

Can You Teach an Old Drug New Tricks? The Use of Salbutamol for Gastrointestinal Anaphylaxis



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During the past decades, food allergy has become a widespread medical concern, affecting the lives of millions of children and their families, and causing considerable morbidity and mortality.¹ Signs and symptoms of a food-related allergic reaction may involve the skin, respiratory system, gastrointestinal tract, and potentially the cardiovascular system. These may range from a mild reaction to lethal anaphylaxis.² Gastrointestinal symptoms are common manifestations after food allergen exposure and may include nausea, vomiting, and diarrhea. The term “gastrointestinal anaphylaxis” is often used to describe severe abdominal symptoms, as the sole allergic reaction or as part of systemic anaphylaxis.³ Current clinical guidelines recommend the prompt use of intramuscular epinephrine as the first and most important treatment for an anaphylactic reaction. Although antihistamines and glucocorticoids are commonly used to treat allergic reactions, there is a lack of solid high-quality evidence to support their benefits.⁴ Importantly, to this date, there is no specific treatment that addresses abdominal pain, when presenting as the sole manifestation of an allergic reaction to food. The use of H1 and/or H2 receptor antagonists to treat abdominal symptoms has thus far not been proven to be effective therapies for this indication.⁵ Medications that have β_2 -agonist activity, such as epinephrine, can alleviate visceral pain due to their relaxing effect on the gastrointestinal tract smooth muscles. However, epinephrine treatment for isolated abdominal pain during allergic reactions to food is not common in clinical practice, likely because these symptoms do not fulfill formal criteria for anaphylaxis.⁶

In the current issue of this journal, Frugier et al⁷ describe the results of their study that used inhaled salbutamol as a novel treatment approach for severe abdominal pain, caused by an IgE-mediated allergic reaction to peanuts. Because inhaled salbutamol is a potent β_2 -agonist that is rapidly distributed through the body and has a systemic effect,⁸ Frugier et al hypothesized that this intervention would result in a rapid clinical resolution of IgE-mediated abdominal pain during an

allergic reaction to peanuts. In this study, which included participants who had significant abdominal pain during a double-blind, placebo-controlled peanuts challenge, Frugier et al compared 26 patients who were treated with high-dose salbutamol (800-1000 mcg) with 31 patients who had similar symptoms during a food challenge but were not treated with salbutamol. All patients, apart from one, were also treated with either H1 or H2 receptor antagonists, and 13 patients were also treated with intramuscular epinephrine, due to lower respiratory tract symptoms or extensive cutaneous or rhinoconjunctival involvement.

The effect of salbutamol treatment was substantial and significant. In the intervention group that was treated with salbutamol, the median time for abdominal pain improvement and resolution was 12.5 and 32.5 minutes, respectively. In the control group that was treated based on the conventional approach, without salbutamol, the median time for abdominal pain improvement and resolution was 65 and 90 minutes, respectively. Importantly, other than tremor and asymptomatic tachycardia, no serious adverse events were observed after treatment with salbutamol. Interestingly, emesis before treatment initiation was also associated with faster improvement and resolution of abdominal pain. However, a sensitivity analysis that excluded the patients who vomited or who were treated with epinephrine showed that the salbutamol effect still remained statistically significant. In multivariate analysis, the effects of salbutamol therapy, and of immediate emesis, remained statistically significant even when other covariates, such as treatment with other medications, eliciting peanut dose, and the severity of the abdominal pain, were included in the regression model. Overall, salbutamol increased abdominal pain improvement rate by 11.35-fold and the rate of resolution by 2.67-fold, whereas immediate emesis increased the rate of improvement by 4.00-fold and the rate of resolution by 2.74-fold.

The authors concluded that salbutamol may be an effective treatment for severe gastrointestinal complaints during a food allergy reaction. There are a few limitations to this study. These results originated from a retrospective case-control study and not from a double-blind, randomized controlled trial. Hence, the results should be considered as hypothesis-generating and should not be directly applied to clinical care at this time. Using historical controls, that were not treated with salbutamol, creates a potential risk of noncontemporaneous control bias. As the authors mentioned in their discussion, patients presenting with more serious symptoms, such as respiratory symptoms, may have had clinical documentation that focused on the more serious symptoms, and potentially overlooked some of the abdominal symptoms, leading to additional bias. Finally, because the study treatment was not blinded, one cannot exclude that treatment

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with salbutamol has a placebo effect that may have contributed to the large magnitude of the observed treatment effect.

Overall, even with the limitations mentioned above, we find this study to represent a unique, out-of-the-box treatment approach for a common medical issue, which up to now has no specific treatment. For years, the treatment for gastrointestinal complaints during IgE-mediated allergic reactions to food has been based on antihistamine use, but without clear evidence supporting its efficacy. Salbutamol is a well-known drug, has an excellent safety profile, is not expensive, and is widely available. By successfully using this medication to treat food allergy-related gastrointestinal complaints, the investigators may have identified a novel treatment approach, which might be added to the limited toolbox we have when facing an allergic reaction. However, this intervention is not ready yet for prime-time clinical use, as a large double-blind, randomized controlled trial will have to confirm the encouraging results of this small retrospective study.

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