

Kiwi pulp hypersensitivity

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Background: Kiwi, or China gooseberry (*Actinidia chinensis*), is an everyday foodstuff in Europe since the 80's. The first documented case of IgE-mediated hypersensitivity to this fruit was reported in 1981. Most series published since that time include only a very small number of patients. **Methods:** We have studied eight patients who developed symptoms suggestive of IgE-mediated reaction after the ingestion of kiwi; one of these patients also developed symptoms while handling the fruit. All eight patients tolerated other foodstuffs, with the exception of one, who reported having fainted while drinking pineapple juice. Skin tests were performed including the prick-by-prick and a modification of the occluded prick test of Dreborg and Foucard with the pulp of various fruits (kiwi, pineapple, papaya and avocado), and prick tests with a kiwi peel extract. The presence of specific IgE was also investigated in all cases by *in vitro* procedures with these same allergens. **Results:** The skin tests with kiwi pulp were positive in all patients, regardless of the actual technique used. Two patients developed clinical symptoms during the prick-by-prick tests with the pulp of this fruit. The one patient who had reported symptoms while manipulating the fruit also evidenced IgE-mediated hypersensitivity to the fruit's rind. Some patients also evidenced positive tests to other fruits, in most cases without clinical relevance. **Conclusions:** In the present study, skin testing was a more sensitive method than the *in vitro* tests in the detection of kiwi pulp hypersensitivity. Because of its greater safety, the modified Dreborg and Foucard technique may represent a diagnostic alternative for the assessment of fruit hypersensitivity in patients reporting severe symptoms. The kiwi pulp appears to contain at least three different allergens, some of which might be shared by the other fruits tested.

KEY WORDS: Hypersensitivity / Kiwi / Fruits.

Hipersensibilidad a la pulpa de kiwi

Fundamento: El kiwi o grosella de China (*Actinidia chinensis*) es un alimento cotidiano en Europa desde los años ochenta. Desde que, en 1981, se describió el primer caso documentado de hipersensibilidad mediada por IgE frente a esta fruta, casi todas las series publicadas hasta la fecha están formadas por muy pocos pacientes. **Métodos:** Se estudiaron ocho pacientes que habían presentado tras la ingestión de kiwi síntomas sugestivos de ser mediados por IgE; uno de ellos también tenía clínica con la manipulación de la fruta. Todos toleraban otros alimentos, excepto uno, que refería haber perdido la consciencia al tomar un zumo de piña. Se realizaron pruebas cutáneas mediante *prick-by-prick* y una modificación del *prick* ocluido de Dreborg y Foucard con pulpa de frutas (kiwi, piña tropical, papaya y aguacate), y *prick* test con extracto de piel de kiwi. En todos los pacientes se investigó la presencia de IgE específica mediante pruebas *in vitro* para estos mismos antígenos. **Resultados:** Las pruebas cutáneas con pulpa de kiwi fueron positivas en todos los casos, con independencia de la técnica utilizada. Dos pacientes presentaron síntomas durante la realización del *prick-by-prick* con pulpa de esta fruta. Mediante técnicas *in vitro* sólo se obtuvo un 37% de positividades frente a la pulpa de kiwi. En el paciente que refería síntomas con la manipulación, se demostró también una sensibilización mediada por IgE frente a la piel de kiwi. Algunos pacientes presentaron también sensibilización a las otras frutas estudiadas, sin relevancia clínica en la mayoría de los casos. **Conclusiones:** Las pruebas cutáneas han sido, en el presente estudio, un método más sensible que las pruebas *in vitro* para detectar sensibilización a la pulpa de kiwi. Dada su mayor inocuidad, la técnica modificada de Dreborg y Foucard podría ser una alternativa diagnóstica para estudiar la sensibilización a frutas en pacientes con una clínica grave. En la pulpa de kiwi parece que podrían existir al menos tres alérgenos diferentes, algunos de ellos compartidos por las otras frutas estudiadas.

PALABRAS CLAVE: Hipersensibilidad / Kiwi / Frutas.

The kiwi fruit or China gooseberry (*Actinidia chinensis*) has its origin in the Yang-Tze valley. The shrub producing it adapts well to temperate climates, and for this reason its cultivation beyond China was first developed in New Zealand, at the beginning of the present century, and from this country it was then introduced into Europe. At present it is an everyday foodstuff in the European diet, and it is consumed either fresh or in the form of juices, ice creams, or as a component of pastry and dessert products.

The rapid penetration this fruit has had in the Spanish market since the early '80s has been due to various reasons: firstly, it became much cheaper after cultivation and production started in the Northwest of the Iberian peninsula; secondly, its high fibre contents led to its being recommended by many dieticians; finally, its consumption vastly increased due to the false belief that its vitamin contents were much higher than those of our traditional fruits.

In 1981, Fine¹ described the first case of IgE-mediated kiwi fruit hypersensitivity. Since that first report, further evidence has been documented in the scientific literature, albeit almost always and with very few exceptions² in the form of series comprising a limited number of patients.

We have studied a group of patients reporting symptoms suggestive of an IgE-mediated sensitization after the ingestion of kiwi fruit.

The main aim of the present work was to assess the risk/benefit ratio of two different techniques for skin testing, that of the "prick-by-prick" and a modification of the occluded prick test described by Dreborg and Foucard³, for the diagnosis of kiwi pulp hypersensitivity. A further aim was to compare the diagnostic yield of these skin tests to that of the *in vitro* tests.

We also assessed the possible relationship between kiwi pulp hypersensitivity and sensitization to other fruits (pineapple, papaya) which also contain proteolytic enzymes⁴. Avocado was also included in these tests because some authors⁵ have reported a correlation between kiwi fruit hypersensitivity and allergy to that fruit.

Sensitization to kiwi rind was also studied in all patients, as well as the possible role of atopy in the development of kiwi pulp hypersensitivity.

PATIENTS AND METHODS

Patients. Eight patients residing in the area of El Ferrol (Corunna province, Spain) were studied. Their mean age was 24.2 years (range, 10 - 57 years), and they had all reported various allergic symptoms immediately after eating kiwi (Table I). One of them (Case 2) had previously evidenced palpebral angioedema in two occasions, while manipulating this fruit.

All the patients tolerated other foodstuffs with one exception (Case 5), a 57-year-old female who reported general malaise and fainting a few minutes after drinking pineapple juice. She had received medical assistance at an emergency ward and had been treated with (unspecified) intravenous medication.

Skin tests. Skin tests were performed in all cases with the pulp of fresh fruits (kiwi, pineapple, papaya and avocado), with a kiwi rind extract prepared in our Laboratory and with a standard pneumoallergen battery including dust mites, animal epithelia, moulds and various pollens, among them birch pollen (ALK-Abelló S.A., Madrid, Spain).

The extracts of pneumoallergens and kiwi rind were tested using the conventional prick test technique.

The tests with fresh fruit pulp were performed using two different techniques: the prick-by-prick one and a modification of the occluded prick described by Dreborg and Foucard³. This technique comprises puncturing the skin of the internal aspect of the forearm with a Morrow-Brown lancet and then placing a piece of the fruit to be tested upon this puncture, keeping it in place for the whole duration of the test. Our modification of the technique described by those authors³ consisted in that the piece of fruit was not kept occluded and fixed to the skin during the test.

The tests were read after 15 minutes in all cases, regardless of the actual technique used. A wheal of 3 mm or more in diameter was considered positive. Normal saline was used as the negative control, and a histamine solution (10 mg/ml) as the positive one.

Preparation of the kiwi rind extract. Through soft brushing of the outer surface of the fruit, 1.5 g of kiwi rind dust were obtained. This dust was then dissolved in 35 ml phosphate-buffered saline

Table I. Symptoms in relation with kiwi, and pneumoallergen sensitizations

Case	Gender	Age (years)	Airborne allergen sensitizations	Clinical features in relation with kiwi
1	F	16	Negative	Palatine pruritus, palpebral angioedema
2	F	13	House dust mites	Pharyngeal and ocular pruritus, palpebral angioedema
3	F	10	House dust mites	Pharyngeal pruritus, sneezing, palpebral angioedema
4	M	42	Grass pollens	Palatine pruritus, nasal obstruction
5	F	57	Negative	Nausea, vomiting, fainting
6	M	11	House dust mites	Palatine pruritus, perioral whealing
7	F	28	Negative	Palatine and lingual pruritus, labial angioedema, vomiting
8	M	17	House dust mites	Generalised urticaria, palatine pruritus, labial angioedema, cough, dyspnoea, nausea

(PBS) and shaken for 24 h at room temperature. The resulting solution was then centrifuged for 10 min at 1000 g. The supernatant was filtered through a 45 mm Millipore filter and divided into aliquots, which were stored in a refrigerator until used.

It was not possible to quantify the final protein concentration in the extract, as our laboratory lacks the required materials.

Quantitation of specific IgE. The possible presence of specific IgE-class antibodies was investigated in the sera of all patients against fresh fruit pulp (kiwi, pineapple, papaya and avocado) and against kiwi rind.

The assessment of specific antibodies to kiwi, pineapple and avocado pulp was performed with an enzymeimmunoassay technique (ELISA, Sanofi-Pasteur), and that against papaya pulp with a Pharmacia Immunocap System (CAP); the manufacturers' instructions were followed in all cases.

For the detection of specific IgE antibodies to kiwi rind, the extract we had prepared was incubated for 24 hours at a temperature of 5°C in the wells of an ELISA plate (Sanofi-Pasteur); after repeated washings with PBS, the wells were blocked with bovine serum albumin (BSA), and then the Sanofi-Pasteur procedure for the ELISA technique was followed.

The results of the *in vitro* studies were expressed in classes, and Class 2 or higher results were considered positive.

The ELISA plates (Sanofi-Pasteur) were read at an absorbance level of 405 nm, and the various Classes corresponded to the following absorbance readings: Class 1, 0.068 - 0.135; Class 2, 0.135 - 0.330; Class 3, 0.330 - 0.910; Class 4, >0.910.

RESULTS

The results of the skin tests performed with fresh kiwi pulp and kiwi rind extract are summarised in Table II.

The skin tests performed with fresh kiwi pulp using the modification of the Dreborg and Foucard technique were positive in all patients.

Prick-by-prick skin tests with fresh kiwi pulp were not performed in Cases 5 and 8, because of the severity of the symptoms reported upon ingestion of the fruit. The skin tests with this technique were positive in the remaining six patients; two of them (Cases 3 and 7) developed symptoms during the tests, requiring oral antihistamines. Patient No. 3 (a female) experienced nasal obstruction, lacrimation and sneezing bouts, and patient No. 7 (also a female) reported generalised skin pruritus without visible skin lesions. No symptoms developed in these two patients when the other skin tests were performed.

The skin tests with kiwi rind extract were positive in the one patient (a female, Case 2) who had reported symptoms while manipulating the fruit, and negative in all other cases in which they were performed. This test was not carried out in Case 5, as she did not give her consent.

Table III shows the results of the skin tests with fresh pineapple, papaya and avocado pulp performed by the prick-by-prick technique. In Case 5 these tests were performed only with the modified Dreborg and Foucard technique because of the severity of the symptoms she had developed after drinking pineapple juice. In all other cases the tests were performed with the two techniques, and no differences were observed in the results achieved with either technique.

The results of the assessments of specific IgE antibodies to the various allergens studied are shown in Tables II and III.

DISCUSSION

The pulp of the kiwi fruit is able to elicit IgE-mediated sensitization, and this sensitization may have many different clinical manifestations: the oral allergy syndrome, vomiting, rhinoconjunctivitis, urticaria-angioedema or even anaphylaxis. There has even been one report of acute pancreatitis caused by hypersensitivity to the pulp of this fruit⁶.

The oral allergy syndrome, defined by the development of labial, lingual and oral mucosal pruritus with the possible association of labial oedema and perioral whealing, immediately after the ingestion of a foodstuff⁷ which is almost always of vegetable origin⁸ is, in our series, the clinical manifestation most often presented by the patients sensitised to kiwi pulp.

In the one patient who had reported symptoms during the manipulation of the fruit we also detected, through both the skin and the *in vitro* tests, an IgE-mediated sensitization to the kiwi rind. The negativity of the skin tests and the absence of specific IgE directed against the rind of the fruit in the remaining seven patients studied suggests the presence of different allergens in the rind and the pulp of the kiwi fruit, a situation that has already been documented and demonstrated in the case of peaches⁹.

There has been only one further case reported in which hypersensitivity to kiwi rind had been demonstrated by skin testing¹. The patient was a female who developed an episode of anaphylaxis while peeling kiwi fruits for the preparation of a fruit salad. In both these cases, the one reported here and the one described by Fine¹, the patients had previously tolerated the ingestion of kiwi fruit. Although further, more comprehensive studies would be necessary, the hypothesis may be advanced that sensitization to the kiwi fruit rind may, through a cross-reactivity mechanism, induce a later sensitization to the pulp of the fruit.

The one patient in our series who had developed an anaphylaxis episode after the ingestion of pineapple juice also evidenced IgE-mediated sensitization to that fruit; this would lend support to the hypothesis of cross-reactivity between kiwi pulp and pineapple pulp¹⁰, possibly because of the presence of proteolytic enzymes with a thiol group in their structures⁴ in the composition of both these fruits. IgE-class antibodies to pineapple, papaya and avocado were also detected in some of the other patients in our study, in all cases without clinical relevance. These observations, which have also been reflected in other studies^{2,5,11,12}, would appear to indicate that minimal or partial cross-reactivity may exist between the pulps of these fruits².

Atopy may represent a predisposing factor for the development of kiwi pulp sensitization, as five of the eight patients studied in this series (62.5%) were atopics. Although there have been speculations regarding the possible association of polle-

Table II. Results of the skin and *in vitro* tests with kiwi fruit

Case	Fruit pulp			Fruit rind (extract)	
	Modified Dreborg and Foucard prick (mm)	Prick-by-prick (mm)	Specific IgE (ELISA class)	Prick test (mm)	Specific IgE (ELISA class)
1	7 x 6	14 x 8	1	Negative	0
2	6 x 6	12 x 8	2	6 x 4	2
3	4 x 4	12 x 10 ^a	1	Negative	0
4	4 x 3	8 x 5	3	Negative	0
5	6 x 4	NP	0	NP	0
6	7 x 5	9 x 9	0	Negative	0
7	3 x 3	10 x 5 ^a	0	Negative	0
8	9 x 5	NP	2	Negative	0

^a Developed systemic symptoms. NP: not performed.

Table III. Results of the test with other fruits: skin and *in vitro* tests

Case	Pineapple		Papaya		Avocado	
	Skin tests	Specific IgE (ELISA class)	Skin test	Specific IgE (CAP class)	Skin tests	Specific IgE (ELISA class)
1	Negative	1	Negative	0	Negative	0
2	Negative	1	Negative	0	Negative	0
3	Negative	0	Negative	0	Negative	0
4	Negative	2	7 x 6	2	8 x 8	2
5	8 x 8 ^a	2	NP	0	3 x 3 ^a	1
6	Negative	0	Negative	0	Negative	0
7	2 x 2	0	Negative	0	Negative	0
8	Negative	0	3 x 3	0	Negative	0

^a Modified Dreborg and Foucard prick test. NP: not performed.

nosis (particularly birch pollen)^{2,15} and kiwi fruit allergy^{13,14}, we, as other authors^{11,16}, have not detected this association. Only one of our patients evidenced sensitization to grass pollens, and the skin tests with birch pollen were negative in all eight cases.

RAST inhibition tests have demonstrated the presence of shared allergens between birch pollen and kiwi pulp²; nevertheless, we believe that the association between pneumoallergen sensitization and kiwi pulp hypersensitivity is in most cases a casual one. One-half of our patients had dust mite allergy; this particular sensitization is responsible for most cases of airborne allergen hypersensitivity in the region of Galicia in Spain.

An analysis of other studies of kiwi pulp hypersensitivity carried out in Spain shows that this particular hypersensitivity is, when at all, associated to sensitization to the airborne allergens usual in the particular area concerned. Thus, in studies performed in coastal regions, the patients are frequently sensitized to dust mites^{11,17}, while in those carried out in the interior of Spain sensitizations to various pollens are most often encountered¹⁴. This might perhaps be explained by the fact that a suspected food allergy, when the symptoms are not severe, is often not a reason for seeking medical consultation.

The skin tests, regardless of the actual technique used, were in our series a valid diagnostic tool in the detection of kiwi pulp hypersensitivity. However, while the modified Dreborg and Foucard technique was in all cases safe and innocuous, two patients developed symptoms during the prick-by-prick tests. It is possible that the

amount of allergen penetrating into the skin may be greater with the latter technique; this might explain these observations, as the skin tests with kiwi pulp were carried out on all patients on the same day and with samples from one and the same piece of fruit.

The extensive clinical experience available shows that the prick-by-prick method is sensitive and generally entails low risk in the diagnosis of food allergies, although exceptionally severe systemic reactions may develop in the course of such tests¹⁸. Such adverse reactions might be explained by the fact that the fresh foodstuff is not a standardised material¹⁹, so that it is not known precisely what is being tested, and by the fact that the ripeness or otherwise of the fruit may be a further conditionant of its allergenicity²⁰.

The modified Dreborg and Foucard technique, because of its good sensitivity and specificity (which are similar to those of the prick-by-prick test) and its greater safety as compared to that of the prick-by-prick, may represent a useful alternative in the diagnosis of fruit allergy, particularly in those cases when the patient has evidenced severe symptoms.

The diagnostic yield of the *in vitro* tests was low in the diagnostic work-up for kiwi pulp hypersensitivity.

Only in three of our cases (37.5%) were IgE-class antibodies to this allergen detected in the sera of the patients. These rather poor results may be due to the fact that, in the population studied, most patients developed only mild symptoms after the ingestion of kiwi fruit. Gall *et al.*² only found specific serum IgE to kiwi in patients who had

had severe and generalised symptoms, but not in those with the oral allergy syndrome.

The *in vitro* tests, because of their low sensitivity as compared to the skin tests, do not seem to be an appropriate diagnostic tool in the routine detection of kiwi pulp hypersensitivity.

Kiwi pulp appears to contain at least three different allergens. One of them seems to be present exclusively in this portion of the fruit, and may represent the major allergen; a further one, perhaps actinidine, might be responsible for the cross reactions appearing between kiwi and other fruits containing proteolytic enzymes, and the third one might be shared by the pulp and the rind of the fruit.

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