

Epidemiological study of the prevalence of allergic reactions to Hymenoptera in a rural population in the Mediterranean area

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Summary

Background Systemic allergic reactions to Hymenoptera venom occur in a percentage that varies from 0.4 to 3.3%. Epidemiological studies indicate that from 15 to 25% of the general population can be sensitized to different Hymenoptera venom as well as the fact that the degree of exposure may be related to the prevalence found in those studies.

Objective The objective of this study was to evaluate the prevalence of insect sting allergy and the venom sensitization in a rural population to three Hymenoptera previously found in the area: *Polistes dominulus* (Pd), *Vespula germanica* (Vg) and honey bee (Hb).

Methods A rural community located in the south-east of Spain, close to the Mediterranean Sea, was selected since the stinging Hymenoptera having been previously identified. A random sample of 310 subjects from the village census was studied. A questionnaire and a serum sample were obtained from every patient. The evaluation was conducted by a family doctor, who focused on the reactions to Hymenoptera sting, age, sex, occupation, atopia, previous Hymenoptera sting, stinging insect, interval to last sting and average stings per year. RAST to Hymenoptera venoms were also determined.

Results The prevalence of systemic reactions was 2.3% (57.6% of them had a positive RAST). Large local reactions were found in 26.4% (only 28.5% of them had a positive RAST). Asymptomatic sensitization (positive RAST) was observed in 16.4% of subjects without reaction. Only a weak correlation between subjects with less than 3 years' interval to last sting exposure and positive RAST results was noted, whether they presented with a clinical reaction or not ($P < 0.05$).

Conclusions The prevalence of systemic sting reactions in our rural community is higher than other general populations in the same Mediterranean area, and similar to other rural populations studied. The degree of exposure influences not only the prevalence found but also the detection of specific serum IgE.

Keywords: epidemiological study, Hymenoptera venom allergy, systemic anaphylactic reaction

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Introduction

Systemic allergic reactions to Hymenoptera venom (bees and wasps) occur in a percentage ranging from 0.4 to 3.3% as reported by different authors [1–4]. In some instances the anaphylactic reaction may cause death, and this

fatal outcome can occur as the first manifestation after a sting [5].

Previous epidemiological studies indicate that from 15 to 25% of the general population can be sensitized to different Hymenoptera venom [6–10]. These studies have been carried out in different groups in different parts of the world and a certain amount in more exposed groups, such as rural communities or bee keepers [11–14]. In Europe,

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several studies have been performed in well-defined populations not including bee keepers [15–19].

Since insect distribution and people's lifestyle vary in different parts of the world, studies on sensitivity of populations in different areas should be done. The present study was carried out in a Spanish rural community of 1600 inhabitants, exposed to three identified Hymenoptera: *Polistes dominulus* (Pd), *Vespula germanica* (Vg) and honey bee (Hb), as we previously reported [20]. The prevalence of systemic reactions (SR) or large local reactions (LLR), the presence of specific IgE antibodies and the association with different parameters such as occupation, degree of exposure and stinging insect, were also determined in a sample of this population.

Materials and methods

Subjects

A rural community of 1600 inhabitants, located at 3000 feet above sea level in the south-east of Spain, close to the Mediterranean Sea, was selected since the distribution of Hymenoptera in this area had been previously determined [20]. Hb and the Vespids Vg and Pd were the three relevant social Hymenoptera identified, Vg being more prevalent than Pd. Taking a previous estimation of 17% of prevalence of Hymenoptera-allergic reactions in this area, a random sample of 310 subjects representing the census of 1600 inhabitants was selected (SE 0.05%; CI 99%) [21].

Evaluation of subjects

The interviews were conducted by a specially trained family doctor, responsible for the community in autumn 1990. The questionnaire used for the interview contained questions on the following: age, sex, occupation, personal atopic history, stinging insect, type of reaction, month of sting, interval to last sting exposure as well as estimated number of sting exposures per year. We adopted the Mueller classification of clinical reaction [22], for establishing systemic reactions (SR) and large local reaction (LLR).

RAST was determined in addition to the evaluation of the questionnaire, given that skin tests were not familiar to the evaluator.

Specific IgE determination

Serum samples were obtained by venipuncture in every subject, frozen and maintained at -20°C till assayed. Pd and Vg were collected locally in summertime and the venom was obtained by sac dissection and extraction by precipitation in B-alanine buffer [23]. Hb venom was obtained from Sigma Chemical (St Louis, MO, USA). Pd,

Vg and Hb venoms were coupled with cellulose disks following the method of Ceska *et al.* [24]. RAST procedure was validated previously and carried out as described [25]. Results were expressed as a percentage of the total number of counts added and were considered positive when double the mean $+2$ SD of a negative control group.

Statistical analysis

The statistical analysis was performed on an IBM computer with the software package SPSS (Ver 6.1.2 for Windows, Chicago, IL, USA). Chi-square tests were employed for analysis of the different ratios between groups. Non-parametric analysis of variance (Kruskal–Wallis method) was used to determine the significant variance between groups. Logistic regression analysis was performed to estimate adjusted odds ratios (OR) when taking several variables into account. OR with 95% confidence intervals (CI) were determined. A *P*-value less than 0.05 was considered significant. Results are presented as percentages and means (SD) [21].

Results

Random sample

The mean age in the sample studied was 42.4 years of age (SD ± 19.6). The percentage of males was 37.3%. However, sex was not balanced owing to the fact that in the local community there was a predominance of females over males as well as no statistical differences in percentage between the sample studied and the community. Farmers represented 43.6% of the subjects, 16.3% had other professions and 40% had no occupation. There were no bee keepers in our sample.

The prevalence of systemic sting reactions was 2.3% (7/303). LLR were reported in 26.4% (77/303) and 72.2% (219/303) of the subjects had no reaction after being stung or failed to remember having been stung previously (9/219). Only seven subjects failed to be interviewed.

Table 1. Type of sting reactions according to age, separated into three categories: less than 20, 20 through 40, and more than 40 years old

Age (years)	Reaction		
	None (%)	Large local (%)	Systemic (%)
< 20	37 (66.0)	17 (30.3)	2 (3.7)
20–40	53 (69.8)	21 (27.6)	2 (2.6)
> 40	129 (75.4)	39 (22.8)	3 (1.8)

Table 2. Calendar of insect stings

Stinging insect	Mar. (%)	Apr. (%)	May (%)	Jun. (%)	Jul. (%)	Aug. (%)	Sep. (%)	Oct. (%)	Nov. (%)
Bees	1 (10)				1 (10)	2 (20)	4 (40)	2 (20)	
Vespid	3 (1.1)	1 (0.4)	1 (0.4)	13 (4.6)	6 (2.1)	85 (30.1)	138 (48.9)	29 (10.3)	3 (1.1)

Table 1 shows the type of reactions in subjects who were stung, with respect to age and separated into three age ranges: less than 20, 20 to 40, and more than 40 years old, without significant statistical differences among them. The 'No reaction' column includes nine subjects, who had failed to remember if they had been stung, as non-reactors.

A vespid was recognized by 84% of subjects as their last stinging insect, Hb in 3% and 13% were not able to identify the insect. The frequency in every type of reaction did not change significantly. In the subgroup of the sample with positive RAST, a vespid was recognized in 91% of subjects, but 28% of the whole sample referred to previous stings from both Hymenoptera. The mean of sting per years in the sample was nearly 2 (1.89 ± 1.65). Table 2 shows a calendar of insect stings.

Specific IgE antibodies in the serum

Of subjects without reaction, 16.4% had a positive RAST. This percentage represents the asymptomatic sensitization of the sample. Positive RAST to the venoms studied occurred more frequently in the group of subjects with SR (57.1%) than in the group with LLR (28.5%) or no reaction at all (16.4%). Among the subjects who reported systemic

reactions, four of the seven had a history of multiple reactions. Details of the SR group are given in Table 3. In the whole sample 20.4% of subjects had a positive RAST to at least one venom. The percentage of subjects with positive RAST to Vg was higher than to the other venoms as shown in Fig. 1.

Parameters correlated with the presence of specific IgE and clinical sting reaction

The indicators of venom sensitivity, RAST and clinical sting reaction, were not correlated with personal atopic history, age, sex or occupation. In the subgroup of subjects with positive RAST, when the RAST was positive to the three insects (three out of seven with SR), the RAST results were significantly associated with SR ($P < 0.005$). In this subgroup also, subjects with less than 3 years' interval to last sting exposure had more positive RAST results whether they presented with a clinical reaction or not ($P < 0.05$). Stinging insect and previous sting reaction were related to severe clinical reaction after adjustment for type of sting reaction in a multiple logistic regression model (Table 4). Neither RAST nor other parameters were correlated.

Table 3. Characteristics of subjects with SR to insect stings

Patient number	Sex	Age (years)	Mueller grade of SR	Specific IgE antibodies (% counts) to:			Stinging insect	Previous sting reaction to first SR	Stings per year	History of atopy
				Vg	Pd	Hb				
1	F	59	4	0	0	0	Vespid	LLR	1	No
2	M	39	4	0.2	0	3.6	Bee	LLR	1	No
3	F	65	4	0.9	0.5	0	Vespid	LLR	1	No
4	F	15	3	3.7	2.1	3	Vespid	None	2	No
5	M	29	3	0	0	0	Vespid	None	2	Yes
6	F	20	2	5.6	2.5	1.8	No ident.	None	2	No
7	M	54	3	10	2.4	29	Vespid	None	4	No

Specific IgE determination: positive > 1.7%. LLR = large local reaction.

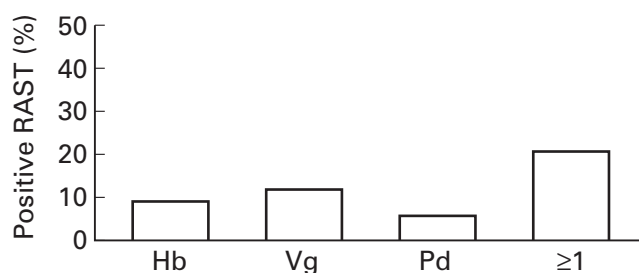


Fig. 1. RAST distribution by insect. Hb = honey bee; Vg = *Vespula germanica*; Pd = *Polistes dominulus*.

Discussion

The epidemiology of hypersensitivity reactions to Hymenoptera is described in a rural population of a well-defined geographical area, in the south-east of Spain, where the relevant Hymenoptera had been previously identified (Hb, Vg and Pd).

The prevalence of SR in our rural population studied was 2.3%. Comparing this result with other surveys, it was found to be lower than 3.3% given by Golden *et al.* [3] in industrial workers in Baltimore, MD, USA or 2.7% by Stuckey *et al.* [6] in 3439 subjects of a general population of Australia, or 5% by Mueller *et al.* [26] in Central Europe, but higher than 2.2% in the study performed by Fuat Kalyoncu *et al.* [17] in Çay town of Afyon, in the western region of Turkey and 1.2% by Charpin *et al.* in Marseille [8,18]. If we were to consider Marseille as a western Mediterranean city, and therefore with similar climatic and insect distribution to our studied area, our data doubles the prevalence found there.

However, when we consider studies which included rural populations, as in the Japanese study [11], the control group being a rural one, the incidence of systemic reactions after Hymenoptera stings was found to be relatively higher (6%) than that of general populations. Although we should add that all of them had mild systemic reactions. As well as this, Schäfer and Przybilla [12] found 3.3% subjects who reported SR to insect stings in a rural population of Bavaria (Germany).

Table 4. Assessment of risk factors for type of sting reaction. Analysis by multiple logistic regression

	OR	95% CI
Vespid as stinging insect	6.87	1.6–29.4*
No previous LLR	4.32	1.9–9.6**

OR = odds ratios, 95% CI = confidence interval. * $P < 0.01$; ** $P < 0.001$.

The degree of exposure in these communities is one possible explanation for the higher prevalence of SR (2.3% in our study) found in rural groups, in spite of the limited reliability we can give to the number of stings reported by the subjects. The time interval between two consecutive stings [27], in communities where there were more than one per year, offers itself as another explanation.

As Golden *et al.* have pointed out [3], the number of individuals who present themselves for medical care represents only the tip of the iceberg. Neither of the subjects with severe sting reactions had sought medical attention in our sample. LLR represent 25.4% of the subjects of our sample and this percentage is not explained according to sex as reported by others [3], owing to no statistical differences being found between LLR, SR and no reaction groups. Lifestyle may be similar in both sexes with regard to exposure to stings in this rural community.

The distribution of stings presented in the calendar in Table 2 shows the predominance of Vespids over Hb in our studied area, with a maximum in late summer. This predominance is also reflected in the RAST results, as it is shown in Fig. 1. The scarce number of Hb stings recorded produces an atypical distribution not comparable with the Vespids.

The percentage of positive RAST in the whole sample was 20.4%, similar to the 21% found by Golden [3] and higher than those found by other authors [4,6,28]. In addition, the degree of asymptomatic sensitization was 16.4%, higher than previously reported in normal controls [29] or in other surveys [6] or even in the rural control group [11]. These RAST percentages seem to better represent the degree of exposure in rural communities than the prevalence of SR. Nevertheless, we should consider the relativity of these figures because of the experimental RAST procedure used and the month the study was carried out [30]. As Zora *et al.* [7] well pointed out, the prevalence is seasonably variable. Also, the RAST results may be influenced by the difference in month of the maximum number of stings in bee and vespids, vespids being earlier (Table 3). Certainly, the use of all Hymenoptera venoms found in the area may increase the detection of specific IgE in the sample, especially with vespid venoms in our case.

Although half of the subjects with systemic reactions had positive RAST, similar to previous studies [11,19], doubling the percentage of LLR group and nearly reaching four times the percentage in the asymptomatic sensitization, RAST is not correlated with clinical sting reaction. However, in the case of subjects with positive RAST to the three Hymenoptera venoms, there were more possibilities of having had a systemic reaction than other sting reactions. Positivity to both vespid venoms was interpreted as the existence of cross-reactivity between them, as we previously reported [18].

Detection of specific IgE antibodies by RAST procedures were of limited predictive value with regard to the reaction to a subsequent sting, but the introduction of the highly sensitive CAP procedure does not improve significantly this predictive value as Müller pointed out [31].

In our population, being stung by a Vespid and not having had a previous LLR are risk factors. Therefore, taking into account the results expressed in Table 4, if the stinging insect is a vespid (OR=6.87) with no previous LLR (OR=4.32), the risk of having an SR is ≈ 29 times ($6.87 \times 4.32 = 29.68$) greater than if the stinging insect was a bee and there were previous LLR. These facts contrast with other risk factors such as male sex, atopy or age found in a different population in Sweden [15]. One of the objectives in any epidemiological study is to define the risk factors in the populations, which as the prevalence is found to do, may change from one community to another.

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