The role of serum interleukin-6 and C-reactive protein levels for differentiating aetiology of neonatal sepsis

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ABSTRACT

***Introduction*:** In our clinical practice, we observed high interleukin-6 (IL-6) levels in gram-negative sepsis.

Objective: To investigate the relationship between IL-6 and C-reactive protein (CRP) levels and early determination of neonatal sepsis of gram-negative or gram-positive aetiology.

***Population and Methods*:** White blood cell count, IL-6 and CRP levels were compared among different groups.

***Results*:** Gram-negative, gram-positive and fungal infection groups consisted of 73, 82 and 15 patients, respectively. The optimal cut-off levels of IL-6 between gram-negative and gram-positive fungal infection groups were 202 and 57 pg/ml. The fungal infection group had higher CRP levels than gram-negative and positive infection groups.

***Conclusions*:** To our knowledge, this is the largest reported study aiming at determining of IL-6 cut-off levels to differentiate neonatal sepsis aetiology. Gram-negative microorganisms led to 10 fold higher IL-6 production. The evaluation of IL-6 and CRP is useful to diagnose and also differentiate neonatal sepsis aetiology.

Key words: *newborn, sepsis, interleukin-6, C-reactive protein, gram-negative infections, fungal disease.*

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INTRODUCTION

Neonatal sepsis continues to be a common and significant health care burden because of high mortality and morbidity rates despite advances in neonatology, especially in developing countries.[1] Several interleukins, tumor necrosis factor (TNF), procalcitonin (PCT), C-reactive protein (CRP), immunoglobins, and other markers have been used in the diagnosis of sepsis.[2]

Early recognition of signs of infection based on clinical or laboratory studies in the early stages of bacteremia could therefore, help to identify those patients who are likely infected with either gram-negative or gram-positive pathogens. Interestingly, some studies have shown significantly greater inflammatory response in gram-negative sepsis than in gram-positive ones.[3-5] Fungal infections also show different inflammatory responses.[6] Recently, we observed high IL-6 levels in some newborn infants with sepsis. During follow up, results showed that most of these patients had gram-negative infection. After this clinical observation, we decided to perform a subgroup analysis with the data obtained from a previously published study reporting cut-off levels of IL-6 and CRP in neonatal sepsis. [7]

OBJECTIVE

1. To investigate the value of IL-6 and CRP in the early establishment in neonatal sepsis aetiology as gram-negative or gram-positive,
2. To determine the cut-off value for each marker of neonatal sepsis,
3. To identify the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each cut-off level.

METHODS

Patients

This retrospective study took place in Zekai Tahir Burak Maternity Teaching Hospital between January 2008 and December 2008; medical records were reviewed and the study was approved by the local Ethics Committee. Clinical findings for sepsis diagnosis required at least three of the following: bradycardia (<100/min), tachycardia (>200/min), hypotension, hypotonia, seizures, apnea, tachypnea, cyanosis, respiratory distress, unusual skin color and perfusion, feeding difficulty, irritability, lethargy, and laboratory results showing elevated levels of IL-6 (>70 pg/ml) or CRP (>10 mg/dl). [8]

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Inclusion criteria of groups

- Group Ia (Proven sepsis; 170 patients): Newborns with positive blood cultures, clinical findings of infection, and elevated IL-6 and/or CRP levels.
- Group Ib (Clinical sepsis; 62 patients): Newborns with clinical findings of infection, elevated IL-6 and/or CRP levels, but with negative blood cultures.
- Group II (Control group; 50 patients): IL-6 and CRP levels of newborns admitted to the hospital for perinatal risk factors such as ablatio placentae, Rh isoimmunization, transverse position in utero, or non-infectious diseases, such as hypoglycemia, intrauterine growth restriction, transient tachypnea, indirect hyperbilirubinemia, without clinical findings of infection.

Statistical analyses

Statistical analyses were performed using the SPSS statistical package (v.15.0). Categorical variables were analyzed using the chi-squared test. The comparison of means was done using a t-test when the data fit a normal distribution, and a Mann–Whitney U test when the data was non-normal. In order to compare more than two groups, ANOVA was used for normal distributions, and the Kruskal–Wallis test for non-normal distributions. ROC analysis was used to determine the power of variables to differentiate groups, and the area under the curve was calculated; significant cut-off levels were calculated using a Youden index. A *p* value of <0.05 was deemed to indicate statistical significance.

RESULTS

There were 232 patients in Group I and 50 in Group II. The characteristics of patients and their distribution within the groups are listed in *Table 1*. Gestational age, birth weight, male/female ratio, and vaginal delivery rate did not differ statistically. The work-up day of IL-6 and CRP was similar between proven and clinical sepsis groups, but was earlier for the control group. Blood culture results are listed in *Table 2*; 29 types of microorganism were isolated from blood cultures. The number of gram-negative microorganisms, gram-positive microorganisms and fungus was 73 (43%), 82 (48%) and 15 (9%), respectively. The most frequently isolated microorganisms were *Klebsiella pneumoniae* (44; 25.8%), *Staphylococcus epidermidis* (29; 17%), fungi (*Candida albicans* and *Candida tropicalis*, 15; 8.8%), and *Staphylococcus aureus* (10; 5.8%).

We previously found cut-off levels of IL-6 and CRP between proven sepsis and control group as 21.5 pg/ml and 5.82 mg/dl, respectively.[7] Levels of IL-6 and CRP in all groups are listed in Table 3. Between the sepsis groups and the control group, there were significant differences for both IL-6 and CRP levels ($p < 0.001$). Levels of IL-6 and CRP in groups of gram-negative, gram-positive and fungal infection groups are listed in Table 4. There were statistically significant differences between gram-negative and other groups according to levels of IL-6 ($p < 0.001$). The optimum cut-off values of IL-6 in the diagnosis of gram-negative infection were found to be 202 pg/ml versus gram-positive infection, and 57 pg/ml versus fungal infection. The optimum cut-off value of IL-6 in the diagnosis of gram-positive infection versus fungal infection was found to be 58 pg/ml. Sensitivity, specificity, NPV and PPV of IL-6 level of 202 pg/ml (gram-negative versus gram-positive infection) are 68%, 58%, 57% and 69%, respectively. Sensitivity, specificity, NPV and PPV of IL-6 level of 57 pg/ml (gram-negative versus fungal infection) are 76%, 42%, 24% and 71%, respectively. Sensitivity, specificity, NPV and PPV of IL-6 level of 58 pg/ml (gram positive versus

TABLE 1. *Clinical and demographic characteristics of proven, clinical sepsis and control groups*

	Group Ia (n= 170)	Group Ib (n= 62)	Group II (n= 50)
Male/Female	87/82	38/24	30/20
Sepsis work-up day	14.3 ± 10.0	14.8 ± 10.2	3.9 ± 3.4
Birth weight, gram	1580 ± 685	1585 ± 718	1735 ± 760
Gestational age, weeks	30.6 ± 3.4 (23-41)	30.8 ± 3.6 (24-38)	31.7 ± 3.9 (25-42)
Vaginal delivery, %	27.6	24.2	30.6
Age of mother, years	26.8 ± 5.2	27.7 ± 6.7	28.4 ± 6.1

mean±standard deviation (interquartile range)

fungal infection) are 76%, 29%, 27% and 55%, respectively. The fungal infection group had higher CRP levels than other groups (p <0.05). Mortality rates of gram-negative, gram-positive and fungal infection groups were 18%, 10% and 20%, respectively (p >0.05).

TABLE 2. *Microorganisms isolated (blood culture)*

	Number of patients (%)
Gram negative microorganisms	**73 (43%)**
Klebsiella pneumoniae	44
Klebsiella oxytoca	8
Escherichia coli	6
Enterobacter cloacae	5
Acinetobacter baumannii, Enterobacter species, Serratia marcescens, Pseudomonas aeruginosa	2
Pantoea agglomerans, Stenotrophomonas maltophilia	1
Gram positive microorganisms	**82 (48%)**
Staphylococcus epidermidis	29
Staphylococcus aureus	10
Staphylococcus hominis	9
Enterococcus faecium	7
Staphylococcus haemolyticus	5
Staphylococcus warneri, Enterococcus faecalis	4
C group *streptococcus, Streptococcus sanguis, Staphylococcus capitis*	2
Streptococcus acidominimus, coagulase negative staphylococcus	
Staphylococcus saprophyticus , Staphylococcus chromogenes,	1
Streptococcus intermedia, Streptococcus mitis	1
Fungus	**15 (9%)**
Candida albicans	11
Candida tropicalis	4
Total	**170**

There was no statistically significant difference between the groups as regards hemoglobin and white blood cell count (p>0.05). Platelet counts of control, gram-negative, gram-positive and fungal infection groups were $199x10^3 \pm 131x10^3$, $153x10^3 \pm 126x10^3$, $207x10^3 \pm 138x10^3$, $101 x10^3 \pm 79 x10^3/\mu L$. According to platelet counts, the gram-negative and fungal infection groups had lower platelet levels than control and gram-positive infection group (p <0.05). The fungal infection group had lower platelet levels than the gram-negative group (p <0.05).

DISCUSSION

IL-6 is an important cytokine of the host's early response to infection. After exposure to bacterial products, concentration of IL-6 increases sharply, and leads the increase of CRP. It has a very short half-life, and the concentration falls with the treatment, becoming undetectable in most infected patients within 24 hr. The CRP is synthesized within 6-8 hr in an inflammatory response by the liver, peaks at 24-48 hr, and diminishes over time as the inflammation resolves.

Differences in mechanisms of bacterial virulence result in differences in the host response, the extent of activation of various signaling cascades and the stimulation/inhibition of host cell apoptosis, which influence the prognosis.[9,10] Pathogen-associated molecular patterns (PAMPs) have been already recognized.[11] PAMPs from gram-negative and gram-positive bacteria are known to act as ligands for mutually different pattern recognition receptors including Toll-like receptors.[12]

TABLE 3. *IL-6 and CRP levels of proven, clinical sepsis and control groups (mean±standard deviation)*

	Group Ia (proven sepsis) (n= 170)	Group Ib (clinical sepsis) (n= 62)	Group II (control) (n= 50)	*p*
IL-6 (pg/ml)	349 ± 422	257 ± 358	35 ± 104	<0.001
CRP (mg/dl)	18.2 ± 14.5	13.6 ± 13.5	1.6 ± 2.6	<0.001

TABLE 4. *IL-6 and CRP levels of gram negative, gram positive, fungal infection and control groups (mean ± standard deviation)*

Infection group	Gram negative (n= 73)	Gram positive (n= 82)	Fungal (n= 15)	Control (n= 50)
IL-6 (pg/ml)	500 ± 439	320 ± 418	45 ± 64	35 ± 104
CRP (mg/dl)	19 ± 14.2	17.9 ± 14.9	22.6 ± 13	1.6 ± 2.6

Our study showed that gram-negative microorganisms lead to a 10 fold increase of IL-6 cut-off level in comparison to the general proven sepsis group. Fungal infection seems to cause lower cytokine production. Studies on predictability of microorganism types according to cytokines are mostly at adult age. Fisher et al. previously reported that plasma IL-6 levels were significantly higher in patients with gram-negative bacteremia and predicts fatal outcome.[13] Abe et al. showed that IL-6 and CRP levels were higher in gram-negative bacteremia in the Intensive Care Unit.[3] They found that the incidence of gram-negative bacteremia and mortality were significantly higher in the septic shock than in the sepsis and severe sepsis groups.

In children with sepsis, IL-6 was found to predict mortality better than clinical or other laboratory tests.[14] In our study, mortality rate of gram-negative group was slightly higher than the gram-positive group with no statistical difference. Kumar et al. showed that TNF-α levels were higher in pediatric gram-negative than gram-positive bacteremia, but found no difference of CRP levels in the study population.[15]

Patients with fungal sepsis have lower IL-6 levels than gram-negative and gram-positive groups, but interestingly, have higher CRP levels. Oguz et al. previously reported high CRP levels in fungal sepsis patients, and showed that fungal sepsis should be suspected in patients with high persistent CRP levels.[6]

Neonatal sepsis treatment is initiated empirically and covers both gram-negative and gram-positive microorganisms. If aetiology is determined, adequate treatment may be started. These findings suggest that differences in host responses and virulence mechanisms of different pathogenic microorganisms should be considered in the treatment of bacteremic patients. Our findings may help clinicians to start adequate therapy and predict outcome.

In conclusion, we think that IL-6 and CRP are useful to determine the aetiology and implement empirical treatment of neonatal sepsis. ■

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Use of component-resolved diagnosis in the follow-up of children with plant food allergy

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ABSTRACT
Food allergy poses a major problem during childhood. Component-resolved diagnosis detects allergy to proteins isolated in food.
This descriptive study analyzes the use of customized and standardized recommendations in a sample made up of 22 children aged 2 to 16 years old with plant food allergy and assesses sensitivity to four plant panallergens.
According to component-resolved diagnosis results, therapy was personalized, guidelines on what foods or components to avoid were provided, and co-factors that may favor food allergic reactions were explained. No new reactions were referred by 20/22 cases. Oral allergy syndrome developed in 2/22 patients with allergy to profilin because they did not follow the recommendations.
Component-resolved diagnosis was useful for the diagnosis and management of these children. Standardized recommendations, based on each patient's component-resolved diagnosis, prevented severe food allergic reactions.
Key words: *component-resolved diagnosis, panallergen, allergy, lipid transfer proteins, child.*

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INTRODUCTION

Allergic reactions to plant foods are a challenge in pediatric allergy practice. Typically, recommendations indicate to avoid the food that causes the allergy,[1] but in pediatric patients, this is hard to implement, therefore hindering treatment compliance.

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Component-resolved diagnosis (CRD) allows to detect an allergy to individual food proteins and, based on their physicochemical characteristics, predict and prevent symptoms.[1-4] Some allergenic proteins are expressed in multiple plant foods and pollens and are called plant panallergens. These include plant defense proteins. At present, only some of these are available for their clinical use.

- Lipid transfer proteins (LTP) present in skin and peel are resistant to pepsin and heat, and may cause allergic reactions to cooked and processed foods.[5,6]
- Birch pollen protein Bet v1 (PR-10) is related to allergy to apple, hazelnut, celery and soybean.[7] Bet v1 and profilin[4,8] are sensitive to heat and digestion, so cooked or processed foods are well tolerated. The most common clinical manifestation is oral allergy syndrome.
- Glycoproteins present in plants and invertebrates contain glycans with carbohydrate determinants capable of inducing specific IgE synthesis in men. This sensitization is rarely associated with clinical symptoms. Its existence may account for certain allergy profiles with a wide reactivity to different foods.[9]

In young children, the main cause of food allergies include milk (2.5%), egg (1.3%) and peanut (0.8%); in most cases, these allergies tend to resolve during school age.[10] In older children, food allergies are a major problem,[10-12] difficult to understand and manage for physicians and the patient's family; many times, management results in an unnecessary food prohibition and an additional risk for nutritional deficiency.

The main objective of this study is to describe the implementation of food recommendations based on component-resolved diagnosis in 22 pediatric patients.

MATERIAL AND METHODS

This is a descriptive, retrospective study that included all consecutive patients aged between

2 and 16 years old who attended the Allergy Department of Hospital Universitario Araba seeking care for adverse reactions suspected to be related to plant food allergy (September 2009-March 2011).

During the first visit of these patients, they had their case history taken, a physical exam and skin tests done, lab tests were requested, a tolerance questionnaire was administered and patients received guidelines based on preliminary results. During their second visit, based on their allergy test result, patients received guidelines regarding what foods to avoid/consume. Six months later, during a follow-up visit, their response to indications was reviewed, and each patient and/or caregiver was questioned on previously referred symptoms and their case history was recorded in order to detect food allergies, defined as the presence of respiratory, gastric, skin or anaphylaxis symptoms in the first four hours following food consumption. If no events had occurred, children were asked to return one year later; if new reactions had been observed, they were referred for a new visit.

Patients' course and response to recommendations were assessed either during the office visit or by reviewing their medical records. If a patient did not return or there was suspicion about their case, their family members were contacted on the telephone so as to verify their course (March 2013). Compliance with guidelines and the presence of food allergic reactions were referred by caregivers.

Patients were considered allergic if they had a positive skin test (papule of, at least, 3 mm x 3 mm) and/or specific IgE test (over 0.36 kU/L)[1] to the food suspected of having caused the reaction. Skin tests used in this study were the prick and the prick-prick tests. A prick test consists in placing a drop of the allergenic extract to be tested on to the skin surface of the forearm and pricking the skin through this drop with a lancet. A prick-prick test consists in pricking the skin after having pricked the food.

Each patient had a specific IgE test and a skin test done *(Table 1)*. A questionnaire on tolerance to different plant foods (more than 100 items), specifying the food and its state (raw/cooked,

Table 1. *Skin tests and IgE determinations performed on participants*

Skin tests			
	Prick test	**Allergen**	**Laboratory**
	Pru p3	Peach LTP with 30 µg/ml of Pru p3	ALK-Abelló
	Profilin	Profilin	ALK-Abelló
	Tree nuts	Peanut, hazelnut, almond, sunflower seed, walnut, pistachio, and pine nut	LETI
	Fruits	Peach (skin and flesh)	ALK-Abelló
	Fruits	Grape, cantaloupe, avocado, strawberry	LETI
	Vegetables	Leek, parsley, lettuce, cardoon, celery	LETI
	Legumes	Pea	LETI
	Flour	Wheat and corn	LETI
	Pollen	Betula, phleum, parietaria	LETI
	Control	Histamine	
		Saline solution	
	Prick-prick technique		
	Fruits	Apple and pear (skin and flesh), banana, kiwi	
	Legumes	Green bean, soybean, lentil, chickpea	
	Vegetables	Carrot, potato, onion, garlic, tomato	
	Spices	Black pepper, paprika, clove, nutmeg, cumin, curry, bay	
Specific IgE			
	LTP	rPru p3 and rPar j2	
	Profilins	rPhp12 and Bet v2	
	CCD	Bromelain and MUXF3	
	PR-10	rBet v1	
	Pollen	Birch, weed and grass pollen	
	Foods involved in each patient		

LTP: lipid transfer proteins; CCD: cross-reactive carbohydrate determinants.

peeled), was administered and the history of each allergic reaction was recorded. Tolerated foods were recorded and co-factors such as exercise or concomitant use of non-steroidal anti-inflammatory drugs, and history of pollinosis were assessed.

Patients were classified into four groups according to sensitization. Patients were considered sensitive to LTP if they had a positive skin test with LTP or a positive specific IgE test with rPru p3 or rPar j. Likewise, patients with a positive skin test or positive specific IgE test with rPhl p12 or rBet v2 were considered sensitive to profilin, and those with a positive specific IgE test with rBet v1 were classified as sensitive to Bet v1. Lastly, patients with a positive specific IgE test with bromelain or MUXF3 were labeled as sensitive to cross-reactive carbohydrate determinants. Patients were defined as monosensitized if they showed sensitivity to one of the four plant panallergens; while polysensitized patients were those with concomitant sensitization to several panallergens.

Based on previous bibliography,[4,6,12,13] guidelines were provided explaining what foods to avoid (fully or partially), conditions for consumption and co-factor avoidance[14,15] according to the panallergen involved *(Table 2)*. If no sensitivity to any of the panallergens was observed, patients were recommended to leave the food that tested positive in the skin test out of their diet.

Continuous outcome measures were described as mean, median, standard deviation and range, while categorical outcome measures were expressed as frequency and percentage. All analyses were done using the SPSS Statistics software (v. 19).

RESULTS

The study included 22 patients; 13/22 were boys; their mean age was 11.4 ± 4.6 years old. A history of previous food allergy was observed in 8/22; this was caused by tree nuts and/or rosaceae fruits in 7/22 cases; the remaining patient (1/8) had banana allergy. The median duration of follow-up was 3 years (1.6-3.9 years); no patients were lost to follow-up.

No new food allergic reactions were referred by 20/22; the other two patients who did have a new reaction were allergic to profilin and developed reactions similar to oral allergy syndrome, with no need for emergency care.

TABLE 2. *Recommendations by panallergen*

Recommendations	LTP	Profilin	BET v1	CCD
Forbidden	1. Tree nuts 2. Peach and similar fruits (nectarine, apricot, saturn peach) 3. Plant foods involved in each patient and those who have confirmed sensitization as per ST or specific IgE	Plant foods that caused a FAR in the patient and those who have confirmed sensitization as per ST or specific IgE	Plant foods that caused a FAR in the patient and those who have confirmed sensitization as per ST or specific IgE	Patients with monosensitization: avoid foods involved
Should be avoided		Cantaloupe, watermelon, citrus fruits, banana, tomato	Apricot, cherry, apple, peach, pear, hazelnut, almond, celery, carrot	Patients with polysensitization: apply recommendations made for concomitant allergy
Conditions for consumption	Avoid skin and fruit peel; eat peeled fruits	Eat fruits, vegetables and juice, either cooked or processed	Eat fruits, vegetables and juice, either cooked or processed	
Co-factors	- Exercise - NSAIDs			
Recommended treatment available	Self-injection of adrenaline, antihistamines and corticosteroids	Oral antihistamines and corticosteroids	Oral antihistamines and corticosteroids	

FAR: food allergic reaction; ST: skin test; NSAIDs: non-steroidal anti-inflammatory drugs.
LTP: lipid transfer proteins; CCD: cross-reactive carbohydrate determinants.

Allergy events were due to non-compliance with the guidelines provided. Main results are shown in *Table 3*.

The most prevalent panallergen was LTP (13/22), alone or in polysensitized patients, followed by profilin (9/22); 13/22 patients showed monosensitization *(Table 4)*. No sensitization to the studied panallergens was detected in 3/22 patients. Sensitization to rosaceae fruits and tree nuts was the most common type, and it occurred in 7/22 patients.

Among LTP-allergic patients, allergy-causing foods were rosaceae fruits in 9/22 and tree nuts in 5/22. In two out of the three children with allergy to profilin, it was related to rosaceae fruits.

DISCUSSION

Component-resolved diagnosis has been applied to the pediatric population to study allergies to specific foods[1,2] or pollen allergy, but no study has been identified that reflects the course of patients following the diagnosis of plant allergen allergy and recommendation implementation.

Advice has been effective, especially in patients with LTP allergy. The level of adherence has been high, possibly because it does not involve significant alterations in daily habits or due to a history of severe reactions. Reactions referred by patients with profilin allergy may be related to the fact that recommendations are

TABLE 3. *Description of patients and their course*

No.	Age	Sex	Panallergen	Foods involved	Clinical manifestation	Course with recommended avoidance
1	16	M	LTP	Peach, walnut	FDEIA	No FAR
2	15	M	LTP	Rosaceae fruits, cantaloupe, kiwi	FAR POLLEN	No FAR
3	6	M	LTP	Peach, apple, apricot, almond, peanut	FAR	No FAR
4	3	M	LTP PROFILIN	Peach, popcorn	FAR	No FAR
5	14	M	LTP	Rosaceae fruits, tree nuts	FAR	No FAR
6	14	F	PROFILIN	Lentil, green bean	FAR POLLEN	No FAR
7	16	M	NEGATIVE	Walnuts	FDEIA	No FAR
8	16	F	NEGATIVE	Cocoa and hazelnut cream	FDEIA	No FAR
9	16	M	LTP PROFILIN CCD	Potato, pepper, asparagus, cantaoupe	FDEIA	No FAR
10	5	M	LTP	Peanut	FDEIA	No FAR
11	13	F	PROFILIN	Apple, pineapple, cantaloupe, watermelon, kiwi	FAR	POLLEN FAR
12	13	M	LTP PROFILIN	Banana, latex	FAR POLLEN	No FAR
13	14	M	PROFILIN CCD	Tree nuts, rosaceae fruits, kiwi	FAR	FAR
14	2	M	LTP PROFILIN	Tomato, kiwi, citrus fruits, banana, plum, tree nuts, corn	FAR	No FAR
15	15	F	BET V1	Apple, nectarine, cherry, peach, pear, hazelnut	FAR POLLEN	No FAR
16	8	F	LTP	Tree nuts, apple, cherry, nectarine	FAR	No FAR
17	12	M	LTP PROFILIN	Sunflower seed	FAR POLLEN	No FAR
18	16	F	LTP	Peach	FAR	No FAR
19	10	F	PROFILIN	Apricot, cantaloupe, nectarine, apple, plum	FAR ASTHMA (DUST MITES)	No FAR
20	13	M	BET V1	Apple, peach	FAR POLLEN	No FAR
21	7	F	LTP	Chickpea	FAR	No FAR
22	6	F	NEGATIVE	Tomato, kiwi	FDEIA	No FAR

FAR: food allergic reaction; FDEIA: food-dependent, exercise-induced anaphylaxis; LTP: lipid transfer proteins; CCD: cross-reactive carbohydrate determinants.

TABLE 4. *Distribution of sensitization among included patients (n= 22)*

Monosensitization (n= 13)	BET V1	2 (9.1%)
	LTP	8 (36.4%)
	PROFILIN	3 (13.6%)
	CCD	0 (0.0%)
Polysensitization (n= 6)	LTP + PROFILIN	3 (13.6%)
	PROFILIN + CCD	1 (4.5%)
	LTP + PROFILIN + CCD	2 (9.1%)
All tests were negative		**3 (13.6%)**

LTP: lipid transfer proteins; CCD: cross-reactive carbohydrate determinants.

generic and involve eliminating raw plant foods. Since these usually cause oral allergy syndrome, patients probably tolerate these symptoms so that they do not have to change their habits; however, given the limited sample size, it is difficult to draw conclusions.

In our sample, as in Southern Europe,[6] sensitization to LTP was most common, followed by profilin. The few patients with allergy to Bet v1 were monosensitized.

Among monosensitized patients, there was a great variability in clinical response to plant foods. For this reason and given the scarce number of patients, it was not possible to define a common response pattern in each group that suggested a set of foods with a higher or lower risk for allergic patients to each studied panallergen, except for rosaceae fruits and tree nuts in the case of patients with LTP allergy.

In this study, no blinding technique or control group were included.

CONCLUSIONS

These preliminary results suggest that using component-resolved diagnosis for this pathology during childhood may be useful to reduce food allergic reactions, especially severe cases. Further studies with more extensive samples and follow-up duration are necessary to confirm this hypothesis. ■

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