



## Anaphylaxis Induced by Nebulized Salbutamol in an Asthmatic Boy

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### Abstract

Salbutamol is a short-acting adrenergic agonist with a higher affinity for  $\beta_2$ -receptors. In the airway, activation of  $\beta_2$ -receptors results in relaxation of bronchial smooth muscle and a widening of the airway. Short-acting  $\beta_2$ -agonists are the first-line drugs for treating reversible airway obstruction, such as in asthma. Adverse effects like tremor, palpitation, headache and metabolic effects after their use have been reported previously. But to our knowledge no cases of anaphylactic reactions with nebulized salbutamol have been reported in childhood. We present 2 years-old boy who developed anaphylaxis episodes after nebulized salbutamol inhalation during asthma attacks.

**Keywords:** Anaphylaxis; Children; Salbutamol

### Introduction

Asthma is a common and potentially serious chronic disease that imposes a substantial burden on patients, their families and the community. It causes respiratory symptoms, limitation of activity and flare-ups (attacks) that sometimes require urgent health care and may be fatal. Short-acting  $\beta_2$ -agonists are the first-line drugs for treating asthma attacks. Adverse effects like tremor, palpitations, headache, paradoxical bronchoconstriction and metabolic effects are commonly described after use of short-acting  $\beta_2$ -agonists [1,2]. Anaphylaxis to the salbutamol has also been documented in adulthood [3]. But in the literature, pediatric patients with anaphylaxis to the nebulized salbutamol have not been reported yet. We present 2 years-old boy who developed anaphylaxis episodes after nebulized salbutamol inhalation during asthma attacks.

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### Case Presentation

A 2 -years - old boy was admitted to our hospital with history of asthma and 2 episodes of anaphylaxis after use of nebulized salbutamol during asthma attacks. On the last episode, he experienced generalized urticaria, vomiting, respiratory distress and fainting after 5 minutes of nebulized salbutamol inhalation and the first episode he had similar symptoms. In both time his symptoms were rapidly improved after intramuscular adrenalin injection. In his history, he was experienced similar symptoms when he took per-oral terbutaline. Skin prick test (SPTs) was positive with nebulized salbutamol (3 mm wheal). When skin test applied he experienced some urticarial rashes on his body. SPTs were negative with nebulized salbutamol in five asthmatics (exposed to beta 2-agonists) and in five non-asthmatic controls. SPTs for common aeroallergens and latex were negative. We decided not to challenge with salbutamol and any other short-acting  $\beta_2$ -agonists because of dramatic response to these drugs. Informed consent was obtained from the patient's family before the case report was presented.

### Discussion

Asthma is major public health problem in many countries. The most commonly used asthma medications are the short-acting inhaled  $\beta_2$ -agonists such as salbutamol (albuterol) first introduced more than 30 years ago and for which there is now extensive clinical experience. Inhaled  $\beta_2$ -agonists can cause both pulmonary and extrapulmonary adverse effects [4]. Inhaled  $\beta_2$ -agonists cause dose-dependent adverse effects because the inhaled drug is absorbed via the lung bed and the drug deposited in the oropharynx is swallowed [5]. If  $\beta_2$ -agonists are absorbed into the systemic circulation, stimulation of adrenergic receptors in non-respiratory tissues will occur. Thus stimulation of cardiac receptors causes positive chronotropic (increased hearth rate) and inotropic (increased force of cardiac contraction) effects, which may be experienced as palpitations [6]. Skeletal muscle

receptor activation causes fine tremor of the hands and contributes to metabolic effects, including hypokalemia, hyperglycemia, metabolic acidosis and elevation of free acids and ketones [7]. Direct vascular effects cause systemic peripheral vasodilatation, which may precipitate headaches and cause a fall in blood pressure [8]. In an acute attack of asthma  $\beta_2$ -agonists may increase hypoxemia by worsening ventilation/perfusion mismatching in the lung [9]. In the literature, a case of Ig E dependent allergy to different short-acting  $\beta_2$ -agonists producing acute bronchoconstriction was described. This patient is a 41 year old man who developed acute respiratory distress within five minutes after inhaled several puffs of salbutamol. SPTs were positive with salbutamol, terbutaline, pirbuterol and negative with formoterol, salmeterol, bambuterol and ipratropium. In this patient tolerance to long-acting  $\beta_2$ -agonists was good [10]. Cross reactive reaction can be seen between  $\beta_2$  agonists [10]. Our patient had also similar symptoms after per-oral terbutaline use. Only one case with anaphylactic reactions to the nebulized salbutamol was reported, until now [3]. This case is a 42-year-old woman diagnosed with asthma due to pollen. She was treated with nebulized salbutamol and budesonide after an acute exacerbation. Ten minutes later, she experienced generalized itching and erythema, eyelid swelling, chest tightness, nausea, and abdominal pain. She had previously tolerated both drugs. Her skin prick tests and intradermal tests with salbutamol and budesonide were found negative. After drug challenge with nebulized salbutamol she experienced anaphylaxis. A basophil activation test to salbutamol was performed to the patient but no activation was detected. In this patient, authors were unable to demonstrate the immunological pathway. But, even though the short time between the inhalation and the reaction onset and the fact that patient was reproducibly rechallenged, suggesting a type I reaction, IgE antibodies could not be detected. In the present report we demonstrated type I immune reaction with SPTs to nebulized salbutamol.

## Conclusion

Our patient is the first reported pediatric patients who developed anaphylaxis after nebulized salbutamol administration. Physicians must be aware of the possibility of anaphylactic reaction after the administration of drugs used in the treatment of allergic disease such as asthma and even anaphylaxis.

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