Allergy to Salbutamol

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Abstract

We report a 10 month old girl known case of Cow's milk protein allergy (CMPA) who presented with an allergic reaction to Salbutamol. She was prescribed salbutamol to be used through nebulizer. She had clear systemic reaction with increased cough and facial and lip swellings that lasted for about 20 minutes. This reaction was observed for three consecutive times after which the medication was held. In the report, we review the literature and found that most reactions can be categorized as either a true anaphylaxis or simply a paradoxical bronchospasm. The true anaphylaxis was mostly associated with a positive skin prick test.

Key words: Allergy, salbutamol, children

Introduction

Salbutamol is a very commonly used medication. It is a cornerstone in treatment of many respiratory diseases. It is a widely available and its relatively cheap cost makes it one of the top 10 medications prescribed in the United States (1). Like almost all medications salbutamol has side effects. It may cause some palpitation, jitteriness, headache, tachycardia, insomnia, nervousness among other symptoms and signs (2). However, having an allergic reaction to salbutamol is very rare. In this publication, we report an infant who presented with typical features of allergic reaction to salbutamol.

The Case

10-month-old baby girl, known case of Cow's milk protein allergy (CMPA). She presented to a local clinic with shortness of breath and cough triggered by upper respiratory tract infection (URTI). There was no fever, no skin rash up to that point, no gastrointestinal symptoms but has a strong family history of asthma and food allergies. The mother was told that she has "tight chest" and was prescribed salbutamol to be nebulized with normal saline. The mother reported that a few minutes into the nebulization the girl started to have lip and facial swelling with increased cough and shortness of breath. These symptoms subsided within 20 minutes. The mother denies any vomiting, change in voice/crying or level of consciousness. This reaction was observed with the two subsequent doses after which the mother held the medication and came to our clinic.

The patient was seen in our clinic a few days later. Her vital signs showed normal pulse oxygen saturation (SPO2) of 99% on room air, afebrile with normal respiratory rate of 28 breaths per minute asleep. Her clinical examination revealed some nasal congestion and on auscultation had mixed wheezing and crackles which is more suggestive of bronchiolitis. Family were educated about the expected outcome of bronchiolitis and the need for supportive treatment only. However, we asked her to avoid using salbutamol until further testing is done and a referral was made for pediatric allergist.

Discussion

Salbutamol is a short acting beta agonist (SABA) which binding to beta receptors on the airway smooth muscles causes it to relax leading to fast bronchodilation (3). Its fast acting nature and fairly good safety record make it the first line management of many respiratory disorders that are associated with bronchoconstriction like asthma and COPD and even some allergic reactions. It replaced subcutaneous adrenaline as the first line management for asthma attacks in the beginning of the 1980s and since then salbutamol became the first line (4).

With this shift of practice the utilization of inhaled/ nebulized salbutamolgreatly increased . Food and drug administration (FDA) estimated that 88 million canisters of albuterol (salbutamol) and 19 million nebulizer solutions were prescribed over 15 years from 1974 to 1988. The adverse reports filed over the same period were 126 for the inhaled MDI and 58 reports for the nebulized form, all of which were reported as paradoxical bronchospasm (PB). These reactions were observed among all age groups and "some" (no exact number mentioned) had a systemic reaction (5).

Since then there have been many similar reports of paradoxical bronchospasm (see Table 1). Most of these reports describe reactions in adults with both asthma and COPD. There was one report describing recurrent anaphylaxis in a two year old boy with asthma (6) and another describes a paradoxical bronchospasm in an 18 year old young man with asthma (7). There were another two clear anaphylaxis incidents reported in adults where a woman aged 41 years and a man aged 60 year had anaphylaxis reactions (8, 9).

It seems that paradoxical bronchospasm after using Salbutamol is more common than we think. In reviewing spirometry data in a large pediatric tertiary center, 32 children (mean age of 8.3 year) had PB with no clear previous clinical observation (10). A similar observation was made in a larger study (pediatric and adults) where 201 (4.4%) out of 4593 subjects, had PB (11). It is important to note that a few other reports describe PB with some stridor in the absence of any other systematic/cutaneous manifestations (12, 13).

It is not clear why these reactions happened. There were some cell lines studies that showed that Salbutamol may have some pro-inflammatory properties where pretreating murine mast cells with salbutamol actually activated mast cells and led to a significant increase in histamine and IL-4 (14). On the other hand, some studies suggest that regular use of salbutamol may increase airway hyper-responsiveness (15, 16).

Conclusion

Salbutamol is a safe medication but adverse reactions including mainly PB and more rarely a true anaphylaxis still may occur. A high index of suspicion and clear time line may help reaching the diagnosis. Furthermore, it seems all patients who had an anaphylaxis had a positive skin prick test that may further confirm the diagnosis. The latter is considered one of the limitations of this report.

Table 1

Study	Diagnosis	Age of subjects	SABA form	Observed Reaction	Notes	ref
Isik 2017 Turkey	Asthma	2 year Boy	Nebulized salbutamol	Anaphylaxis	Positive SPT	(6)
Bonniaud 2007 France	Asthma	41 year woman	Inhaled salbutamol	Anaphylaxis	Positive SPT	(8)
Manso 2015 Spain	COPD	60 year Man	Inhaled salbutamol	Anaphylaxis	Negative SPT	(9)
Raghunathan 2006 USA	COPD	80 year man	Nebulized salbutamol	Paradoxical bronchospasm		(17)
Chitikela 2018 India	Asthma	18 year Woman	Inhaled salbutamol	Paradoxical bronchospasm		(7)
Rubio 2012 Spain	Asthma	32 children mean age 8.3 year	Inhaled salbutamol during spirometry	Paradoxical bronchospasm	56% males obesity in 34.3%	(10)
Schissler 2018 USA	Asthma	201 (4.4%) of a total 4593 subjects	Inhaled salbutamol during spirometry	Paradoxical bronchospasm	Age ranged from 7-98 year	(11)
Magee 2018 USA	Asthma	25 year Man	inhaled salbutamol during spirometry	Paradoxical bronchospasm	Similar attacks over the previous 4 weeks	(18)
Spooner 2005 USA	COPD	92 year Man	Reacted to both inhaled and nebulized forms	Paradoxical bronchospasm with stridor		(13)
Mutlu 2000 USA	Asthma	22 year woman	Nebulized salbutamol	Paradoxical bronchospasm with stridor (laryngospasm)		(12)
Broski 2008 USA	Asthma	36 year Man	Inhaled salbutamol	Paradoxical bronchospasm		(19)
Ayed 2020 Tunisia	Asthma	50 year Man	Inhaled salbutamol and nebulized terbutaline	Paradoxical bronchospasm	Didn't react to ipratropium bromide	(20)
Nicklas 1990 USA	FDA report		Inhaled (126 events) and nebulized (58) salbutamol	Paradoxical bronchospasm	FDA adverse reaction reports over 15 year (1974-1988)	(5)

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