

CASE REPORT

# Intentional salbutamol poisoning: report of two siblings and review of the literature

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## ABSTRACT

**Background:** About 65% of poisoning cases are related to children and of these, more than half of the patients are 5-year-old or less. While non-accidental poisoning is rare. We report two cases of intentional salbutamol poisoning in two young siblings presenting separately multiple times over a period of two years with similar presentations of tachycardia, hyperglycemia and hypokalemia.

**Case Presentation:** Two siblings, one 3-year-old boy and the other one, 1 year old girl, presented at emergency department. Both presented with tachycardia and vomiting, while the boy also had hyperglycemia and hypokalemia, and girl also had subjective fever and poor oral intake. Other vital signs, physical examination, HbA1c, genome sequence, and upper gastrointestinal tract examination were all normal. Child protective team was called due to suspicion of Salbutamol toxicity and lab work confirmed it. The mother was interviewed who became resentful and refused to undergo any psychological assessment and left the hospital with the children. The mother is suspected of Munchausen syndrome by proxy.

**Conclusion:** Emergency medicine physicians should scrutinize medication side effects and presentation. Active investigation to recognize similar cases of suspected Munchausen Syndrome by proxy in the Saudi community is also warranted. Policymakers should introduce a protocol to deal with victims and affected families.

**Keywords:** Albuterol, toxicity, poisoning, Munchausen syndrome by proxy, case report.

## Introduction

Poisoning is a frequently encountered phenomenon worldwide. It is estimated that 65% of all poisoning occurs in the pediatric population and of these 51.3% are children less than 5 years old [1]. Ingestion is the commonest route of entry for poisons, accounting for 77% of exposures and 75% of lethal poisoning. Inhalation follows ingestion as the second most common poisonous route [1]. Non-accidental poisoning is relatively rare. However, Meadow and Rogers [2] stated that occasionally parents may intentionally harm their children by overdosing a drug.

Salbutamol is a synthetic and relatively selective  $\beta_2$ -adrenergic agonist, most commonly prescribed for childhood asthma. The use of inhaled salbutamol has supplanted oral formulations due to the lower therapeutic index and reported overdoses. Its side effects include tachycardia, central nervous system (CNS) stimulation, and vasodilation which are seen to a milder degree in inhalation than in ingestion. Hence, it is very rare for salbutamol to be prescribed orally, though it is still available and overdoses are also reported [3].

We report two cases of intentional salbutamol poisoning in two young siblings presenting separately multiple

times over a period of 2 years with similar presentations of tachycardia, hyperglycemia, and hypokalemia.

## Case Presentation

### Case 1

A 3-year-old boy presented to the Emergency Department (ED) with tachycardia, hyperglycemia, hypokalemia, and vomiting. Cardiac monitors and electrocardiogram (ECG) showed sinus tachycardia with normal QRS at 190 beats per minute (Figure 1). His respiratory rate was 25 breaths/minute. The remaining vital signs were within normal range: oxygen saturation on room air

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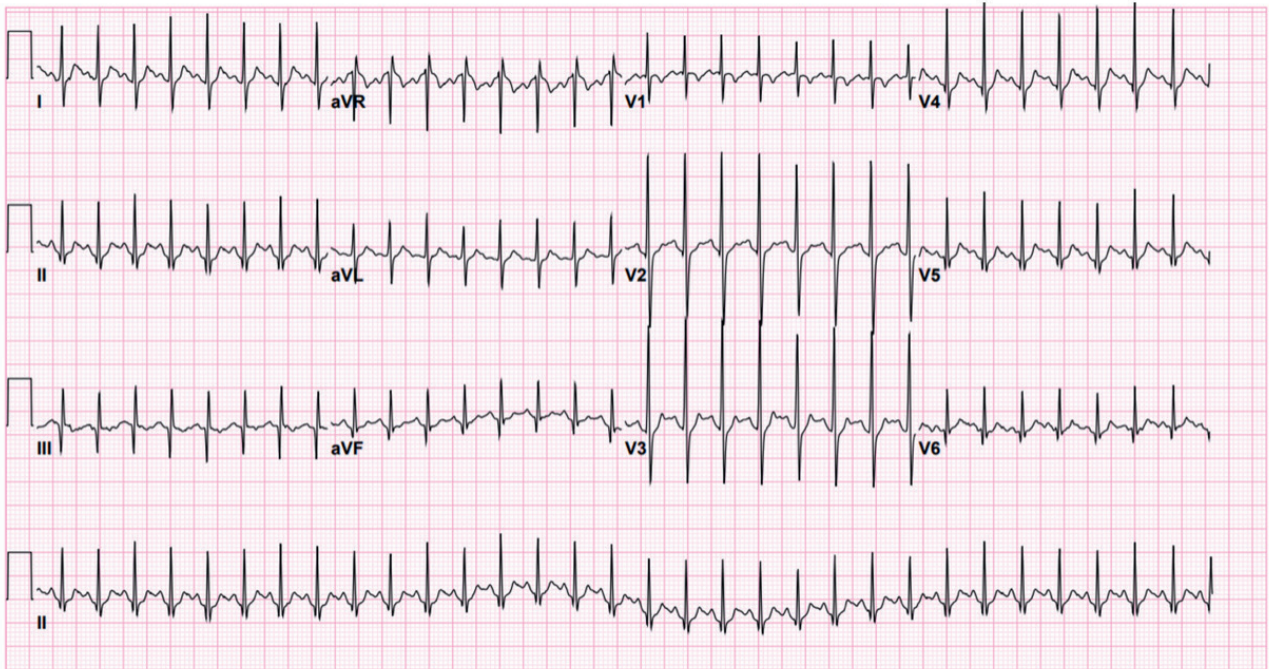
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**Figure 1.** ECG showing narrow QRS complex tachycardia in the patient at the rate of 190 beats/minute.

100%, blood pressure 100/63 mmHg, and temperature 36.5°C. His point of care glucose was measured at 14.8 mmol/l. The patient was accompanied by his mother, a 24-year-old woman who reported a similar history of this presentation in the past month for which the patient was discharged after a period of observation in the ED. She reported multiple episodes of food-content vomiting at home, accompanied by poor oral intake and occasional shortness of breath. She denied history of fever, cough, rash, or diarrhea. The patient's medical history was significant for grade II left hydronephrosis with normal voiding cystourethrogram and multiple previous hospital admissions due to upper respiratory tract infection. The mother denied history of any family illness, medication or herbal use. The child had been delivered at full term vaginally. Regarding his immunization history, the mother reported that he did not receive his one-year immunizations.

On physical examination, the patient was awake and oriented, playful, with no increased work of breathing or airway compromise. The patient's chest was clear on auscultation, with no wheezes or crackles. Cardiac exam revealed a fast and regular rhythm, with no murmurs. Pulses were equal in all four extremities with no significant difference in blood pressure measurement. Abdominal and screening neurological exams were unremarkable.

The blood work was significant for potassium 3.2 mmol/l, phosphate 0.76 mmol/l (reference range 0.92-1.55 mmol/l). The anion gap was 13 mmol/l and osmolar gap was normal. Chest radiograph showed no significant findings (Figure 2).

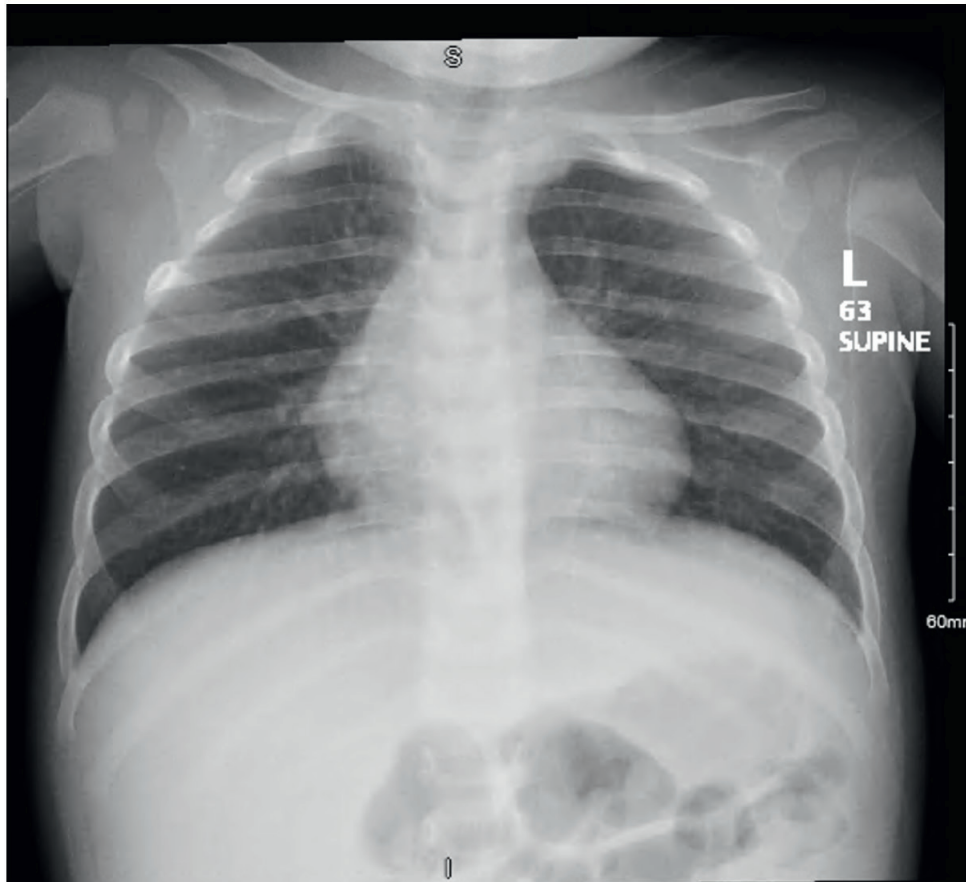
The patient was fluid resuscitated with 20 cc/kg of normal saline intravenous (IV) bolus as well as potassium replacement. Patient was accordingly admitted under

the Pediatric Cardiology service for further assessment and investigation. Echocardiography was done showing normal cardiac structure with no evidence of congenital heart diseases. Patient was also seen by Endocrinology, Genetics and Gastroenterology services where he underwent testing of HbA1C, whole genome sequencing and upper gastrointestinal (GI) series studies respectively, of which all yielded normal results.

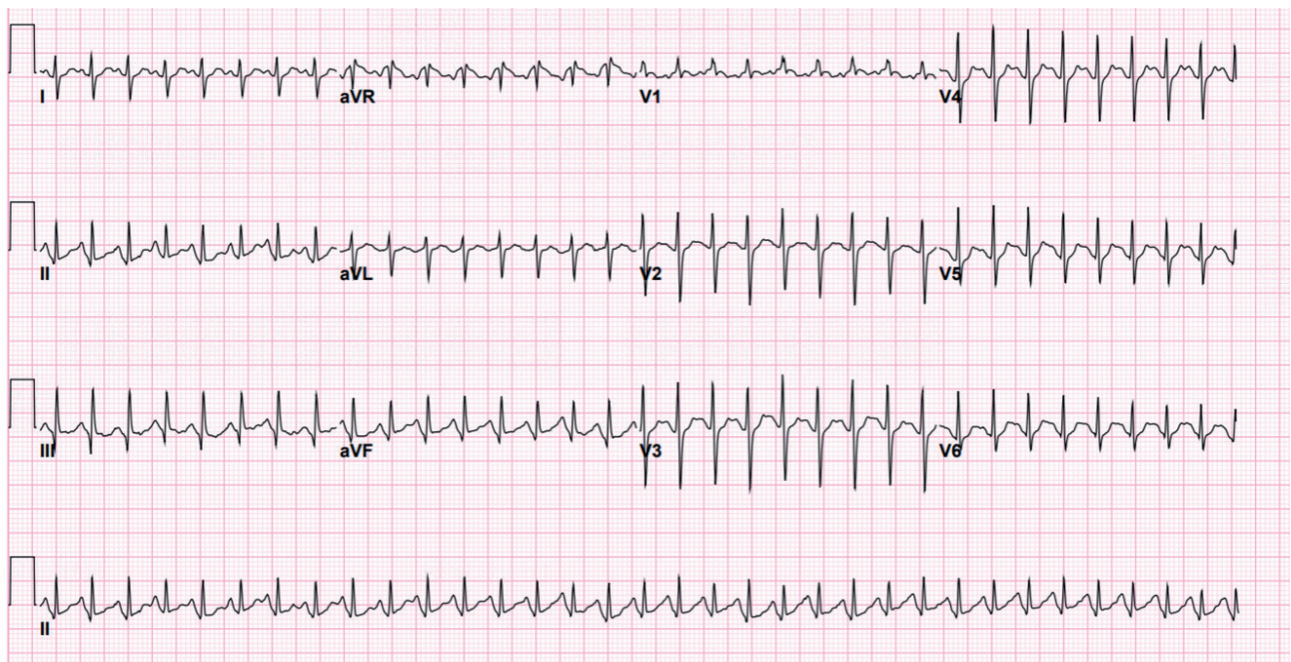
Throughout patient's hospital admission, no clear identifiable cause was found. It is worth mentioning that the patient had not developed any event of tachycardia or electrolyte imbalances during his stay in the hospital. The patient was subsequently prescribed propranolol 4 mg/ml syrup 8 mg three times daily orally as discharge medication.

### Case 2

A 1-year-old girl presented to the ED with a history of vomiting, subjective fever, and poor oral intake. Cardiac monitors and ECG showed sinus tachycardia of 210 beats/minute (Figure 3). Her respiratory rate was 28 breaths/minute. The remaining vitals were unremarkable. Her point of care glucose was 22.8 mmol/l. The patient was accompanied by her mother who reported a history of multiple food content vomiting, subjective fever, flushing, and irritability at home. She noticed that the patient's heart is pounding and fast when she touched her chest. The mother reported that her illness started two days ago when she noticed poor oral intake followed by multiple non projectile, non-bloody vomiting episodes. She measured the patient's temperature rectally and it was 37.5°C with flushing of the face and fast pounding of the heart. She denied a history of rash, diarrhea, trauma, or any medication use. The patient's medical history was significant for fenestrated atrial septal defect, grade I



**Figure 2.** Chest radiograph showing normal cardiomeastinal silhouette and clear lungs.



**Figure 3.** ECG showing narrow QRS complex tachycardia in the patient at the rate of 210 beats/minute.

hydronephrosis and bilateral developmental dysplasia of the hip with dislocation. There were no previous surgical interventions and immunization was up to date. The patient was a product of spontaneous uneventful vaginal delivery. On physical examination, the patient was awake

and oriented, well hydrated and perfused with a <2 seconds capillary refill. She expressed normal milestones for her age. The patient's chest was clear on auscultation with transmitted sound. Her cardiovascular examination showed normal heart sounds without murmurs. Pulses

were equal in all four extremities with no significant difference in blood pressure measurement. Abdominal and screening neurological exams were unremarkable.

Patient was started on normal saline bolus of 20 cc/kg IV. Due to the concerns for supra-ventricular tachycardia (SVT) based on the short PR interval and the fluctuating heart rate reaching 240 beats/minute, vagal maneuvers were attempted after discussion with the Cardiologist. However, the maneuvers failed to revert the tachycardia. Subsequently, 0.1 mg/kg of adenosine was given via IV route which successfully controlled her heart rate. Her laboratory result was significant for white blood cell count of  $18.36 \times 10^9/l$  (reference range 6.00-16.00  $\times 10^9/l$ ), potassium 2.9 mmol/l, creatinine 36  $\mu\text{mol/l}$  (reference range 18-35  $\mu\text{mol/l}$ ), with venous blood gas showing metabolic acidosis with a pH of 7.252 and a normal anion gap. Patient was admitted accordingly to the hospital as a case of gastroenteritis inducing SVT for investigation and observation. She was started on broad spectrum antibiotics and fluid maintenance. The patient underwent echocardiography during admission which was insignificant apart from her already known diagnosis of the fenestrated atrial septum. The patient was also investigated by Endocrinology, Genetics, and Gastroenterology services where she underwent testing of HbA1C, whole genome sequencing, and upper GI series studies respectively, all of which yielded normal results.

She was started on propranolol 1 mg orally in the hospital which successfully controlled her heart rate and was subsequently discharged on propranolol 4 mg/ml syrup 1 mg three times daily with a diagnosis of SVT with atrioventricular reentrant tachycardia.

Due to the challenge in reaching a reasonable medically explained diagnosis, both cases were referred to the child protective team. When no specific cause for both siblings' presentations was elicited, the diagnosis of salbutamol toxicity was suspected based on the similar manifestation of hyperglycemia, hypokalemia, and tachycardia which could be attributed to Beta-agonist drug toxicity. Toxicology advised that, with a potential future presentation, a serum salbutamol level should be collected. During the next visit, it was found that serum salbutamol was elevated in the younger sibling (140 mcg/l). A subsequent level was obtained for the older sibling as well.

It was noted by medical staff that the mother hardly left the unit during admissions or emergency room department (ER) visits. The mother admitted to having a salbutamol nebulizer machine at home, but completely denied using it prior to visits and admissions and did not believe it to be the reason for her children's illness. It is worth mentioning that the mother herself had multiple visits to the ER and underwent multiple diagnostic tests for different presentations, all of which yielded negative results. She is a homemaker with no professional healthcare experience. Upon further questioning about marital status, she mentioned that her husband (father of both siblings) works in a remote city and visits his family few times a year. The mother denied any psychological or further social disorders during her childhood or adult life. She denied undergoing surgeries or equivalent procedures

in the past. With further questioning, she became resentful and refused to undergo any psychological assessment and she was eager to leave the hospital. The children were, hence, released from the hospital after providing mental health and social follow-up for both patients and mother to ensure safety measures. Following the case, a year later, both siblings were well and never presented to the hospital with the earlier mentioned symptoms again.

## Discussion

Salbutamol has  $\beta_2$  adrenergic activity that provides rapid bronchodilation effects, through cyclic adenosine monophosphate mediated relaxation of smooth muscles [4].

Beta-adrenergic agonists initially cause a rapid transient elevation in serum glucose concentration through stimulation of glycogenolysis in muscles and liver, followed by hypoglycemia resulting from direct stimulation of the  $\beta_2$  receptors on the pancreas leading to a rise in insulin levels [5]. Hypoglycemia can be seen as late as 16 hours after exposure [6]. Salbutamol causes hypokalemia primarily through  $\beta_2$  stimulation of  $\text{Na}^+ \text{K}^+$  ATPase, which shifts potassium intracellularly [4].

$\beta_2$  agonists can also cause imbalance between fast and slow-twitch muscle fascicles resulting in muscular tremors in arms and legs [7]. They also have a poor ability to cross the blood-brain barrier hence CNS manifestations are rare [7]. However, a reported case of seizure in a child after Terbutaline overdose has been reported [8].

Sinus tachycardia is also a commonly reported side effect following salbutamol overdose.  $\beta_2$  agonists can stimulate the peripheral vasculature which in turn leads to tachycardia. Moreover, following  $\beta_2$  agonist overdose the specificity of the receptors is lost, and stimulation of either  $\beta_1$  or  $\beta_2$  or both receptors can lead to tachycardia including SVT, atrial fibrillation and ventricular tachycardia [9].

Most reported cases of salbutamol overdose described in the literature are in the form of ingestion. However, this medication is now used in a form of inhalation (Meter dosed inhalers, Nebulization) ensuring a minimal systemic dose and keeping the incidence of adverse events low [10]. Salbutamol varies over formulation and dosages. The aerosol for inhalation contains 90 mcg per metered (200 puffs per container), nebulizer solution contains 5 mg/ml (3 ml per container), oral syrup 2 mg/5 ml and tablet forms of 2 and 4 mg. Inhalation has an onset of action in 15 minutes and a duration of 3 to 4 hours, reaching peak serum concentration in 2-5 hours, whereas the onset is <30 minutes in ingestion with a duration of 4-8 hours and peak serum concentration reaching in 2-2.5 hours. Both have a similar half-life of 2.7-5 hours [4].

A dosage of 1 mg/kg or 3 to 10 times larger dose than normal is widely accepted as a threshold toxic dose and can lead to the development of 3 or more signs [5]. Its treatment and management are largely symptomatic and supportive [4]. One of the studies found that no patients with toxic levels required any specific treatment and 72% were discharged from medical care after 6 hours of ingestion [5]. Activated charcoal has been recommended

to prevent further absorption of the drug for patients presenting within 30-60 minutes of ingestion [4].

Munchausen Syndrome by proxy is considered a mental condition in which a parent, mostly a mother, fabricates an illness or induces an illness in their child to gain attention as a caregiver. The scope of Munchausen syndrome by proxy is unknown, owing to the difficulty of diagnosing such cases. It was first described by a British pediatric nephrologist, Dr. Roy Meadow, who reported two cases in 1977 in which one mother poisoned her baby with excessive amounts of salt and the other added maternal blood into the urine of her baby [2]. Nonetheless, an estimate indicates that approximately 1,000 of the 2.5 million recorded annual cases of child abuse were related to Munchausen syndrome by proxy with a confirmed death rate of 7.4% [11]. In addition, Yates and Bass [12] meta-analysis found that 97.6% of the offenders were women, and 95.6% were the mothers of the victims. Forty-five percent of caregivers have been in a healthcare-related occupation and most of them were diagnosed with a mental illness. Therefore, Munchausen syndrome by proxy is a serious condition that has the potential to cause significant morbidity and mortality and should be taken seriously by the medical community. To the authors' knowledge, this is the second case report of suspected Munchausen syndrome by proxy in the Saudi community with the first being reported in a 17 months old baby boy who presented with hematemesis and rectal bleeding [13].

## Conclusion

We report a case of inhaled salbutamol toxicity in two siblings, complicated by suspected Munchausen Syndrome by proxy. Inhaled Salbutamol toxicity can present with pronounced tachycardia, hyperglycemia and hypokalemia. Emergency Medicine Physicians are suggested to scrutinize over medication side effects and presentation. Importance should also be given to recognizing similar cases of suspected Munchausen Syndrome by proxy in the Saudi community, thereby developing and forming a formal approach and social support programs for dealing with victims and affected families.

## List of Abbreviations

|     |                               |
|-----|-------------------------------|
| CNS | Central nervous system        |
| ECG | Electrocardiogram             |
| ER  | Emergency room department     |
| GI  | Gastrointestinal              |
| IV  | Intravenous                   |
| SVT | Supra-ventricular tachycardia |

## Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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## Consent for publication

Not required.

## Ethical approval

Ethical approval is not required at our institution to publish an anonymous case report.

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