

Hymenoptera Venom Allergy: Time Course of Specific IgE Concentrations during the First Weeks after a Sting

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Key Words

Hymenoptera venom · Specific IgE · CAP · Anaphylaxis/ allergy

Abstract

Detection of IgE antibodies specific to honeybee or *Vespula* venoms is an important criterium firstly for the diagnosis of sensitization and secondly for the indication for a specific immunotherapy. Some authors recommend to postpone blood analysis after an insect sting for a certain time because circulating IgE antibodies might be consumed by the allergic reaction, which would result in a false-negative test outcome. We investigated IgE concentrations during the first weeks after an insect sting in 31 patients with an unequivocal history of an anaphylactic reaction after a honeybee ($n = 13$) or *Vespula* ($n = 18$) sting. Blood samples for analysis of specific IgE concentrations (CAP system, Pharmacia Diagnostics, Sweden) were collected within 2 weeks and 5 ± 2 weeks after the insect sting. 12/13 patients with honeybee venom and 14/18 patients with *Vespula* venom sensitization had CAP classes 1 or higher within the first 2 weeks. Those 5 patients with CAP class 0 within the first 2 weeks had detectable IgE concentrations a few weeks later. We conclude that testing for specific IgE to hymenoptera venoms is in most cases useful even during the first 2 weeks after the hymenoptera sting.

This allows early decisions on further diagnostic procedures and the therapeutic way to choose. Patients with no detectable IgE should, however, be retested after a few weeks.

Introduction

Hypersensitivity reactions to hymenoptera venoms are most often mediated by IgE antibodies specific to honeybee or *Vespula* venom and therefore represent anaphylactic reactions of the immediate type (type I allergy) [1–3]. Diagnosis and indication for specific immunotherapy are based not only on patient history and skin tests with hymenoptera venoms but also on in vitro assays for IgE antibodies specific to hymenoptera venoms [4].

Some studies suggest that specific IgE concentrations depend on the time interval between an insect sting and withdrawal of blood [5, 6]. Low to undetectable IgE concentrations have been found shortly after the sting. It has been speculated that this was due to consumption of circulating IgE antibodies, resulting in low or undetectable IgE concentrations as measured by RAST [2]. A considerable increase in specific IgE concentrations has been reported 3–4 weeks after the sting [7]. On the other hand, a decrease under the detection threshold has been noticed 3–18 months [5] after the sting or even 5 years later [6].

Table 1. Patients with hymenoptera venom allergy: characteristics and severity of anaphylactic reactions

	Allergy Patients	M/F ratio	Age range years	Severity of anaphylactic reaction [9]				
				grade I	grade II	grade III	grade IV	unclassifiable
Honeybee venom	13	9/4	8–65	2	8	2	1	0
Vespula venom	18	8/10	17–70	4	7	5	0	2

Since specific IgE concentrations are crucial for diagnostic and therapeutic decisions, we have studied IgE concentrations during the first 9 weeks after a sting in 31 patients with a history of allergic reaction following a hymenoptera sting.

Materials and Methods

Patients

31 patients with an obvious history of anaphylactic reaction of the immediate type to either honeybee or *Vespula* venom and detectable specific IgE antibodies were included. Patient characteristics and severity of anaphylactic reaction according to Ring and Messmer [9] are given in table 1. None of the patients had undergone specific immunotherapy before.

IgE Detection (CAP-FEIA)

The commercial CAP system (Pharmacia Diagnostics, Sweden) was used to determine concentrations of specific IgE antibodies to honeybee and *Vespula* venoms. Since not all sera were tested in the same assay, interassay reproducibility was studied by analyzing 19 sera of patients not included in this study twice on 2 different days; the 19 sera included 5 sera negative for antibodies to honeybee and *Vespula* venoms. The mean relative coefficient of variation was 15% for honeybee venom and 11% for *Vespula* venom results.

In patients with hymenoptera venom allergy, the first blood sample (sample 1) was taken 1–16 days (median 2) after the sting. The second blood sample (sample 2) was drawn 18–59 days (median 35 days) after the sting. Time points of blood samples are visualized in figure 1. All sera were stored frozen and thawed immediately before analysis.

Statistical Analysis

All statistical analyses were performed with SPSS for Windows, release 6.0 (SPSS). Pearson's relative coefficient of variation was calculated to test interassay variability. Specific IgE antibody concentrations of the first and the second blood sample were compared with the Wilcoxon matched-pairs signed-ranks test.

Results

In patients with honeybee venom allergy, 12 out of 13 had CAP class 2 or higher immediately after the sting. There was no significant increase in specific IgE concentra-

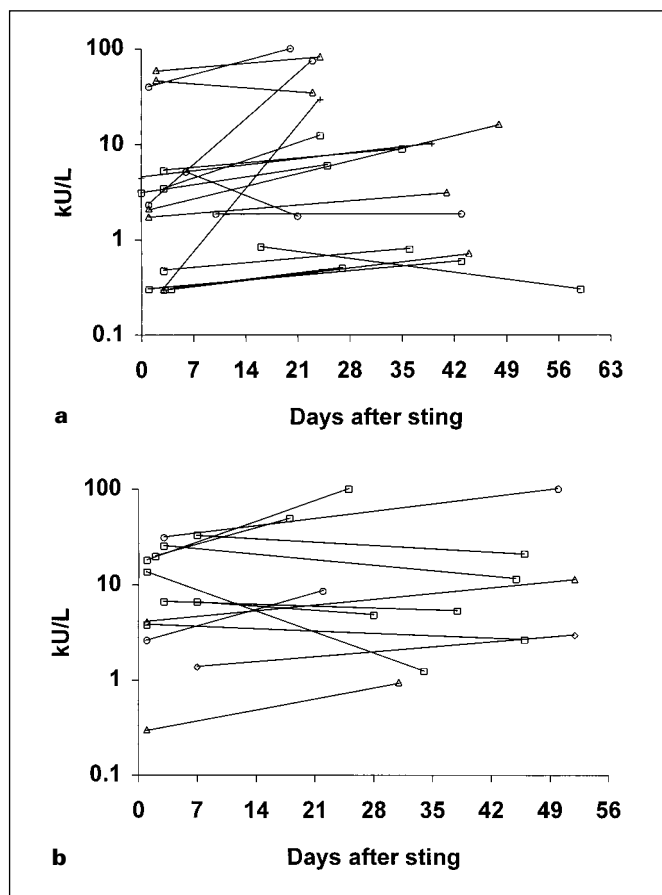


Fig. 1. Concentrations of specific IgE antibodies to honeybee (a) and *Vespula* (b) venom during the first weeks after the insect sting. Pairs of blood samples are connected by lines. The severity of anaphylactic reactions according to Ring and Messmer [9] is visualized by symbols: grade 1 (○), 2 (□), 3 (△) and 4 (◇). + = Unclassifiable. Note logarithmic scale of y-axis.

tions from the first to the second blood sampling (first sample: mean 12.8 kU/L, standard deviation $\pm$ 11.5; second sample: 24.6 $\pm$ 35.9 kU/L; Wilcoxon matched-pair signed-rank test: $p > 0.50$). IgE concentrations increased in 7 patients but decreased in 6 patients (fig. 1a).

In patients with *Vespula* venom allergy, 14 of 18 had CAP class 1 or higher in the first blood sample. All patients

with CAP class 0 had CAP classes 1 or higher in the second blood sample. One patient dropped from CAP class 2 to 0. There was a significant increase in specific IgE concentrations from the first to the second blood test (first sample: mean 9.9 kU/l, standard deviation $\pm$ 18.3; second sample: 21.4 $\pm$ 31.5 kU/l. Wilcoxon matched-pair signed-rank test: $p < 0.02$). IgE concentrations increased in 14 patients and decreased, however, in 3 patients, 1 patient remained unchanged (fig. 1b).

Discussion

In patients with *Vespula* venom allergy, we found lower concentrations of specific IgE antibodies than in patients with honeybee venom allergy. This finding is consistent with reports from the literature [1, 3, 7]. Possible explanations are an incomplete cross-reactivity between venoms of different *Vespula* genera or a higher purity of honeybee venom preparations used for CAP, which are collected by electric stimulation as compared to *Vespula* venom preparations, which are collected directly from the venom sac.

Despite the fact that skin prick tests are generally considered at least as sensitive and specific as IgE determination, we did not perform skin tests with insect venoms for the following reasons: the aim of the study was not a comparison of the relevance of different test methods but the investigation of the time course of specific IgE antibody concentrations after the sting. In many of our patients, a skin test would not have been useful shortly after the sting (median time span 2 days) because of medication with antihistamines and/or corticosteroids. Furthermore, low sensitivity of skin tests during the first weeks after a sting has been well documented [10].

Generally, concentrations of specific IgE increased during the first weeks after the sting. This increase was statistically significant only in patients with *Vespula* venom allergy. 84% of our patients had detectable specific IgE concentrations during the first 2 weeks after the sting. Differences between our results and earlier investigations may be due to an increase in sensitivity of present commercial in vitro assays as compared to formerly used assays [11]. In a recent study, Goldberg and Confino-Cohen [8] used an immunoenzymometric assay and detected specific IgE antibodies in 10/19 patients with honeybee and 7/12 patients with *Vespula* venom sensitization within the first 2 weeks after the sting. This is well in accordance with our results, although the detection rate of specific IgE antibodies was higher (honeybee: 12/13, *Vespula*: 14/18) in our study. This may be due to a higher sensitivity of the CAP system used in our study.

We conclude that CAP assays are useful even during the first 2 weeks in order to make an early decision on further diagnostic procedures and the therapeutic way to choose. It has, however, to be considered that the concentration of specific IgE does not predict the severity of the following anaphylactic reaction [5]. If specific IgE is not detectable during the first 2 weeks a repeat analysis should be performed several weeks after the sting.

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References

- 1 Stieger M, Wüthrich B, Wyss S, Kopper E: Zur Klinik und Diagnostik der Bienengiftallergie. *Hautarzt* 1978;29:632–636.
- 2 Przybilla B, Ring J, Wielgosch J: Der Basophilen-Histamin-Freisetzungstest als diagnostische Methode bei Hymenopterengift-Allergie. *Hautarzt* 1988;39:662–670.
- 3 Müller U: Klinik, Diagnose und Therapie der Insektenstichallergie. *Schweiz Med Wochenschr* 1989;49:1761–1768.
- 4 Schlenvoigt G, Müller M, Jäger L, Wenz W: In-vitro-Untersuchungen zum Auftreten von Doppelsensibilisierungen und ihre Charakterisierung bei Insektengiftallergikern. *Allergologie* 1996;19:461–464.
- 5 Przybilla B, Ring J: Hyposensibilisierungsbehandlung der Hymenopterengiftallergie: Aspekte der Indikationsstellung und Dosierung. *Allergologie* 1986;9:2–10.
- 6 Settiple GA, Carlisle CC: A critical evaluation of RAST to venoms of hymenoptera. *Clin Allergy* 1980;10:667–673.
- 7 Heinig JH, Engel T, Weeke ER: Allergy to venom from bee or wasp: The relation between clinical and immunological reactions to insect stings. *Clin Allergy* 1988;18:71–78.
- 8 Goldberg A, Confino-Cohen R: Timing of venom skin tests and IgE determinations after insect sting anaphylaxis. *J Allergy Clin Immunol* 1997;100:182–184.
- 9 Ring J, Messmer K: Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet* 1977;i:466–468.
- 10 Müller UR: Insektenstichallergie. Klinik, Diagnostik und Therapie. Jena, Fischer, 1988, p 78.
- 11 Aberer W, Kränke B, Hager A, Wick G: In vitro allergy testing needs better standardization – Test results from different laboratories lack comparability mostly due to missing effective standards. *Int Arch Allergy Immunol* 1995;108:82–88.

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