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Original Article

Self-reported hypersensitivity to exotic fruit in birch pollen-allergic patients

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Abstract

Background: The majority of Swedish birch pollen (BP)-allergic patients report hypersensitivity to some fruits, nuts and vegetables. Some BP-allergic patients complain 'I can't tolerate any fruit'. The main aim of the present study was to answer the question, 'can BP-allergic patients tolerate some of the exotic fruit, not at present common in Sweden?'

Methods: Consecutive patients (n = 397) visiting the participating Allergy Clinics, who had a BP allergy and reported a food hypersensitivity, were asked to fill out questionnaires regarding 66 different fruits and vegetables. Subjects had three alternatives as an answer to each of the food questions: (i) 'I tolerate it'; (ii) 'I get symptoms from it'; or (iii) 'I have not tried this food'. Skin prick tests were performed with pollen allergens.

Results: Most patients had experienced reactions to several foods; only 31 patients (8%) reported hypersensitivity to one food only. Some of the fruit had been tried by only a few patients. In addition to earlier well-known BP-related foods, more than 40% of patients who had knowingly eaten Japanese pear and pomegranate said that they had experienced symptoms after eating the fruit. Most patients tolerated pineapple, melon, grapes and citrus fruits, as well as zucchini, lychee, rambutan, mangosteen, ugli, melon pear and cherimoya.

Conclusions: Although an allergy to fruit is common among BP-allergic patients, there are several widely available fruits that most patients tolerate; for instance, pineapple, melon, grapes and citrus fruit. Furthermore, there are many exotic fruits that most patients have not yet tried.

Key words: allergy, birch pollen, exotic fruit, food hypersensitivity, pollen-related food.

Introduction

The majority of Swedish birch pollen (BP)-allergic patients report a hypersensitivity against some fruits, nuts and vegetables.[1,2] In pollen-related food hypersensitivity (FH), the symptoms are most often located in the mouth and the term 'oral allergy syndrome' (OAS) is used for these symptoms.[3] *In vitro* studies have shown immunological cross-reactions between BP and several of these foods. The major BP allergen Bet v 1, a 17 kDa protein, as well as a minor BP-allergen, the 14 kDa profilin, share common epitopes with proteins of similar size in various fruits and vegetables (for a review, see Caballero *et al.*[4]).

Some BP-allergic patients complain 'I don't tolerate any fruit'. The main aim of the present study was to determine whether BP-allergic patients are able to tolerate some of the exotic fruits, not so commonly eaten at present in Sweden.

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METHODS

Consecutive patients, having BP-allergic asthma or hay fever, attending the participating Allergy Clinics and reporting a FH, were asked to fill out questionnaires regarding 66 different fruits and vegetables. The foods listed were exotic fruits and vegetables available in Sweden, as well as some other foodstuffs known to be related to pollen allergy.[1,2,5,6] The participants had to choose one of the following three alternatives as an answer to each of the foods: (i) 'I tolerate it'; (ii) 'I get symptoms from it'; or (iii) 'I don't know because I have not tried this food'. A booklet with photos showing the various exotic fruits was available as an aid. The specific allergic symptoms were not asked for.

A total of 397 patients (295 adults > 18 years of age and 102 children or adolescents 4–18 years old) were included in the study.

Skin prick tests (SPT) were performed in accordance with international recommendations[7] using commercially available standardized BP, Timothy pollen and mugwort pollen extract with an activity of 10 histamine equivalent prick (HEP; Soluprick; ALK Abello, Hörsholm, Denmark). Histamine hydrochloride, 10 mg/mL, was used as a positive control. Test results were recorded in accordance with Nordic guidelines.[8] Thus, a weal reaction the same size as that of the histamine reference was recorded as 3+. A weal with an area double that of a 3+ weal was recorded as 4+, whereas a weal that was double the size of a 4+ weal was recorded as 5+. A weal half the size of a 3+ weal was recorded 2+ and a weal that was smaller than a 2+ weal but larger than the negative control was recorded 1+. Fourteen patients had a weak (1+) BP reaction only; 64 patients had a reaction graded as 2+, whereas 319 patients had a reaction graded as ≥ 3+ to BP. Two hundred and seventy-four patients had positive reactions to Timothy pollen and 134 had positive reactions to mugwort pollen.

Statistics

SPSS statistical software (SPSS, Chicago, IL, USA) was used for statistical analysis. ANOVA was used for comparisons between groups. $P < 0.05$ was regarded as significant.

Ethics

The ethics committees in the participating centers approved the study.

RESULTS

Most patients had experienced reactions to several foods; 31 patients (8%) had reported hypersensitivity against one food only (Table 1). Nobody reported hypersensitivity against all foods listed. The mean (±SD) number of foods giving symptoms was 9.6 ± 7.2. The number of foods giving symptoms was greater in adults and adolescents than in children (Table 2; $P < 0.001$). There was a non-significant ($P = 0.07$) tendency towards increasing number of foods giving symptoms with increasing size of the SPT with BP (Table 3). No relationship was

Table 1 Number of foods eliciting symptoms

No. foods	No. patients (%)
1	31 (7.8)
2	21 (5.3)
3	28 (7.1)
4	25 (6.3)
5	30 (7.6)
6–10	116 (29.2)
11–20	109 (27.4)
21–30	29 (7.3)
31–38	8 (2.0)

Table 2 Relationship between patient age and the number of foods eliciting symptoms

Age group (years)	No. patients	No. foods*
4–12	57	5.2 (4.2–6.3)
13–18	45	9.5 (7.6–11)
>18	295	10 (9.7–11)

*Data show the mean with 95% confidence intervals given in parentheses. $P<0.001$ for the difference between children and adolescents and between children and adults.

Table 3 Relationship between results of the skin prick test with birch pollen and the number of foods eliciting symptoms

SPT with birch pollen	No. patients	No. foods*
1+	14	5.6 (3.0–8.3)
2+	64	8.2 (6.8–9.7)
3+	212	9.8 (8.8–11)
4+	87	11 (9.2–13)
5+	18	11 (6.8–15)
6+	2	7 (0–76)

*Data show the mean with 95% confidence intervals given in parentheses.

For the skin prick test (SPT) scores, a 3+ weal is the same size as that obtained with the histamine control (for details, see Methods).

seen between the number of foods giving symptoms and SPT results with Timothy or mugwort.

Some of the fruit in question had been tried by only a few patients. Fewer than 50% of patients had tried the fruits listed in Table 4.

Nuts, apple, pear, stone fruit and kiwi fruit were the fruits having the highest figures for 'Yes, I get symptoms' (Fig. 1). Among exotic fruits, in addition to kiwi fruit, Japanese pear, pomegranate, guava and tree tomato showed the highest proportion of 'Yes I get symptoms' responses (Table 5). Several fruits were tolerated by most patients who had tried the particular fruit (Fig. 2).

There were some differences between children and adults. Reactions to apricot, cherry, plum, potato peel and pear were more common in adults, whereas more children said that they did not tolerate peanuts (Table 6).

No significant correlation was seen between SPT results with Timothy or mugwort pollen and symptoms from any of the individual fruits and vegetables.

Table 4 Fruits and vegetables that more than 50% of patients had not eaten

Food	No. patients who have not eaten the food (%)
Salak	397 (100)
Sapodilla chicle	391 (98)
Pitaya	383 (96)
Passionfruit	380 (96)
Mangosteen	375 (94)
Okra	374 (94)
Horned melon	369 (93)
Melon pear	367 (92)
Durian	364 (92)
Guava	362 (91)
Indian fig	361 (91)
Japanese pear	360 (91)
Cherimoya	359 (90)
Rambutan	354 (89)
Tamarillo	347 (87)
Ugli	346 (87)
Pomelo	336 (85)
Kumquat	328 (83)
Ogen melon	327 (82)
Lychee	324 (82)
Kaki	285 (72)
Pomegranate	264 (66)
Cantaloupe	259 (65)
Cape gooseberry	258 (65)
Date	233 (59)
Papaya, pawpaw	231 (58)
Galia melon	213 (54)
Brazil nut	204 (51)

Discussion

It should be kept in mind that the present study was based on admitted patients and, thus, it is possible that our material is not quite representative of all BP-allergic patients. However, the list of fruits and vegetables most frequently eliciting symptoms contains nuts, apple, pear and stone fruits, similar to earlier reports.[1,2,5] Among exotic fruit, kiwi fruit is the one most often giving rise to symptoms. The considerable number of patients reporting symptoms to kiwi fruit obviously reflects the fact that kiwi fruit has become a more common Swedish everyday food. Radioallergosorbent test (RAST) inhibition studies have revealed cross-reacting antigens between BP and kiwi fruit.[9] *In vitro* studies have also shown cross-reactions between BP and lychee, mango, banana and orange, which are dependent on a 35 kDa protein.[10]

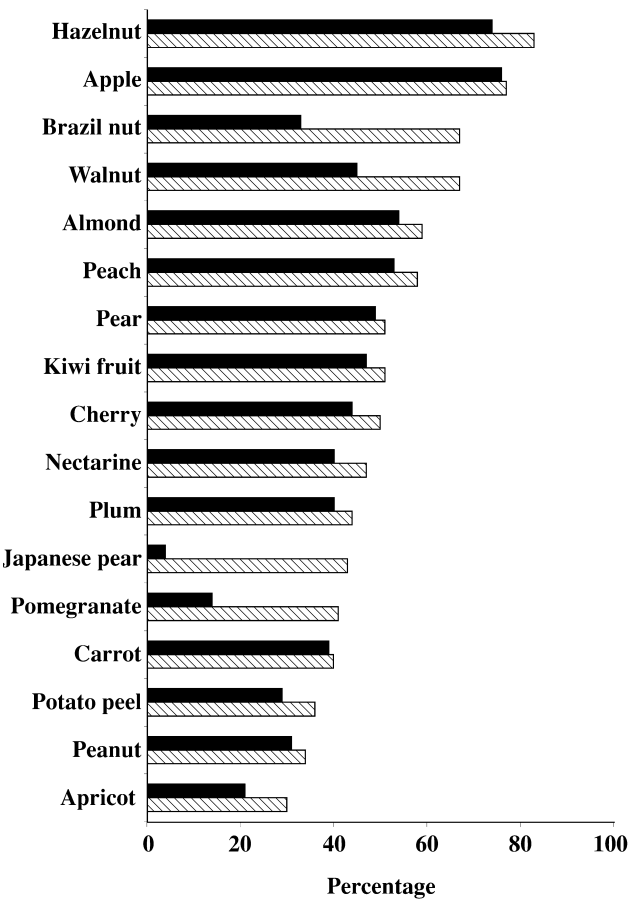

Fig. 1 Fruits and vegetables most often eliciting symptoms according to the patients' opinions. (▨), patients who get symptoms after consuming the fruit or vegetable as a percentage of those who know; (■), patients who get symptoms after consuming the fruit or vegetable as a percentage of all subjects.

Table 5 Patients' answers and botanical classification of fruits and vegetables included in the questionnaire

English name	Family	Latin name	No. patients who have eaten the food	'Yes, I get symptoms'		
				n	% of those who know	% of all
Chinese gooseberry, kiwi fruit	*Actinidiaceae*	*Actinidia deliciosa*	364	185	51	47
Mango	*Anacardiaceae*	*Mangifera indica*	237	49	21	12
Cherimoya/custard apple/ Jamaican apple	*Annonaceae*	*Annona cherimola*	38	4	11	1
Carrot	*Apiaceae*	*Daucus carota*	384	155	40	39
Celery or celeriac	*Apiaceae*	*Apium graveolens*	248	31	13	8
Parsnip	*Apiaceae*	*Pastinaca sativa*	237	16	7	4
Date	*Arecaceae*	*Phoenix dactylifera*	164	24	15	6
Salak	*Arecaceae*	*Salacca edulis*	0	0	0	0
Sunflower seed	*Asteraceae*	*Helianthus annuus*	266	28	11	7
Durian	*Bombacaceae*	*Durio zibethinus*	33	6	18	2
Pineapple	*Bromeliaceae*	*Ananas comosus*	354	51	14	13
Pitaya	*Cactaceae*	*Hylocereus undatus*	14	2	14	1
Indian fig	*Cactaceae*	*Opuntia ficus-indica*	36	5	14	1
Papaya, pawpaw	*Caricaceae*	*Carica papaya*	166	23	14	6
Mangosteen	*Clusiaceae*	*Garcinia mangostana*	22	2	9	1
Sweet potato	*Convolvulaceae*	*Ipomoea batatas*	229	12	5	3
Hazelnut	*Corylaceae*	*Corylus avellana*	350	292	83	74
Cantaloupe	*Cucurbitaceae*	*Cucumis melo* var. *cantalupa*	138	20	14	5
Galia melon	*Cucurbitaceae*	*Cucumis melo* cultivar	184	23	13	6
Honeydew melon	*Cucurbitaceae*	*Cucumis melo* cultivar	352	44	13	11
Horned melon	*Cucurbitaceae*	*Cucumis metuliferus*	28	6	21	2
Musk melon	*Cucurbitaceae*	*Cucumis melo reticulatus*	255	28	11	7
Ogen melon	*Cucurbitaceae*	*Cucumis melo* cultivar	70	10	14	3
Squash/zucchini	*Cucurbitaceae*	*Cucurbita pepo* cultivar	292	5	2	1
Watermelon	*Cucurbitaceae*	*Citrullus lanatus*	377	30	8	8
Kaki	*Ebenaceae*	*Diospyros kaki*	112	19	17	5
Peanut	*Fabaceae*	*Arachis hypogaea*	354	122	34	31
Walnut	*Juglandaceae*	*Juglans regia*	269	179	67	45
Avocado	*Lauraceae*	*Persea americana*	303	50	17	13
Brazil nut	*Lecythidaceae*	*Bertholletia excelsa*	193	130	67	33
Okra	*Malvaceae*	*Hibiscus esculentus, Abelmoschus esculentus*	23	4	17	1
Fig	*Moraceae*	*Ficus carica*	223	42	19	11
Banana	*Musaceae*	*Musa* × *acuminata*	392	65	17	16
Guava	*Myrtaceae*	*Psidium guajava*	35	10	29	3
Starfruit/Carambola	*Oxalidaceae*	*Averrhoa carambola*	195	21	11	5
Poppy seed	*Papaveraceae*	*Papaver somniferum*	295	13	4	3
Passionfruit/yellow granadilla	*Passifloraceae*	*Passiflora edulis f. flavicarpa*	17	3	18	1
Purple granadilla	*Passifloraceae*	*Passiflora edulis f. edulis*	236	41	17	10
Pomegranate	*Punicaceae*	*Punica granatum*	133	55	41	14
Almond	*Rosaceae*	*Prunus dulcis*	358	213	59	54
Apple	*Rosaceae*	*Malus domestica*	393	302	77	76
Apricot	*Rosaceae*	*Prunus armeniaca*	286	85	30	21
Cherry	*Rosaceae*	*Prunus avium*	348	175	50	44
Japanese pear	*Rosaceae*	*Pyrus pyrifolia* var. *culta*	37	16	43	4
Nectarine	*Rosaceae*	*Prunus persica* var. *nucipersica*	341	160	47	40
Peach	*Rosaceae*	*Prunus persica*	359	210	58	53
Pear	*Rosaceae*	*Pyrus communis*	383	196	51	49
Plum	*Rosaceae*	*Prunus domestica*	359	157	44	40
Clementine	*Rutaceae*	*Citrus* × *reticulata*	380	55	14	14

Table 5 cont.

English name	Family	Latin name	No. patients who have eaten the food	'Yes, I get symptoms' *n*	% of those who know	% of all
Grapefruit	*Rutaceae*	*Citrus × paradisi*	311	35	11	9
Kumquat	*Rutaceae*	*Fortunella japonica*	69	12	17	3
Lemon	*Rutaceae*	*Citrus limon*	368	21	6	5
Lime	*Rutaceae*	*Citrus aurantii folia*	244	13	5	3
Orange	*Rutaceae*	*Citrus sinensis*	383	84	22	21
Pomelo	*Rutaceae*	*Citrus maxima*	61	5	8	1
Satsuma	*Rutaceae*	*Citrus reticulata* cultivar *unshiu*	297	38	13	10
Ugli	*Rutaceae*	*Citrus × reticulata*	51	5	10	1
Lychee	*Sapindaceae*	*Litchi chinensis*	73	4	5	1
Rambutan	*Sapindaceae*	*Nephelium lappaceum*	43	3	7	1
Sapodilla chicle	*Sapotaceae*	*Manilkara zapota*	6	1	17	0
Cape gooseberry	*Solanaceae*	*Physalis peruviana*	139	21	15	5
Eggplant/aubergine	*Solanaceae*	*Solanum melongena*	232	10	4	3
Melon pear	*Solanaceae*	*Solanum muricatum*	30	3	10	1
Potato (peel)	*Solanaceae*	*Solanum tuberosum*	326	117	36	29
Tree tomato/tamarillo	*Solanaceae*	*Solanum betaceum*	50	11	22	3
Grape	*Vitaceae*	*Vitis vinifera*	380	68	18	17

Table 6 Differences between age groups regarding foods eliciting symptoms

	Children <13 years	Adolescents 13–18 years	Adults >18 years	*P*
Peach	31	52	64	0.001
Pear	39	44	55	0.05
Cherry	15	42	57	0.001
Nectarine	29	39	51	0.05
Plum	16	43	49	0.001
Potato peel	12	30	41	0.001
Peanut	53	48	29	0.001
Apricot	7	21	34	0.01

Figures indicate percentages of patients in a particular group. *P* values refer to the significance of differences between children (<13 years) and adults.

Very few of these fruits were reported to elicit symptoms by BP-allergic patients in the present study. It was shown earlier that immunological cross-reactions, as indicated by results from *in vitro* tests, do not always have a clinical significance.[11] Such clinically irrelevant sensitization is very common with exotic fruits cross-reacting with latex.[12,13] In contrast, clinical reactions to various exotic fruits have been reported (e.g. kiwi fruit, banana, melon, mango, passionfruit, pineapple, fig, grape, lychee, kaki, cherimoya, date, durian and tamarillo).[13–19]

Reports of subjective FH are not equivalent to real FH. All diagnostic methods regarding FH have limitations. For example, IgE tests and SPT give many positive reactions despite negative double-blind placebo-controlled food challenge (DBPCFC),[20] as well as negative reactions despite positive challenges.[20,21] It is considered that a definite diagnosis should be based upon a DBPCFC.[22] It is difficult for practical reasons to perform DBPCFC with a large number of foods in hundreds of patients; a questionnaire is more practical. The diagnostic accuracy of the patient's history is very high for some fruits and nuts.[23] However, the answers to the questionnaires should be interpreted prudently, especially with regard to some of the foods whose names have similarities that may make some patients think that they are allergic to particular foods that they do, in fact, tolerate. Thus, patients may have confused Japanese pear with pear, and pomegranate (Swedish 'granat-apple') with apples. For that reason,

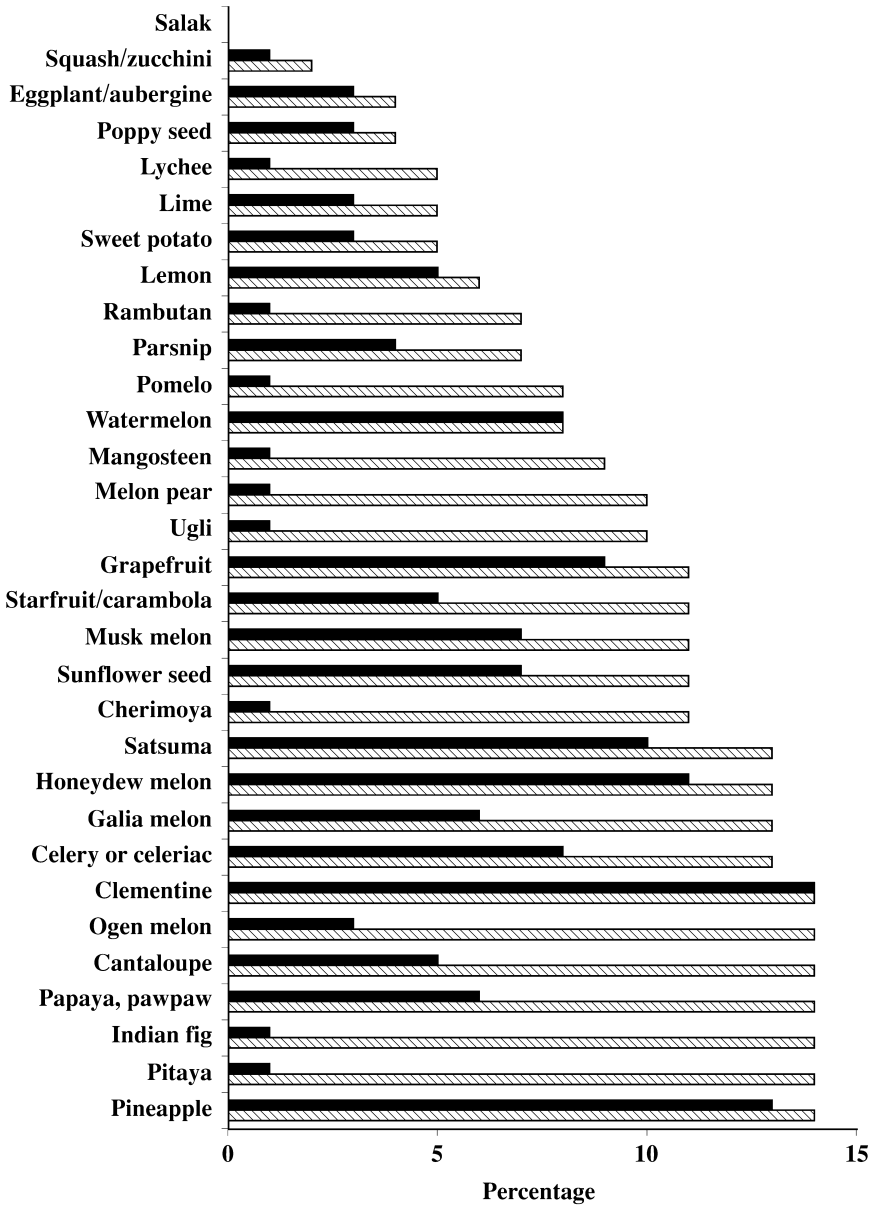

Fig. 2 Fruits and vegetables most seldom eliciting symptoms according to the patients' opinions. (▨), patients who get symptoms after consuming the fruit or vegetable as a percentage of those who know; (■), patients who get symptoms after consuming the fruit or vegetable as a percentage of all subjects.

the high figures for symptoms in response to the consumption of Japanese pear and pomegranate should be regarded with caution and our results should be confirmed by controlled challenges.

It should be noted that self-reported hypersensitivity includes IgE-mediated reactions as well as reactions other than those mediated by IgE. Hypersensitivity reactions to oranges, identified by 84 patients in the present study, may, to some extent, be mediated by non-allergic mechanisms.

Some spices and vegetables belonging to the family *Apiaceae* (celery/celeriac, carrot, parsnip) have been found to cross-react with BP.[5,24,25] For this reason, we included these foods in our questionnaire, although they are not exotic. Of these vegetables, only carrot was a common offender among our patients. The absence of symptoms for celery/celeriac probably reflects the fact that some of these allergens are heat labile, so that BP-allergic patients tolerate them in cooked food,[25] and that raw celery is not often eaten in Sweden.

The number of foods causing allergy symptoms was higher in adults than in children. We did not ask patients about the duration of their hay fever. The study of Asero *et al*.[26] indicates that the proportion of BP-allergic

patients with FH increases from 40% in patients having had hay fever for 1 year to a maximum of 85% in patients who have had hay fever for more than 15 years. Thus, the difference between children and adults in the present study may be related to differences in the duration of their BP sensitization.

Positive correlations have been shown between the degree of BP sensitization and the occurrence of FH.[2,27] In the present study, where the inclusion criterion was the existence of a BP allergy and FH, a tendency was seen towards hypersensitivity against more foods with an increasing size of the BP skin test, although this was not statistically significant. Other studies have shown a relationship between the degree of BP sensitization and the number of foods giving symptoms.[2]

In conclusion, although allergy to fruit is common among BP-allergic patients, there are several commonly available fruits that most patients tolerate; for instance, pineapple, melon, grapes and citrus fruit. Furthermore, there are many exotic fruits that most patients have not tried. There is a need to expand our knowledge about these matters so that patients can be given proper advice as to which fruit may be eaten safely.

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