

Is Self-injectable Epinephrine Being Used by Children With Food Allergy?

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Anaphylaxis can be defined as a serious allergic reaction that is rapid in onset and might cause death [1]. The incidence of pediatric anaphylaxis has been increasing in the last decade [2], probably owing to the increasing frequency of food allergy, which remains the most important trigger of anaphylaxis in the pediatric population [3].

Epinephrine is the medication of choice for the immediate treatment of anaphylaxis, and autoinjectors are the preferred method for administration in the community setting. Autoinjectors should be prescribed to patients with a history of anaphylaxis and a high probability of recurrence [1]. However, evidence has shown that many patients do not carry them or use them when needed [4].

The purpose of this study was to describe the use of self-injectable epinephrine for pediatric patients with food allergy.

We performed an observational, cross-sectional study of patients with food allergy attended in the Pediatric Allergy Unit of Hospital General Universitario Gregorio Marañón, Madrid, Spain between October and November 2016. Participants were invited to fill in an anonymous survey if they had already been diagnosed with food allergy. The survey included questions about reactions within the previous year and their management. Most of the questions were asked in a dichotomous format to facilitate responses and analysis. A detailed description of the survey has been published elsewhere [5]. The characteristics of the reactions were extracted from the clinical records by the investigators. This post hoc analysis includes only patients who had been prescribed an autoinjector, following recommendations by international guidelines [1]. The study was approved by the local ethics committee. Written informed consent was obtained from all participants.

The statistical analysis was performed with IBM SPSS Statistics Windows, Version 20.0 (IBM Corp). Qualitative variables are expressed as frequency and quantitative variables are expressed as median (IQR). Categorical variables were compared using the χ^2 test and Fisher exact

test; quantitative variables were compared using the Mann-Whitney test. Post hoc statistical power was calculated for the main variables, ie, rate of anaphylaxis (0.84) and use of epinephrine (0.88).

An autoinjector was prescribed to 103 patients (40 girls [38.8%] and 63 boys [61.2%]); median age was 9 (5) years. A history of anaphylaxis was recorded in 79 cases (76.7%); of these, 19 (18.4%) had been prescribed an autoinjector owing to allergy to ubiquitous triggers, 4 (3.9%) had experienced reactions with tiny amounts of food, and 1 (1%) had concomitant unstable asthma.

Table. Characteristics of the Pediatric Patients With Food Allergy Who Had Been Prescribed an EAI^a

	EAI-Carrying Patients (n=88)	Non-EAI-Carrying Patients (n=15)	P
Sex			
Female	55 (62.5%)	7 (46.7%)	.5
Male	33 (37.5%)	8 (53.3%)	
Median (IQR) age, y	9 (5)	10 (6)	.3
History of anaphylaxis	69 (78.4%)	10 (66.7%)	.3
Other allergic diseases			
Asthma	55 (62.5%)	8 (53.3%)	.5
Rhinoconjunctivitis	29 (33%)	7 (46.7%)	.3
Atopic Dermatitis	23 (26.1%)	4 (26.7%)	.9
Food allergy			
Peanuts and tree nuts	47 (53.4%)	9 (60%)	.6
Cow's milk	35 (39.8%)	2 (13.3%)	.09
Egg	30 (34.1%)	5 (33.3%)	.9
Fruit	19 (21.6%)	4 (26.7%)	.7
Fish	16 (18.2%)	0	.1
Legumes	5 (5.7%)	1 (6.7%)	.9
Shellfish	2 (2.3%)	1 (6.7%)	.4
Other	2 (2.3%)	0	.9
Allergic to ≥ 2 foods	42 (46.6%)	7 (46.7%)	.9
Time since diagnosis			
<1 y	4 (4.5%)	2 (13.3%)	.2
1-5 y	18 (20.5%)	5 (33.3%)	.2
>5 y	66 (75%)	8 (53.3%)	.1
Reactions within the previous year			
Anaphylaxis	46 (52.3%)	8 (53.3%)	.9
Other allergic reactions	20 (43.5%)	0	.02
Other allergic reactions	26 (56.5%)	8 (100%)	.04
Use of epinephrine			
Self-injected	10 (11.4%)	0	.3
Health care center	4 (40%)	0	.9
Health care center	9 (90%)	0	.3

Abbreviations: EAI, epinephrine autoinjector.

^aHochberg-Benjamini and Bonferroni corrections did not alter the findings in this table.

Eighty-eight patients (85.4%) reported that they usually carried the devices with them. There were no statistically significant differences between patients who carried an autoinjector and those who did not with respect to sex ($P=.5$), age ($P=.3$), history of anaphylaxis ($P=.3$), triggers, or time since the diagnosis of food allergy (Table).

Fifty-four patients (52.4%) had a food-triggered allergic reaction within the previous year; the reaction was anaphylaxis in 20 (19.4%). The frequency of reactions was similar in the autoinjector-carrying group and the non-autoinjector-carrying group ($P=.9$). However, anaphylaxis was significantly more common among the former (43.5% vs 0; $P=.02$) (Table).

Only 10 of the patients who experienced a reaction received epinephrine (18.5%). There were no statistically significant differences between the patients who received epinephrine and those who did not with respect to sex ($P=.3$), age ($P=.9$), concomitant allergic diseases ($P=.9$), or triggers. Nevertheless, anaphylaxis was more common among those who had received epinephrine than among those who had not (100% vs 22.7%; $P<.0001$) (Supplementary Material).

Only 4 patients (7.4%) used their autoinjector to treat their reactions; 9 (16.7%) received epinephrine in a health center with a standard injection. Three patients (75%) who used their device received a second dose in a health center with a standard injection.

Avoidance is standard treatment for food allergy [1]. However, in our study, over half of the patients with a previous diagnosis of food allergy had had a reaction during the previous year, in many cases resulting in anaphylaxis. Studies of adverse food reactions in food-allergic people are scarce. One systematic review reported an incidence rate of self-reported anaphylaxis of 4.93/100 person-years [6], which is lower than the 19.4% we recorded. However, comparison of these figures might be limited owing to methodological differences. Other studies have focused on the frequency of accidental exposure in children with known peanut allergy [7] and cow's milk allergy [8] (11.9% and 40%, respectively). As the latter figure was recorded in a pediatric allergy unit in Madrid, the population represented can be considered similar to ours.

In our study, most of the patients who were prescribed an autoinjector reported that they usually carried it with them. However, the device was used in a very small number of reactions. It is possible that some of them were mild and did not require treatment with epinephrine, as anaphylaxis was more common among patients who received epinephrine. However, previous studies have demonstrated that, regardless of severity, many patients do not have an epinephrine autoinjector readily available [9]. In fact, we found that fewer than half of the patients with anaphylaxis used epinephrine. Furthermore, most patients who received epinephrine for treatment of their reactions did not use their autoinjector. A survey among survivors of anaphylaxis showed similar results [4]. This observation has various explanations, including unavailability, inability to recognize anaphylaxis, severity of the reaction, inadequate training in the use and indications of the autoinjector, use of antihistamines, and concern about adverse effects [4,10].

Our study is subject to a series of limitations owing to its cross-sectional design, from which only associations, rather than causality, can be established. The data were collected in the pediatric allergy unit of an urban tertiary hospital, thus indicating a lack of external validity. Given that this is a post hoc analysis, some minor differences between groups may have gone undetected because of a potential lack of statistical power or recall bias. However, given the strength of the associations, it seems unlikely that this would alter the conclusions.

In summary, allergic reactions due to accidental exposure are not uncommon among children already diagnosed with food allergy. While many children report that they usually carry epinephrine, they rarely use it. Anaphylaxis in the community remains undertreated.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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