

Oral viscous budesonide can be successfully delivered through a variety of vehicles to treat eosinophilic esophagitis in children



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Clinical Implications:

- Swallowed topical corticosteroids, such as oral viscous budesonide, comprise the main pharmacologic therapy for eosinophilic esophagitis. Various vehicles can successfully deliver oral viscous budesonide to treat eosinophilic esophagitis in children.

TO THE EDITOR:

Eosinophilic esophagitis (EoE) is a clinicopathologic disorder characterized by eosinophilic infiltration of the esophagus. Symptoms vary, with infants and young children typically presenting with feeding difficulties or failure to thrive, older children presenting with abdominal pain or vomiting, and adolescents and adults presenting with dysphagia or food impaction.¹⁻³ Diagnosis must be confirmed on esophagogastroduodenal endoscopy, with esophageal biopsy showing at least 15 eosinophils (eos)/hpf. Gastroesophageal reflux disease and proton pump inhibitor-responsive esophageal eosinophilia must be excluded with high-dose proton pump inhibitor therapy. The main treatments currently available for EoE are dietary therapy and corticosteroids. Systemic corticosteroids are reserved for emergency cases such as severe dysphagia or stricture and weight loss, whereas swallowed topical corticosteroids comprise the main pharmacologic therapy for EoE.²⁻⁴ One option is oral viscous budesonide (OVB), created typically by mixing liquid budesonide (Pulmicort Respule) intended for nebulized administration with sucralose (Splenda) to create a slurry consistency.⁴⁻⁶ Some patients, however, are wary of using artificial sweeteners such as Splenda. A recent study compared the use of Splenda and Neocate Nutra, a hypoallergenic food powder, as the vehicle for delivering OVB and found that they were similarly effective.⁷ We report the various vehicles that have been used by patients with EoE at the Children's Hospital of Philadelphia.

The study protocol was approved by the Institutional Review Board of the Children's Hospital of Philadelphia. We reviewed the electronic medical records of all patients with EoE treated with OVB during a 5.5-year period between November 2008 and May 2014. Charts were reviewed for demographic data, the vehicle used to mix budesonide, and esophageal biopsy data. *Active EoE* was defined as a peak esophageal eosinophil count of 15 eos/hpf or more. We compared the peak esophageal

eosinophil count on the biopsies performed immediately before and after the initiation of OVB. All follow-up biopsies were performed at least 6 weeks after initiation. Some patients did not respond by the first biopsy following OVB initiation but did show response on a subsequent biopsy after the dose of OVB was increased. For these patients, we used the peak eosinophil count from the biopsy showing response. Patients were considered responsive if peak eosinophil count improved from 15 eos/hpf or more to less than 15 eos/hpf. The starting dose of OVB was determined by a standardized dosing schedule based on the patient's weight: 0.5 mg daily for less than 20 kg, 1 mg daily for 20 to 40 kg, and 2 mg daily for more than 40 kg.

Seventy patients were treated with OVB during the time period studied. Three patients were excluded because the vehicle used to mix budesonide could not be confirmed. Six patients were excluded because they were started on OVB during a time of inactive EoE (<15 eos/hpf) because of unavailability of previous therapy or desire to switch from dietary therapy. Of the 61 remaining patients, 49 were male (80%). Ages ranged from 1 to 17 years (median, 8 years) at the time of OVB initiation.

The various vehicles with associated budesonide doses used by all 61 patients are presented in Table I. The most frequently used vehicle was Splenda (N = 30 [49%]). Twenty-seven of the 30 patients using Splenda responded (90%), demonstrating improvement in their peak eosinophil count to less than 15 eos/hpf. The 3 patients without response did have decreased peak eosinophil counts but not less than 15 eos/hpf. The mean peak eosinophil count for all 30 patients using Splenda decreased from 56.5 eos/hpf to 3.9 eos/hpf after the initiation of OVB.

Following Splenda, applesauce (N = 19) and honey (N = 7) were the next most commonly used vehicles. Fifteen of the 19 patients using applesauce responded (79%). Of the 4 patients without response, 1 patient did ultimately respond when switched to honey. The mean peak eosinophil count for all patients using applesauce decreased from 56.3 eos/hpf to 9.8 eos/hpf after the initiation of OVB. Six of the 7 patients started on OVB using honey responded (86%). The patient without response had documented poor compliance. The mean peak eosinophil count for all patients using honey decreased from 53.7 eos/hpf to 8.6 eos/hpf after the initiation of OVB.

The following vehicles were also used, by 1 patient each: hot cocoa mix, pear sauce, xanthan gum, and rice cereal. One patient used a compounded formulation of OVB prepared by a compounding pharmacy. The patient using rice cereal did show some improvement from more than 100 eos/hpf to 40 eos/hpf but not to less than 15 eos/hpf. The patients using hot cocoa mix, pear sauce, xanthan gum, and a compounded formulation all responded. The specific peak eosinophil counts for each of these patients are presented in Table I.

In summary, we report success using various vehicles to deliver OVB to treat EoE in children. Similar to previous findings,⁷ we show that there are promising alternatives to Splenda. Although Splenda remains the standard and is highly successful, most of the patients using applesauce and honey have also been effectively treated with OVB. In addition, individual patients using hot cocoa mix, pear sauce, xanthan gum, and a compounded formulation have responded to OVB.

TABLE I. Summary of vehicles used with associated budesonide doses and peak esophageal eosinophil counts

Vehicle	No. of patients	No. of patients who responded	Total daily budesonide dose	Peak esophageal eosinophil count before OVB	Peak esophageal eosinophil count after OVB
Splenda	30	27	1 mg (n = 15) 2 mg (n = 15)	56.5 eos/hpf* (range, 18-120 eos/hpf)	3.9 eos/hpf* (range, 0-70 eos hpf)
Applesauce	19	15	0.5 mg (n = 1) 1 mg (n = 7) 2 mg (n = 11)	56.3 eos/hpf* (range, 20-100 eos/hpf)	9.8 eos/hpf* (range, 0-40 eos/hpf)
Honey	7	6	1 mg (n = 2) 2 mg (n = 5)	53.7 eos/hpf* (range, 15-100 eos/hpf)	8.6 eos/hpf* (range, 0-50 eos/hpf)
Compound	1	1	1 mg	30 eos/hpf	0 eos/hpf
Hot cocoa mix	1	1	1 mg	30 eos/hpf	0 eos/hpf
Pear sauce	1	1	1 mg	30 eos/hpf	0 eos/hpf
Rice cereal	1	0	2 mg	100 eos/hpf	41 eos/hpf
Xanthan gum	1	1	2 mg	70 eos/hpf	0 eos/hpf

*Mean counts are provided for the patients using Splenda, applesauce, and honey.

There are several limitations to our study. We reviewed data retrospectively, and patients may not have had comparable compliance. We noted only 1 patient with documented poor compliance. And although we aim to standardize the desired consistency of OVB delivered—for example, 5 packets of Splenda, or 1 teaspoon of applesauce or honey, mixed with a Pulmicort Respule vial—the ultimate consistency created may differ among patients. Patients using hot cocoa mix, pear sauce, xanthan gum, and rice cereal were instructed to achieve a slurry consistency. With a less viscous consistency than desired, the maximal efficacy of swallowed topical budesonide may not be achieved. It is also important that patients not rinse, eat, or drink for 30 minutes after using the medication.

Despite these limitations, our results suggest that a variety of different vehicles can be offered to patients starting OVB for EoE. These options may be particularly beneficial to patients who are wary of consuming Splenda.

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Conflicts of interest: M. Shuker has received lecture fees from Greenville Hospital System, Division of Gastroenterology. L. Gober has received consultancy fees from Deerfield Consulting. C. A. Liacouras has received lecture fees from Abbott and Nutricia. J. M. Spergel has received research support from the National Institutes of Health (NIH), DBV Technology, NIH/National Heart, Lung, and Blood Institute, FARE, AImmune Therapeutics, and Stanford Food Allergy Center; is on the American Academy of Allergy, Asthma & Immunology board, FARE Medical

Advisory Board, APFED Scientific Advisory Board, and the International Association for Food Protein Induced Enterocolitis Medical Advisory Board; has received consultancy fees from Nutricia; has received lecture fees from Meetings & Events International; and has stock/stock options in DBV Technology. The rest of the authors declare that they have no relevant conflicts of interest.

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REFERENCES

1. Spergel JM, Brown-Whitehorn TF, Beausoleil JL, Franciosi J, Shuker M, Verma R, et al. 14 years of eosinophilic esophagitis: clinical features and prognosis. *J Pediatr Gastroenterol Nutr* 2008;48:30-6.
2. Liacouras CA, Furuta GT, Hirano I, Atkins D, Attwood SE, Bonis PA, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol* 2011;128:3-20.
3. Cianferoni A, Spergel J. Eosinophilic esophagitis: a comprehensive review. *Clinic Rev Allergy Immunol* 2016;50:159-74.
4. Contreras EM, Gupta SK. Steroids in pediatric eosinophilic esophagitis. *Gastroenterol Clin N Am* 2014;43:345-56.
5. Aceves SS, Bastian JF, Newbury RO, Dohil R. Oral viscous budesonide: a potential new therapy for eosinophilic esophagitis in children. *Am J Gastroenterol* 2007;102:2271-9.
6. Dohil R, Newbury R, Fox L, Bastian J, Aceves S. Oral viscous budesonide is effective in children with eosinophilic esophagitis in a randomized, placebo-controlled trial. *Gastroenterology* 2010;139:418-29.
7. Rubinstein E, Lee JJ, Fried A, Logvinenko T, Ngo P, McDonald D, et al. Comparison of 2 delivery vehicles for viscous budesonide to treat eosinophilic esophagitis in children. *J Pediatr Gastroenterol Nutr* 2014;39:373-7.

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