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ORIGINAL ARTICLE

EVALUATION OF SERUM ELECTROLYTE CONCENTRATION DISTURBANCES AMONG ASTHMATIC PATIENTS

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ABSTRACT:
Introduction: Abnormal electrolyte concentrations in asthma patients can be attributed to low intake or secondary to asthma medications. Hypokalemia, hypomagnesaemia and hypocalcaemia are well known causes of cardiac arrhythmias. Thus the purpose of present study was to detect the frequency of electrolyte (Na^+, K^+, Ca^{++}, Mg^{++} and P) disturbances in asthmatic patients (chronic stable and acute exacerbation) and their effect on lung function parameters. **Material and Methods:** The present prospective study was conducted over 100 subjects including 50 asthmatic patients and 50 healthy age and sex matched controls. Asthmatic patients within 14 to 60 years age group were enrolled to evaluate the electrolyte disturbances in asthma patients. Baseline values of pulmonary function tests were measured before including the patient into the study. Serum levels of electrolytes: sodium, potassium, magnesium, calcium and phosphorus of both asthmatics and control group were observed. **Results:** Electrolyte disturbances were found in forty three patients out of fifty (86%).In 32% of patients, there was one electrolyte disturbance. 32% had two electrolyte disturbances; 30% had three electrolyte disturbances and 4% had four electrolyte disturbances. Hypomagnesemia (48%) and hypophosphatemia (48%) were found to be the two most common electrolyte disturbances in adult asthmatic patients.40% of patients had hypocalcemia with mean serum calcium levels of 8.8±0.64 mg/dl. Hypokalemia was observed in 14 out of 50 (28%) asthmatic patients with mean serum potassium levels of 3.93±0.69 meq/L with statistically significant results. **Conclusion:** Serum electrolytes should be checked during admission and atleast 2 hours of nebulisation. In patients with chronic asthma and exacerbation, care should be taken during acute management to avoid the adverse effects of bronchodilator therapy.
Keywords: Asthma, Electrolyte imbalance, Hypokalemia, Hypomagnesaemia, Hypocalcaemia

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INTRODUCTION

Asthma is a serious public health problem throughout the world affecting people of all ages.[1] Abnormal electrolyte concentrations in asthma patients can be attributed to low intake or secondary to asthma medications. Hypokalemia was the earliest electrolyte disturbance reported in acute asthma, and it was related to the use of β_2 agonist and aminophylline therapy.[2,3-5] Tremors, tachycardia, palpitation, and anxiety are well known side effects of β_2-agonists.[6]

Recently hypomagnesaemia, hypophosphatemia and hypocalcaemia have also been reported after the administration of beta 2 agonist in normal subject and asthmatic patient as well.[7,8-10] In acute asthma, an increase in the urinary excretion of calcium has also been reported in patients treated with IV aminophylline.[8] Electrolyte levels directly influence excitability of airways smooth muscles(ASM) by influencing the state of ion exchangers and Na^+/K^+ pump,[11-13] for example, hyponatremia inhibits Na^+/K^+ exchange, potassium free solution inhibit Na^+/K^+ pump and the addition of K^+ activates Na^+/K^+ pumping. Possible hypothesis that may lead to airway reactivity include a direct effect of electrolytes on bronchial smooth muscle contractility as well as potential enhancement of the release of mast cell-derived inflammatory mediators, possibly through airway osmolarity changes.[14] The mortality rate in patients with asthma is still rising and has been partly attributed to the adverse effects of beta 2 agonist administered for asthma management.[15-17] Hypokalemia, hypomagnesaemia and hypocalcaemia are well known causes of cardiac arrhythmias.[18-20] In addition, hypophosphatemia can worsen respiratory failure in severely ill asthmatic patients through impairment of respiratory muscle performance.[20] The prevalence of hypomagnesaemia in asthma is variable, although there are reports of significantly high prevalence of hypomagnesaemia both in acute asthma and chronic stable asthma when compared with general non asthmatic population.[21,22]

Thus the purpose of present study was to detect the frequency of electrolyte (Na^+, K^+, Ca^{++}, Mg^{++} and P) disturbances in asthmatic patients (chronic stable and acute exacerbation) and their effect on lung function parameters.

MATERIAL AND METHODS

The present prospective study was conducted at Guru Gobind Singh Medical College and Hospital, Faridkot, Punjab. Asthmatic patients within 14 to 60 years age group were taken from OPD and Indoor wards of TB and Respiratory Department. A total of 50 asthmatic patients and 50 controls were recruited.

Patients were diagnosed as asthmatic as per GINA guidelines. All patients were subjected to detailed history after taking written and informed consent and detailed systemic examination was carried out as per the Performa attached. Pregnant and lactating females and patients with history of other systemic disorders were excluded from the study.

Routine investigations i.e. Haemoglobin, total leukocyte count (TLC), differential leukocyte count (DLC), electrolytes (sodium, potassium), with standard laboratory technique were done. Chest X ray (PA view) was done. Special investigations Electrolytes (calcium, magnesium and phosphorus) with standard laboratory technique were done. The investigations were carried out by fully auto analyzer machine. Baseline values of pulmonary function tests were measured before including the patient into the study. Serum levels of electrolytes: sodium, potassium, magnesium, calcium and phosphorus of both asthmatics and control group were observed. Chi-square was used to evaluate data statistically with p value <0.005 considered as significant value.

RESULTS

Table 1 shows electrolyte disturbances among the study and control group. It was found in forty three patients out of fifty (86%) in study group. In 32% of patients, there was one electrolyte disturbance. 32% had two electrolyte disturbances; 30% had three electrolyte disturbances and 4% had four electrolyte disturbances. Electrolyte disturbance was found in twenty one patients out of fifty in control group. In 58% of patients, there was no electrolyte disturbance. 36% had one electrolyte disturbance and 6% had two electrolyte disturbances.

Table 2 shows the ranking of the most commonly disturbed electrolytes. Magnesium and phosphorus showed equal and the highest proportion of disturbance, followed by calcium and potassium. Sodium disturbance was found in least number of patients. In this study in case group twenty four patients were having hypomagnesemia (table 3) and 26 were having normal magnesium levels.

Table 1: Proportion of electrolyte disturbances in study and control group

Proportion of electrolyte disturbances	Cases	Controls
No electrolyte disturbance	**7**	**29**
One electrolyte disturbance	**14**	**18**
Two electrolyte disturbances	**14**	**3**
Three electrolyte disturbances	**13**	**0**
Four electrolyte disturbances	**2**	**0**
Total	**50**	**50**

Table 2: Serum level, frequency and percentage of cases with disturbed electrolytes in study group (n-50)

Electrolytes	Serum levels	Frequency
Magnesium	1.47±0.56	24 (48%)
Phosphorus	3.46±0.74	24 (48%)
Calcium	8.83±0.64	20 (40%)
Potassium	3.93±0.69	14 (28%)
Sodium	139±9.86	09 (18%)

But in control group only three were having hypomagnesemia. Data was statistically significant with p-value <0.05. In this study, in case group twenty four patients were having hypophosphatemia (table 4) and twenty six were having normal phosphorus levels. But in control group only two were having hypophosphatemia. Data was statistically significant with p-value <0.05. In this study, in case group twenty patients were having hypocalcemia (table 5) and thirty were having normal calcium levels. But in control group also fifteen were having hypocalcemia. Data was not statistically significant with p-value >0.05. Difference between calcium disturbances among the cases and control group was not statistically significant.

In this study, in case group fourteen patients were having hypokalemia (table 6) and thirty six were having normal potassium levels. But in control group only three were having hypokalemia. Data was statistically significant with p-value <0.05.

Table 3: Frequency of magnesium disturbance and its comparison between two groups

Magnesium levels	Cases	Controls
Hypomagnesemia	24	3
Normal	26	47
Total	50	50
p-value	0.000 (S)	

Table 4: Frequency of phosphorus disturbance and its comparison between two groups

Phosphorus levels	Cases	Controls
Hypophosphatemia	24	2
Normal	26	48
Total	50	50
p-value	0.000 (S)	

Table 5: Frequency of calcium disturbance and its comparison between two groups

Calcium levels	Cases	Controls
Hypocalcemia	20	15
Normal	30	35
Total	50	50
p-value	0.000 (S)	

Table 6: Frequency of potassium disturbance and its comparison between two groups

Potassium levels	Cases	Controls
Hypokalemia	14	3
Normal	36	47
Total	50	50
p-value	0.003 (S)	

Table 7: Frequency of sodium disturbance and its comparison between two groups

Sodium levels	Cases	Controls
Hyponatremia	9	1
Normal	41	49
Total	50	50
p-value	0.008 (S)	

In this study, in case group nine patients were having hyponatremia (table 8) and forty one were having normal sodium levels. But in control group only one was having hyponatremia. Data was statistically significant with p-value <0.05. Difference between sodium disturbances among the cases and control group was statistically significant.

DISCUSSION

Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. Asthma involves a complex interaction of airflow obstruction, bronchial hyperresponsiveness and an underlying inflammation. The chronic inflammation causes recurrent episode of wheezing, breathlessness, chest tightness, and cough, particularly at night and in early morning. These episodes are usually associated with wide spread but variable airflow obstruction that is often reversible either spontaneously or with treatment.[23]

The magnesium (Mg^{++}) is the most abundant intracellular cation. Magnesium plays a crucial role in the regulation of bronchial smooth muscle contractility and hyper-responsiveness. There have been many studies on the relationship between asthmatic exacerbation and blood magnesium level.[24] In addition, there are links between magnesium deficiency with increasing tracheobronchial hyperreactivity and decreasing lung function.[25,26] The intracellular influx of calcium (Ca^{++}) causes bronchial smooth-muscle contraction. Recently, experimental evidences suggest that modification of potassium channel activity may induce bronchodilation, reduce cough and mucus production and inhibit airway inflammation and remodelling.[27-28] In addition, controlling voltage gated sodium channel in the central nervous system and lung tissue can lead to safer strategies for asthma prevention and treatment. Deficiency enhances the action of calcium on the airway smooth muscles and vice versa. Animal experiments have shown that the hyperreactivity of sensitized bronchial smooth muscle is associated with an exaggerated influx of sodium across the cell membranes.[29] It is possible that this inhibits the exchange mechanism of sodium and calcium ions resulting in raised intracellular calcium and thus increased contractility.[30] High sodium consumption may enhance this abnormality. High sodium intake has been shown to inhibit Na^+/K^+ ATPase in erythrocytes of normotensive males.[31] The resulting inhibition of the Na^+/K^+ pump would be expected to increase levels of intracellular sodium and, in turn, to increase intracellular calcium via inhibition of Na^+/Ca^{++} exchange. Serum phosphate or phosphorus (P) normally ranges from 2.5 to 4.5 mg/dl (0.81–1.45mmol/l) in adults. Hypophosphatemia is defined as mild (2–2.5 mg/dl or 0.65–0.81mmol/l), moderate (1–2 mg/dl or0.32–0.65mmol/l), or severe (<1 mg/dl or 0.32mmol/l).[32] Phosphorus is a vital component of cellular membranes, enzyme systems, nucleic acids and various nucleoproteins.[33] Serum phosphorus concentrations lower than 1 mg/dl for two or more days can lead to serious complications, such as rhabdomyolysis, respiratory failure, acute hemolytic anemia and arrhythmias.[34]

In our study electrolyte disturbances were found in forty three patients out of fifty (86%). In 32% of patients, there was one electrolyte disturbance. 32% had two electrolyte disturbances; 30% had three electrolyte disturbances and 4% had four electrolyte disturbances. In the study conducted by Alamoudi OSB[35] 2001 electrolyte disturbances were found in 43% of the patients; 85% of the patients had one electrolyte disturbance, 10% had two electrolyte disturbances, and 5% had three electrolyte disturbances. Mohammad HA et al[36] in a prospective study detected electrolyte disturbances in up to 68% of patients with chronic stable asthma and a higher percentage in acute severe asthma (98%).

In the present study, hypomagnesemia (48%) and hypophosphatemia (48%) were found to be the two most common electrolyte disturbances in adult asthmatic patients (serum levels were 1.47±0.56 mg/dl and 3.46±0.74mg/dl respectively) followed by hypocalcemia (serum levels were 8.83±0.64 mg/dl). The lowest proportions were for potassium (28%) and sodium (18%) [serum levels were 3.93±0.69 meq/L and 139±9.86 meq/L respectively]. In the study conducted by Alamoudi OSB[35] 2001 the highest proportions were for magnesium (26.9%) and phosphorus (15.1%) [serum levels were 0.69 +/- 0.04 mg/dl and 0.64 +/- 0.09 mg/dl, respectively], the lowest proportions were for potassium (5.4%) and sodium (4.3%) [serum levels were 3.3 +/- 0.01 meq/L and 133 +/- 0.01 meq/L, respectively] and no patient had a calcium disturbance. A study conducted by Mohammad HA et al[36] stated that hypomagnesemia was the most common electrolyte disturbance in patients with chronic stable asthma and in those with acute attacks, with a prevalence of 50% and 92%, in both groups respectively. In our study the mean levels of magnesium in asthmatic patients was 1.47±0.56

mg/dl with 48% patients having hypomagnesemia. Agin K et al[37] reported that hypomagnesemia occurred in 40.5% of chronic stable asthmatic patients and the mean levels of magnesium in those patients was 1.85±0.28 mg/dl. In our study a statistically significant decrease in serum magnesium levels was found in patients with asthma as compared to normal controls. Some reports in the past have showed an association between magnesium deficiency and an increased airway hyper reactivity which suggests that magnesium ions participate in numerous biochemical and physiological processes that directly influence lung function and respiratory symptoms.

In our study the mean levels of phosphorus in asthmatic patients was 3.46 ±0.74 mg/dl and 48% of the asthmatic patients were having hypophosphatemia which was higher than other studies in the past. In our study a statistically significant decrease in serum phosphorus levels was found in patients with asthma as compared to normal controls. Alamoudi OSB[35] 2001 reported that hypophosphatemia occurred in 15.5% of patients with chronic stable asthma with mean phosphorus levels of 0.64±0.09 mg/dl.

Hypophosphatemia has also been reported in patients with acute asthma treated with nebulized β_2 agonists, IV aminophylline and hydrocortisone. IV infusion of β_2 agonists can cause dose related hypophosphatemia probably through intracellular shifts of phosphorus ions. Hypophosphatemia can cause myocardial depression, respiratory muscle fatigue, and reduction of tissue oxygen extraction in patients with acute asthma. Therefore, patients with chronic asthma and hypophosphatemia may be at high risk if they have an exacerbation.[35]Hypokalemia was observed in 14 out of 50 (28%) asthmatic patients with mean serum potassium levels of 3.93±0.69 meq/L with statistically significant results. Priyadarshini G et al[38] found hypokalemia in 8% of the patients in the beginning of the study, which increased to 26%, 18% and 12% at 90min, 180min and 24hours respectively after starting nebulization. The present work confirmed that the incidence of hyponatremia is low (18%) in adult asthmatic patients and this is consistent with the results of Alamoudi OSB[35] who reported hyponatremia in 4.3% of the patients with stable bronchial asthma. In our study a statistically significant difference in serum sodium levels was found between the asthmatic patients and the control group This may be related to the fact that theophylline increases production of urine and enhances excretion of water and electrolytes. Although the total number of patients with chronic asthma and low serum levels were too small to draw a clear conclusion about its prevalence. In our study, prevalence of electrolyte disturbances in asthmatic patients was found to be high. Therefore, in patients with chronic asthma and exacerbation, care should be taken during acute management to avoid the adverse effects of bronchodilator therapy. In presence of one or more abnormal electrolyte levels (hypomagnesemia, and/or hypophosphatemia, and/or hypokalemia), the use of therapies like β_2 agonists and IV aminophylline can increase the derangement of the existing abnormal electrolyte levels.

CONCLUSION

Current data suggests that electrolyte disturbances are common in asthma. Hypomagnesemia (48%) and hypophosphatemia (48%) were found to be the most common electrolyte disturbances in our study. Therefore, serum electrolytes should be checked during admission and atleast 2 hours of nebulisation. In patients with chronic asthma and exacerbation, care should be taken during acute management to avoid the adverse effects of bronchodilator therapy.

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