

A. ARENA

Anaphylaxis to apple: is fasting a risk factor for LTP-allergic patients?

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KEY WORDS

Food allergy, Lipid transfer protein, Apple allergy, Allergens

SUMMARY

Background: Primary apple allergy is frequent in Mediterranean countries where hypersensitivity to lipid transfer protein (LTP) is common. Due to its stability upon pepsin digestion, LTP may cause systemic allergic reactions. This study investigated the potential risk associated with an isolated intake of apple while fasting in LTP-hypersensitive patients with clinical allergy to peach but not to apple. **Patients and methods:** Based on the observation of 6 patients who experienced 7 apple-induced anaphylactic reactions that in 6 cases followed the ingestion of the fruit after fasting, open food challenges were carried out in 12 patients LTP-hypersensitive patients with peach allergy but tolerant to apple. **Results:** Four out of the 12 patients (33%) reacted to apple upon oral challenge. **Conclusion:** Fasting seems to play a relevant role in the clinical expression of allergy to LTP. It is possible that in an empty gastrointestinal tract the allergen is absorbed more rapidly. Alternatively, pepsin might digest the food matrix more efficiently, thus increasing the concentration of the purified allergen that comes in contact with the gut mucosa.

Introduction

Primary allergy to Rosaceae fruits is frequent in the Mediterranean area (1-3). In central and northern Europe Rosaceae allergy is associated with birch pollinosis and is clinically mild and restricted to the oropharyngeal mucosa (4, 5), whereas in Southern Europe primary sensitization to Lipid transfer protein (LTP) is frequent (6, 7). LTPs are heat- and pepsin-stable, and can cause systemic reactions (6, 8). It is generally accepted that Pru p 3, the peach LTP, represents the primary sensitizer to this allergen (7). In LTP-hypersensitive patients allergic to peach, apple allergy may occur due to the high homology between Mal d3, the apple LTP and Pru p3 (7, 9).

In LTP-hypersensitive subjects the clinical presentation of apple allergy can be severe and not always preceded by other symptoms, as the OAS (1, 10, 11).

The observation of a group of six LTP-allergic patients, who experienced seven anaphylactic episodes induced by apples with peel, that in 6 cases were ingested at least two hours after a meal and without eating anything else, prompted us to investigate the potential risk associated with the isolated intake of apple in patients with peach allergy.

Patients and methods

Patients

29 LTP-hypersensitive patients with a history of peach allergy but clinically apple-tolerant, negative on SPT with birch pollen extract, seen at the Allergy center of Azienda Sanitaria of Messina (Italy) from 2007 to 2009 were asked to participate to the study.

All the patients scored positive on SPTs with Golden Delicious (GD) fresh apple (peels and pulp separately), according to prick-by-prick method (12), and with a commercial peach extract containing uniquely lipid transfer protein (Alk Abellö ; LTP 30 µg/ml). SPTs were carried out and read following the EAACI recommendations (13) using histamine hydrochloride (10 mg/mL) and saline as positive and negative controls, respectively.

Specific IgE

Specific IgE against apple and Pru p 3 were measured by CAP-System (Phadia©, Uppsala, Sweden), according to the instructions of the manufacturer.

Challenge tests

Twelve out of 29 subjects accepted to undergo the apple challenge. An informed consent was obtained from each patient before the challenge. GD apples, bought at the local market, were used in the

challenges. Open food challenges (OFC) were performed by administering slices of fresh apple with peel on patients fasting for at least two hours. One slice of apple (approximately 10 g) was administered at the beginning and the dose was then doubled every 60 min. The test continued until the patient had convincing symptoms, or a total of approximately 70 g of apple had been ingested (3 h). Before all challenges and SPTs, medication was discontinued according to the guidelines on skin testing of the European Academy of Allergology and Clinical Immunology (EAACI) (14).

Results

Results are shown in Table 1. Four out of 12 (33%) subjects scored positive upon apple challenge. All 4 experienced itch, urticaria, abdominal pain and nausea. No significant differences were found in Pru p 3 and apple IgE between subjects who responded or tolerated apple on oral challenge (Table 2).

Table 1 - Patients submitted to oral challenge with fresh, unpeeled apple

N.	Age	Sex	Peach*	Cap Pru p3	Cap Apple	Other food allergies**	Clinical symptoms during OFC*** *	Dose challenge
1	44	F	U, AP	22,7	69,3	Ha (U-A)	I,N,AP	10
2	18	F	OAS, P	1,85	7,11	Al (U)	T	70
3	33	F	OAS	6,31	19,8	Ha (OAS)	T	70
4	38	F	OAS	4,75	63,8	Pn (OAS)	T	70
5	20	F	CU	1,35	0,8	W (U)	T	70
6	19	F	OAS	0,95	0,61	-----	T	70
7	46	F	OAS	1,5	0,5	Pn, Al (SOA)	AP, I	30
8	23	M	OAS	2,34	2	-----	T	70
9	20	M	OAS	9,57	1,8	Pn(SOA)	T	70
10	32	F	OAS	3,8	0,61	-----	T	70
11	29	M	D, CU	12,3	13,4	Pn (U)	U, N	30
12	28	M	CU	3,96	1,2	-----	N, I	30

* A, angioedema; AP, abdominal pain; D, dyspnoea; N, nausea; I, itch; U, urticaria; UC, contact urticaria; OAS, oral allergy syndrome

** Apr, apricot; Al, almond; Ha, hazelnut; Pn, peanut; W noce;

*** T, tolerated

Table 2 - Specific IgE

		Positive on apple oral challenge (n= 4)	Negative on apple oral challenge (n= 8)
Pru P3	kU/l (mean[range])	10,1 (1,5-22,7)	3,8 (0,9-6)
Apple	kU/l (mean[range])	21,1 (0,5-69,3)	12,06 (0,6-63,8)

Discussion

The observation that in 6/7 (85%) cases of apple-induced anaphylaxis the fruit had been eaten while fasting prompted us to carry out the present study. In a group of LTP-hypersensitive subjects with a history of peach allergy but clinically tolerant to apple (albeit sensitized to apple on SPT and in-vitro assays) submitted to open food challenge with increasing doses of unpeeled apple, one third experienced a systemic reaction following apple ingestion while fasting.

Recent guidelines recognize that there is no absolute correlation between pepsin digestion and allergenicity but suggest that rapid and extensive degradation may be helpful in increasing allergen availability (15). The proteolysis of food allergens is strongly dependent on the pepsin to allergen ratio (16). Pepsin secretion by human stomach is influenced by quantity and type of food ingested (17). Digestibility and allergenicity of some proteins, such as peanut and β -lactoglobulin, is the of interactions between allergens and other food ingredient (18-20).

It is possible that in an empty gastrointestinal tract the LTP is absorbed more rapidly. Alternatively, pepsin might digest the food matrix more efficiently, thus increasing the concentration of the purified allergen that comes in contact with the gut mucosa.

There are several different facilitating factors in food allergy: exercise (21-23), various drugs (24) or both (25). Fasting has never been described as a risk factor for systemic reaction to foods.

These observations allow to hypothesize that the absence of food in the stomach may influence allergen presentation to the immune system, thus representing an eliciting factor for clinical allergy in apple-allergic subjects.

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