

Clinical Communications

Oral viscous mometasone is an effective treatment for eosinophilic esophagitis

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Clinical Implications

- In this study, we show that swallowed viscous mometasone is an effective alternative for the treatment of eosinophilic esophagitis, achieving histologic response in 76% of patients, including 72% of patients previously unresponsive to other swallowed steroids.

TO THE EDITOR:

Eosinophilic esophagitis (EoE) is an allergic immune-mediated condition characterized by eosinophilic infiltration of the esophageal mucosa and clinical symptoms of esophageal dysfunction. Pharmacologic treatment options for EoE are limited, consisting largely of swallowed topical corticosteroids fluticasone and oral viscous budesonide (OVB). Although studies have shown efficacy in achieving histologic remission in EoE,¹⁻³ a number of patients are refractory to these medications. Practical issues around palatability, medication mixing, and administration technique can make taking these medications difficult. Furthermore, concerns exist regarding potential for adrenal suppression in patients on chronic corticosteroid therapy.⁴

Mometasone furoate is a corticosteroid used for the treatment of allergic conditions with a well-documented safety profile.^{5,6} A study of intranasal corticosteroids has shown that the systemic bioavailability of mometasone is approximately 0.1%, 10 times lower than that of fluticasone (~1% bioavailability) and 340 times lower than that of budesonide (34% bioavailability).⁷ Mometasone is the most lipophilic of the 3, allowing for greater deposition in the targeted mucosa, higher binding affinity at the corticosteroid receptor, and consequently, less unbound drug to interact with systemic glucocorticoid receptors to potentially cause adverse effects.⁸

We analyzed the effectiveness of swallowed viscous mometasone as a novel medication for EoE treatment. This retrospective study was approved by the Boston Children's Hospital institutional review board (IRB-P00025308). Data were collected from electronic medical records. For study inclusion, patients required endoscopy with biopsies demonstrating active EoE (>15 eosinophils per HPF [eos/HPF] on any 1 esophageal biopsy) before mometasone initiation and follow-up endoscopy with biopsies 1 month or more after mometasone initiation. Patients were classified as "prior steroid failure" if they had active EoE while on previous swallowed steroid therapy (OVB doses ranging from 1 to 3 mg daily, fluticasone doses ranging from 440 to 1320 µg daily) before mometasone initiation. Patients were

"steroid-naïve" if they had never been on swallowed steroid therapy for EoE. Patients with documented concern for medication noncompliance were excluded. Histologic response to mometasone was defined as less than or equal to 15 peak eos/HPF, and remission less than or equal to 5 peak eos/HPF on all follow-up biopsies. The paired change in peak eos/HPF from pretreatment to posttreatment was examined by 2-sided Wilcoxon signed-rank test. Data analysis was performed with SAS version 9.4 (SAS Institute, Cary, NC).

Mometasone dosage was based on patient stature as a proxy for esophageal length. Patients shorter than 110 cm received 750 µg (5 mL), 110 to 149 cm received 1125 µg (7.5 mL), and 150 cm or higher received 1500 µg (10 mL) mometasone. Mometasone was formulated as a viscous suspension at 150 µg/mL, composed of powder forms of mometasone furoate United States Pharmacopeia (USP) (Medisca, Letco), hydroxypropyl methylcellulose USP (Methocel E4M), potassium sorbate NF, citric acid USP (anhydrous), stevia (stevioside), sodium benzoate NF, and liquid flavoring agent (PCCA, Flavorx, Letco). A compounding pharmacist weighed all components and prepared the suspension with strict quality control guidelines in adherence with USP standards. Methocel E4M 2% suspension was gradually added to the powders and flavoring, mixing well to ensure uniform distribution of all components. The suspension was dispensed in a plastic amber bottle with a plastic bottle adaptor cap and syringes. Patients were instructed to store the compounded mometasone suspension in the refrigerator and discard the medication after 30 days per USP guidelines. Patients were instructed to shake the medication well before each use and not to eat or drink for 30 minutes after taking the medication.

Thirty-four patients who started mometasone for EoE at Boston Children's Hospital between April 2016 and June 2018 met the aforementioned inclusion criteria (Table I). Twenty-six

TABLE I. Subjects' characteristics (n = 34)

Characteristic	Value
Age at mometasone initiation (y), median (range)	9.4 (1.4-28.3)
Age ≤18 y	30 (88)
Age >18 y	4 (12)
Age at first postmometasone EGD (y), median (range)	10.0 (1.5-28.5)
Sex: male	25 (74)
History of asthma	14 (41)
History of environmental allergies	16 (47)
History of immediate food allergies	14 (41)
History of reactive skin prick testing (≥5 positive foods), among n = 24 tested	11 (46)
Concomitant PPI therapy	20 (59)
Reason for mometasone initiation	
Initial treatment	9 (26)
Prior failed steroid therapy	18 (53)
Prior failed diet therapy	23 (68)
Behavior concerns on prior steroid regimen	6 (18)
Growth concerns on prior steroid regimen	1 (3)

EGD, Esophagogastroduodenoscopy; PPI, proton pump inhibitor. Values are n (%) unless otherwise indicated.

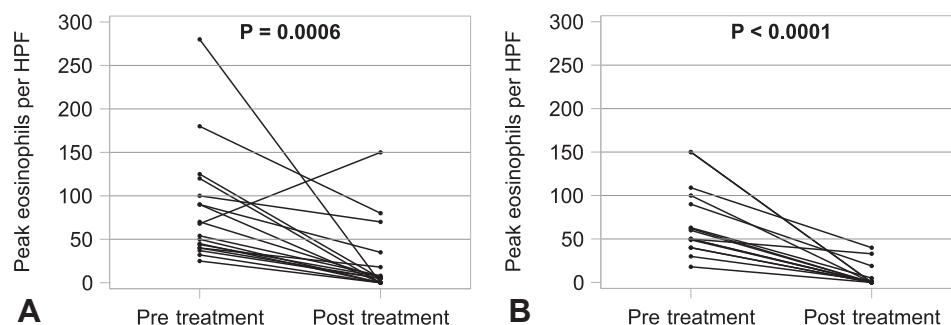


FIGURE 1. Comparison of peak eosinophil counts pretreatment and posttreatment with mometasone in (A) patients who previously failed swallowed steroid therapy and (B) steroid-naïve patients. The median paired change was -46 (range, -280 to 82) and -54 (range, -150 to -17) peak eosinophils per HPF (eos/HPF), respectively, with P value for change from the Wilcoxon signed-rank test. There was no difference in paired change for those who were steroid-naïve compared with those who experienced prior steroid failure ($P = .54$ by Wilcoxon rank-sum test).

(76%) patients experienced histologic response to mometasone and 23 (68%) achieved remission, with median change in peak eos/HPF of -50 (range, -280 to 82 ; $P < .001$). A decrease in peak eos/HPF was seen in all but 1 patient, who previously had poor response to OVB and also had IgE-mediated food allergies, asthma, and environmental allergies.

Eighteen patients had experienced prior steroid failure. Thirteen (72%) demonstrated histologic response, and 10 (56%) achieved remission after mometasone treatment, exhibiting a median change of -46 eos/HPF (range, -280 to 82 ; $P = .0006$) (Figure 1, A). Sixteen patients were steroid-naïve, 13 (81%) of whom achieved histologic response and remission after treatment with mometasone, with median change of -54 eos/HPF (range, -150 to -17 ; $P < .0001$) (Figure 1, B). Although response and remission rates were higher for steroid-naïve patients compared with those with prior steroid failure, these were not statistically significant ($P = .54$ and $P = .11$, respectively; Pearson χ^2 test).

Six patients had idiosyncratic reactions on their previous OVB regimen, including aggression, mood swings, hyperactivity, and disrupted sleep. Each achieved remission and parent-reported improvement in behavior after switching to mometasone.

All 34 patients maintained linear growth trajectory (defined as maintenance of height within 2 percentile curves on World Health Organization/Centers for Disease Control and Prevention growth charts) throughout the study period. One patient had a history of slowed linear growth on his previous OVB regimen, dropping from the 15th to the 3rd percentile over 6 years. After switching to mometasone, his height percentile stabilized but did not recover.

To assess adrenal axis function, dehydroepiandrosterone sulfate (DHEA-S) levels were monitored.⁹ Of the 13 patients with DHEA-S levels available, 1 had low DHEA-S (<0.1 ; normal, 5–40 for patient age) confirmed with low morning cortisol (1.6; normal, 5–25) and abnormal adrenocorticotrophic hormone stimulation testing, diagnostic of adrenal suppression. Levels from his previous OVB regimen were unavailable for comparison. This patient was receiving multiple corticosteroid-containing medications, including inhaled fluticasone daily, inhaled budesonide 1 or more times weekly, and prednisolone

bursts 1 or more times yearly for asthma, in addition to 7.5 mL (1125 μ g) mometasone daily. The cause of adrenal suppression was likely from the cumulative effects of multiple steroids rather than mometasone alone.

Topical therapy with fluticasone or OVB is currently standard of care in EoE pharmacologic treatment. Previous studies investigating their efficacy have demonstrated remission rates ranging from 55% to 93%.^{1–3} The extremely low systemic bioavailability of mometasone compared with that of fluticasone and budesonide, combined with high lipophilicity allowing for more effective mucosal tissue targeting, makes mometasone an attractive long-term treatment option in EoE management. In addition, mometasone can be dosed once daily, potentially increasing compliance, and can be flavored, making it more palatable than sucralose-based suspensions.

This study is the first to show the effectiveness of swallowed viscous mometasone for treatment of EoE, demonstrating a 76% response rate and 68% remission rate in our population. Mometasone also induced histologic response in 72% of patients with prior steroid failure, and shows promise as an alternative for patients with behavior concerns. Prospective studies are needed to determine whether mometasone is superior to other swallowed steroid therapies for EoE treatment.

Acknowledgments

We thank nurse Kathryn Vukson, CPN, for her work communicating with compounding pharmacies and patients and their families to provide education about appropriate medication dosage, administration, and compliance, and we also acknowledge ACC Apothecary (Newton, Mass) and Acton Pharmacy (Acton, Mass) for compounding of the mometasone suspension. For further details regarding preparation of mometasone for patient use, please contact pharmacist Arthur Margolis at ACC Apothecary (email: arthur@accrx.com, phone: 617-527-1563).

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Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication May 14, 2019; revised July 31, 2019; accepted for publication August 19, 2019.

Available online ■ ■

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2213-2198

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<https://doi.org/10.1016/j.jaip.2019.08.042>

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