Abstract:
Objective To compare the serum magnesium levels in chronic stable asthmatics with nonasthmatic healthy controls.
Design Case control study.
Materials and Methods This is a case control study which was performed on patients with chronic stable asthma and non asthmatic healthy controls. Thirty patients attending the outpatient department of respiratory medicine with stable asthma were randomly selected and assessed clinically and their serum magnesium levels were measured. This was compared with the serum magnesium levels of thirty non asthmatic healthy controls.
Results Significant difference between the two groups was noted (P<0.001). Mean (SD) serum magnesium concentration of 1.18 (0.26) meq/l observed in the asthmatics was significantly lower compared to the controls which was 1.93 (0.42) meq/l, P<0.001.
Conclusion Chronic stable asthmatic patients have statistically significant lower serum magnesium levels compared to healthy controls.

Keyword: Serum magnesium, Stable asthma, Chronic asthma.

INTRODUCTION:
Magnesium, the second most abundant intracellular cation (1) has modulatory effects on the contractile state of smooth muscle cells in various tissues. It has shown to be an in vitro relaxant on bronchial smooth muscle (2), first described by Rossello and pla in 1936 (3) and magnesium has been shown to bronchodilate asthmatic airways in vivo. Recently there has been considerable interest generated in the possible importance of magnesium ions in the regulation of bronchial smooth muscle tone either directly or indirectly (4). Diverse clinical manifestations have been reported in conjunction with magnesium deficiencies of which asthma is one of them (5). These factors have aroused the possible utilization of magnesium salts in the management of asthma both in acute and chronic cases (6, 7). Bronchial asthma is a disease characterized by inflammation of the airways and increased
responsiveness of the tracheobronchial tree to a multiplicity of stimuli \(^8\). Epidemiological evidence suggests that a low dietary intake of magnesium is associated with impaired lung function, bronchial hyperactivity, wheezing \(^9\) and could be involved in the aetiology of asthma and it constitutes a decompensatory factor for asthma \(^10\). The present study was done to evaluate the levels of serum magnesium in chronic stable asthmatics, and also to determine if magnesium deficiency occurs in them. This will serve as a baseline for future intervention studies on the possible effects of magnesium in asthmatics. MATERIALS AND METHODS: Thirty patients with chronic stable asthma registered at outpatient department of thoracic medicine, Govt. Rajaji Hospital, Madurai, a tertiary care hospital and a teaching institution were included in this study. All patients were on oral bronchodilators, few patients were using salbutamol inhalation along with oral bronchodilator as and when required. The control group included medical post graduate students, laboratory technicians, hospital workers who were found to be in good health. Written informed consent was obtained from each subject after their requirements for participation in the study were explained. The study was preapproved by the ethical committee of our institution review board.

Inclusion criteria:

a) The chronic stable asthmatic patients who had no exacerbations at the time of presentation or within last two weeks.

b) Non smoker.

c) Age more than 14 years.

Exclusion criteria:

a) Medical disorders like diabetes mellitus, cardiac disease, and renal disorder.

b) Patients on diuretic therapy.

c) Patients and controls on any form of magnesium supplements. All the patients were evaluated with detailed history, general examination, and examination of the respiratory system. The height and weight of the subjects were measured by using standard methodology with inch tape and weighing machine. Blood pressure was determined in all the subjects by using sphygmomanometer by auscultatory method in right upper arm in sitting posture. Examination of the Respiratory system: Respiratory rate was counted and chest expansion was measured with an inch tape placed around the chest just below the nipples. The diagnosis of asthma was confirmed by the presence of spirometric evidence of asthma, by measuring FEV1, the forced expiratory volume during the first second, by asking the subject to exhale rapidly and forcibly in to the spirometer after taking a maximum inspiration and also improvement of FEV1 by 12% after salbutamol inhalation.

Peak expiratory flow rate was measured by using Wright’s peak expiratory flow meter. The patients and controls were asked to inspire maximally and blow out as fast as they can in to the flow meter. Normal PEFR is 400-600 l/mt.

Biochemical Analysis:

Five ml of venous blood was obtained from antecubital fossa of both patients and controls, by using Dispovan. The blood samples were allowed to clot and centrifuged at 3000 r.p.m for 10 minutes. Clear serum was separated and the estimation of serum magnesium was carried out with semi-auto analyzer using Calmagite as the dye reagent. A normal serum magnesium level by this method is 1.3-2.5 meq/l.
**Statistical analysis:**
Data were expressed as mean (SD). The student's ‘t’ test was used for comparison of mean magnesium values between asthmatics and normal groups. This was done using SPSS (statistical package for social science) software, sigma stat version 3.5. Level of significance was considered to be p <0.05 throughout the analysis.

**RESULTS:**
A total of thirty patients with chronic stable asthma were compared with thirty healthy subjects. Results of the analysis are presented in the following table:

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases n=30 Mean (SD)</th>
<th>Controls n=30 Mean (SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.2 (10.2)</td>
<td>39.7 (5.96)</td>
<td>0.499</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>154.66 (8.18)</td>
<td>158.2 (7.43)</td>
<td>0.086</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50.26 (8.44)</td>
<td>58.36 (11.09)</td>
<td>0.002</td>
</tr>
<tr>
<td>Systolic B.P (mm of Hg)</td>
<td>129.4 (11.19)</td>
<td>131.13 (10.01)</td>
<td>0.53</td>
</tr>
<tr>
<td>Diastolic B.P (mm of Hg)</td>
<td>79.6 (6.18)</td>
<td>78.4 (6.3)</td>
<td>0.713</td>
</tr>
<tr>
<td>Chest expansion (cm)</td>
<td>4.2 (0.60)</td>
<td>4.83 (0.69)</td>
<td>0.002</td>
</tr>
<tr>
<td>Respiratory rate (No/min)</td>
<td>18.56 (1.07)</td>
<td>14.73 (0.78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PEFR (litre/min)</td>
<td>187.86 (67.02)</td>
<td>386.16 (43.48)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum magnesium (meq/lit)</td>
<td>1.18 (0.26)</td>
<td>1.93 (0.42)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The mean (SD) age was 41.2 (10.2) for the patients and 39.7 (5.96) for the controls. The mean duration of asthma was 7.3 years. The mean weight of the asthmatic patient is 50.26 (8.44) and is significantly lower than that of the non asthmatic which is 58.36 (11.09). There is no significant difference in systolic and diastolic blood pressure between the asthmatics and non asthmatics (Table 1).

**Fig.1 Comparison of serum magnesium level (meq/lit) between cases and controls**
The mean (SD) serum magnesium concentration (Fig. 1) in asthmatic patients was significantly lower than that obtained in the controls with p <0.001 (Table 1).

Fig. 2 Comparison of Peak expiratory flow rate between cases and controls
The mean (SD) peak expiratory flow rate (PEFR) (fig.2) in asthmatic patients was significantly lower than that in controls with p value <0.001 (Table 1).

Fig. 3 Changes in serum magnesium level (meq/lit) with PEFR (litres/min) among Asthmatics
There was a linear relationship between serum magnesium level and PEFR. As the PEFR increases there was an associated increase in the serum magnesium levels. (fig.3)

Fig. 4 Changes in serum magnesium concentration (meq/lit) with different bronchodilators
There was a significant increase in Respiratory rate in asthmatics with mean (SD) 18.56 (1.07) when compared to the controls which was 14.73 (0.78) with p<0.001 whereas there was a significant decrease in the chest expansion in asthmatics with mean (SD) 4.2 (0.80) when compared to the controls which was 4.83 (0.69) with p=0.002 (Fig. 5).

In asthmatic patients, using inhaled bronchodilator along with oral brochodilator the mean serum magnesium level was decreased when compared with patients only on oral bronchodilator but it was not significant. Hence, there was no effect of therapy on serum magnesium levels in patients with chronic stable asthma (Fig.4).
There was a positive correlation between the duration of asthma and hypomagnesaemia. As the duration of asthma increases, the serum magnesium level decreases (fig.6).

**DISCUSSION**

Magnesium has been found to play a role in the pathophysiology of allergic reactions especially asthma.(11). The pulmonary function test has been shown to improve with the administration of intravenous magnesium (12) and magnesium appears to be additive to the bronchodilating effect of anti-asthmatic drugs salbutamol and terbutalin (13). 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 enzyme and myosin phosphatase is calcium-dependent enzyme (1). Since magnesium is involved in calcium transport across the cellular membrane (14), both types of enzymes are directly or indirectly influenced by magnesium levels. 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 controls. The study also shows high prevalence of hypomagnesaemia and association of hypomagnesaemia with asthma as proved by the correlation between PEFR and serum magnesium level.

Fedoseev et al. (15) 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. The magnesium deficiency in asthma may favour 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 hyperactivity. Other mechanisms by which magnesium deficiency increases bronchial hyperreactivity include increased production of acetylcholine in cholinergic nerve endings (16), increased histamine release from mast cell (17), increased production of interleukin-1&6, Degranulation of basophils, and enhanced production of IgE. Causes of magnesium deficiency in asthma may be multifactorial. It may be genetically determined. Though reports say hypomagnesaemia as a side effect of bronchodilators, decreased magnesium level was reported in the patients who were not on treatment with bronchodilators, corticosteroids or even after withdrawal of the drugs (18). This study also shows that bronchodilators in any form did not affect the serum magnesium levels significantly. 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 \(^{(5)}\). Magnesium supplementation has been shown to be of a large preventive advantage for disorders such as asthma \(^{(5)}\). A sustained increase in serum magnesium level augments the bronchodilator effect of salbutamol possibly through increased affinity for \(\beta\) receptors \(^{(14)}\). Thus isotonic magnesium can be administered safely in patients with stable asthma either in an inhaled form, or as a vehicle for salbutamol through nebulizer \(^{(19)}\).

**CONCLUSION:**

It is concluded that hypomagnesaemia is more prevalent in chronic stable asthmatics than non-asthmatic controls. There is a statistically significant lower serum magnesium levels in asthmatics when compared to non asthmatic controls. Expanded version of this study would emphasize the significance of magnesium in the patho-physiology and management strategies of bronchial asthma.


7. Harrison’s principle of internal medicine, edi-17, 1596.


10. Halpren H J. Magnesium physiopathology II.


