk factor for asthma occurrence. Current literature concerning magnesium supplementation recommends that on national basis magnesium should be added to the water supplies of large areas [11]. Magnesium supplementation has been shown to be of large preventive advantage for disorders such as asthma [11].

A sustained increase in serum magnesium level augments the bronchodilator effect of salbutamol possibly through increased affinity for β-receptors [8]. Thus isotonic magnesium can be administered safely in patients with stable asthma either in an inhaled form, or as a vehicle salbutamol through nebulizer.

Conclusions

It can be concluded from the present study that hypomagnesaemia is more prevalent in stable asthmatics than non-asthmatic control. There is statistically significant correlation of hypomagnesaemia with severity of asthma. We measured serum concentration of magnesium which may not be representative of actual body store. We did not consider the amount of dietary magnesium in the patients. So, further studies using large number of patients, and measuring Mg^{++} level in RBC, WBC, or muscle cell in addition to serum Mg^{++} will give better insight in this field. The cause of hypomagnesaemia in asthmatics and whether magnesium supplementation has a role in asthmatic population are important fields of further research.

Conflict of Interest: None declared

Acknowledgement: None

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