



## Electrolytes levels in asthmatic patients

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### ABSTRACT

**Background:** abnormal electrolytes concentrations in asthma patients can be attributed to low intake or secondary to asthma medications.

**Objectives:** to identify the pattern of changes in electrolytes concentrations among asthmatic patients and to detect correlations between concentrations of electrolytes and pulmonary function measurements.

**Materials and Methods:** the study involved a control group of 56 non-asthmatic subjects matched for gender and age with a study group of 100 patients with a medical history of asthma but no other respiratory diseases. IQ TQ Spirometer was used to assess pulmonary function according to ATS/ERS standards. Sodium, potassium, calcium and magnesium concentrations were measured from venous blood samples.

**Results:** There were significant positive correlations between potassium concentration and FEV<sub>1</sub>, FEV<sub>50%</sub>, FEV<sub>25-75%</sub> (P < 0.05) and negative correlation between sodium concentration and FEV<sub>1%</sub>, FEV<sub>1</sub>/FEV<sub>6</sub>, FEV<sub>25%</sub>, FEV<sub>75%</sub>, FEV<sub>25%-75%</sub>, FEV<sub>85%-75%</sub> (P < 0.05). None of the electrolytes showed significant differences in the mean when asthmatic patients were compared with control group (P > 0.05).

**Conclusion:** sodium and magnesium concentrations of asthmatic patients showed no significant differences in the means when compared with the control group, but elevated levels of sodium were associated with poor ventilatory function. High levels of potassium were associated with better pulmonary ventilation.

**Keywords:** electrolytes, asthma, pulmonary function.

### 1. INTRODUCTION

Abnormal electrolytes concentrations in asthma patients can be attributed to low intake<sup>1-4</sup> or secondary to asthma medications<sup>5-8</sup>. Electrolytes levels directly influence excitability of airways smooth muscles (ASM) by influencing the state of ion exchangers and Na<sup>+</sup>/K<sup>+</sup> pump<sup>9-11</sup>. For example, hyponatremia inhibits Na<sup>+</sup>/Ca<sup>++</sup> exchange<sup>10</sup>, K<sup>+</sup>-free solution inhibit Na<sup>+</sup>/K<sup>+</sup> pump and the addition of K<sup>+</sup> (10 or 30 mM) activates Na<sup>+</sup>/K<sup>+</sup>-pumping<sup>11</sup>. Recently, experimental evidences suggest that modification of K<sup>+</sup> channel activity may induce bronchodilation, reduce cough and mucus production and inhibit of airway inflammation and remodeling<sup>12-13</sup>. In addition, controlling voltage-gate sodium channel in the central nervous system and lung tissue can lead to safer strategies for asthma prevention and treatment<sup>14</sup>. Possible

hypotheses that may lead to airway reactivity include direct effect of electrolytes on bronchial smooth muscle contractility<sup>10</sup> as well as potential enhancement of the release of mast cell-derived inflammatory mediators, possibly through airway osmolarity changes<sup>15,16</sup>. Hypocalcaemia had been reported in healthy subjects following administration of intravenous  $\beta$ 2-agonists that cause an increase in the urinary excretion of calcium<sup>17</sup>. In acute asthma, an increase in urinary excretion of calcium has also been reported in asthmatic patients treated with intravenous aminophylline<sup>8</sup>. Recently, there has been increasing interest in the possible link between vitamin D and asthma. Further clarification of the role of vitamin D in the lung functions and immunity may hold profound implications for the prevention and treatment of

asthma<sup>3,18,19</sup>. In contrast, short-term magnesium supplementation trials to assess the effects of supplemental magnesium on lung function and symptoms among patients with asthma have had mixed results. High magnesium intake was associated with improvement in asthma symptom, though not in measures of airflow or airway reactivity<sup>20</sup>. This study aims to detect the effects of electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Ca<sup>++</sup> and Mg<sup>++</sup>) on lung function parameters.

**2. PATIENTS AND METHODS**

The study received an ethical approval from the ethical committee at the faculty of medicine – University of Khartoum - Sudan. All volunteers were informed about the purpose and methods of the study prior their examinations.

The study involved fifty-six healthy subjects recruited mainly from university students and employees and one hundred asthmatic patients selected from chest clinics of teaching hospitals in Khartoum state – Sudan. Asthma history and drug therapy were recorded to assess asthma activity at the time of examination. Patients were grouped according anti-asthma medications taken during the time of examination into asthmatics not taking beta agonists and steroids, asthmatics taking beta agonists only, asthmatics taking steroids only and asthmatics taking both beta agonists and steroids. IQ TQ Spirometer (Version 5.18 - Clement Clarke International Limited – U. K) was used for assessing pulmonary function according to ATS/ERS standards<sup>21</sup>. BS-200 Chemical analyzer (Shenzhen Mindray Bio-Medical Electronics – China) was used for estimation of calcium and magnesium concentrations. Flame photometer 410 (Sherwood Scientific Limited – U. K) was used for estimation of sodium and potassium concentrations. Ten calcium and three magnesium samples were damaged and give zero results and therefore were not considered in data analysis.

Screening studied variables for significant differences in the means between the groups was performed using analysis of variance. When significant differences were identified, individual groups were compared using the Student two-tailed, unpaired T-test. Significant correlations between electrolytes levels and pulmonary function were assessed using bivariate correlations. Adjustment for asthma medications was performed using the general linear model and partial correlations. In all of these statistical tests, only P < 0.05 was considered significant.

**3. RESULTS:**

Asthma medications, namely beta agonists and steroids, were introduced as a covariate when comparing serum electrolytes concentrations of asthmatics with control group (figures 1 and 2) and correlating spirometric measurements with electrolytes concentrations (table 1).

There were significant positive correlations between potassium concentration and FEV1, FEF<sub>50%</sub>, FEF<sub>25%-75%</sub> (P < 0.05) and negative correlation between sodium concentration and FEV<sub>1%</sub>, FEV<sub>1</sub>/FEV<sub>6</sub>, FEF<sub>25%</sub>, FEF<sub>75%</sub>, FEF<sub>25%-75%</sub>, FEF<sub>85%-75%</sub> (P < 0.05). None of the electrolytes showed significant mean differences when asthmatics are compared with control group. There was a significant difference in the mean of calcium concentration between asthmatic and control group (P = 0.002), which disappeared on adjustment for treatment.

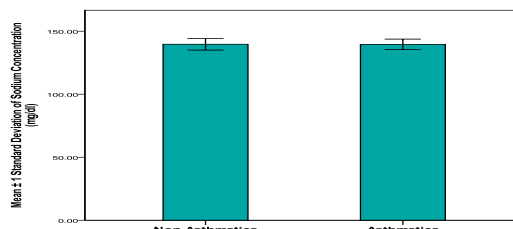


Figure-1: Comparison of sodium Concentrations between asthmatic patients and the control Groups.

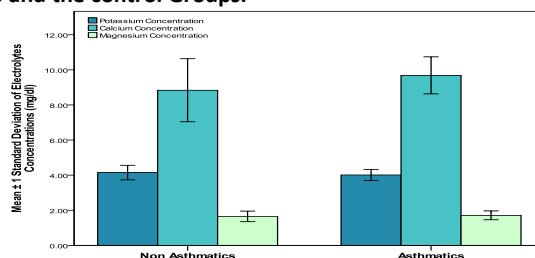


Figure-2: Comparison of potassium, calcium and magnesium Concentrations between asthmatic patients and the control Groups.

		S.[Na+]	S.[K+]	S.[Ca++]	S.[Mg++]
FEV1	CC	-0.149	0.175	0.037	0.003
	Sig.	0.076	0.036*	0.975	0.665
FVC	CC	-0.031	0.130	0.111	0.043
	Sig.	0.712	0.122	0.189	0.612
FEV1%	CC	-0.227	0.075	-0.132	-0.105
	Sig.	0.006*	0.370	0.117	0.214
FEV1/FEV6	CC	-0.223	0.085	-0.117	-0.092
	Sig.	0.008*	0.313	0.164	0.273
PEFR	CC	-0.157	0.141	-0.077	-0.028
	Sig.	0.061	0.094	0.364	0.739
FEF25%	CC	-0.191	0.154	-0.099	-0.033
	Sig.	0.022	0.067	0.237	0.692
FEF50%	CC	-0.142	0.170	-0.075	-0.056
	Sig.	0.091	0.043*	0.376	0.509
FEF75%	CC	-0.186	0.159	0.014	-0.037
	Sig.	0.026*	0.057	0.868	0.665
FEF25%-75%	CC	-0.169	0.176	-0.056	-0.050
	Sig.	0.044*	0.036*	0.504	0.551
FEF85%-75%	CC	-0.192	0.143	0.050	-0.023
	Sig.	0.022*	0.089	0.550	0.790

CC = Correlation Coefficient

Sig = Significance of the correlation

Table-1: Correlations between Spirometric Measurements and Electrolytes Concentrations Following Controlling for Drug Therapy in asthmatic group.

#### 4. DISCUSSION

Most previous studies on electrolyte disturbance in asthmatics have focused on asthma treatment as a contributing factor. This was especially true for Hypokalaemia<sup>7</sup>, Hypocalcemia<sup>6,17</sup> and hypomagnesaemia<sup>6,7</sup>. Therefore, asthma medication was introduced as a covariate during statistical analysis. In spite of the significant positive correlation of potassium and negative correlation of sodium with some spirometric measurements in asthmatics, none of these electrolytes showed significant mean differences when asthmatic patients were compared to control group. This is probably due to weakness of these correlations (correlation coefficients  $\leq 0.230$  for all significant correlations).

Association between sodium intake and asthma has been reported in some previous studies<sup>22,23</sup> but not in others<sup>24,25</sup>. The findings of the present study are consistent with lack of agreement of these studies. This is because sodium concentrations showed no significant differences in the means when asthmatic patients were compared with the control group, yet elevated levels of sodium were associated with poor ventilatory function. The reverse was true for potassium in which high levels were associated with better pulmonary ventilation. Possible mechanisms that may lead to airway reactivity include direct effect of sodium and potassium on ASM contractility<sup>10</sup> as well as augmentation of the release of inflammatory mediators, possibly through airway osmolarity changes<sup>15</sup>. The influences of salts on release of inflammatory mediators is further supported by Mickleborough et al study which demonstrated that dietary salt loading exacerbated the development of airway narrowing in guinea pigs by modifying leukotrienes secretion<sup>16</sup>.

It is noteworthy that insulin resistance<sup>26</sup> and high activity of renin-angiotensin system activity<sup>27,28</sup> were both reported to coexist with asthma. Insulin resistance and renin-angiotensin system have contradictory effects on  $\text{Na}^+/\text{K}^+$  pump and therefore may explain part of the lack of consistency of the results regarding sodium and potassium levels in asthmatics independently of dietary intake and asthma medication. However, studies in this field are scanty and the subject needs further exploration. In the present study there was no significant difference in the mean of the body mass index when asthmatic patients were compared with the control group. This precludes from drawing a conclusion that insulin resistance is linked to the present findings.

Interestingly, although there was significant difference in the mean of calcium concentration between asthmatic and the control group, it disappears on adjustment for treatment. However, hypocalcaemia had been reported in healthy subjects following administration of intravenous  $\beta_2$ -agonists that cause an increase in the urinary excretion

of calcium<sup>17</sup>. In acute asthma, an increase in urinary excretion of calcium has also been reported in asthmatic patients treated with IV aminophylline<sup>8</sup>. The findings of this study did not contradict previous studies, as none of asthmatic patients were receiving intravenous  $\beta_2$ -agonists or intravenous aminophylline during the measurement of their electrolytes concentrations.

Magnesium concentrations were not statistically different in asthmatic patient compared with that of the control group and there was no significant associations between magnesium concentrations and studied spirometric measurements. However, studies in asthma patients indicate that dietary magnesium intake and serum magnesium levels are lower than healthy controls<sup>4,23,24</sup>. The evidence suggests that magnesium ions participate in numerous biochemical and physiologic processes that directly influence lung function and respiratory symptoms. The mechanisms for effects on lung function include alteration in ASM function<sup>29</sup>, immune function<sup>30</sup> and oxidative stress<sup>31</sup>. When magnesium is deficient, the action of calcium is enhanced and an excess of magnesium blocks calcium. These interactions are important to the patient with respiratory diseases because the intracellular influx of calcium causes bronchial smooth-muscle contraction<sup>32</sup>.

It is important to remember that serum electrolyte levels, mainly magnesium and potassium, may not correctly reflect their intracellular levels. Skeletal muscle biopsies of asthmatics had lower magnesium and potassium concentrations compared with healthy controls, both with and without oral beta 2-agonists therapy<sup>6</sup>. Whether the findings are related to asthma pathophysiology or treatment remain for further investigations. A shortcoming of this study is that intracellular levels of electrolyte were not considered. Correlations between intracellular electrolyte levels of ASM and pulmonary function measurements, as well as, comparing electrolyte concentrations differences between intracellular and extracellular fluids in asthmatic patients and healthy subjects could offer better understanding about effects of electrolytes on ASM. The evaluation of intracellular electrolyte levels in ASM is technically difficult and additional studies are desirable to explore it.

In conclusion, the findings of the present study are consistent with lack of agreement of previous studies on electrolyte levels in asthmatic patients. For example, sodium concentrations showed no significant differences in the means when asthmatic patients were compared with the control group, yet elevated levels of sodium were associated with poor ventilatory function. The reverse was true for potassium in which high levels were associated with better pulmonary ventilation. Calcium concentrations were higher in asthmatics but did not achieve statistical

significance. Magnesium concentrations were not statistically different in asthmatic patient compared to the control group.

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