
Contamination of nebulizer equipment with cockroach allergen: there's a bug in the system!

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Background: Physicians often have anecdotal reports of patients describing increased asthma symptoms after the use of nebulizers; however, there are few published reports of nebulizer-associated exacerbations.

Objective: To present 2 cases of asthmatic children who experienced a life-threatening exacerbation of their symptoms after nebulizer use.

Methods: Case 2's nebulizer was tested for cockroach allergen by washing the medication reservoir with 2 mL of sterile filtered 1% phosphate-buffered saline, 0.05% bovine serum albumin, and Tween 20 overnight with rotation. The patient's sealed albuterol nebulizer medication was used as a control. The control albuterol and test solutions were analyzed for *Blattella germanica* 1 and 2 allergens using a monoclonal antibody-based immunoassay.

Results: The reservoir from case 2 was found to have measurable levels of both Bla g 1 and Bla g 2. The control albuterol solution had no measurable cockroach allergen. An insect found in the nebulizer box of case 2 was identified as an infantile German cockroach.

Conclusions: Nebulizer use provides an opportunity for antigen exposure directly to small airways, which may lead to severe allergic reactions in patients using contaminated equipment.

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INTRODUCTION

Nebulizers are used by many asthmatic patients, particularly children. It is estimated that one third of children with asthma use nebulizers for dispensing asthma medications.¹ Most nebulizers are used to deliver rescue β -agonist treatment for acute asthma symptoms; however, with the introduction of nebulized budesonide onto the market, some patients also use nebulizers daily to dispense controller asthma medications. Physicians often have anecdotal reports of patients describing increased asthma symptoms after the use of nebulizers; however, there are few published reports of nebulizer-associated exacerbations. Several proposed mechanisms for worsening symptoms following nebulizer use have included the development of tachyphylaxis or increased bronchial hyperresponsiveness due to β -agonist overuse or possibly an adverse reaction to the medication or excipient. We report 2 cases of asthmatic patients who had severe life-threatening respiratory deterioration following the use of a nebulizer for administering rescue albuterol. These exacerbations may have been

related to the contamination of their nebulizer equipment with cockroach allergen.

CASE REPORTS

Case 1

A 12-year-old boy awoke one morning with dyspnea. This child was a former 23-week premature infant with severe persistent asthma, with a history of several asthma admissions and prior intubations and food allergy. The patient had a history of medication misuse and poor compliance with follow-up and medication directions, including β -agonist overuse and independent dosing of oral steroids. He dosed himself with albuterol nebulizer at his home after which he measured a peak flow of 175 L/m (baseline, 200 L/m; personal best, 225 L/m). He then went to school, where throughout the day he used his albuterol inhaler on 5 occasions (2 puffs each) but continued to have dyspnea. He had no known exposures to his food allergy triggers. On arrival at his grandmother's home after school, he was given an albuterol treatment, with subsequent acute worsening dyspnea. Emergency medical services (EMS) were notified, and he was then given an additional double dose of his albuterol nebulizer treatment, with acute mental status changes. He was transported to the emergency department (ED) and was rapidly intubated. Arterial blood gas before intubation was a pH (arterial) of 6.94, a Paco_2 of 144 mm Hg, and a Pao_2 of 260 mm Hg on 100% nonrebreather oxygen mask. In the ED, he responded to 3 doses of subcutaneous epinephrine and albuterol treatments. On examination by one of the resident physicians, the grandmother's nebulizer was noted to have 3

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small cockroaches in the reservoir. He had an uneventful course in the pediatric intensive care unit. He was readily weaned off the ventilator and responded well to systemic steroids. The boy was discharged at his baseline respiratory status. Replacement equipment was provided for his nebulizer.

Allergies. The patient had positive puncture skin test responses to shellfish, scaled fish, peanut, egg, natural rubber latex, and multiple environmental allergens, including dust mite and German cockroach (latter produced a wheal-flare response of 10 and 20 mm and 10 and 15 mm for histamine control).

Medications. Before this episode, the patient had taken fluticasone and salmeterol, 250 and 50 μ g 2 times daily, respectively; budesonide, 400 μ g 2 times daily; montelukast, 10 mg/d; loratadine, 5 mg/d; hydroxyzine, 15 mg/d as needed; olopatadine as needed; albuterol nebulizer and inhaler as needed; and injectable epinephrine (EpiPen) as needed.

Case 2

A 13-year-old boy with a history of moderate persistent asthma awoke one morning with dyspnea. His asthma had been poorly controlled due to poor adherence with his control medications, but he had not been previously hospitalized for asthma. His nebulizer was retrieved from storage in the garage. He was given an albuterol treatment at his home after which he felt acutely worse and was taken to a local ED. While in the ED he was treated with methylprednisolone sodium succinate (Solu-Medrol) and nebulized albuterol and observed overnight. He was released and instructed to use his home nebulizer throughout the day at home. After his first subsequent nebulizer treatment at home, he experienced sudden worsening of his symptoms, which he associated with the treatment. He then attempted to use his inhaler and he collapsed in respiratory failure. He required emergency intubation by the EMS and treatment with subcutaneous epinephrine. He was transferred to the local ED, where he received ventilatory support and was transferred to the intensive care unit. A chest x-ray examination performed on arrival showed a left pneumothorax. A chest tube was placed, with resolution of the pneumothorax. He was weaned off the ventilator without issue. The patient's father provided the home nebulizer with the tubing and reservoir attached. On examination of the equipment, a number of small insects were found still in the box and apparatus. The father had also seen a cockroach in the tubing before his son's treatments. Tryptase level at the time was 2 ng/mL (reference range, <11.5 ng/mL).

Allergies. The patient had no known drug, food, or environmental allergies (not previously tested). Subsequent allergy test results were positive for German cockroach (wheal and flare response of 12 and 30 mm and 12 and 35 mm for histamine control) and dust mite.

Medications. Albuterol inhaler with a spacer was used at least 2 times daily, and fluticasone inhaler was used intermittently before this episode.

MATERIALS AND METHODS

The nebulizer (Sunrise Co, Somerset, PA) used by patient 2 during his exacerbation was obtained from the patient. The box containing the nebulizer was visually observed to contain 2 small insects. All testing of the equipment for cockroach allergen was performed by the Clinical Laboratory Improvement Act–licensed Johns Hopkins Dermatology, Allergy, and Clinical Immunology (DACI) Reference Laboratory in Baltimore, MD. The nebulizer was tested for cockroach allergen by washing the medication reservoir with 2 mL of sterile filtered 1% phosphate-buffered saline, 0.05% bovine serum albumin, and Tween 20 overnight with rotation. The patient's sealed albuterol nebulizer medication found in the box was used as a control. The control albuterol and test solutions were analyzed for *Blattella germanica* 1 and 2 allergens using a monoclonal antibody–based immunoenzymetric assay (Indoor Biotechnologies, Charlottesville, VA). The limit of detection of these assays for Bla g 1 and Bla g 2 was 0.01 U/mL. For Bla g 2 only, 1 U is equivalent to 40 ng of allergen protein. Bla g 1 and Bla g 2 levels are expressed as units, since the DACI Laboratory did not have a conversion factor for Bla g 1 to mass per volume units. The insects found in the box containing the nebulizer for case 2 were photographed and sent to the Department of Entomology at the University of Maryland, College Park, for species identification.

RESULTS

As presented in Table 1, the reservoir from case 2 was found to have measurable levels of both Bla g 1 and Bla g 2. The control albuterol solution had no measurable cockroach allergen. A photograph of the insect found in the nebulizer box of case 2 is shown in Figure 1 and was identified by entomologist Dr. Nancy Breisch as an infantile German cockroach.

DISCUSSION

Nebulizers are used by asthmatic patients primarily for dispensing rescue albuterol medication, although they may also be used to dispense daily controller medications. Many physicians and health care providers have heard anecdotal reports of patients who have described acute worsening of their asthma symptoms after the use of a nebulized medication. A MEDLINE review of the literature from 1965 to 2003, using the keywords *worsening asthma* and *nebulizer*, *asthma* and *treatment* and *decline*, *storage* and *nebulizer*, *contaminants* and *worsening asthma*, *allergic reactions to albuterol*, *tachy-*

Table 1. Cockroach Allergen Levels in Nebulizer Washes

Cockroach allergen specificity	Case 2 nebulizer reservoir, U per reservoir	Case 2 albuterol nebulizer solution (from sealed container), U/mL
Bla g 1	0.36*	<0.01
Bla g 2	0.44†	<0.01

* 0.18 U/mL $\times$ 2 mL.

† 0.22 U/mL $\times$ 2 mL.



Figure 1. Bug found in box containing the nebulizer in case 2. Left, Top of bug; right, head of bug (which was detached during processing).

phylaxis, and β -agonist, yielded no published reports of such acute exacerbations. Possible explanations for such nebulizer reactions may include tachyphylaxis or increased bronchial hyperresponsiveness due to β -agonist overuse or allergic reactions to the medication or the excipient. There are no previous published reports of accidental nebulization of allergen, although many clinical studies that used nebulized allergens, such as cat, ragweed, and grass, have been performed to study allergic asthmatic populations.^{2,3} There are a few published bronchial challenge studies that used nebulized cockroach allergen; however, the allergen levels described are in units of allergen.^{4–6} Since there are no conversion factors for units per milliliter of Bla g, it is difficult to make comparisons between the levels of allergen found in the medication reservoir of case 2 and clinical studies.

Both patients had significant skin test reactivity to German cockroach (equal to the histamine control), although skin test reactivity is not necessarily predictive of asthma severity.⁷ Despite years of education and care by several asthma specialists, patient 1 continues to have poorly controlled, severe, persistent asthma despite additional recommendations specific to nebulizer care and cleaning. His poor control is most likely due to poor adherence, significant environmental allergies, and exposures and psychosocial issues. Patient 2 underwent evaluation by an allergist for the first time after this incident and received extensive education about environmental controls, appropriate use of controller medications, and specific education about nebulizer care and cleaning. His asthma has been well controlled since that episode with low-dose inhaled steroids.

Review of manufacturer guidelines for proper care of nebulizers revealed instructions for proper cleaning but not for proper storage. It is well known that many patients fail to follow manufacturer guidelines for proper cleaning of nebulizer equipment. If proper cleaning of nebulizers is performed, potential contamination of the equipment with environmental allergens may be reduced, although this remains to be studied. Further study of the frequency of contamination of nebulizer equipment with environmental allergens and the impact that it may have on asthmatic patients is needed. The 2 case reports presented herein suggest that an environmental

contaminant introduced by improper storage or cleaning of the nebulizer may have played a role in both children's acute respiratory failure.

CONCLUSION

These 2 cases of pediatric asthma demonstrate that contamination of nebulizer equipment with environmental allergens is possible. Nebulizer use may provide significant opportunity for antigen exposure directly to the small airways, which may lead to severe allergic reactions in patients using contaminated equipment. Guidelines are needed to educate patients about proper cleaning and storage of nebulizer equipment to avoid potential life-threatening exposures.

Further study is warranted to evaluate the prevalence and extent of this problem given the potentially severe outcomes that may result from allergen contamination of nebulizers. Guidelines for appropriate storage of nebulizer equipment to avoid environmental contamination are needed to alleviate nebulizer contamination, which may lead to morbidity in children with asthma.

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