Acta Biomed 2019; Vol. 90, N. 2: 265-268 DOI: 10.23750/abm.v90i2.7611

Original article

Pru p 3 sensitization in children with allergy to Parietaria pollens

Giorgio Ciprandi[1], Paolo Del Barba[2], Michela Silvestri[3], Salvatore Barberi[4], Maria Angela Tosca[3]

[1]Casa di Cura Villa Montallegro, Genoa, Italy; [2]Pediatric School, Università Vita Salute San Raffaele, Milan, Italy; [3]Pediatric Allergy, IRCCS Istituto Giannina Gaslini, Genoa, Italy; [4]Pediatric Department, ASST Fatebenefratelli-Sacco, Milan, Italy

Summary. *Background:* Pru p 3 is the major allergen of the peach and belongs to the LTP family. Pru p 3 sensitization has been associated with severe allergic symptoms after eating LTP-containing foods. However, a previous experience partially downsized the potential danger of Pru p 3 sensitization in a group of adult rhinitics. This study aimed to evaluate the real impact of Pru p 3 sensitization in children in a real-world setting. *Methods:* 82 consecutive paediatric patients (55 males and 27 females, mean age 8.19±4.23 years) with allergic rhinitis due to Parietaria pollen allergy and sensitization to Pru p 3, documented by ISAC test, were evaluated. Serum IgE was measured by ImmunoCap method. Allergic symptoms occurring after ingesting LTP-containing foods were considered and scored as oral allergy syndrome, food allergy, and anaphylaxis. *Results:* About one-quarter of Pru p 3-sensitized children reported anaphylaxis after ingesting LTP-containing foods, about half reported food allergy or oral allergy syndrome. Only ¼ was merely sensitized. *Conclusions:* Pru p 3 sensitization deserves careful attention in children contrary to what might occur in adult patients. It could depend on the age and the serum IgE level. Thus, Pru p 3 sensitization should be adequately interepreted and managed in clinical practice. (www.actabiomedica.it)

Key words: Pru p 3, sensitization, allergy, pollen food syndrome, pollen allergy, children

Introduction

Lipid transfer protein (LTP) belongs to the prolamins super-family and is implicated in cuticle formation and defence against pathogens (1). LTP is present in several plant food sources, such as fruits, vegetables, nuts, pollens, and in latex. LTP is a genuine food allergen as can sensitize throughout the digestive tract and may be a potent food allergen as resistant to thermal and acid processing (2, 3). LTP is the most frequent cause of both primary food allergy and food-dependent anaphylaxis in Italy (2, 4), although of course cow's milk and egg are the most frequent offending foods in Italian children (5). The LTP allergen Pru p 3 is the major peach allergen and is primarily present in the peel (1). Pru p 3 is commonly considered a pan-allergen as it is shared by several foods (4). It is well known that the peach may be considered the primary sensitizer to LTP in the Mediterranean area. It has been reported that high levels of serum IgE to Pru p 3 were associated with increased probability to have systemic allergy to peach (6). A further study partially confirmed these outcomes, as high levels could not be associated with true allergy (7). In addition, it has been reported that only 20% of children with LTP sensitization showed symptoms after LTP ingestion (8).

Pollen-food syndrome (PFS) is defined by the symptom occurrence after eating fruits or vegetables in patients with pollen allergy, because of a primary pollen sensitization due to cross reactivity between pollen and food allergen proteins. The severity of symptoms may vary from mild intensity, such as symptoms confined to

oral cavity (the so-called oral allergy syndrome, OAS) to life-threatening reactions. In this regard, LTP sensitization has been considered as a potential risk factor for severe allergic reaction after eating LTP-containing foods. Consequently, there are some allergists who prescribe restricted dietary regimen suggesting avoidance of many fruits and vegetables potentially cross-reacting with Pru p 3 and sometimes deliver auto-injectable epinephrine also in patients with Pru p 3 sensitization alone, fearing potential severe reaction. In this regard, a recent study, conducted in 3,937 Italian subjects, reported that the prevalence of Pru p 3 sensitization was 16.7% (6). More interestingly, Pru p 3 IgE production depended on age concerning both positive test and serum level: older age lower level (9, 10). As this matter is particular intriguing, we would like to test the hypothesis about the clinical and pragmatic relevance of Pru p 3 sensitization in clinical practice. So, a real-world study was conducted in a group of adult patients suffering from allergy to Parietaria pollen exploring this issue (11). In those clinical cases, no subject had anaphylactic reaction after eating LTP-food, even though those patients were a selected group, such as suffering from allergic rhinitis (11). Therefore, we retrospectively analysed a consecutive series of children with pollen allergy and Pru p 3 sensitization with the aim of defining the clinical relevance of IgE production toward LTP and comparing findings with those adult subjects.

Materials and Methods

A retrospective analysis of the medical records of 82 consecutive paediatric patients (55 males and 27 females, mean age 8.19±4.23 years) with allergic rhinitis due to Parietaria pollen allergy and sensitization to Pru p 3, documented by ISAC test, has been performed. All of them referred to the Allergy Center.

Inclusion criteria were the documented pollen allergy and Pru p 3 sensitization. In particular, all children had an IgE-mediated pollen allergy diagnosed on the consistency between positive skin prick test and symptoms occurrence after exposure to sensitizing allergen. Sensitization was defined as below described.

The study conformed to the ethic criteria concerning the management of personal data and was it was approved by the local Ethics Committee, consequently all the parents of the children gave a written informed consent to this pourpose.

Children were subdivided in 4 sub-groups: sensitized alone (such as without clinical reaction after eating LTP-containing foods), OAS (such as reporting oral symptoms alone after ingesting LTP-containing foods), food allergy (such as reporting systemic symptoms after eating LTP-containing foods, but without anaphylaxis), anaohylaxis (such as reporting anaphylactic reaction after eating LTP-containing foods).

Serum levels of specific IgE for Pru p 3 were detected by the IFMA (immunofluorimetric) procedure (ImmunoCAP Thermo Fisher Scientific, Uppsala, Sweden) in peripheral blood samples from patients. Serum was collected into gel-separator tubes, centrifuged and stored at -20°C until analysis. Measurement of circulating specific IgE antibodies was performed according to manufacturer's instructions (12). Specific Ig E levels were expressed in kUA/L (kilo Unit of Allergen) according to the traceable calibration to the 2nd IRP WHO (Implementation Research Platform of World Health Organization) for Human IgE and 0.35 kUA/L has been considered as a cut-off for defining sensitization (13).

In addition, a group of adult patients, with allegic rhinitis due to Parietaria allergy and sensitized to Pru p 3, and living in the same geographic area, were compared with the current pediatric cases. Details on these subjects were reported elsewhere (11).

Age was reported as mean with standartd deviation in parenthesis; IgE levels were non-normally distributed (as evaluated by the Shapiro-Wilk test), summarized as medians with lower and upper quartiles (LQ and UQ) and compared using the Mann U Whitney test (in case of comparison between two groups) or Kruskal Wallis test (in case of comparison among more groups). Categorical variables (i.e. groups of pediatric patients with clinical reaction after ingestion of LTP- containing foods) were reported as absolute frequency and percentage; comparison between or among absolute frequencies were made using chi-square test of Fisher's exact test in case of expected frequencies lower than 5. All the tests were two-sided and a p value <0.05 was considered as statistically significant. Statistica software 9.0 (StatSoft Corp., Tulsa, OK, USA) was used for all the analyses.

Results

Table 1 reports demographic and clinical characteristics of the paediatric and adult study populations. The frequency of reaction after ingestion of LTP-containing foods was almost double in children as compared to adults: 73.2% and 37.3% respectively (p=0.0007). Particularly, anaphylaxis to LTP- containing foods was only reported by children, whereas no adult referred this severe reaction; in contrast, about ¾ of adults reported oral allergic syndrome to LTP-containing foods, whereas only about ¼ of children referred this kind of reaction.

Notably, Pru p 3 levels were significantly higher in children as compared to adults being 4.91 (1.07-9.37) KuA/L and 1.62 (0.98-2.48) KuA/L, respectively (p=0.042). In children, serum IgE to Pru p 3 levels tended to become higher in relation with the severity of the reaction being lower in children with Oral Allergy Syndrome and higher in those with anaphylaxis (p=0.15), as reported in Table 2.

Analyzing the absolute frequency of anaphylaxis, food allergy and/or oral allergy syndrome in pediatric patients due to each specific LTP-containing food, we found that peach was the most common culprit food, followed by walnut, apple and nut. Peach was also the most frequent food able to induce anaphylaxis or oral allergy syndrome, whereas walnut was more frequently responsible for food allergy (Table 3).

Table 2. Serum IgE to Pru p 3 levels (KuA/L) in different groups of pediatric patients with clinical reaction after ingestion of LTP-foods

Anaphylaxis No. 20	Food Allergy No. 24	Oral Allergy Syndrome No. 16
6.05 (4.54-12.2)	4.06 (0.81-6.78)	2.84 (0.86-8.71)

Table 3. Absolute frequency of anaphylaxis, food allergy and/or oral allergy syndrome in pediatric patients due to each specific LTP-food

	Anaphylaxis	Food Allergy	Oral Allergy Syndrome	Whole
Peach	6	13	11	30
Walnut	4	15	5	21
Apple	0	4	9	13
Nut	4	4	4	11
Kiwi	1	1	8	10
Cherry	1	3	4	8
Peanut	2	3	1	6
Strawberry	0	3	3	6
Apricoat	1	1	3	5
Pear	0	3	1	4
Plum	1	1	0	2
Soy	1	1	0	2
Grapes	2	0	0	2
Orange	1	0	0	1
Chestnut	1	0	0	1
Wheat	1	0	0	1
Almond	0	1	0	1

Discussion

The current study demonstrates that Pru p 3 sensitization in children with allergic rhinitis due to Parietaria pollen allergy deserves adequate attention in this age group. Indeed, about one-quarter of children with Pru p 3 sensitization reported anaphylaxis ingesting LTP-containing foods. In addition, one half of these children had anyway clinical reaction after eating LTP-containing foods, including food allergy or OAS. Thus, about ¾ of all of these children had LTP allergy and only one-quarter were merely sensitized to Pru p 3. On the other hand, these outcomes are very differ-

Table 1. Demographic and clinical characteristics

	Children (No. 82)	Adults (No. 29)	P value
Age (yrs) [mean (standard deviation)]	8.19 (4.23)	39.54 (14.96)	-
Gender	55 m 27 f	15 m 14 f	0.14
Patients with reaction after ingestion of LTP-foods [No. (%)]	60 (73.2%)	11 (37.3%)	0.0007
Anaphylaxis to LTP-foods	20 (30.0%)	0	0.0071
Food Allergy to LTP-foods	24 (29.3%)	3 (27.2%)	
Oral allergic syndrome to LTP-foods	16 (26.7%)	8 (72.8%)	

ent in the adults with Pru p 3 sensitization, previously reported, as only about one third had clinical reaction after LTP-containing foods ingestion. Interestingly, peach and nuts were the most common LTP-containing foods accountable for anaphylactic reaction in our geographic area.

These conflicting findings could be dependent also on the level of serum IgE: in fact, IgE to Pru p 3 production significantly diminishes with age, as previously reported (9.10). Really, a noteworthy outcome is the relevance of serum IgE level: the higher is serum level the higher is the odds of true allergy, both in children and in adults. This outcome is consistent with Par j 2 IgE level assessment: in this regard, it was reported that also IgE to Parietaria significantly diminished over time (14). Interestingly, it has to be noted that Par j 2 belongs to LTP family, even though it is an allergen able to induce only respiratory allergy and not food allergy.

Of course, the current study has some limitations: the setting concerning respiratory allergy outpatients, the relatively restricted number of patients, the lack of a follow-up, the peculiarity of the considered geographic area. Anyway, a pragmatic message is that to find Pru p 3 sensitization does not automatically mean to diagnose true allergy to Pru p 3 food allergen. Only the demonstration of a close relationship between ingestion of a sensitizing Pru p 3 allergen and consistent symptom occurrence is mandatory for allergy diagnosis that should be confirmed by a double-blind food oral challenge. Thus, a thorough work-up is fundamental in Pru p 3 sensitized patients. Avoidance diet should be prescribed only to true food allergic patients and epinephrine should be deliver only when an anaphylactic reaction is undoubtedly documented.

On the other hand, the current study highlights the relevant difference between adult and paediatric subjects: in fact, severe reactions are more frequent in children.

In conclusion, Pru p 3 sensitization needs adequate interpretation and management in clinical practice. Indeed, children with pollen allergy to Parietaria and Pru p 3 sensitization deserve careful attention, as anaphylaxis may be not a rare occurrence at a young age.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

1. Pastorello EA, Robino AM. Clinical role of lipid transfer protein in food allergy. MolNutr Food Res 2004; 48: 356-62.
2. Asero R, Piantanida M, Pinter E, Pravettoni V. The clinical relevance of lipid transfer protein. Clin Exp Allergy 2018; 48: 6-12.
3. Asero R, Antonicelli L, Arena A, et al. EpidemAAITO: features of food allergy in Italian adults attending allergy clinics: a multi-center study. ClinExp Allergy 2009; 39: 547-55.
4. Asero R, Mistrello G, Roncarolo D, et al. Immunological cross-reactivity between lipid transfer proteins from botanical unrelated plant-derived foods: a clinical study. Allergy 2002; 57: 900-6.
5. Caffarelli C, Coscia A, Ridolo E, et al. Parents' estimate of food allergy prevalence and management in Italian school-aged children. Pediatrics Internat 2011; 53: 505-10.
6. Rossi RE, Monasterolo G, Canonica WC, Passalacqua G. Systemic reactions to peach are associated with high levels of specific IgE to Pru p 3. Allergy 2009; 64: 1795-6.
7. Asero R, Arena A, Cecchi L, et al. Are IgE levels to foods other than Rosaceae predictive of allergy to lipid trabsfer protein-hypersensitivity patients? Int Arch Allergy Immunol 2011; 115: 149-54.
8. Mastrorilli C, Tripodi S, Caffarelli C, et al. Endotypes of pollen-food syndrome in children with seasonal allergic rhinoconjunctivitis: a molecular classification. Allergy 2016; 71: 1181: 91.
9. Ciprandi G, DeAmici M, DiMarino ML, Barocci F, Comite P. The impact of age on Pru p 3 IgE production in Italy. Asian Pacific Allergy 2017; 7: 42-7.
10. Tosca MA, Silvestri M, Olcese R, et al. Allergen-specific IgE to food molecular components and age: From early childhood to adulthood. Allergol Immunopathol 2017; 45: 87-92.
11. Ciprandi G, Ferrero P, Comite P. The pragmatic relevance of Pru p 3 sensitization in patients with pollen allergy. Rev Francaise Allergologie (in press)
12. Leimgruber A, Mosimann B, Claeys M, et al. Clinical evaluation of a new in-vitro assay for specific IgE, the immuno CAP system. Clin Exp Allergy 1991; 21: 127-31.
13. Seagroatt V, Anderson SG. The second international reference preparation for human serum immunoglobulin E and the first British standard for human serum immunoglobulin E. Journal of Biological Standardization 1981; 9: 431-7.
14. Tosca MA, Silvestri M, Olcese R, Pistorio A, Rossi GA, Ciprandi G. The impact of age on serum allergen-specific IgE to inhaled molecular components. Allergologia et Immunopathologia 2017; 45265-71.

Received: 8 August 2018
Accepted: 13 February 2019
Correspondence:
Giorgio Ciprandi, M.D.
Casa di Cura Villa Montallegro - Genoa, Italy
Tel. 00 39 10 35338120
E-mail: gio.cip@libero.it