Large Local Reactions to Hymenoptera Stings Negatively Affect Quality of Life to the Same Degree as Systemic Reactions

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J Investig Allergol Clin Immunol 2021; Vol. 31(6): 502-504
doi: 10.18176/jiaci.0688

Key words: Allergy to Hymenoptera. Quality of life. Hymenoptera stings. Large local reactions. Systemic reaction.

Palabras clave: Alergia a himenópteros. Calidad de vida. Picaduras de himenópteros. Reacción local aumentada. Reacción sistémica.

Reactions to Hymenoptera venom usually produce pain, pruritus, erythema, and mild inflammation at the site of the sting. Some patients present a large local reaction (LLR), which leads to inflammation greater than 10 cm in diameter and lasts for between 24 hours and 5-10 days [1].

Quality-of-life questionnaires are useful tools in daily clinical practice. In the case of Hymenoptera allergy, Oude Elberink et al [2] developed a quality-of-life questionnaire for patients who experience systemic reactions following Hymenoptera stings (Vespid Allergy Quality of Life Questionnaire [VQLQ]).

Between 2008 and 2015, the Hymenoptera Allergy Committee of the Spanish Society of Allergology and Clinical Immunology (SEIAC) undertook the translation into Spanish and subsequent cultural adaptation of the VQLQ, as well as a cross-sectional and longitudinal validation [3,4]. The questionnaire (HiCaVi) was validated in patients allergic

to *Apis*, *Vespula*, and *Polistes* species. HiCaVi consists of 14 questions, each with 7 possible answers, and yields a score of between 1 and 7, representing low to high quality of life.

The hypothesis of our study was that the quality of life of patients with LLR is also impaired. Furthermore, we sought to compare our findings with those of patients who experience systemic reactions due to Hymenoptera venom allergy.

Between 2016 and 2018, the Hymenoptera Allergy Committee of SEAIC conducted a cross-sectional observational study in 9 hospitals in Spain. The study population comprised consecutive patients older than 14 years who attended allergy departments reporting an LLR following a Hymenoptera sting in the previous 2 years. Professional beekeepers were excluded. After the statistical analysis, we performed a post hoc comparison with a historical control group of patients with systemic reactions included in the cross-sectional and longitudinal validation of the original questionnaire.

The study was approved by the Ethics and Research Committees of the participating hospitals. All patients gave their written informed consent to participate.

Qualitative variables are presented with their distribution as absolute and relative frequencies. Quantitative variables are summarized with means and standard deviations or medians and interquartile ranges in the case of a nonnormal distribution.

Qualitative variables were compared using the χ^2 test or the Fisher exact test, when necessary. Means were compared between 2 independent groups using the *t* test. For all tests, statistical significance was set at $P<.05$. Data were processed and analyzed using SPSS Version 21.0 (IBM Corp.).

A total of 186 patients with a mean age of 43.87 (14.99) years were included in the study. The results are included in the Supplementary Table.

The mean score on the HiCaVi for the whole group was 4.1 (1.53). We found no significant differences when we analyzed the questionnaire scores by age, sex, culprit insect, place of residence, or location of the reaction. However, significant differences were found for the type of reaction, as patients who experienced an immediate reaction had a significantly lower score than patients who experienced a delayed reaction (3.87 vs 4.36; $P=.031$).

The results from the quality-of-life questionnaire for the patients with LLR (4.1 [1.53]) were compared with those obtained from the 186 patients with systemic reactions included in the cross-sectional and longitudinal validation of the questionnaire (3.86 [1.55]). This yielded a nonsignificant difference between means of 0.23 ($P=.145$).

Our results show that quality of life is reduced in patients with LLR due to Hymenoptera venom. This loss of quality of life is similar to that observed patients who experience systemic reactions to insect stings.

The prevalence of LLR ranges from 2.4% to 26.4% of the general population, depending on the series consulted, and is lower in children and higher in professional beekeepers (38%) [1,5]. Such variability may be related to the lack of homogeneity in the definition of LLR, the methodology used, and the population studied [1,6].

It is estimated that the risk of developing a systemic reaction following an LLR is relatively low, ranging from 2% to 24%. Therefore, treatment should target symptoms, and immunotherapy is not routinely recommended [1,7,8]. Immunotherapy may be recommended in patients with high exposure to stings, those who live far from health care facilities, and those whose fear of a new sting may affect their quality of life [9-10]. Therefore, measuring quality of life in daily clinical practice may prove useful in the initial approach and in the decision on which treatment to implement in patients who experience an LLR following a Hymenoptera sting.

The significantly lower score in immediate reactions may be because patients perceive a reaction that occurs closer in time to the insect sting as being more dangerous. However, it is also possible that they had received treatment early. Reactions occurring several hours after the sting are seen as being more innocuous, even though in both cases the score obtained was low.

When we compared the results from the quality-of-life questionnaire, patients with systemic reactions obtained a slightly lower score than patients with LLR although the difference was not statistically significant.

Our study is limited by the clinical management of this type of patient. As we mentioned above, treatment of patients with LLR targets symptoms; therefore, performing in vivo and in vitro studies does not form part of daily clinical practice. However, given that the objective of our study was different, the absence of these data has no effect on our overall conclusions. Furthermore, since ours was a multicenter study conducted in Spain, further studies are required at the international level to confirm our findings.

This is the first controlled study to directly examine the difference in quality of life between patients with LLR and systemic reactions and to show that both groups experience a reduction in their quality of life. The use of quality-of-life questionnaires may help in the initial assessment of these patients and support the decision to implement specific treatment with immunotherapy.

Acknowledgments

The study was carried out within the framework of the Hymenoptera Allergy Committee of the SEAIC.

Funding

The authors declare that no funding was received for the present study.

Conflicts of Interest

Dr T Alfaya declares personal fees from ALK-Abelló outside the submitted work. The remaining authors declare that they have no conflicts of interest.

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Manuscript received February 15, 2021; accepted for publication March 12, 2021.

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