STUDY OF SERUM MAGNESIUM AND OTHER ELECTROLYTES IN PATIENTS OF ACUTE SEVERE ASTHMA RECEIVING PARENTERAL BETA ADERENERGIC AGONISTS.

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ABSTRACT

Asthma is a very common disease with immense social impact. Its acute exacerbations are commonly treated with salbutamol. The study intends to determine the magnitude of changes in serum magnesium, potassium, phosphate and calcium during treatment of acute severe asthma with parenteral salbutamol. This is a prospective study comprising of 80 patients who presented to casualty with symptoms of acute severe asthma and met the inclusion criteria. Baseline serum magnesium, potassium, phosphate and calcium levels were measured. Nebulised salbutamol was administered every thirty minutes till symptoms subsided. After 80 minutes, repeat serum levels of electrolytes were determined. Treatment followed with Parenteral salbutamol administration during the emergency treatment of acute severe asthma is associated with statistically significant decreases in serum magnesium, potassium, and phosphate levels. It is also associated with decrease in serum calcium levels, although the decrease was not statistically significant. The mechanism and clinical significance of these findings are currently unknown and warrant further study.

KEYWORDS: Asthma; Parenteral nebulisation; Salbutamol, Magnesium

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INTRODUCTION

Asthma is a very common disease with immense social impact. Bronchial asthma occurs at all ages, with slight male preponderance. The WHO defines asthma as, “A chronic condition characterized by recurrent bronchospasm resulting from a tendency to develop reversible narrowing of airway lumen in response to stimuli of level or intensity not inducing such narrowing in most individuals”. Asthma is defined as chronic inflammatory disease of airways that is characterized by increased responsiveness of the tracheobronchial tree to narrowing of the air passages, which may be relieved spontaneously or as a result of therapy, and clinically by paroxysms of dyspnoea cough and wheezing. Asthma is an episodic disease with acute exacerbations interspersed with symptom free periods, attacks are short lived, lasting minutes to hours, and clinically the patient seems to recover completely after an attack. Acute episodes of asthma are one of the most common respiratory emergencies. Asthma is a multifactorial disease with atopy as single largest risk factor. Other risk factors include genetic factors, pharmacological stimuli, environmental factors, occupational factors, infections, exercise and emotional stress. Avoidance of allergen and desensitization are less successful modes of treatment. Drug therapy is the most commonly used mode of treatment. Drugs used to treat asthma are β-adrenergic agonists, methyl xanthenes, glucocorticoids and mast cell stabilizing agents. β-Adrenergic agonists have been the primary focus of emergency management of acute severe asthma for over 50 years. Multiple inhalations of short acting sympathomimetic drugs, such as salbutamol, are the cornerstone of most regimens. Administration of nebulised salbutamol during emergency treatment of acute severe asthma was shown to be associated with significant decreases in serum magnesium, potassium and phosphate levels. Serum potassium concentrations decreased significantly 75 minutes after initiation of treatment with salbutamol. Magnesium relaxes the bronchial smooth muscle and produces dilatation of airways, may be by modulating calcium ion movement. Hypomagnesaemia conversely may produce bronchoconstriction. Hypomagnesemia may upset the neuromuscular mechanism to such an extent as to make certain individuals more susceptible to bronchial spasms. It is of interest that β-adrenergic agonists administered for bronchodilatation, cause hypomagnesemia, which in turn can cause bronchoconstriction. Studies have shown that magnesium sulphate used with salbutamol helps in poor responders of acute severe asthma. This study intends to measure and evaluate the changes in serum magnesium and other electrolyte levels on administration of β-adrenergic agonists in patients of acute severe asthma.

MATERIALS AND METHODS

Study included 80 clinically diagnosed cases of acute severe asthma getting admitted to the Casualty who fulfilled the inclusion criteria. Study spanned over a period of 15 months from August 2011 to October 2012. Inclusion and Exclusion criteria: Clinically diagnosed cases of acute severe asthma those were treated with parenteral β-adrenergic agonists. Study only included patients aged more than 16 years. All patients with chronic liver diseases, chronic renal failure and acute myocardial infarction were excluded. Patients of age less than 16 years, normal volunteers, pregnant women and psychiatric patients were also excluded from study group. Sample collection: Blood samples were drawn under aseptic precautions from clinically diagnosed cases of acute severe asthma before and after administration of β-adrenergic agonists. Both the blood samples...
were analyzed for study parameters. 3ml of blood sample was collected in a disposable syringe before the start of β–adrenergic agonist therapy. Precaution was taken to prevent sepsis and hemolysis. Repeat blood sample was drawn 80 minutes after starting β–adrenergic agonist therapy and processed similarly to separate serum. Serum levels of magnesium, calcium, potassium and phosphate were measured in both sets of serum samples. Serum magnesium levels were assessed by 'The Wako Magnesium B test kit method', which is an in vitro colorimetric method. Serum Calcium levels were measured by modified O- Cresolphthalein Comlexone (OCPC) method using semi auto analyzer using kit. Serum phosphorus levels were estimated by ammonium molybdate method using kit based on modified Daly and Ertingshausen’s method. Serum potassium is measured with the by a K⁺ ion selective electrode and For the tests conducted suitable controls were run according to protocols.

RESULTS

Statistical analysis: The levels of four variables (Magnesium, Calcium, Phosphate, and Potassium) were estimated twice, before and after the administration of salbutamol in same study group. Study group consisted of 80 clinically diagnosed cases of acute severe asthma. Results were tabulated and analyzed using “Paired ‘t’ test”. Difference between two sets of readings (A) was calculated and tabulated. Age and Sex Distribution in Table 1 and figure 1

<table>
<thead>
<tr>
<th>Age group</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30 years</td>
<td>1</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>31-50 years</td>
<td>2</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 50 years</td>
<td>0</td>
<td>07</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>32</td>
<td>8</td>
</tr>
</tbody>
</table>

1) Males are more affected by asthma than females can be appreciated from the figure.
Blood samples were drawn twice, first at admission, and repeat samples were drawn 80 minutes after administration of salbutamol for measurement of serum levels of magnesium, calcium, phosphate and potassium.

**Table 2**

*Changes in Serum Electrolyte Levels*

<table>
<thead>
<tr>
<th>Serum electrolytes</th>
<th>Mean Serum levels Before treatment with Salbutamol</th>
<th>After treatment with Salbutamol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium (mg/dl)</td>
<td>1.958</td>
<td>2.048</td>
</tr>
<tr>
<td>Calcium (mg/dl)</td>
<td>9.632</td>
<td>9.532</td>
</tr>
<tr>
<td>Phosphate (mg/dl)</td>
<td>3.743</td>
<td>3.689</td>
</tr>
<tr>
<td>Potassium (mEq/L)</td>
<td>4.154</td>
<td>4.054</td>
</tr>
</tbody>
</table>

![Figure 2](changes_in_serum Electrolyte Levels.png)

Changes in Serum Magnesium, Phosphate, Potassium Levels decreased significantly (p < 0.001) 80 minutes after administration of salbutamol, Changes in Serum Calcium Levels decreased which was statistically not significant (p > 0.10).

**DISCUSSION**

Bronchial asthma is a very common disease with prevalence of 10-12%. Although many modes of therapy are available, like avoidance, immunotherapy and drug therapy, none cure the disease. Drug therapy is the most commonly used mode of treatment, and in emergency situations, salbutamol is the cornerstone of the therapy. Few studies have demonstrated a significant reduction in serum magnesium levels after
treatment with salbutamol. Hypomagnesemia may upset the neuromuscular mechanism to such an extent as to make certain individuals more susceptible to bronchial spasms. It's noteworthy that, hypomagnesemia causing bronchoconstriction is a side effect of salbutamol which is a potent bronchodilator. The present study intends to determine the magnitude of changes in serum magnesium, potassium, phosphate and calcium during treatment of acute severe asthma with salbutamol. The study group consisted of 80 subjects, out of them 65 were aged<50 years and the rest 15 were aged >50 years. Among the 65 persons, 40 were men and 25 were women. In the 15 patients aged >50 years, 8 were men and 7 were women. The overall incidence of bronchial asthma is higher in males than in females in age group of <50 years so the incidence in men increases, as seen in our study group. In our study, serum magnesium levels were measured in patients of acute severe asthma before initiation of therapy and 80 minutes after administration of salbutamol. Serum magnesium reduced significantly (p < 0.001) after treatment with salbutamol. Bodenhamer J. and vittal also observed in their study, which was performed in similar clinical setting, that serum potassium levels decreased significantly (p = 0.0001). Hieronymus H. Vincent and co workers studied the effect of different β2 agonists on plasma potassium levels in hypertensive persons. They infused isoproterenol (a non selective β agonist), prenolterol (selective β1 agonist) and salbutamol (selective β2 agonist) in a stepwise increasing dose. This caused a dose dependent decrease in potassium with all three drugs, but the decrease was much greater with salbutamol. They inferred that the greater effect of salbutamol in reducing serum potassium levels is a β2 receptor mediated effect. Rolf Smith S. and co workers in their study also demonstrated a significant decrease of potassium levels when asthma patients were treated with inhaled bronchodilators such as salbutamol. Leitch AG and co workers studied effect of different β2 agonists on plasma potassium levels in hypertensive persons. Gregory and co workers studied the effect of intravenous salbutamol infusion on serum potassium levels in pregnant women. Both groups demonstrated a significant reduction in plasma potassium levels after salbutamol infusion. Hypokalemia is shown to occur in therapeutic and excessive doses of β2 agonists. This effect is attributed to activation of Na⁺-K⁺-ATPase enzyme and/or β2 receptor mediated insulin release, with consequent intracellular shift of potassium. There are also studies done on various diseases about levels of potassium which show significant changes.

In our study, serum phosphate levels showed a statistically significant (p < 0.001) decrease. Bodenhamer J and co workers studied the effect of frequently nebulised salbutamol on serum phosphate levels in patients of asthma. Effect of salbutamol on serum calcium in patients of acute severe asthma was included as an experimental
parameter. Serum calcium levels decreased but the decrease was not statistically significant (p > 0.10). Many studies suggest that intravenous magnesium sulphate (MgSO4) may be a beneficial adjunct to salbutamol therapy while treating acute severe asthma, as many patients showed better clinical improvement after addition of MgSO4 to the salbutamol therapy.3,7,20,21 Magnesium probably mediates its action by its inhibitory action on smooth muscle contraction, histamine release from mast cells, acetylcholine from nerve terminals, and sedative action.20 Hypomagnesemia in some asthmatic patients, both during and not during attack, has been reported.6 Probably magnesium sulphate corrects the hypomagnesemia in asthmatics due to salbutamol and adds to beneficial effect

SUMMARY AND CONCLUSION

Asthma is a very common disease with aetiology of complex phenomenon and it is a multi factorial disease. Asthma is an episodic disease with acute exacerbations interspersed with symptom free periods. Although symptomatically treated, asthma cannot be cured. So our treatment modalities and the drugs used should be understood to perfection. This study intends to evaluate the effects of salbutamol, most frequently used drug in the treatment of asthma, on selected serum electrolytes (magnesium, potassium, phosphate, and calcium). The study included 60 patients of acute severe asthma who were treated with nebulised salbutamol. Pre and post treatment levels of the electrolytes were measured and evaluated using statistical methods. Study results demonstrated a statistically significant decrease of serum magnesium, phosphate, and potassium levels after treatment with salbutamol.

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REFERENCES

9. Mann CK, Yoe JH, Spectrophotometric


19. K.sameera et.al ;Evaluation of serum LDH levels in thyphoid fever ;Int J Pharm Bio sci 2013 Jan;4(1);(B)944-950


21. S Mittal, KK Dwivedi, VK Goel, TN Malhotra, VS Singh. Effect of Intravenous Magnesium Sulphate on β2 stimulant aerosol therapy in acute bronchial asthma. JAPI 1991; 39/1: 42-43