

Are There Any Links between Hop Japanese Pollen and Other Weed Pollens or Food Allergens on Skin Prick Tests?

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ABSTRACT

Recent investigations suggest that the importance of Hop Japanese pollen, which has been known as one of the major causative weed pollens, is increasing in this country. There have been few data dealing with the allergenic relationship between Hop J pollen and other food or inhalant allergens. Among 2909 patients who visited the Allergy Clinic of Ajou University Hospital, Suwon, Korea, 471 patients sensitized to Hop J, mugwort, or ragweed pollens on skin-prick test were enrolled. Positive rates to common inhalant or food allergens and their allergenic relationships with other pollens or food allergens were analyzed based upon skin-prick test results. The positive rates to sunflower, fat hen, nettle, grass (*Bermuda*, *Orchard*) and tree (alder, birch, and poplar) pollen were significantly higher in those sensitized to Hop J pollen than in those of negative responders ($p < 0.05$, respectively). No significant associations were noted with ragweed or mugwort pollen ($p > 0.05$, respectively). In regard to food-related allergens, an association was noted between Hop (*Humulus lupulus*) or celery allergens in those sensitized to Hop J pollen

($p < 0.05$, respectively). Hop J pollen may have possible links with celery, Hop, and sunflower pollens on skin-prick test. Further *in vitro* investigations will be needed to evaluate the possibility of cross-reacting components between them. (Allergy and Asthma Proc 22:43–46, 2001)

Hop J (*Humulus japonicus*), a weed of the Cannabaceae family and Urticales order, which grows 60–80 cm high, is widespread in both rural and urban areas of Korea.¹ It is wind-pollinated, with a flowering period lasting from August to October in our region.² Kim et al.³ reported two cases of asthma showing positive responses to skin-prick tests (SPTs) and bronchial challenges with this pollen, but the first prospective study using skin-prick test and serum-specific IgE determination failed to detect significant sensitization to Hop J pollen.⁴ Ten years later, the second study,⁵ which was carried out in Suwon, Korea ~40 km south of Seoul, using pollen collected in the locality during peak season, emphasized the emerging importance of Hop J pollen as one of the major causative allergens during the autumn season.

There have been some studies suggesting cross-allergenicity between mugwort or tree pollen and food allergens, such as vegetables and fruits.^{6–9} However, to the best of our knowledge, there have been no studies concerning the allergenic relationships between Hop J pollen and other taxonomically unrelated food or inhalant allergens.

In this study, we observed skin test reactivity to common inhalant and food allergens in patients sensitized to Hop J pollen.

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Subjects and Methods

Patients were selected from the Allergy Clinic of Ajou University Hospital in Suwon, Korea. Between April 1995 and May 1997, 2909 patients examined for treatment of asthma, rhinitis, or conjunctivitis were skin-tested with Hop J pollen extract (Torii Co., Japan). Patients who showed a positive response ($\geq 1+$ antigen-to-histamine (A/H) ratio) to Hop J, mugwort, or ragweed pollen on skin test were enrolled. Routine SPTs were performed on the backs of the patients with 50 common inhalant allergens and 20 food allergens used simultaneously. The results were read 15 minutes later. The size of the wheal produced by each antigen and histamine test was expressed as the maximum diameter and vertical length at the midportion of the maximal length. Skin reactivity was expressed as the ratio of wheal size of allergen to histamine according to the criteria of the Scandinavian Society of Allergy.¹⁰ If the A/H ratio was from 0.1 to 1 and the erythema had a diameter of <21 mm, it was read as 1+. If the A/H ratio was from 0.1 to 1, but the erythema was >21 mm, it was read as 2+. If the A/H ratio was from 1 to 2, it was read as 3+. If the A/H ratio was from 2 to 3, it was read as 4+. If the A/H ratio was greater than 3, it was read as 5+. If the A/H ratio was greater than 4, it was read as 6+. A positive responder was defined as a responder demonstrating a response greater than 2+ on the SPT. Two-hundred ninety (8.9%) patients showed positive responses ($\geq$ A/H 2+) to Hop J pollen, while 400 (13.8%) showed positive responses ($\geq$ A/H 2+) to mugwort pollen, and 285 (9.8%) to ragweed pollen. The prevalence of positive responses to inhalant and food allergens was analyzed.

Statistical Analysis

Cross-tab analysis using SPSS version 7.0 (Chicago, IL) was used to evaluate the statistical differences in the allergenic relationships observed between two allergens. A p value of 0.05 or less was regarded as significant.

RESULTS

Fig. 1 summarizes the prevalence of positive responses on skin-prick test to inhalant and food allergens in 260 patients sensitized to Hop J pollen. Statistically significant associations were noted between Hop J pollen and weed pollens such as nettle, fat hen, sunflower, and grass pollens such as rye, orchard, Bermuda, and tree pollens such as alder, birch, hazel, and poplar ($p < 0.05$, respectively). There were no significant associations between Hop J pollen and two house dust mites, mugwort, or ragweed pollens ($p > 0.05$, respectively). With respect to food-related allergens, significant associations were noted between Hop J pollen and Hop (*Humulus lupulus*), and celery allergens ($p < 0.05$, respectively). No associations were found with apple, carrot, other fruit, vegetables, and wheat grain allergens ($p > 0.05$, respectively).

Table I summarizes the association of skin reactivity

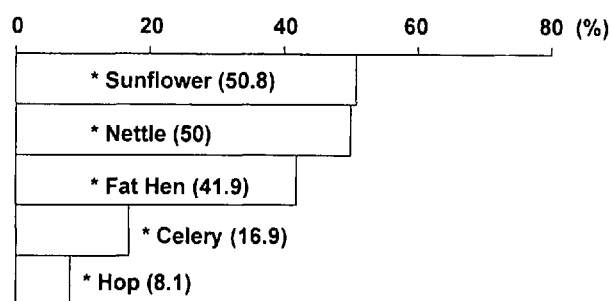


Figure 1. Prevalence of positive responders on skin-prick test to weed pollen and food allergens in 260 patients sensitized to Hop Japanese pollen. *Statistical significances were noted with each allergen by cross-tab analysis.

between Hop J pollen and sunflower pollen. Statistical significance was noted between them ($p < 0.05$). Table II summarizes the association of skin reactivity between Hop J pollen and nettle pollen. Statistical significance was also noted between them ($p < 0.05$). Table III summarizes the association of skin reactivity between Hop J pollen and celery allergen. Statistical significance was noted between them ($p < 0.05$).

DISCUSSION

There are two pollen seasons, in the spring from March to May and in the autumn from mid-August to the beginning of October, in this country.² In the spring, tree pollen from elder, oak, hazel, beech, birch, pine, and poplar is abundant. In the autumn, high levels of pollen arise from mugwort, ragweed, grasses, and Hop J. The flowering period of these three pollens is concurrent. More than 30% of respiratory allergy patients in this country had positive responses to more than one kind of pollen allergen on skin-prick test.¹¹ The sensitization rate to mugwort was highest (18.6%), followed by Hop J (13.8%), and ragweed (10%).¹² Our two-year study (1995–1997), which was based on positive skin test responses to major weed pollens in Korea, showed the highest prevalence in mugwort (13.8%), followed by Hop J (8.9%) and ragweed pollens

TABLE I

The Association of Skin Reactivity to Hop Japanese and Sunflower Pollen

Hop Japanese Pollen (A/H Ratio)	Sunflower (A/H ratio)					
	1	2	3	4	5	6
1	36	14	6	2		1
2	5	10	2			
3	5	4	7	1	1	1
4	2	1	2	1	1	
5		2				2
6	3	5	9	2	1	3

$p < 0.001$ by cross-tab analysis.

TABLE II

The Association of Skin Reactivity between Hop Japanese and Nettle Pollens

Hop Japanese Pollen (A/H Ratio)	Nettle Pollen (A/H Ratio)					
	1	2	3	4	5	6
1	32	10	8	2	1	2
2	9	20	1	3	2	
3	4	4	8	1		2
4	2	1				1
5		1				
6	4	3	4			3

$p = 0.001$ by cross-tab analysis.

TABLE III

The Association of Skin Reactivity between Hop Japanese and Celery

Hop Japanese Pollen (A/H Ratio)	Celery (A/H Ratio)					
	1	2	3	4	5	6
1	13	3	2			
2	4	6	4			
3		1				
4		2		1		
5		1	1			
6	3		1	1	1	

$p < 0.05$ by cross-tab analysis.

(9.8%). The pollination period of the Hop J plant in our geographic area lasts from August to October². The Hop J pollen counts recorded in Seoul during the autumn season have been greater than those of mugwort and ragweed pollens.² Despite its high pollen count, it was underestimated as an allergenic source when the first prospective study⁴ failed to detect significant sensitization.⁸ However, the second study,² performed 10 years later in our region, revealed that 6.1% of the respiratory allergy patients who visited Ajou University Hospital Allergy Clinic showed a larger than +2 of A/H ratio to Hop J pollen; moreover, 73.4% of them showed a larger than +3 of A/H ratio response. Based upon these results, Hop J has been considered one of the major causes of autumn pollinosis in this country.¹³

For the diagnosis of Hop J pollinosis, ELISA was used on sera of subjects showing positive responses on skin-prick tests. The prevalence of specific IgE binding increased according to skin reactivity: 33.3% in +2 reactors, 27.3% in +3 reactors, 33.3% in +4 reactors, and 92.3% in +5 reactors. These results suggest that the skin-prick test and antigen-specific IgE determination by ELISA may be valuable methods for identifying Hop Japanese pollinosis patients.

There have been a few studies dealing with allergenic relationships among these three major weed species: mugwort, ragweed, and Hop J. Our previous study² using Hop J ELISA inhibition assays with addition of ragweed and mugwort pollen demonstrated minimal inhibition between Hop J pollen and the other two weed pollens, suggesting limited cross-allergenicity between them. The other *in vitro* data¹³ using crossed immunoelectrophoresis revealed a very low possibility of cross-antigenicity between mugwort and ragweed pollens. However, a recent publication dealing with the allergenic relationship between ragweed and mugwort pollen demonstrated the presence of cross-reacting allergens between them.¹⁴ Further investigations will be needed to clarify the allergenic relationship between these two major weed pollens. Moreover, there have been no data dealing with allergenic relationships between Hop J pollen and major food allergens, although several studies have suggested the possible cross-allergenicity between mugwort and food allergens, especially celery, carrot, and spice allergens, referred to as "mugwort-celery-spice syndrome." In this study, significant associations were found between Hop J and nettle or sunflower pollen. Sunflower pollen has not been found in the pollen survey of this area; however, sunflower seed is commonly consumed as food in this country. In fact, some of the patients, having concurrent positive responses to these two allergens, experienced the same allergy symptoms upon eating sunflower seed, although no *in vitro* data have been found to identify the cross-allergenic components between them. The possibility exists that sunflower pollen could be contaminated within the sunflower seed.¹⁵ Also, a significant association was noted with celery and Hop which has been widely used as raw material to make beer in this country. No associations were found with other common fruit or vegetable allergens. No one has experienced the occurrence of the same allergy symptoms with beer or celery. Further laboratory investigations will be needed to identify the presence of cross-allergenic components between Hop J and celery or Hop, nettle, and sunflower pollen.

In conclusion, the analysis based upon skin-prick test results suggested that Hop J pollen may be linked with celery, Hop allergens, and nettle and sunflower pollen allergens.

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