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Comparison of Cetirizine to Diphenhydramine in the Treatment of Acute Food Allergic Reactions

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To the Editor:

Diphenhydramine has been commonly used as the antihistamine of choice for acute food allergic reactions given its prompt onset of action (15–60 minutes)¹ and ready availability, though epinephrine is still the first-line therapy for anaphylaxis. However, sedation is a common side effect of diphenhydramine, which, in our clinical experience, can complicate the assessment of a patient being treated for an acute allergic food reaction. Cetirizine is a second generation antihistamine with a similar onset (15–30 minutes) but longer duration of action (≥24 hours) compared to diphenhydramine^{2,3}. Furthermore, CNS effects are less commonly reported^{2,4,5}. Cetirizine has been used by patients in our outpatient clinic for the treatment of acute allergic food reactions, but a direct comparison of the efficacy and side effect profile of cetirizine to diphenhydramine has not been investigated for the treatment of allergic food reactions. Therefore, the aim of this study was to compare the presence of medication-related sedation of cetirizine to diphenhydramine and the efficacy of these medications in the treatment of acute food allergic reactions in subjects undergoing oral food challenges.

This was a randomized, double-blind study of 70 allergic reactions during oral food challenge involving 64 patients ages 3 to 19 years (5 patients presented for multiple food challenges). There were 35 reactions included in each treatment arm. Written informed consent was obtained from each subject, and the study was approved by the Mount Sinai Institutional Review Board. Subjects who reacted to the challenged food were blindly randomized to receive either liquid diphenhydramine (1mg/kg) or liquid cetirizine (0.25mg/kg). Of note, 5 patients presenting for multiple food challenges were re-randomized at each challenge. When indicated, all other medications were administered as per the standard oral food challenge protocol⁶. After administration of the antihistamine, each patient was

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monitored at 10-minute intervals for allergic symptoms and sedation by nursing staff blinded to the medication. Patients were assessed for sedation using a 5-point validated sedation score (Table 1), which has been used in pediatric anesthesiology studies^{7,8}. The primary outcome of the study was the percent of patients experiencing sedation in the two treatment groups. Patients with sedation score of 1 or 2 were considered as experiencing sedation. Additionally, the mean time to resolution of urticaria and pruritus was determined in each group to assess the efficacy of diphenhydramine and cetirizine. While all symptoms experienced by patients were recorded, the cutaneous symptoms were used for analysis as these are the symptoms effectively treated by antihistamines. Additionally, urticaria is an objective finding, which enhances the validity of study outcome. An unpaired *t* test (GraphPad Software) was utilized for statistical analysis.

The median age for the diphenhydramine-treated group was 8.42 years (3–19 years), and that for cetirizine-treated group was 8.92 years (4–17 years). Milk, egg, and peanut constituted 88.6% of foods challenged in both groups. In the diphenhydramine-treated group, 28.6% experienced sedation as compared to 17.1% for the cetirizine-treated group, reflecting a difference in sedation of 11.4% (CI -8.4% to 30.2%); however, this did not reach statistical significance, likely due to the small sample size. The distribution of sedation scores is presented in Table 1; both the mean and median sedation scores between the two treatment groups were not significantly different. The mean time to resolution of urticaria and pruritus was similar in both groups. In the diphenhydramine-treated group, the mean time to resolution of the urticaria was 42.3 minutes (SD 23.15); in the cetirizine-treated group, the mean time to its resolution was 40.8 minutes (SD 22.11) [*p*=0.86]. For pruritus, the mean time to its resolution was 28.6 minutes (SD 20.54) for the diphenhydramine-treated group; in the cetirizine-treated group, the mean time to resolution was 31.3 minutes (SD 20.07) [*p*=0.67]. Similarly, the mean time to first onset of urticarial or pruritus relief was similar in the two treatment groups. There was no difference in administration of other medications. Specifically, 9 patients in each group required administration of steroid or epinephrine for symptoms of abdominal pain, nausea, cough, wheezing, and angioedema. The reactions were promptly resolved by these additional medications, and all patients were discharged home the same day.

In this randomized, double-blind study involving 70 allergic reactions during oral food challenges, cetirizine demonstrated similar efficacy as compared with diphenhydramine in treating cutaneous symptoms in acute food allergic reactions. No significant difference in the mean time to resolution of urticaria and pruritus by either cetirizine or diphenhydramine was noted. This finding is consistent with the results of prior studies assessing the efficacy of second generation antihistamines in acute allergic reactions².

Although the primary outcome of the study was not met as the study was not sufficiently powered to demonstrate a statistically significant difference in sedation, the observed trend showed a higher percentage of sedation in patients receiving diphenhydramine in comparison to cetirizine with a difference of 11.4%. In studies assessing antihistamine-related sedation in other, non-food allergic reactions, the results suggest a higher incidence of sedation in patients treated with diphenhydramine in comparison to those treated with the second generation antihistamines, including cetirizine^{2,4,5}. However, our study on food allergic reactions did not replicate these results. It should also be noted that liquid formulations of antihistamine were used in our study; other formulations which may have different bioavailability may yield different results. In regards to the safety, our study showed no adverse events related to the administration of cetirizine, and a number of studies in the past have documented and confirmed the safety of cetirizine in young children^{9,10}.

In summary, cetirizine has similar efficacy and onset of action as compared with diphenhydramine in treating acute food allergic reactions. With added benefits of similar efficacy but longer duration of action compared with diphenhydramine, cetirizine is a good treatment option for acute food allergic reactions. Further studies involving a larger sample size will better elucidate the difference in sedation between the two antihistamines.

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Table 1

Description of sedation scores and their distribution in the two treatment groups

Sedation Score	Description	Diphenhydramine (% experiencing sedation)	Cetirizine (% experiencing sedation)
1: Unconscious	Asleep; does not respond to minor motor stimulation	8.6	2.9
2: Drowsy	May close eyes but responds to minor motor stimulation	25.7	17.1
3: Normal	Calm, sitting/lying comfortably with eyes open	100 [*]	100 [*]
4: Anxious	Looks frightened but not clinging to parent; may whimper but not crying	22.9	22.9
5: Very agitated	Crying, struggling, or clinging to parent	2.9	11.4

* All subjects started or ended the observation period with this score.

** Some of the patients who experienced sedation moved along the sedation score scale during the observation period (for example, a patient could have started with a sedation score of 3, then received a score of 1 when heavily sedated, then moved up to a score of 2 while gradually getting more alert, and ended the observation period again with a score of 3). Therefore, these patients received more than 1 sedation scores, and this explains why the percentages of the scores sum up to >100.