

Efficacy of Venom Immunotherapy in Beekeepers

K Münstedt,¹ D Wrobel,¹ M Kalder²

¹Department of Obstetrics and Gynecology, University Hospital Giessen and Marburg, Justus Liebig University, Giessen, Germany

²Department of Gynecology and Gynecological Endocrinology and Oncology, University Hospital Giessen and Marburg, Philipps University, Marburg, Germany

■ Abstract

Introduction: We previously found that some beekeepers continue beekeeping even after experiencing systemic allergic reactions. The present study was performed to collect data on the experience of beekeepers who underwent desensitization and continued beekeeping. The results are important for future counseling in this group of patients, and they show the effectiveness of desensitization under real conditions.

Methods: With the help of German and American beekeeping journals, we asked beekeepers who had undergone desensitization to participate. Data were obtained using a newly developed questionnaire and supplemented by reports obtained from the physicians who treated the allergy.

Results: We sent a questionnaire to each of the 73 beekeepers who responded to our call, and 63 (86.3%) questionnaires were returned. The vast majority of participants were hobby beekeepers who developed signs of allergy after a median of 2 years' beekeeping (mean, 4.27 years) and a median of 15 stings (mean, 51 stings). Additional allergies were reported by 35 beekeepers. Forty-three beekeepers were evaluated to determine the effectiveness of desensitization. The average number of bee stings after desensitization was 107 (median 18). All but one reported no longer having allergic responses; however, in the case of those that did, the severity of the allergic symptoms improved significantly.

Conclusion: To our knowledge, this study is the first to provide data on the experience of beekeepers who continue their activity after desensitization. Our results show that desensitization can result in a complete absence of symptoms after re-exposure to bee stings.

Key words: Bee venom. Allergy. Beekeeper. Venom immunotherapy. Desensitization.

■ Resumen

Introducción: Anteriormente habíamos observado que algunos apicultores alérgicos continúan criando abejas incluso después de experimentar reacciones alérgicas sistemáticas. Este estudio se realizó con el fin de recoger datos sobre la experiencia de apicultores que se sometieron a desensibilización y siguieron criando abejas. Los resultados son relevantes para un asesoramiento futuro en este grupo de pacientes, y muestran la eficacia de la desensibilización en condiciones reales.

Métodos: Con la ayuda de revistas alemanas y americanas especializadas en apicultura, se solicitó a apicultores que cumplieran con las características previamente mencionadas que participaran en el estudio. Los datos se obtuvieron utilizando un cuestionario de reciente creación, y se complementaron con los informes obtenidos de los médicos que trataban la alergia.

Resultados: Se envió un cuestionario a cada uno de los 73 apicultores que respondieron a nuestra llamada, de los cuales 63 fueron devueltos cumplimentados (86,3%). La inmensa mayoría de los participantes eran apicultores aficionados que mostraron signos de alergia tras una mediana de 2 años dedicados a la cría de abejas (media, 4,27 años) y una mediana de 15 picaduras (media, 51 años). Treinta y cinco apicultores notificaron además otras alergias. Se evaluó a 43 apicultores con el objetivo de determinar la eficacia de la desensibilización. El promedio de picaduras después de la desensibilización fue de 107 (mediana 18). Todos, salvo uno, notificaron que ya no presentaban respuestas alérgicas. Sin embargo, en el caso afirmativo, la intensidad de los síntomas alérgicos disminuyó significativamente.

Conclusión: Según sabemos, este estudio es el primero en proporcionar datos sobre la experiencia de apicultores que continúan su actividad después de la desensibilización. Los resultados muestran que la desensibilización puede dar lugar a una ausencia completa de síntomas tras la reexposición a picaduras de abeja.

Palabras clave: Veneno de abeja. Alergia. Apicultor. Inmunoterapia con veneno. Desensibilización.

Introduction

The likelihood of a member of the general public being stung by a bee at least once during their lifetime ranges between 55% and 95%, depending mainly on climate. In warm parts of the world, bees are active throughout the year and are considered to be relatively more aggressive, whereas in colder climates they are active and numerous only in late spring and summer [1,2]. Accordingly, the reported prevalence of systemic allergic reactions to bee venom ranges from 0.3% to 7.5%. Annual mortality from bee stings ranges from 0.09 to 0.45 per million inhabitants [3]. The recommendations for preventing a fatal outcome in patients at risk are to avoid contact with stinging insects, carry emergency kits during the bee season, and/or undergo desensitization/venom immunotherapy (VIT). Due to its high cost, desensitization is recommended mainly in patients who are more likely to be re-stung.

In cases of venom-allergic beekeepers, this likelihood is high when beekeeping is continued. Despite the risks, between 5% and 43% of beekeepers continue beekeeping [4-8]. Financial necessity has been cited as the principal reason, and the proportion of allergic beekeepers is lower among hobby beekeepers [8]. We previously showed that most affected beekeepers wore protective clothing, and we also observed that some beekeepers underwent desensitization and then continued beekeeping [8]. In the present study, we analyzed the experience of beekeepers who underwent desensitization and continued beekeeping. Our results show the effectiveness of desensitization and provide useful information for future counseling of this patient group.

Methods

Patients

In the December 2006 issue of the beekeeping journals *Die Biene*, *Der Imkerfreund*, and *ADIZ* (readership 35 000) and in the February 2007 issue of the *Bienenjournal* (readership 17 000) and the *American Bee Journal*, we asked beekeepers who had experienced an allergic reaction to bee venom and undergone specific treatment to contact us. They were asked to complete and return a questionnaire.

Study Questionnaire

As there are no previous studies on this subject, we had to develop a suitable instrument for data collection, namely, the Questionnaire for the Assessment of Beekeepers' Venom Allergy and Desensitization. The questionnaire was based on previous research in other fields of medicine and on reports of various disorders in beekeepers [4,8-11]. We used the classification devised by Ring and Messmer, as it is the basis of German guidelines for the treatment of Hymenoptera venom allergy [12]. The symptoms of the various degrees of allergy were assessed and beekeepers were asked to choose the condition which best described their situation before and after desensitization. The instrument was piloted in 10 volunteers to ensure its intelligibility. A copy of the questionnaire is available on request. In order to prove the beekeepers were allergic, we also requested copies of their medical reports and/or permission to contact the treating physician for any information

that could prove necessary to evaluate the questionnaire. The questionnaire was sent to German participants along with a postage-paid envelope and stamps to compensate the expenses of copying relevant medical documents. Participants from outside Germany were asked to submit their expenses, which were reimbursed when the questionnaire was returned.

Statistical Analysis

SPSS version 14.0 (SPSS, Chicago, Illinois, USA) was used for data management and statistical analysis.

Ethics

The study was submitted to and approved by the ethics committee of the Justus-Liebig-University (application number 127/2006).

Results

Table. Characteristics of the Study Groups

Parameter	Entire group N=63
Age, y	
Mean value	52.2
Median	51.4
SD	10.2
Range	10.0-77.0
Gender	
Female, No. (%)	21 (33.3%)
Male, No. (%)	42 (66.7%)
Marital status	
Single, No. (%)	6 (9.5%)
Married, No. (%)	56 (88.9%)
Widowed, No. (%)	1 (1.6%)
Body mass index	
Mean value	25.5
Median	25.5
SD	3.3
Range	14.7-32.6
Place of residence	
Town, No. (%)	18 (28.6%)
Country, No. (%)	45 (71.4%)
Country of Origin	
Germany	59
USA	2
Switzerland	1
United Kingdom	1
Time spent as a beekeeper, y	
Mean	14.9
Median	8.5
SD	12.2
Range	2-57
Number of bee hives tended	
Mean	19.6
Median	7
SD	75.4
Range	2.0-600.0

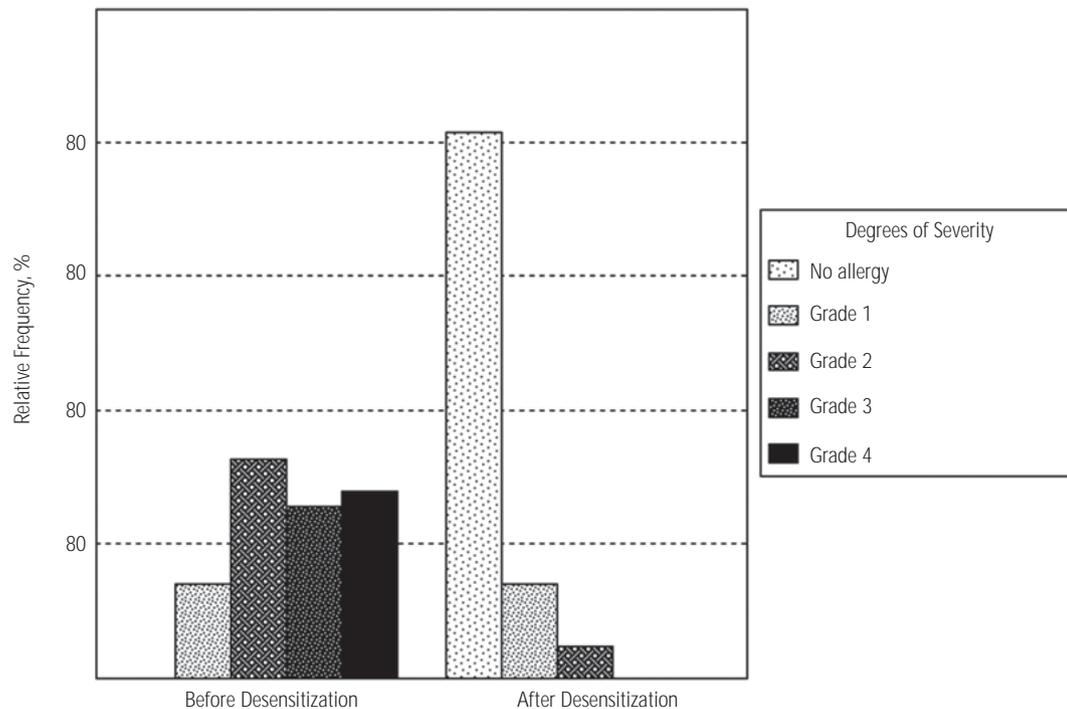


Figure 1. Severity of allergy based on the classification of Ring and Messmer before and after desensitization.

In all, 73 beekeepers responded to our call, and 63 (86.3%) returned their questionnaires. The characteristics of the participants are summarized in the Table. As shown, the vast majority of the participants were hobby beekeepers who tended a median of 7 hives.

It took a median (range, 1-38) of 2 years' beekeeping until signs of allergy developed (mean [SD], 4.27 [6.7]) and a median of 15 stings (mean, 51 [118.5]; range, 1-760). Thirty-five respondents reported that they also suffered from other allergies: wasp venom (14), coryza/hay fever (12), asthma (8), animal hair (7), house dust mites (5), foods (5), antibiotics (4), propolis (3), bee dust (2), bumblebee (1), and neurodermatitis (1).

After diagnosis, 27 (42.9%) respondents were initially counseled to give up beekeeping, 30 (47.6%) to wear sting-proof protective clothing, 53 (84.1%) to always carry an emergency kit, and 34 (54.0%) to undergo desensitization. Twenty beekeepers were told that they could continue beekeeping after desensitization. The beekeepers in this study, however, did not follow the advice to give up beekeeping and underwent desensitization.

We evaluated the response to sensitization in 43 beekeepers. The prerequisite for analysis was that the beekeeper had to have been stung at least once after desensitization. Desensitization was performed using Reless-Bienengift (Alk-Scherax Arzneimittel GmbH, Wedel, Germany) in 9 (20.9%) of these cases and Venomil Biene (Bencard Allergie GmbH, Munich,

Germany) in the other 34 (80.1%). The mean time of VIT was 3.7 years (median 3 years). Ultrarush treatment was administered to 9% of the patients, and 58% underwent rush Hymenoptera VIT. The remaining cases received conventional VIT. Figure 1 compares the severity of allergy based on the classification of Ring and Messmer before and after desensitization [12]. It clearly shows that, after desensitization, all but one patient no longer had an allergic response. In the 1 remaining case, the severity of the allergy decreased significantly. The average number of bee stings after desensitization was 107 (median, 18; range, 1-800). Most beekeepers were unconcerned about possible allergic reactions (Figure 2). Interestingly, concern over allergic reactions increased with the number of stings, although they did not cause allergic responses ($r=0.451$; $P=.01$). Sixteen (37.2%) of the 43 beekeepers carried an emergency kit for safety reasons.

Five of the beekeepers we evaluated used complementary and alternative methods to treat their allergy. Three relied on homeopathy. In 1 case, the grade of allergy decreased from grade 3 to 0; the other 2 were not evaluated, as they had not been stung. One beekeeper used meditation and received psychological support from a colleague. Interestingly, despite having a grade 3 reaction, he was no longer sensitized. After his alternative treatment, he was stung about 500 times with no further allergic reactions. The remaining beekeeper relied on his emergency kit, although he was able to avoid being stung after diagnosis.

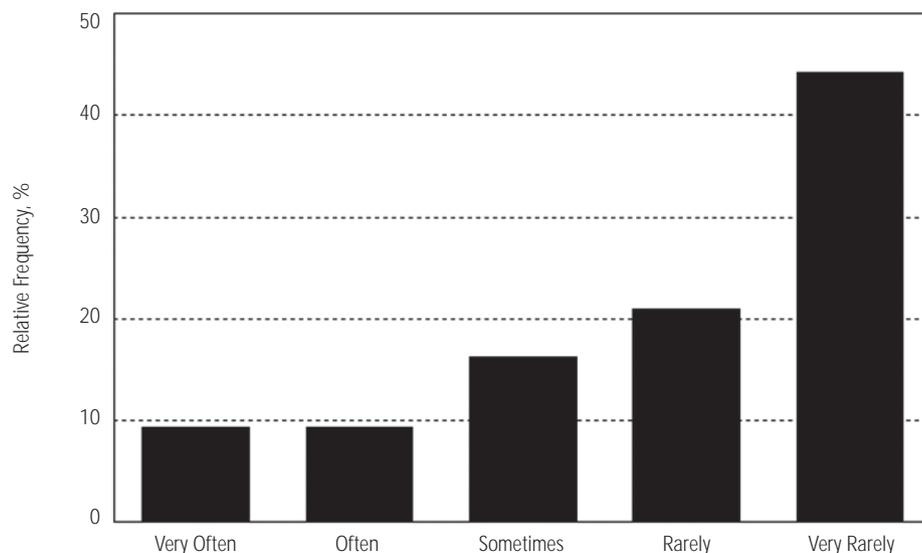


Figure 2. Frequency of concern over possible allergic reactions after desensitization.

Discussion

This is the first report of the experience of beekeepers continuing their hobby after desensitization. We show that it is possible to normalize the immune system and to avoid allergic reactions to the extent that even beekeeping is possible. The value of our results lies in the fact that previously sensitized individuals experienced many bee stings after desensitization. Only one other study mentions reactions after desensitization (2 cases) [13].

Few data are available on the efficacy of desensitization to bee venom allergy, as patients who have experienced an anaphylactic reaction to a bee sting will be told to avoid being stung again and are likely to follow this advice. Therefore, they will avoid situations in which they could be exposed to bee stings. In a recent study evaluating the long-term outcome of desensitization in 146 successfully treated patients with allergy to bee and wasp venom (mean follow-up, 6.5 years), 41.1% were stung again, although only a few were stung more than once [14]. The authors conclude that patients with allergy to Hymenoptera venom benefit significantly from desensitization, as the psychological outcome is favorable and the severity of the reactions decreases [14]. However, the low exposure of these patients limits general conclusions on the efficacy of desensitization.

Our study has several limitations. It seems likely that only beekeepers whose desensitization was successful answered the questionnaires, and we might assume that beekeepers whose desensitization was not effective will give up beekeeping, especially when it is only a hobby. As beekeepers with allergic reactions to bee venom are frequently counseled to give up

beekeeping, many might have followed the advice of their allergologist, thus leading to a selection bias.

Nevertheless, our data provide valuable information on how to counsel beekeepers with bee venom allergy. As allergic reactions to future stings can be effectively prevented by desensitization, affected beekeepers willing to continue beekeeping should be advised to undergo desensitization. Knowing that the procedure is effective and will enable them to continue beekeeping may encourage them to seek treatment. However, a very interesting study from Italy [15] that analyzed the outcome of beekeepers with allergic reactions who did not undergo desensitization showed that symptoms improved spontaneously in half of the beekeepers, remained unchanged in 30%, and worsened in “only” 20%. These findings explain why alternative methods appear to be effective.

These and our findings may have little relevance in countries like Germany, with a high prevalence of hobby beekeepers; however, they could be of interest in countries with a high percentage of commercial beekeepers. Other studies have shown that the prevalence of bee venom-allergic beekeepers is much higher [7,14]. Nevertheless, even in Germany, the ability to successfully treat bee venom allergy is important because of the fact that allergy obliges beekeepers to discontinue their activity. Furthermore, effective treatment can safeguard the role of bees in the ecosystem and prevent the continuous decline in beekeeping observed in recent years. The number of beekeepers in Germany is falling, and those who continue are increasingly older. Desensitization could perhaps ease the problem to some extent [8]. We intend to continue recording the experience of venom-allergic beekeepers in order to confirm these findings and to provide a solid basis for consultation in this group of patients.

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References

1. Mingomataj E, Ohri D, Dhimitri V, Priftanji A, Qirko E, Pani L, Fischer TC, Dinh QT, Peiser C, Fischer A, Groneberg DA. Hymenoptera sting anaphylactic reactions in the Mediterranean population of Albania. *J Investig Allergol Clin Immunol*. 2003;13:272-7.
2. Antonicelli L, Bilo MB, Bonifazi F. Epidemiology of hymenoptera allergy. *Curr Opin Allergy Clin Immunol*. 2002;2:341-6.
3. Annala I, Saarinen JV, Nieminen MM, Moilanen E, Hahtola P, Harvima IT. Bee venom induces high histamine or high leukotriene C4 release in skin of sensitized beekeepers. *J Investig Allergol Clin Immunol*. 2000;10:223-8.
4. Annala IT, Karjalainen ES, Annala PA, Kuusisto PA. Bee and wasp sting reactions in current beekeepers. *Ann Allergy Asthma Immunol*. 1996;77:423-7.
5. Celikel S, Karakaya G, Yurtsever N, Sorkun K, Kalyoncu AF. Bee and bee products allergy in Turkish beekeepers: determination of risk factors for systemic reactions. *Allergol Immunopathol (Madr)*. 2006;34:180-4.
6. Bousquet J, Menardo JL, Michel FB. Allergy in beekeepers. *Allergol Immunopathol (Madr)*. 1982;10:395-8.
7. Garcia-Robaina JC, de la Torre-Morin F, Vazquez-Moncholi C, Fierro J, Bonnet-Moreno C. The natural history of Apis-specific IgG and IgG4 in beekeepers. *Clin Exp Allergy*. 1997;27:418-23.
8. Münstedt K, Hellner M, Winter D, von Georgi R. Allergy to bee venom in beekeepers in Germany. *J Invest Allergol Clin Immunol*. 2008;18:100-5.
9. Müller UR. Bee venom allergy in beekeepers and their family members. *Curr Opin Allergy Clin Immunol*. 2005;5:343-7.
10. Eich-Wanger C, Müller UR. Bee sting allergy in beekeepers. *Clin Exp Allergy*. 1998;28:1292-8.
11. Light WC, Reisman RE, Wypych JI, Arbesman CE. Clinical and immunological studies of beekeepers. *Clin Allergy*. 1975;5:389-95.
12. <http://www.uni-duesseldorf.de/AWMF/II/061-020.htm> (Accessed November 26, 2009).
13. Annala IT, Karjalainen ES, Mörsky P, Kuusisto PA. Clinical symptoms and immunologic reactivity to bee and wasp stings in beekeepers. *Allergy*. 1995;50:568-74.
14. Roesch A, Boerzsoenyi J, Babilas P, Landthaler M, Szeimies RM. Outcome survey of insect venom allergic patients with venom immunotherapy in a rural population. *J Dtsch Dermatol Ges*. 2008;6:292-7.
15. Pastorello EA, Incorvaia C, Sarassi A, Qualizza R, Bigi A, Farioli L. [Epidemiological and clinical study on bee venom allergy among beekeepers]. *Boll Ist Sieroter Milan*. 1988;67:386-92.

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■ Prof Dr Karsten Münstedt

Universitätsfrauenklinik Giessen
Klinikstrasse 32
35392 Giessen
Germany
E-mail: karsten.muenstedt@gyn.med.uni-giessen.de