JOURNAL OF CLINICAL AND DIAGNOSTIC RESEARCH

How to cite this article:
VITTAL B G, RUDRESHA B M, ALIYA N, PRIYADARSHINI K S. A STUDY OF SERUM ELECTROLYTE LEVELS DURING NEBULISED SALBUTAMOL THERAPY. Journal of Clinical and Diagnostic Research [serial online] 2010 December [cited: 2010 December10]; 4:3460-3464.

Available from
http://www.jcdr.in/article_fulltext.asp?issn=0973-709x&year=2010&volume=4&issue=6&page=3460-3464&issn=0973-709x&id=822

ORIGINAL ARTICLE

A Study Of Serum Electrolyte Levels During Nebulised Salbutamol Therapy

VITTAL B G*, RUDRESHA B M*, ALIYA N*, PRIYADARSHINI K S*

ABSTRACT

Background and objectives: Asthma is a very common disease with immense social impact. Nebulised salbutamol is the mainstay of therapy in acute severe asthma. This prospective study was done to determine the magnitude of changes in serum magnesium, potassium, phosphate and calcium during the treatment of acute severe asthma with nebulised salbutamol alone in a larger sample size, as previous studies were carried on a smaller sample size and yielded ambiguous results. **Subjects and Methods:** Sixty patients who met the inclusion criteria were included and their baseline electrolyte levels were measured. Nebulised salbutamol was administered every thirty minutes till the symptoms subsided and repeat serum levels of electrolytes were determined after 90 minutes. **Results:** Serum magnesium levels decreased significantly ($p < 0.001$) from 2.058 ± 0.0263 mg/dl to 2.048 ± 0.0268 mg/dl. Serum potassium levels decreased from 4.053 ± 0.0485 mEq/L to 3.983 ± 0.0482 mEq/L ($p < 0.001$). Serum phosphate levels decreased significantly ($p < 0.001$) from 3.899 ± 0.0299 mg/dl to 3.872 ± 0.0296 mg/dl, but no statistical difference was seen in the Serum calcium levels. **Interpretation and Conclusion:** Nebulised salbutamol therapy is associated with statistically significant decreases in serum magnesium, potassium and phosphate levels.

Key words: Asthma, electrolyte levels, salbutamol therapy.

*MD Biochemistry, Department of Biochemistry, Adichunchanagiri Institute of Medical Sciences, BG Nagar, Mandya District, Karnataka
Corresponding Author:
Dr. Vittal BG,
Assistant Professor,
Department of Biochemistry,
Government Medical College,
Hassan-573 201,
Karnataka
Mobile No: 09141400766
Email: vittal.bg@gmail.com

INTRODUCTION

Bronchial asthma is one of the most common diseases globally and it currently affects ~ 300 million people. Asthma is a very common disease with immense social impact, with a prevalence of ~10-12% in adults and 15% in children. It is known to occur at all ages, with a slight male preponderance [1].

Asthma is defined as a chronic inflammatory disease of the airways, that is characterised by increased responsiveness of the tracheobronchial tree, leading to the 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. It is an episodic disease with acute exacerbations which are interspersed with symptom free periods. Typically, most attacks are short lived, lasting minutes to hours and clinically, the patient seems to recover completely after an attack. However, there can be a phase in which the patient experiences some degree of airway obstruction daily. This phase can be mild or

serious, with severe obstruction persisting for days or weeks; the latter condition is known as acute severe asthma. Acute episodes of asthma are one of the most common respiratory emergencies [2].

Drug therapy is the most commonly used mode of treatment for asthma. The drugs which are used to treat asthma are β–adrenergic agonists, methyl xanthines, glucocorticoids and mast cell stabilizing agents.

β – Adrenergic agonists have been the primary focus of the emergency management of acute severe asthma for over 50 years [3]. Multiple inhalations of short acting sympathomimetic drugs such as salbutamol, are the cornerstone of most regimens [2]. The administration of nebulised salbutamol during the emergency treatment of acute severe asthma was shown to be associated with a significant decrease in serum magnesium, potassium and phosphate levels [4],[5].

Literature search revealed few groups that have studied the changes in electrolyte levels during nebulised salbutamol therapy. Previous studies were conducted on a very small sample size and yielded ambiguous results.

This study intended to measure and evaluate the changes in serum magnesium and other electrolyte levels on the administration of nebulised salbutamol in 60 patients of acute severe asthma.

METHODS

This study included 60 clinically diagnosed cases of acute severe asthma who got admitted to the emergency department of a teaching hospital, who fulfilled the inclusion criteria and who gave consent to participate in the study. The study spanned over a period of 15 months from August 2008 to October 2009.

Clinically diagnosed patients of acute severe asthma who were treated with nebulised salbutamol were included in the study. All patients with chronic liver diseases, chronic renal failure and acute myocardial infarction were excluded. Patients who were aged less than 16 years, those with metabolic disorders, pregnant women and psychiatric patients were also excluded from this study group.

Blood samples were drawn under aseptic precautions from clinically diagnosed cases of acute severe asthma before and after the administration of nebulised salbutamol. Both the blood samples were analysed for the study parameters.

After getting the written consent, 3ml of venous blood sample was drawn in a disposable syringe before the start of nebulised salbutamol therapy. Precaution was taken to prevent sepsis and haemolysis. The sample was then transferred to a mineral free acid washed glass test tube and was allowed to stand for 20-30 minutes, after which it was centrifuged to separate serum. Nebulised salbutamol (2.5mg) was administered every 30 minutes until the patient was discharged from the emergency department. Each dose was administered over a period of 10 minutes. Apart from inhaled oxygen supplementation, no other drug was administered during the course of the treatment. A repeat blood sample was drawn 90 minutes after starting nebulised salbutamol therapy, as the peak serum concentration of salbutamol is reached at 90 minutes [6]. The repeat samples were processed similarly to separate serum.

The serum levels of magnesium, calcium, potassium and phosphate were measured in both the sets of the serum samples.

Serum magnesium levels were assayed by Mann and Yoe's Xylidyl blue method, which is an in vitro colourimetric method for the quantitative determination of magnesium in serum [7]. Serum Calcium levels were measured by the modified O- Cresolpthalein Complexone method [8]. Serum phosphorus levels were estimated by the ammonium molybdate method, based on the modified Daly and Ertingshausen's method [9]. Serum potassium was measured by an electrolyte analyser that measures ionic potassium by a K^+ ion selective electrode.

The levels of the four electrolytes (Magnesium, Calcium, Phosphate, and Potassium) were

estimated twice, before and after the administration of nebulised salbutamol to the same study group. The study group consisted of 60 clinically diagnosed cases of acute severe asthma. The results were tabulated and analysed by using the "Paired 't' test" for any statistically significant changes in the electrolyte levels before and after the treatment.

RESULTS

Among the 60 subjects who were a part of the study, 36 (60%) were men and 24 (40%) were women. 24 of the 60 patients were aged less than 30 years, while 30 patients were between the age group of 31 to 50 years and 6 were aged more than 50 years. [Table/Fig 1]

[Table/Fig 1]: Age – Sex Distribution of Study Group

Age group	Male	Female	Total
= 30 years	12	12	24
31-50 years	20	10	30
> 50 years	04	02	06
	36	24	60

The changes in serum magnesium, potassium, phosphate, and calcium levels before and 90 minutes after nebulised salbutamol therapy were measured and tabulated. [Table/Fig 2]

[Table/Fig 2]: Changes in Serum Electrolyte Levels

Serum electrolytes	Serum levels before treatment with salbutamol	Serum levels after treatment with salbutamol
Magnesium (mg/dl)	2.058 ± 0.0263	2.048 ± 0.0268
Potassium (mEq/L)	4.053 ± 0.0485	3.983 ± 0.0482
Phosphate (mg/dl)	3.899 ± 0.0299	3.872 ± 0.0296
Calcium (mg/dl)	9.532 ± 0.0515	9.532 ± 0.0507

Serum concentrations are depicted as Mean± Standard Error

The baseline magnesium level before the administration of salbutamol in patients of acute severe asthma was 2.058 ± 0.026 mg/dl (Mean ± Standard error) and it decreased significantly ($p < 0.001$) 90 minutes after the administration of salbutamol, to 2.048 ± 0.027 mg/dl.

The serum potassium level which was measured before the administration of salbutamol was 4.053 ± 0.048 mmol/L, which decreased after treatment with salbutamol to 3.983 ± 0.048 mmol/L. This decrease was found to be statistically significant ($p < 0.001$) on applying the paired t test to find the level of significance.

The baseline serum phosphate level which was measured at admission was 3.899 ± 0.030 mg/dl, which decreased to 3.872 ± 0.029 mg/dl after the administration of β–adrenergic agonists. This decrease was statistically significant ($p < 0.001$).

The serum calcium level which was measured before the administration of the β–adrenergic agonist, salbutamol (base line calcium levels) was 9.532 ± 0.051 mg/dl and it decreased after the administration of salbutamol to 9.532 ± 0.050 mg/dl. This decrease was statistically not significant ($p > 0.10$).

DISCUSSION

The patients of acute severe asthma were treated with nebulised salbutamol alone and serum electrolytes were measured before and after 90 minutes of therapy to determine the magnitude of change in the serum concentrations.

Serum magnesium, potassium, and phosphate levels decreased significantly after the initiation of nebulised salbutamol therapy, as compared to the baseline levels or the electrolyte levels before the initiation of nebulised salbutamol therapy. Serum calcium levels did not show any significant changes during the course of the study.

The cause of hypomagnesaemia due to the β_2–adrenergic agonists is still unclear, which can probably be explained by the epinephrine like action of the β_2–adrenergic agonists on magnesium uptake by the adipocytes. Hypomagnesaemia is associated with tremor, low potassium and ventricular ectopic activity. Interestingly, these adverse effects are seen in therapeutic or excessive doses of salbutamol. Therefore, hypomagnesaemia can be considered as a common denominator to help explain these effects of β_2–adrenergic agonists [10].

Hypomagnesaemia may increase the neuromuscular irritability, thus making a few individuals more susceptible to the bronchial spasms. It is noteworthy that hypomagnesaemia which causes bronchoconstriction is a side effect

of salbutamol, which is a potent bronchodilator. However, this bronchoconstriction might be of a very small magnitude.

A statistically significant decrease ($p<0.001$) in serum magnesium levels was observed in our study after the treatment with nebulised salbutamol, when compared with the baseline levels. A serial and statistically significant decrease ($p<0.001$) was also observed by Bodenhamer in his study, with an aggressive administration of nebulised salbutamol [4]. Khilnani also reported a decrease in serum magnesium levels with the use of the β_2– adrenergic agonists [10]. However, a few studies have reported that no statistically significant change of serum magnesium levels was observed in patients who were treated with nebulised salbutamol [11].

In our study, serum potassium levels were found to decrease significantly after the treatment with nebulised salbutamol ($p<0.001$). A statistically significant decrease in serum potassium levels was also observed after salbutamol therapy in other studies [4], [10], [12], [13] and also in a study on patients of the paediatric age group [14]. Nevertheless, a study pointed out that only intravenous salbutamol led to a decrease in serum potassium levels, while nebulised salbutamol did not result in significant changes [15].

Hypokalaemia is known to occur in therapeutic and excessive doses of β_2– agonists. This effect is attributed to the activation of the Na^+-K^+-ATPase enzyme and β_2 receptor mediated insulin release, with a consequent intracellular shift of potassium [12].

The serum phosphate levels were found to decrease significantly in our study ($p<0.001$) after treatment with nebulised salbutamol and a similar observation was made by Bodenhamer in his study [4].

Serum calcium levels did not show any statistically significant changes during the salbutamol therapy in our study.

The limitation of this study was that randomisation and placebo control were not done, as they were not practically feasible in our setup. If the study had taken into account, the history of the asthma medications that the patients took before therapy, the results could have been attributed more directly to salbutamol therapy.

Our study results indicated that serum electrolytes like magnesium potassium and phosphate decreased significantly in patients with acute severe asthma who were on treatment with nebulised salbutamol. The decrease in electrolyte levels was only statistically significant and the levels did not decrease below the decision limits. The mechanism and clinical significance of these findings are unclear and they warrant further studies.

It is recommended that further studies must be carried out on a larger sample size and also, the clinical findings should be correlated with the dose dependent variation in electrolyte levels during salbutamol therapy.

REFERENCES

[1] Waltraud Eder, Markus J Ege, Erika von Mutius. The Asthma Epidemic. N Engl J Med 2006;355:2226-35.
[2] Casper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson L. Harrison's Principles of Internal medicine. 17th ed. McGraw-Hill Medical publications; 2008: 1596-1599p.
[3] Skobeloff EM, Spivey WH, McNamara RM, Greenspon L. Intravenous Magnesium Sulphate for the Treatment of Acute Severe Asthma in the Emergency Department. JAMA 1989; 262: 1210-1213.
[4] Bodenhamer J., Bergstrom R, Brown D, Gabow P, Marx JA, Lowenstein SR. Frequently nebulised beta agonists for Asthma- Effects on serum electrolytes. Ann Emerg Med Nov 1992; 21(11): 1337-1342.
[5] Dickens GR. et al. Effect of nebulised albuterol on serum potassium and cardiac rhythm in patients with asthma or chronic obstructive pulmonary disease. Pharmacotherapy 1994; 14(6): 729-733.
[6] Mohamed MH, Lima JJ, Eberle LV, Self TH, Johnson JA. Effects of gender and race on albuterol pharmacokinetics. Pharmacotherapy 1999; 19: 157-161.
[7] Mann CK, Yoe JH, Spectrophotometric determination of magnesium with xylidyl blue. Anal Chem Acta 1957; 16: 155-160.

[8] Moorehead WR, Briggs HG. 2-Amino 2-methyl 1-propanol as the alkalysing agent in the improved continuous flow cresolpthalein complexone procedure for calcium in serum. Clin Chem 1974; 20: 1458-1460.
[9] Daly JA et al, Estimation of serum inorganic phosphorus by ammonium molybdate. Clin Chem 1972; 18: 263.
[10] G Khilnani, H Parchani, G Toshniwal. Hypomagnesemia due to β_2 agonist use in bronchial asthma. JAPI 1992; 40/5: 346.
[11] B. J. Lipworth, R. A. Clark, C. G. Fraser, D. G. McDevit. The biochemical effects of high dose inhaled salbutamol in patients with asthma. Eur J Clin Pharmacol 1989; 36: 357-360.
[12] Kung M, White JR, Burki NK. The effect of subcutaneously administered terbutaline on serum potassium in asymptomatic adult asthmatics. Am Rev Respir Dis 1984; 129: 329-332.
[13] D. DaCruz, C. Holburn. Serum potassium responses to nebulised salbutamol administered during an acute asthmatic attack. Archives of Emergency medicine 1989; 6: 22-26.
[14] Hung CH, Chu DM, Wang DL, Yang KD. Hypokalemia and salbutamol therapy in asthma. Pediatric Pulmonology 1999; 27(1): 27-31.
[15] A Neville, J B D Palmer, J Gaddie, C S May, K N V Palmer, L E Murchison. Metabolic effects of salbutamol: comparison of aerosol and intravenous administration. BMJ 1977; 1: 413-414.