Original Article

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Association between Serum Magnesium to Calcium Ratio with Level of Asthma Control in Children

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Abstract

Introduction: Bronchial asthma is an inflammatory reversible obstructive airway disease. This study aims to determine the association between serum magnesium to calcium ratio with level of asthma control in children by comparing serum magnesium to calcium ratio between - children with well controlled, partly controlled and uncontrolled asthma.

Methods: An analytical cross sectional study was done on 90 children diagnosed with bronchial asthma between five to 12 years age from January 2019 to June 2020. Children were selected from the outpatient and inpatient departments of paediatric medicine of a tertiary care medical college hospital. They were classified into well controlled, partly controlled and uncontrolled groups as per Global Initiative for Asthma (GINA) assessment of asthma control in children. The serum magnesium to serum calcium ratio of these children were compared between the groups classified.

Results: Mean level of serum magnesium to calcium ratio in well controlled group was 0.29857 (SD 0.07633), partly controlled 0.2439 (SD 0.0532), uncontrolled 0.2545 (SD 0.04467), respectively. Serum magnesium to calcium ratio more than or equal to 0.3 was positively correlated with well controlled asthma. Comparisons of serum magnesium to calcium ratio of well controlled group with partly controlled, uncontrolled and both partly and uncontrolled were statistically significant.

Conclusions: Higher serum magnesium to calcium ratio is associated with well controlled asthma. In our study, serum magnesium to calcium ratio more than 0.3 is significantly associated with well controlled asthma.

Introduction

Bronchial asthma is a chronic inflammatory reversible obstructive airway disease with bronchial hyper-responsiveness resulting from heterogenous genetic and environmental interaction which is still not clearly understood.[1] It is a common cause of morbidity in children. It has a problem of partly controlled and poorly controlled status. There has been a search to find a marker for bronchial asthma

control. It was serum magnesium,[2,3] erythrocytic magnesium,[4,5] polymorphonuclear magnesium,[6] hypomagnesemia and hypophosphatemia[7,8] in different studies.

Precise mechanism by which magnesium produces smooth muscle relaxation is not known.[9] But review of literature shows magnesium possibly has beneficial effect in bronchial asthma through its action at different sites through different mechanisms. It is supposed to enhance calcium uptake in the sarcoplasmic reticulum and / or as a calcium antagonist.[10] Magnesium regulates a number of enzymatic and cellular activity as a cofactor.[11] Other beneficial effect in asthma is through inhibition of release of acetylcholine from cholinergic nerves[12] and reduced release of histamine from mast cells.[13] Increased bronchial smooth muscle contractility with consequent bronchial hyper-reactivity is characteristic pathophysiological event of asthma. Magnesium constitutes an important determinant of contraction / relaxation state of bronchial smooth muscle.[14] Calcium ions (Ca^{2+}) participate in the pathogenesis of asthma. Increased cytosolic concentration of free Ca^{2+} must develop among others to trigger smooth muscle contraction.[3] Magnesium has a beneficial effect in bronchial asthma acting through a number of ways including direct bronchodilating action and being a natural calcium antagonist.

Search is on to find markers of bronchial asthma control in the form of serum magnesium,[2,3] erythrocytic magnesium,[4,5] polymorphonuclear magnesium,[6] hypomagnesemia and hypophosphatemia.[7,8] But none has become popular. As magnesium and calcium are antagonistic to each other and magnesium has beneficial bronchodilating effect and reduces bronchial hyperreactivity[15] while calcium causes contraction, the ratio of magnesium and calcium can have an association between level of asthma control. The objective of this study is to find the correlation between serum magnesium to calcium ratio and level of control of asthma.

Methods

An analytical cross sectional study was done on 90 children between five to 12 years age group diagnosed as bronchial asthma in the Department of Paediatrics in a tertiary care medical college hospital in India. Children with diagnosed asthma either admitted in the Paediatric Medicine ward or attended outpatient department (OPD) including Asthma clinic were included in the study. Children with respiratory tract infection like pneumonia, bronchiolitis, tuberculosis, those with any chronic illness and malnutrition were excluded from the study. The study was done between January 2019 to June 2020 for a period of one and half years. They were classified into well controlled, partly controlled and uncontrolled groups as per Global Initiative for Asthma (GINA) assessment of asthma control in children. Ethical clearance was taken from the institutional ethics committee. Serum magnesium to calcium ratio of the children were compared between the above mentioned classified groups. The data were tabulated using Microsoft excel software. For comparison between the groups, Mann Whitney U test was employed.

Results

Table 1 shows the distribution of serum magnesium to calcium ratio in the groups with different levels of asthma control. Number of subjects in the well-controlled group 21, partly controlled group 31 and uncontrolled group 38, total 90. Mean level of serum magnesium to calcium ratio in well controlled group was 0.29857 (SD 0.07633, Range 0.181-0.470), in partly controlled group was 0.2439 (SD 0.0532, Range 0.172-0.398) and in uncontrolled group was 0.2545 (SD 0.04467, Range 0.191-0.369).

Table 1. Distribution of serum magnesium to calcium ratio according to the level of asthma control

A	B	C	D	F	F
Well controlled	21	0.29857	0.07633	0.181	0.470
Partly controlled	31	0.2439	0.0532	0.172	0.398
Uncontrolled	38	0.2545	0.04467	0.191	0.369

Note: A = Level of asthma control, B = Number of Subjects, C = Mean, D = SD, E = Minimum value, F = Maximum value

Mean serum magnesium to calcium ratio in the well-controlled group in our study was 0.29857. Rounded value was taken as 0.3. The number of cases in well - controlled group were 21 and those with serum magnesium to calcium ratio more than or equal to 0.3 in this group were eight. Number of cases in the partly and uncontrolled groups were 69 and those with serum magnesium to calcium ratio more than or equal to 0.3 in these groups were 8. The odds ratio was calculated to be 4.6923 which shows that serum magnesium to calcium ratio more than 0.3 is positively correlated with well controlled asthma.

When we compared the serum magnesium to calcium ratio in well controlled group with partly controlled and uncontrolled group combined together, it was statistically significant with a Z score of 2.80945 and p-value of 0.00496. Similarly, while comparing well controlled group with uncontrolled group, it was also statistically significant (Z score of 2.38259, p-value 0.01732). The ratio was also statistically significant when well controlled group was compared with partly controlled group (Z score 2.67617, p-value 0.00736). (Table 2)

Table 2. Comparison of serum magnesium and calcium ratio between different level of asthma control groups

S.No.	Comparison groups	Z score	p-value
1	Well controlled vs both partly controlled and uncontrolled	2.80945	0.00496
2	Well controlled vs uncontrolled	2.38259	0.01732
3	Well controlled vs partly controlled	2.67617	0.00736

Discussion

A study by V.M. Daliparty et al showed that serum magnesium levels have positive correlation with the level of symptom of asthma control. In uncontrolled asthma, significantly low magnesium levels were present hence showing its utility as a biomarker in assessing

control or severity of asthma.[16] In contrary, study by Chitamanni P et al showed that the prevalence of hypomagnesaemia was much lower than the earlier studies and there seems to be no significant association between serum magnesium and asthma symptom control.[2]

In a study done by Sein HH et al to determine the relationship of erythrocytic magnesium levels with the level of control of asthma in children, no significant intracellular magnesium deficiency was present in children with chronic bronchial asthma.[4] In another study lower erythrocyte magnesium was associated with acute asthma while plasma levels of magnesium (Mg) remained unchanged. This decrease in intracellular Mg content occurred regardless of the severity of the exacerbation and returned to normal values after achievement of control.[5] In a study done by Fantidis P et al which measured polymorphonuclear magnesium content in patients with asthma, low polymorphonuclear magnesium content was seen in patients with bronchial asthma.[6] In a study by Kilic et al[7] and OS Alamoudi[8], hypomagnesemia and hypophosphatemia were found to be the most common electrolyte abnormalities in patients with chronic stable asthma. There is no popular marker for association with level of control of asthma.

We observed that mean serum magnesium to calcium ratio in the well-controlled group was significantly more than that in the partly controlled and uncontrolled asthma. Serum magnesium to calcium ratio in the well controlled group was 0.29857 in our study. The figure was rounded to 0.3. Then we took magnesium to calcium ratio of 0.3 as the cut off value and compared those above or equal to it in the uncontrolled, partly controlled groups together and well controlled group. Odds ratio was calculated and a positive association between magnesium to calcium ratio of more than or equal to 0.3 with well controlled asthma was found. Serum magnesium to calcium ratio of 0.3 may be considered as optimum level of contribution from magnesium towards achieving well controlled asthma.

Also significantly higher level of serum magnesium to calcium ratio had a positive correlation with well controlled asthma when compared with partly controlled and uncontrolled groups combined together (Z score 2.80945, p-value 0.00496), uncontrolled group alone (Z score 2.38259, p-value 0.01732) and partly controlled group alone (Z score 2.67617, p-value 0.00736).

In an individual patient serum level of magnesium and calcium may be within normal reference range but the ratio between magnesium to calcium will determine the status of asthma control. If the ratio between magnesium to calcium is more than or equal to 0.3, it is in favour of magnesium and is associated with better asthma control status. Interventions can be done with fortification of food or supplementation with magnesium to maintain serum magnesium to calcium ratio above 0.3 to have beneficial effect in asthma control. Magnesium may be used as an adjunct to conventional treatment of bronchial asthma. The limitations in our study were single centred study, small sample size, patients were not longitudinally followed up to see whether fall or rise in serum magnesium to calcium ratio causes loss or gain of asthma control.

Conclusions

Higher serum magnesium to calcium ratio is associated with well controlled asthma and lower serum magnesium to calcium ratio is associated with partly controlled and uncontrolled asthma. When serum magnesium to calcium ratio is more than or equal to 0.3, it is associated significantly with well controlled asthma. It remains to be seen through larger studies whether 0.3 may be considered as optimum level of contribution from magnesium towards achieving well controlled asthma.

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