Section: Biochemistry

Original Research Article

STUDY OF SERUM ELECTROLYTES WITH PARTICULAR REFERENCE TO SERUM MAGNESIUM IN BRONCHIAL ASTHMA PATIENTS IN A TERTIARY CARE HOSPITAL

Prabhat Kumar Singh[1], Musarrat Parveen[2], Rajiv Ranjan Sinha[3]

[1]Assistant Professor, Department of Biochemistry, Nalanda Medical College, Patna, Bihar, India.
[2]Assistant Professor, Department of Biochemistry, Nalanda Medical College, Patna, India.
[3]Professor, Department of Biochemistry, Nalanda Medical College, Patna, Bihar, India.

Received : 28/11/2022
Received in revised form : 03/01/2023
Accepted : 17/01/2023

Keywords:
Serum Electrolytes, Serum Magnesium, Bronchial Asthma.

Corresponding Author:
Dr. Musarrat Parveen
Email: drmusarratpraveen79@gmail.com

DOI: 10.47009/jamp.2023.5.2.68

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (2); 330-333

Abstract

Background: 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. **Materials and Methods:** This prospective observational study was done in Department of Biochemistry, Nalanda Medical College, Patna, Bihar, a Tertiary Care Hospital. The study duration was 12 months July 2020 to June 2021. A total of 42 patients were included, who fulfilled the inclusion criteria and who gave consent to participate in the study. The study received an ethical approval from the ethical committee. 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, 5ml 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. **Result:** All 42 patients clinically diagnosed with acute severe asthma who were treated with nebulised salbutamol were included in the study. Out of 42 patients in which 17(40.47%) were female and 25(59.52%) were male. The baseline magnesium level before the administration of salbutamol in patients of acute severe asthma was 1.983 ± 0.0221 mg/dl (Mean ± Standard error) and it decreased significantly ($p < 0.001$) 85 minutes after the administration of salbutamol, to 1.975 ± 0.0223 mg/dl. **Conclusion:** Serum magnesium 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.

INTRODUCTION

Asthma is a very common disease with immense social impact. Nebulised salbutamol is the mainstay of therapy in acute severe asthma. 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]

Magnesium (Mg) is one among the most abundant cations in the human body with normal serum value ranges of 1.5–2.3 mg/dl. It has a vital role in cellular metabolism, cardiac contractility, and muscle contractility. Among these, the effect of Mg on smooth muscle warrants further attention. Mg is involved in mechanisms such as inhibition of

ISSN (O): 2687-5365; ISSN (P): 2753-6556

vascular and bronchial smooth muscle contraction and inhibition of acetylcholine release from cholinergic nerves. It is also engaged in the promotion of nitric oxide and prostacyclin generation and smooth muscle stabilization. Hence, Mg has a significant role in causing muscle relaxation. Hypomagnesaemia leads to muscle contraction and hypermagnesaemia to muscle relaxation. There are studies documenting usefulness of Mg in treating acute asthma.[3,4] There are several studies on serum Mg levels in asthma patients which show that hypomagnesaemia is commonly seen in asthmatics.[5,6,7] However, there are no studies that correlate the asthma symptom control and serum Mg level. We aimed at estimating the serum Mg levels and asthma control.[8,9,10,11] Magnesium as the second most plentiful intracellular cation and an important part of bone mineralization has a crucial function in synthesis and metabolism of vitamin D. Lower level of serum magnesium are associated with hypovitaminosis D which can also worsen the clinical condition in asthma by tracheo-bronchial hyperactivity and by increasing susceptibility to respiratory infections.

MATERIALS AND METHODS

This prospective observational study was done in Department of Biochemistry, Nalanda Medical College, Patna, Bihar, a Tertiary care Hospital. The study duration was 12 months July 2020 to June 2021. A total of 42 patients were included, who fulfilled the inclusion criteria and who gave consent to participate in the study. The study received an ethical approval from the ethical committee.

Inclusion criteria: All 42 patients clinically diagnosed with acute severe asthma who were treated with nebulised salbutamol were included in the study.

Exclusion criteria: Patients who were aged less than 18 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, 5ml 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 25-30 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 85 minutes after starting nebulised salbutamol therapy, as the peak serum concentration of salbutamol is reached at 85 minutes (6). The repeat samples were processed similarly to separate serum.

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 42 clinically diagnosed cases of acute severe asthma.

RESULTS

All 42 patients clinically diagnosed with acute severe asthma who were treated with nebulised salbutamol were included in the study. Out of 42 patients in which 17(40.47%) were female and 25(59.52%) were male.

Table 1: Age and sex distribution

Age group	Male	Female	Total
<25 years	7	3	10
26-45 years	9	6	15
>46 years	9	8	17
	25	17	42

Among the 42 subjects who were a part of the study, 25 (59.52%) were male and 17 (40.47%) were female. 10 of the 42 patients age was less than 25 years, while 15 patients were between the age group of 26 to 45 years and 17 were more than 46 years old.

Table 2: Changes in Serum Electrolyte Levels

Serum Electrolytes	Serum level before treatment with salbutamol	Serum level after treatment with salbutamol
Magnesium (mg/dl)	1.983±0.0221	1.975±0.0223
Potassium (mEq/L)	3.053±0.0358	2.987±0.0356
Phosphate (mg/dl)	3.000±0.0300	2.985±0.0298
Calcium (mg/dl)	8.555±0.0324	8.555±0.320

Serum concentrations are depicted as Mean± Standard Error (SD)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

The baseline magnesium level before the administration of salbutamol in patients of acute severe asthma was 1.983 ± 0.0221 mg/dl (Mean ± Standard error) and it decreased significantly ($p < 0.001$) 85 minutes after the administration of salbutamol, to 1.975 ± 0.0223mg/dl.

The serum potassium level which was measured before the administration of salbutamol was 3.053 ± 0.0385 mmol/L, which decreased after treatment with salbutamol to 2.987 ± 0.0356 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 3.000 ± 0.0300 mg/dl, which decreased to 2.985± 0.0298 mg/dl after the administration of adrenergic agonists. This decrease was statistically significant ($p < 0.001$).

The serum calcium level which was measured before the administration of the adrenergic agonist, salbutamol (base line calcium levels) was 8.555 ± 0.0324 mg/dl and it decreased after the administration of salbutamol to 8.555± 0.320 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 85 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 β2 adrenergic agonists is still unclear, which can probably be explained by the epinephrine like action of the β2 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 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 adrenergic agonists.[8] 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, 15, 16,17] 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 agonists. This effect is attributed to the activation of the Na+-K+-ATPase enzyme and β2 receptor mediated insulin release, with a consequent intracellular shift of potassium.[18,19,20,21]

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.[22,23]

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.[24,25]

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

CONCLUSION

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

ISSN (O): 2687-5365; ISSN (P): 2753-6556

calcium levels did not show any significant changes during the course of the study.

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. Harrisonâ€™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 cresolpthaleincomplexone 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 β2 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.
16. Singh AK, Gaur S, Kumar R. A randomized controlled trial of intravenous magnesium sulphate as an adjunct to standard therapy in acute severe asthma. Iran J Allergy Asthma Immunol. 2008;7:221–9.
17. Ciarallo L, Brousseau D, Reinert S. Higher-dose intravenous magnesium therapy for children with moderate to severe acute asthma. Arch PediatrAdolesc Med. 2000;154:979–83.
18. Shaikh MN, Malapati BR, Gokani R, Patel B, Chatriwala M. Serum magnesium and Vitamin D levels as indicators of asthma severity. Pulm Med 2016. 2016:1643717.
19. Lee SH, Song WJ, Park HW, Kim SH, Park HK, Kim SH, et al. Serum micronutrients levels and clinical features of elderly asthmatics. Allergy Asthma Respir Dis. 2017;5:223–7.
20. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. Behav Res Methods. 2009;41:1149–60.
21. Saris NE, Mervaala E, Karppanen H, Khawaja JA, Lewenstam A. Magnesium. An update on physiological, clinical and analytical aspects. Clin Chim Acta. 2000;294:1–26.
22. Emelyanov A, Fedoseev G, Barnes PJ. Reduced intracellular magnesium concentrations in asthmatic patients. Eur Respir J. 2019;13:38–40.
23. Das SK, Haldar AK, Ghosh I, Saha SK, Das A, Biswas S, et al. Serum magnesium and stable asthma: Is there a link? Lung India. 2020;27:205–8.
24. Hatipoglu N, Hatipoglu H, Turel O, Aydogmus C, Engerek N, Erkal S, et al. Serum magnesium concentration in children with asthma. Eurasian J Pulmonol. 2021;16:36–9.
25. Rude RK. Magnesium. In: Ross AC, Caballero B, Cousins RJ, Tucker KL, Ziegler TR, editors. Modern Nutrition in Health and Disease. 11th ed. Baltimore, Mass: Lippincott Williams & Wilkins; 2022. pp. 159–75.

ISSN (O): 2687-5365; ISSN (P): 2753-6556