ISSN Print: 2664-7591
ISSN Online: 2664-7605
Impact Factor: RJIF 5.2
IJAN 2023; 5(2): 06-08
www.pharmaceuticaljournal.in
Received: 11-05-2023
Accepted: 15-06-2023

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Salbutamol-induced hypokalemia: A case report

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DOI: https://doi.org/10.33545/26647591.2023.v5.i2a.54

Abstract
Asthma is a chronic lung disease caused by inflammation and muscle tightening around the airways, which makes it difficult to breathe. The pharmacological treatment mainly includes bronchodilators such as salbutamol and steroids which can deliver medication directly to the lungs through inhaler. Salbutamol opens up the medium and large airways in the lungs and is used in asthma attacks, chronic obstructive pulmonary disease and exercise induced bronchoconstriction. Serious side effects of salbutamol may include worsening bronchospasm, irregular heartbeat and low potassium levels. Normal potassium levels include 3.5-5.0 mmol/L. potassium levels below 3.5 mmol/L is defined as hypokalemia. Hypokalemia induced by salbutamol is due to overdosage and can be serious. It has potential toxic effects on the heart and sometimes can increase the risk of an abnormal heart rhythm which is too slow and cause cardiac arrest. Hypokalemia can be treated with oral potassium replacement accompanied with plenty of fluids with close follow-up, continuous ECG monitoring and serum potassium levels. Patient must be counselled about their treatment options, triggers to avoid and to manage their symptoms accordingly.

Keywords: Bronchial asthma, salbutamol, hypokalemia

Introduction
Brochial asthma is characterised by hyper responsiveness of tracheobronchial smooth muscle to a variety of stimuli, resulting in narrowing of air tubes, often accompanied by increased secretion, mucosal edema and mucus plugging. Symptoms include dyspnoea, wheezing, cough and may be limitation of activity asthma is now recognized to be a primarily inflammatory condition: inflammation underlying hyper reactivity. An allergic basis can be demonstrated in many adult, and higher percentage of pediatrics patients. In others a variety of trigger factors: infection, irritants, pollution, exercise, exposure to cold air, psychogenic may be involved. Two principal varieties are recognised: extrinsic asthma: it is mostly episodic, less prone to status asthmaticus. Intrinsic asthma: it tends to be perennial, status asthmaticus is more common [1].

The current international and national guidelines for the treatment of acute asthma seem entirely appropriate in recommending high-dose inhaled β2-agonist in conjunction with systemic corticosteroid, and reserving second-line therapy with ipratropium bromide or intravenous bronchodilators for refractory or more severe cases. A greater awareness of the severity markers in acute asthma is also required, although when in doubt the safest axiom is always to over treat rather than undertreat to prevent a potentially fatal attack. Further large-scale studies are required to resolve issues such as the use of large-volume spacers and the role of intravenous β2-agonists in acute severe asthma [2]

Salbutamol a highly selective β2 agonist, cardiac side effects are less prominent. Selectivity is further increased by inhaling the drug. Inhaled salbutamol delivered mostly from pressurized metered dose inhaler pMDI produces bronchodilatation within 5 min and action lasts for 2-4 hours. It is therefore used to abort and terminate attacks of asthma, but is not suitable for the round the clock prophylaxis. Muscle tremors are the dose related side effect. Palpitations, restlessness, nervousness, throat irritation and ankle edema can also occur. Hypokalaemia is a possible complication. Because of more frequent side effects, oral beta2 agonist therapy is reserved for patients who cannot correctly use inhalers or as alternative/adjuvant medication in severe asthma [1].

Hypokalemia is a well known side effect of overdosage with salbutamol and other beta-adrenergic agonists that are now the main stay of acute asthma therapy. Although it has been reported occasionally, despite its infrequency it is important because of its potentially toxic effects on the heart, especially against the background of hypoxia, acidosis, increased adrenergic drive and dysrhythmia which can be associated with the disease or its treatment [3].

Treatment of hypokalemia has four aims: (a) reduction of potassium losses (b) replenishment of potassium stores, (c) evaluation for potential toxicities and (d) determination of the cause, in order to prevent future episodes, if possible. Major goal of treatment should be the management of the underlying disease or elimination of the causative factor. Discontinuation of laxatives, use of potassium-neutral or potassium-sparing diuretics (if diuretic therapy is required, such as in heart failure), treatment of diarrhea or vomiting, use of H2 blockers in patients with nasogastric suction and effective control of hyperglycemia, if glycosuria is present, are some measures in this direction. Whether oral or intravenous potassium will be administered, this should be decided according the severity of the hypokalemia. It is important to remember that every 1 mEq/L decrease in serum potassium, represents a potassium deficit of approximately 200–400 mEq. However, this calculation could either overestimate or underestimate the true potassium deficit. Patients with potassium levels of 2.5–3.5 mEq/L (representing mild to moderate hypokalemia), may need only oral potassium replacement. If potassium levels are less than 2.5 mEq/L, intravenous (i.v.) potassium should be given, with close follow-up, continuous ECG monitoring, and serial potassium levels measurements [4].

ED physicians should be aware that albuterol-induced hypokalemia can occur at normal therapeutic doses. Manufacturers of beta agonists and drug regulatory agencies should modify their side-effect profiles for beta-agonist drugs to increase physician and patient awareness of hypokalemia as a side effect. It would be useful to study serum potassium levels before and after nebulizer use in asthmatic patients visiting emergency departments. The authors acknowledge the use of Saudi Aramco Medical Services Organization facilities for the study and data that resulted in this paper. The authors were employed by Saudi Aramco during the time the study was conducted and the paper written [3]

Case Study

A 55 year old female patient came to casualty with chief complaints of SOB since 5 days, fever and productive cough since 4 days. Patient was apparently asymptomatic five days ago, developed SOB (shortness of breath), gradual onset, progressive, grade 1 to 3, with no orthopnea and PND (paroxysmal nocturnal dyspnea). History of illness includes: c/o-fever (low grade, intermittent associated with chills) relieved by medications. c/o-Ronchi, c/o-productive cough, no blood in sputum. There's no history of chest pain, decreased urine output, abdominal distension, B/L pedal edema, weight loss, decreased appetite. Past medical history includes known case of bronchial asthma on beclomethasone and levosalbutamol inhaler, montelukast and levocitrizine and prednisolone dispersible tablets. Known allergies: dust. General examination: patient is febrile and conscious coherent, PR-88 bpm, GRBS-147 mg/dl, per abdomen-soft, nontender, CVS-S1S2+, RS-BAE+, B/L wheezing, CNS-NFND, SPO2-93%.

Table 1: Blood pressure levels

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
BP (mmHg)	160/100	150/60	140/80	110/60	120/70	140/90	120/80	110/70	150/90

Lab Investigations: Lab investigation findings: WBC-16.66 x 103/µl, RBC-4.25 x 106/µl, HGB-9.7 g/dl, HCT-31%, MCV-72.9 fl, MCH-22.8 pg, PLT-325 x 103/ µl, Neu-78.8%, Neu-13.12 x 103/ µl, Eos-0.2%, (imp-microcytic hypochromic, neutrophilic leucocytosis) ESR-45 mm, Crea-1.57 mg/dl, Urea-27.82 mg/dl, BUN-13 mg/dl, Cl-97 mmol/L, Na-142 mmol/L, CHOL-244.5 mg/dl, TRIG-345 mg/dl, HDL-49 mg/dl, LDL-141 mg/dl, VLDL-69 mg/dl, ABG: pH-7.479, pCO_2-43.8, pO_2-79.8, ctHb-10.6 g/dl, SO_2-95.6%, HCO_3-31.8 mmol/L. ECG-sinus tachycardia ST-T abnormality (V4) pair PVC.

Table 2: Serum Potassium levels

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
K+conc (mmol/L)	2.83	3.23	2.16	2.4	2.8	2.5

Final Diagnosis: Acute exacerbations of Asthma with LRTI with CAD with hypokalemia secondary to salbutamol inhalation.

Treatment

Initially O2 Inhalation 6L/min, nebulization with asthalin and budecort 8th hourly, Inj hydrocort 100 mg IV TID, Inj Deriphylline 100 mg IM BD, Inj Pan 40 mg PO OD, Syr Ambroxyl 10 ml PO OD, Tab PCM 500 mg PO BD, Tab azithromycin 500 mg PO OD, Inj Augmentin 1.2gm IV BD, Tab Telmisartan 40 mg PO OD, Inj Methyl prednisolone 80 mg IV OD. Later treatment was changed to the following medications-Inj Piptaz 4.5 gm IV BD, Inj Metrogyl 500mg IV TID, Neb with Duolin and Budecort 8th hourly, Inj Deriphylline 100 mg IV BD, Inj Hydrocort 100 mg IV TID, Tab Monteleukast 10 mg PO OD, Syr Potchlor 15 ml in 1 glass of water PO TID.

Hypokalaemia was recovered later and there was moderate improvement in the serum potassium levels with syr potchlor. Patient was counselled about importance and continuation of drug therapy after the discharge with routine follow ups.

Discussion

Salbutamol, a selective β2 adrenoceptor agonist, is widely used as a bronchodilator in the treatment of asthma and chronic obstructive airways disease. Administration is usually by inhalation or by mouth but in severely ill patients it may be administered by intravenous boluses or infusion. There have been a number of reports of falls in serum

potassium following salbutamol. Reports of hypokalemia occurring following intravenous doses and in cases of self-poisoning with salbutamol have, in recent years, been followed by reports of hypokalemia with lower doses of salbutamol and other similar selective-β2 adrenoceptor agonists administered subcutaneously and by inhalation. The mechanism of salbutamol-induced hypokalemia has not been fully elucidated. Some authors have attributed it to the action of salbutamol on insulin release. A rise in insulin levels has been reported with salbutamol infusion and insulin is released by stimulation of β2-adrenoceptors. The rise in serum insulin concentration could result in a shift of potassium into cells from the extracellular compartment resulting in hypokalaemia. This hypothesis must now be questioned. There is a membrane-bound-β2 adrenoceptor linked Na+/K+ ATPase on skeletal muscle cells which causes insulin independent potassium flux. Adrenaline-induced hypokalaemia has been known for 50 years. But has only recently become the subject of intensive investigation. Pathophysiological increases of circulating adrenaline to levels similar to those seen during acute severe illness, such as acute myocardial infarction or hypoglycaemia, results in a fall in serum potassium of 0.8-1.0 mmol 1-1 and the fall in serum potassium is prevented by, Beta-selective adrenoceptor antagonist. This discovery of the Na+/K+ ATPase pump linked to β2-adrenoceptor stimulation has raised the possibility of an alternative explanation for salbutamol-induced hypokalaemia. In addition to the risk of hypokalaemia induced by salbutamol therapy during episodes of bronchoconstriction there may also be increases in circulating adrenaline. Further stimulation by adrenaline of the Na+/K+ ATPase pump could occur increasing the degree of hypokalaemia. We have administered salbutamol or placebo to subjects in whom adrenaline or placebo has been infused to achieve circulating adrenaline concentrations similar to those seen in acute stress. We have examined the effects on plasma potassium, glucose and insulin and on cardiac rhythm and blood pressure in a single-blind crossover study [5].

Conclusion

Hypokalemia if left untreated can lead to potential toxic effects on the heart causing abnormal heart rhythm and cardiac arrest. This case study have shown that proper patient counselling on asthma, its obvious triggers, the treatment plan with drug compliance, the symptomatic management and the need for monitoring blood pressure, blood glucose levels and serum potassium levels while salbutamol therapy is indicated, continuous ECG monitoring and follow up can have better outcomes in improving the quality of life. Its important for patients to know how to increase their treatment when their symptoms are worsening to avoid a serious attack.

Conflict of Interest

There is no Conflict of interest behind this study.

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