Studying Serum Magnesium in Metabolic syndrome with Endothelial dysfunction: A Drug History Scenario

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Abstract: The magnesium has a crucial role in the occurrence of various factors of metabolic syndrome, however not much study has been absolutely convincing on this issue. This study was conducted to determine possible association of serum magnesium (Mg) concentrations with the parameters of metabolic syndrome (MetS) and endothelial dysfunction. Out of the total 100 subjects, on the basis of drug history for diabetes among the patients with MetS, they were grouped as with medication (n=19) and without medication (n=31) patients. The data obtained was compared via paired t-test and correlated by bivariate analysis. It was observed that the serum level of magnesium was significantly reduced (p<0.001) in the patient's group compared to control and there was a slight increase in the level of serum magnesium in the patients under medication compared to patients without medication. But medication did not show any significant role in alleviating the condition.

1. Introduction

Metabolic syndrome, itself is not a disease, however the clusters of various factors that could aggregate to result in cardiovascular complications. It is characterized by hypertension, hyperglycemia, insulin resistance, dyslipidemia, and abdominal obesity. [1] Generally, in the obese people the reactive oxygen species ie. Oxidative stress tends to be higher thus affecting the visceral adipose tissue. In addition, under oxidative stress, the adipose tissue generates more pro-inflammatory cytokines and less adiponectin which tends to affect the generation of nitric oxide via endothelial cells.[2,3] As a consequence bioavailability of nitric oxide (NO) is reduced leading to the impairment in the regulation of blood flow in response to increased oxygen demand and energy utilization.[4] Mg, which has very important roles in body metabolism under these sort of circumstances, magnesium, a bivalent cation, has been found to be associated, as it plays a fundamental role in carbohydrate metabolism by stimulating glucose uptake in the insulin sensitive tissues such as the adipose tissue and skeletal muscle. It also enhances the production of nitric oxide as well as acts as a natural physiologic calcium channel blocker to modulate the vascular tone to influence the blood pressure.[5] Apart From this, magnesium is a cofactor for hundreds of enzymes, especially those involved in the transfer, storage, and use of energy. It is involved in the metabolism of carbohydrate, protein, and fat and its deficiency in the body can lead to various metabolic abnormalities. The metabolic syndrome (MetS) is a condition that individually and more specifically in combination, elevate the risk of cardiometabolic disease. [6] Magnesium is found to lower the LDL cholesterol and TG content and raise the HDL level by enhancing the activity of lecithin cholesterol acyl transferase (LCAT) and lipoprotein lipase (LPL). This is done by inhibiting the activity of HMG-CoA reductase which is responsible for converting 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) to mevalonate. [7] Magnesium balance is regulated by the interaction between intake through the diet, its absorption, and renal excretion. Although, how plasma magnesium concentration is kept within narrow limits, the exact physiological mechanisms which regulate this are not fully understood.[8,9] The present study was done to find out the level of serum magnesium levels in MetS patients and to find out its association with different components of the syndrome as well as oxidative stress and endothelial dysfunction.
“2. Method”

“2.1. Study type” A Cross-sectional study

“2.2. Study design”

“2.2.1. Place” This study was carried out in the Department of Biochemistry in collaboration with the Department of Medicine, School of Medical Sciences and Research and Hospital, Sharda University, Knowledge park III, Greater Noida, UP., India.

“2.2.2. Duration of study” 01/05/2016 to 03/10/2016

“2.2.3. Sample size and Sampling method”

A total of 100 subjects were enrolled into this study. Overnight fasting peripheral venous blood sample was collected into plain (5ml) vials from the study subjects after informed consent and appropriate questionnaire. The samples were centrifuged at 2000 rpm for 15 minutes. The separated serum (plain vial) were stored at –80˚C until further analysis. After estimation of above-mentioned parameters by a chemical method and semi auto analyzer, Among the metabolic syndrome (MetS) subjects recruited, 19 had already progressed to diabetes and were under medication and 31 were not diabetic and not taking medication. Rest of the subjects who did not have MetS served as an age-matched control group. The study was conducted on 100 outdoor subjects who visited Sharda Hospital, Greater Noida, UP. These subjects were categorized as Control group with 50 normal healthy individuals of age group 20 – 50 years and a Patient group comprised of 50 individuals suffering from the Metabolic syndrome.

The main parameters estimated were Magnesium, Malondialdehyde, Ceruloplasmin, Uric Acid, Nitric oxide, Fasting blood plasma sugar and lipid profile. The serum magnesium level was estimated using Accurex kit. Nitric oxide was determined by the use of Vanadium III chloride and Griess reaction method. The Griess reagent consists of sulfanilamide and N-(1-naphthyl) ethylenediamine. The method is based on a two-step process. The first step is the conversion of nitrate to nitrite using nitrate reductase. The second step is the addition of Griess reagent, which converts nitrite into a deep purple azo compound; photometric measurement of the absorbance at 540 nm due to this azo chromatophore accurately determines the nitrite concentration. while rest were estimated using readily available enzymatic kits. Serum HDL was determined by Accurex kit.

“2.2.4. Ethical Approval and Patient consent”

Ethical approval and appropriate patient consent were obtained prior conduct of the study.

“2.2.5. Inclusion and exclusion criteria”

Those diabetic patients with MetS taking drugs for diabetes were included under med patient group and Mets without diabetic and not taking the drug for diabetes were grouped as a non-med patient group. Total 50 MetS patients according to the National Cholesterol Education Programme / ATP III criteria and above 20 years of age were included. Patients aged above 50 and below 20 years, Magnesium supplements, vitamin supplements, hormone replacement therapy and those with a history of infections, abnormal renal function, and malignancy were excluded from the study.

“2.2.6. Statistical analysis and software used”

Paired t-test and bivariate analysis were performed using SPSS version 21.

“3. Observations and Results”

Table 1.1. The demographic profile of Control and Patient groups (Mean±SD).

<table>
<thead>
<tr>
<th>S.N.o.</th>
<th>Particulars</th>
<th>Control N=50</th>
<th>Patients N=50</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Age (years)</td>
<td>33.23±2</td>
<td>35.63±7</td>
<td>0.82</td>
</tr>
<tr>
<td>2.</td>
<td>BMI</td>
<td>23±8.0</td>
<td>29.56±5.6</td>
<td>0.07</td>
</tr>
<tr>
<td>3.</td>
<td>Waist Circumference (cm)</td>
<td>82.68±10</td>
<td>96.30±9.9***</td>
<td>0.01</td>
</tr>
<tr>
<td>4.</td>
<td>Systolic pressure (mmHg)</td>
<td>116±8.12</td>
<td>128.7±12**</td>
<td>0.43</td>
</tr>
<tr>
<td>5.</td>
<td>Diastolic pressure (mmHg)</td>
<td>78.46±0.5</td>
<td>83.7±8.8*</td>
<td>0.46</td>
</tr>
</tbody>
</table>

where, * p < 0.1: Non-significant; ** p<0.05 significant,
Table 1.2. Comparison of Serum Mg and NO level between Control and Patients Group. (Mean ± SD)

<table>
<thead>
<tr>
<th>S.No.</th>
<th>Particulars</th>
<th>Control</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mg (mg/dl)</td>
<td>1.82±0.04</td>
<td>1.55±0.16***</td>
</tr>
<tr>
<td>2</td>
<td>NO (µM/l)</td>
<td>750±264</td>
<td>628±272**</td>
</tr>
</tbody>
</table>

Table 1.4. Correlation of Serum Magnesium with NO.

<table>
<thead>
<tr>
<th>S.NO.</th>
<th>Medication</th>
<th>Serum magnesium</th>
<th>Nitric oxide</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes (n=19)</td>
<td>r</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.13</td>
<td>0.95</td>
</tr>
<tr>
<td>2</td>
<td>No (n=31)</td>
<td>r</td>
<td>p value</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.59</td>
<td>0.75</td>
</tr>
</tbody>
</table>

where, *p < 0.1: Non-significant; **p<0.05 significant, *** p < 0.001 : Highly Significant.

“4. Discussion”

Magnesium is the second most abundant intracellular cation and the fourth most abundant cation in the body. Magnesium has various vital biochemical functions in the body[10]. The present study was conducted to find out the association of serum magnesium with components of MetS and endothelial dysfunction. Our study showed that mean serum magnesium levels were significantly lower in patients with MetS when compared with that of a healthy adult. Similar results were observed in these study.[9,11,12] Also, mean serum level of non-med patients were even slightly lower than the medicated patients. Low magnesium levels have been implicated as an important pathogenic factor in most of the disorders of MetS.[13] Its low levels promote endothelial cell dysfunction. Endothelial dysfunction forms the basis of development of several components of MetS including hypertension, blood lipid disorders, and thrombosis.[10]. Also, acts as a modulator of contraction of smooth muscle of vessel wall. Magnesium stimulates the production of vasodilator substances such as prostacyclin and nitric oxide and decreases the production of endothelial-derived vasoconstrictors such as endothelin-1,[14] which was similar to this study. Deficiency of this cation causes increased...
sympathetic nervous system activity thereby leading to elevated BP.[15]
A case-control study showed that both serum and intracellular magnesium were inversely related with body mass index (BMI) in patients with MetS. [16] which supported our study. Despite many studies showing the positive impact of drug intake on metabolic diseases[17], our study hypothesized that drug effect on serum magnesium, endothelial health as well as components of MetS on short duration was not only weak but also weakly correlated among the parameters.

"5. Conclusion"

Unlike the anticipation, serum magnesium showed a very obscure correlation with endothelial function and basic criteria of Metabolic syndrome given by ATP III, speculating that medication as such have no sole drastic impact in short duration on the overall health of patients. Hence, indicating an opting for healthy life practices to aid the drug effect.

"6. Limitation"

The severity of the case was ambiguous, as well as the drug applied among patients, varied. Furthermore, most of the patient were illiterate which hindered the questionnaire session contributing to reduced sample size.

"7. Acknowledgment"

We extend my heartiest gratitude towards Department of Biochemistry, SMS&R, Sharda University, Greater Noida for being very supportive.

"8. Conflicts of Interest"

No conflict of interest

"9. References"

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