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Study of defect in calcium Homeostasis in Asthmatic children

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Abstract: Calcium and magnesium exert a major role upon diverse physiological process. Defect in calcium homeostasis have been seen in the asthma process. Antagonism of calcium and magnesium in the asthma and the beneficial effect of magnesium therapy in asthma have also been found in many studies. Children being the major target of asthma, we studied the blood levels of ionized calcium, total calcium, magnesium, sodium and potassium in 50 asthmatic children attending the pediatric OPD and compared with similar number of age and sex matched control. It was found that there was significant decrease in the levels of serum ionized calcium (1.15 ± 0.01 mmol/L), total calcium (8.93 ± 0.96mg/dl) and serum magnesium (1.91 ± 0.23 mg/dl)in asthmatic children as compare to the normal controls (1.24 ± 0.01 mmol/L), (9.35 ± 0.90 mg/dl) and (2.05 ± 0.23 mg/dl) respectively. The significant decrease was irrespective with the age, gender of patients and the severity of disease. In study group serum sodium (138 ± 3.4 mmol/L) and potassium (4.13 ± 0.46 mmol/L) showed no significant difference as compared to normal control group (139 ± 3.4 mmol/L) and (4.2 ± 0.53 mmol/L) respectively. A defect in calcium homeostasis may lead to increased utilization and translocation i.e. higher influx of calcium ions in bronchial smooth muscle cells and variety of other cells for e.g. mast cells which might have caused its lowering in plasma, ionized calcium being a physically active fraction which account for nearly half of the total calcium levels. These results suggest that airway hyper-responsiveness may be associated with altered calcium mobilization in airway smooth muscles. Utilization of magnesium for antagonism of calcium in the asthma process might have caused significant lowering in serum magnesium levels in asthmatic children as compare to normal controls.

Key words: asthma, hyper-reactivity, ionized calcium, magnesium.

Introduction:

In all living being calcium exerts a major role upon diverse physiological processes. Ionic calcium is a physiological active fraction. With respect to asthma its potential role may influence many interrelated processes such as, smooth muscle tone and contraction, mucocilliary function, mast cell mediator release, involvement in inflammatory process, cellular permeability, neurotransmitter function and host of intracellular biochemical events. Its intracellular function is so vital that any drug or agent capable of regulating the entry of calcium into the cell can influence cellular events and metabolism as specific physiological changes [1].

Major element of smooth muscle tension development in asthma is due to an increase in intracellular calcium concentration after a variety of chemical, electrical or mechanical stimuli has been suggested [2].There is a possibility of disturbance of calcium homeostasis [3] in asthma due to the fact that calcium plays a crucial role in the control of bronchial smooth muscles. Calcium also affects the vascular smooth muscle function [4] and low ionized calcium has been found in the patient of arterial hypertension. In vivo studies have shown that calcium antagonist have both an antihypertensive effect and also an attenuating effect on bronchial hyper reactivity [5]. Low level of ionized calcium has been observed in patients with exercise induced asthma [6]. With the possibility of defect in calcium metabolism it was our hypothesis that ionized calcium concentration might be reduced in asthmatic children.

Several authors have reported a beneficial effect with magnesium therapy in different type of asthma, including the inhibition of bronchoconstriction in asthmatic patients, challenged with a methacholine or histamine bronchoprovocation test [7]. It has been postulated that, the therapeutic effect of magnesium in asthma derives from its action in modulation of smooth muscle contractility and in mediator release through its antagonism of the action of calcium at any one of the several sites. [8, 9]

Material and Method:

Present study was carried out in Department of Biochemistry. The permission of the ethical committee was also sought to carry out the present study. Blood samples of 50 (26 males, 24 females) children who came to pediatrics OPD with asthmatic episodes were included in the study. Informed written consent was taken from the

parents of the asthmatic children for this study. Blood sample was collected and analyzed for below given parameters. Serum ionized calcium sodium and potassium were analyzed on ISE based [10] electrolyte analyzer, Easylyte, from Transasia. Total calcium was measured by O cresolphthalein complexone [11] method on semiautomatic analyzer. Serum magnesium [12, 13] was estimated by spectrophotometric method using Randox kit called as magnesium calmagite. Out of total 50 children 18 were having severe symptoms. Equal number of healthy age and sex matched controls (28 males, 22 females) were selected for comparison. All the statistical comparisons were done by using Paired student's t test.

Observations and Results:

In the present study, the result was expressed as mean ± SD in a tabular form. A p value of < 0.05 was considered statistically significant. The total number of 50 asthmatic children was in the age group of 2 to 12 years with similar age matched controls. It was observed that the serum ionized calcium concentration in the asthmatic children (1.15 ± 0.01mmol/l) was significantly low as compared to the normal controls (1.24 ± 0.01mmol/l) P< 0.001. Total serum calcium and magnesium level in asthmatic children were also significantly low in asthmatic children (8.93 ± 0.96 mg/dl) and (1.91± 0.23 mg/dl) respectively as compare to the normal controls (9.35 ± 0.90 mg/dl) and (2.05 ± 0.23) respectively P< 0.05. The highly significant low level in asthmatic children was irrespective of gender of subjects and severity of symptoms. The levels of other electrolytes like serum sodium and potassium were not significantly different from that of normal controls.

Table 1: **Serum electrolytes in asthmatic children**

Serum Electrolytes	Normal Controls (50)	Asthmatic children (50)
Ionized calcium mmol/L	1.24 ± 0.01	1.15 ± 0.01**
Total calcium mg/dl	9.35 ± 0.90	8.93 ± 0.96*
Magnesium mg/dl	2.05 ± 0.23	1.91± 0.23*
Sodium mmol/L	139± 3.4	138± 3.4
Potassium mmol/L	4.2 ± 0.53	4.13 ± 0.46

Number in parenthesis indicate number of individuals incorporated in the study
***P< 0.05 ,**P< 0.001**

Table 2: **Serum electrolytes and sex variation in asthmatic children**

Serum Electrolytes	Normal controls		Asthmatic children	
	Male (26)	Female (24)	Male (28)	Female (22)
Ionized calcium mmol/L	1.24 ± 0.01	1.24 ± 0.02	1.16 ± 0.01	1.15 ± 0.01**
Total calcium Mg/dl	9.37 ± 0.76	9.34 ± 0.76	8.95 ± 0.82	8.90 ± 0.80*
Magnesium mg/dl	2.05 ± 0.36	2.04 ± 0.29	1.91 ± 0.21	1.90 ± 0.19*
Sodium mmol/L	139 ± 3.3	139 ± 3.5	139 ± 3.4	137 ± 3.6
Potassium mmol/L	4.2 ± 0.61	4.17 ± 0.40	4.11 ± 0.52	4.13 ± 0.35

Number in parenthesis indicate number of individuals incorporated in the study
***P< 0.05, **P< 0.001**

Table 3: **Serum electrolytes according to the severity of asthma**

Serum Electrolytes	Normal Controls (50)	Severe Asthmatics (18)	Mild Asthmatics (32)
Ionized calcium mmol/L	1.24 ± 0.01	1.16 ± 0.02**	1.15 ± 0.01**
Total calcium Mg/dl	9.35 ± 0.90	8.91 ± 0.95*	8.89 ± 0.94*
Magnesium mg/dl	2.05 ± 0.23	1.92 ± 0.14*	1.91 ± 0.21*
Sodium mmol/L	139 ± 3.4	139 ± 3.6	137 ± 3.5
Potassium mmol/L	4.2 ± 0.53	4.02 ± 0.32	4.2 ± 0.50

Number in parenthesis indicate number of individuals incorporated in the study
***P< 0.05, **P< 0.001**

Discussion:

It has been well established that the principle pathogenic features of asthma are ultimately calcium [14] related phenomenon, such as smooth muscle contraction, mast cell chemical mediator secretion, mucous gland secretion and vagal cholinergic reflex activity. More specifically in the cell types, the availability of the free calcium ion for excitation-contraction coupling, stimulus-secretion coupling and nerve impulse conduction, determines significantly the smooth muscle contractility, mast cell mediator secretion, mucous gland secretion and vagus nerve activity etc.

During the course of present study the mean serum calcium and ionized calcium concentration in the asthmatic children was found to be significantly low as compared to the normal controls. It may be contented that such lowering may be due to the increased infiltration of calcium ions into the tissue cells. This contention gains support from the findings of Kuruda S et al. [15], who confirmed beyond doubt that an elevation in the levels of intracellular calcium in asthmatic adults.

The characteristic features of asthma are due to extreme sensitivity of the airway to physical, chemical and pharmacological stimuli. Exposure of the airway to antigen, bacterial infection and environmental pollutants such as fog, smoke may cause a defect in calcium homeostasis [16], leading to increased permeability, translocation and utilization of calcium in a variety of cells such as mast cells, neutrophils and respiratory smooth muscle cells. Thus with its increased utilization and translocation i.e. higher influx of calcium ions in these cells, might have caused its lowering in plasma. It is also well understood that the ionized calcium is a physically active fraction which account for nearly half of the total calcium levels. [17]

Another important divalent cation, serum magnesium in the asthmatic children was found to be decreased significantly. Similar type of finding has been reported by Rolla G et al. [18] in the individuals with bronchial hyper-reactivity. The reason for such significantly low levels of serum magnesium in asthmatic children is not clearly understood. However, it would be pertinent to mention here that, the role of magnesium as a cation, which has a modulatory effect on the contractile state of smooth muscle cells in the various tissues: Hypomagnesaemia leads to

contraction, [19, 20] hypermagnesaemia to relaxation [19, 21]. The relationship between the hypomagnesaemia and increased contractile state may be explained by the antagonism between magnesium and calcium in the cell, and the inhibitory effect of magnesium on the secretion of acetylcholine from the presynaptic neurons [19, 22]. As asthma is characterized by widely varying degrees of contraction of bronchial smooth muscle, magnesium deficiency could have a negative effect on the asthmatic patient, increasing the contracting state of the bronchial smooth muscle. This notion could also be supported by the fact that magnesium infusion was found to improve the pulmonary function in asthmatic adults [8, 23].

The level of serum sodium and potassium shows no signification variation in asthmatic children as compared to normal controls.

In conclusion, we suggest that serum calcium specially the ionized calcium and serum magnesium levels should be checked in children with bronchial asthma and the low levels should be promptly corrected, not only for its deleterious effect on respiratory muscle power but also for its possible contribution to bronchial hyper-reactivity.

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