

# Debilitating beliefs and emotional distress in patients given immunotherapy for insect sting allergy: A prospective study

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## ABSTRACT

*Patients who receive venom immunotherapy (VIT) for systemic reactions (SRs) to insect stings are advised that once they reach the maintenance dose they are almost 100% protected against future SRs. However, initial evidence indicates that some patients continue to perceive themselves as highly debilitated by the allergy and are preoccupied with the allergic event. These factors have significant impact on their emotional well-being and allergy-related quality of life (ARQOL). We aimed to explore prospectively whether patients would experience these adverse psychological outcomes after receiving VIT coupled with professional explanation and reassurance of protection. Thirty-four patients who received VIT for systemic insect allergy and were under close medical surveillance were included. Before and 1 year after initiation of treatment, patients completed a questionnaire that measured debilitating beliefs, preoccupation with the SR event, emotional distress ARQOL, and QOL in general. Physician-graded severity of the reaction was recorded as well. VIT had a beneficial effect on all allergy-related variables. Self-imposed debilitating beliefs, preoccupation with the anaphylactic event, and ARQOL significantly but modestly improved over time. No association was found between ARQOL and QOL in general. The later variable as well as emotional distress remained unchanged after the VIT. This study shows that patients with sting allergy guided by trained personnel and treated with VIT show a reduction in dysfunctional beliefs and an improvement in ARQOL. Disputing medically unfounded beliefs that persist in some patients might improve their ARQOL.*

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**Key words:** Adverse psychological outcomes, debilitating beliefs, emotional distress, health-related quality of life, Hymenoptera, immunotherapy, insect sting allergy, venom

A systemic allergic reaction (SR) to an insect sting is an acute event that occurs within minutes after the sting and results in one or more of the following symptoms: diffuse urticaria and pruritus, cutaneous or laryngeal edema, bronchospasm, nausea and vomiting, hypotension, and loss of consciousness.<sup>1</sup> Affected patients are referred to an allergy clinic for primary evaluation and, subsequently, for immunotherapy with the relevant venom. A few months after beginning treatment, most patients reach the maintenance dose and are at no greater risk for SR than the general population.<sup>1</sup> Severe allergic reaction is a frightening event that may have adverse psychological consequences that can lead to impairments in mobility, outdoor activities, and social and even occupational functioning.<sup>2</sup> Such consequences may lead to perceived impairment in quality of life (QOL) in general. To our knowledge, this possibility was never tested.

A previous cross-sectional study of patients receiving immunotherapy for an SR to insect stings<sup>2</sup> revealed that

some of these patients found the event of the reaction very traumatic and that it continued to influence their lives long after they had been fully protected by the immunotherapy with the threat to their health being almost nonexistent. This observation is consistent with the general findings of studies of patients' illness perception. They repeatedly showed that lay people react not as much to their objective physical state, but rather to the cognitive representation of the threat to their health.<sup>3–6</sup> This might involve a variety of beliefs concerning the seriousness, controllability, duration, and consequences of the medical symptoms and these beliefs affect their overall emotional state and avoidance behaviors. Findings from the aforementioned cross-sectional study indicated that as much as one-third of these patients had displayed self-imposed, debilitating, illness-related beliefs. They were continuously preoccupied with the events of the SR, experiencing disturbing uncontrolled thoughts that hampered individual adjustment to insect venom allergies and impaired allergy-related QOL (ARQOL). No difference in the psychological response was found between patients at the beginning of treatment, when they were not yet protected and patients after 5 years of full treatment, when the risk of a sting reaction was very low. This finding was fairly disappointing, because it suggested that despite successful immunotherapy, there was no improvement in the patients' psycho-

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logical well-being. The shortcoming of that study was that it was not a follow-up study, and different patients were examined at discrete points in time after immunotherapy and no baseline data were available. The current prospective study was designed to overcome this shortcoming and to explore whether patients who experienced anaphylactic reaction to insect sting would experience the aforementioned adverse psychological outcomes as well as impaired QOL in general, after receiving venom immunotherapy (VIT) coupled with professional explanation and reassurance of protection.

## MATERIALS AND METHODS

### Subjects and Procedure

Thirty-seven consecutive patients with SRs to insect sting and positive skin tests or serum-specific IgE, who attended an outpatient allergy clinic for VIT were invited to participate in this study. Thirty-four (92% response rate) agreed to be treated with VIT after a thorough explanation of the protective effect as well as its side effects. Explanation included the incidence of recurrent SRs if re-stung when the patient was treated or not treated, the safety of the VIT procedure, and its side effects. Explanation was modified according to the patient's age and understanding and questions were answered unreservedly. VIT was given once a week until the maintenance dose of 100  $\mu$ g was reached (2–6 months after the initiation of treatment). Thereafter, the interval between the injections was gradually extended to once every 1–3 months. The same certified allergists and qualified nurses gave the explanations to all patients. They were available for further discussion, if needed, during the entire treatment period. Before commencement of VIT (T1) and 12 months later (T2) patients were asked to take part in the study and to complete a five-part questionnaire (see later). Children <12 years old, a minority of the sample ( $n = 3$ ), were assisted by their parents in this process.

Physician-graded severity of the SR was 1, mild (diffuse rash only); 2, moderate (diffuse rash and shortness of breath); or 3, severe (anaphylaxis). The study was approved by the Institutional Review Board. All participants gave oral informed consent.

### Questionnaires

*Debilitating beliefs* were measured by a 12-item scale developed by Confino-Cohen *et al.*<sup>3</sup> Sample items are "People who are allergic to insect stings should always be under medical surveillance," "It is preferable that people allergic to insect stings avoid participating in sporting activities in open areas," "Persons who are allergic to insect stings may be limited in doing certain types of work" (the response scale ranged from 1, not true at all, to 6, very true). It should be emphasized, however, that all these beliefs were unfounded once

the patient reached the protective maintenance dose. Some of the beliefs had no medical basis at all. The reliability (internal consistency) coefficient (Cronbach's  $\alpha$ ) for this scale was 0.81 (a value of  $\geq 0.80$  is considered desirable and indicates that all scale items are measuring the same attribute).

*Preoccupation with the SR event* was assessed by 10 items adopted from the Impact of Event Scale.<sup>7</sup> Sample items were "I think about it [the systemic reaction] when I do not mean to," "I try to remove it from my memory," "I have waves of strong feelings about it." Responses ranged from 1 (not at all) to 4 (often). Cronbach's  $\alpha$  for this scale was 0.83.

*Emotional distress* was gauged by the somatization (physical complaints; 12 items), anxiety (10 items), and depression (13 items) subscales of the SCL-90.<sup>8</sup> Cronbach's  $\alpha$  for these subscales were 0.87, 0.89, and 0.88, respectively.

ARQOL was assessed by three items: (1) "My allergy to insect stings is restricting" (2) "My quality of life is impaired due to my insect sting allergy." (3) "The need to continuously carry the EpiPen [Epinephrine Auto-Injector Center Laboratory] auto-injector is restricting." The response scale ranged from 4 (not at all) to 1 (to a large extent). The average intercorrelation between these items was 0.61, pointing to the internal consistency of the scale items.

QOL in general was measured by eight items of the general positive affect in the Rand Mental Health Inventory.<sup>9</sup> Sample items are "How happy, satisfied, or pleased have you been with your personal life during the last month?" (6, extremely happy, could not have been more satisfied or pleased; 1, very dissatisfied, unhappy most of the time). "During the past month, how much of the time have you generally enjoyed the things you do?" (6, all of the time; 1, none of the time). Cronbach's  $\alpha$  for this scale was 0.84

In addition, patients were asked about their adherence to carrying the EpiPen auto-injector (1, never; 2, seldom; 3, most of the time; 4, regularly) and their treatment beliefs, gauged by two questions: (1) "What do you think will be your reaction if re-stung?" (1, not severe at all; 6, very severe); (2) "Do you believe that the VIT protects against the risk of severe reaction if re-stung?" (1, not at all; 6, very much)

### Statistical Analysis

The association between the study variables before and after receiving VIT was examined by computing Pearson correlations between these variables. The significance of change in these variables after the VIT was tested by paired *t*-tests.

## RESULTS

Of the 34 participants in this study, 5 (14.7%) experienced a mild reaction, 23 (67.6%) had a moderate

Table 1 Correlations among the major study variables#

| Variable                        | Debilitating Beliefs | Preoccupation with the SR Event | ARQOL   | Somatic Complaints | Anxiety | Depression | QOL in General |
|---------------------------------|----------------------|---------------------------------|---------|--------------------|---------|------------|----------------|
| Debilitating beliefs            | —                    | 0.57**                          | −0.34*  | 0.29               | 0.39*   | 0.08       | −0.05          |
| Preoccupation with the SR event | 0.70**               | —                               | −0.52** | 0.44**             | 0.76**  | 0.62**     | −0.36*         |
| ARQOL                           | −0.35*               | −0.50**                         | —       | −0.15              | −0.45** | −0.34*     | 0.17           |
| Somatic complaints              | 0.17                 | 0.10                            | −0.18   | —                  | 0.68**  | 0.67**     | −0.43**        |
| Anxiety                         | 0.40*                | 0.41*                           | −0.32   | 0.47**             | —       | 0.86**     | −0.35*         |
| Depression                      | 0.50**               | 0.56**                          | −0.21   | 0.37*              | 0.67**  | —          | −0.52**        |
| QOL in general                  | −0.37*               | −0.29                           | 0.10    | −0.26              | −0.37*  | −0.66**    | —              |

#The correlations between T1 measures are presented above the diagonal, and for T2 measures are presented below the diagonal.

\* $p < 0.05$ ; \*\* $p < 0.01$ .

ARQOL = allergy-related quality of life; QOL = quality of life; SR = systemic allergic reaction.

Table 2 Mean scores of the major study variables before immunotherapy (T1) and 1 yr after commencement of treatment (T2)

| Variable                    | Before VIT (T1) | After VIT (T2) | <i>p</i> Value |
|-----------------------------|-----------------|----------------|----------------|
| Debilitating beliefs        | 25.1            | 22.0           | 0.04           |
| Preoccupation with SR event | 18.2            | 17.1           | 0.01           |
| ARQOL                       | 2.5             | 2.9            | 0.02           |
| Somatic complaints          | 16.8            | 16.7           | 0.9            |
| Anxiety                     | 13.9            | 11.7           | 0.07           |
| Depression                  | 20.9            | 20.1           | 0.51           |
| QOL in general              | 26.7            | 25.6           | 0.37           |

ARQOL = allergy-related quality of life; QOL = quality of life; SR = systemic allergic reaction; VIT = venom immunotherapy.

reaction, and 6 (17.6%) had a severe reaction. There were 26 male and 8 female patients. Most of the participants ( $n = 24$ ) were native-born Israelis and the rest were immigrants. The average age was 28.9 (range, 6–71 years) years, with an average of 12.5 (range, 6–17 years) years of education.

No association was found between the severity of the SR event and the demographic variables (age, gender, and education) or any of the major study variables (debilitating beliefs, preoccupation with the SR event, emotional distress symptoms, ARQOL, and QOL in general) at the two phases of the study (T1 and T2). In a similar vein, no association was found between any of the demographic variables and the major study variables (with the exception of a positive correlation between gender [male patients, 1; female patients, 2] and anxiety at T1 [ $r = 0.34$ ;  $p = 0.04$ ] and depression at T2 [ $r = 0.41$ ;  $p = 0.01$ ], which reflects the trend in the general population).<sup>10</sup>

In contrast, many of the major study variables positively intercorrelated. The correlations at T1 and T2 are given in Table 1. Before commencement of VIT (T1), there was a positive association between debilitating

beliefs and preoccupation with the SR event ( $r = 0.57$ ). Both of these variables were negatively associated with ARQOL (−0.34 and −0.52, respectively). Furthermore, preoccupation with the SR event was positively associated with psychological distress (manifested by somatic complaints, anxiety, and depression,  $r$  ranged from 0.44 to 0.76) and was negatively associated with QOL in general (−0.36). At T1, 16 of the 21 correlations were statistically significant. At T2 (12 months later) 13 correlations remained significant. There was no longer a significant association between emotional distress symptoms and ARQOL after VIT. No association was found between ARQOL and QOL in general, both at T1 and T2 ( $r = 0.17$  and 0.10, respectively).

The major finding was that the intensity of allergy-related thoughts and beliefs was reduced with time. The mean scores of the study variables are presented in Table 2. Paired  $t$ -test of significance revealed a significant reduction in debilitating beliefs and preoccupation with the SR event. This was coupled with a significant increase in ARQOL. Close inspection of the scores on individual items (not presented here) indicates that the most pronounced changes in the debili-

tating beliefs were in two items: "people allergic to insect stings should avoid going outdoors" and "people allergic to insect stings should always be under medical surveillance." The most pronounced changes in the scale measuring preoccupation with the SR event were in two items: "I try to eliminate the stinging event from my thoughts" and "I am aware that I still have a lot of fear from the event." In the scale measuring ARQOL, the most significant change was in the item, "My allergy to insect stings is restricting."

No corresponding change was observed in psychological distress symptoms and in QOL in general. On the other hand, a significant change was found in other variables associated with the treatment beliefs. Before VIT, 71.2% of the patients rated their expected reaction if re-stung as very severe. This percentage dropped to 46.8% after treatment ( $p < 0.01$ ). Similarly, before treatment only 51.5% believed that VIT would protect them against the risk of severe reaction if re-stung. This figure increased to 72.7% after treatment ( $p < 0.001$ ). A parallel change was observed in the frequency of carrying the EpiPen auto-injector. At T1, 83.8% indicated that they carried it regularly or most of the time, whereas at T2 only 51.5% reported doing so ( $p < 0.001$ ).

## DISCUSSION

SR to insect sting is an acute traumatic event that has major emotional consequences as well as an impact on functioning. The physical hazard is well controlled with specific VIT and once the maintenance dose is reached, which usually happens several months after commencement of VIT, the risk to the patient's health is almost nonexistent.<sup>1</sup> Our previous cross-sectional study of patients with allergic reaction to stings treated with VIT suggested that the psychological effects seemed to be long lasting.<sup>3</sup> In contrast, the findings of the present prospective follow-up study of a new group of patients over a 1-year period, showed that the VIT had a beneficial effect on all allergy-related variables.

After VIT, there was a statistically significant reduction in medically unfounded debilitating beliefs, in preoccupation with the SR event, and an increase in ARQOL. These parameters are idiosyncratic and were found both here and in other studies to be unrelated to the severity of the sting reaction<sup>2,3</sup> but rather dependent on the patient's interpretation of his/her medical condition. Because self-imposed debilitating beliefs are medically unfounded, the aforementioned changes may have resulted primarily from information about the disease and its treatment as well as from emotional support provided by the treating team.

Furthermore, VIT coupled with professional explanation and reassurance of protection appears to increase the patients' confidence with respect to treatment efficacy. Compared with the responses before

commencing the treatment, significantly fewer patients (a 34% reduction) expected their reaction to be severe if re-stung. In addition, after the treatment, 72.7% of the patients believed that VIT protected them against the risk of severe reaction if re-stung. Their sense of protection was also manifested in the significant drop in the percentage of patients who continued carrying the EpiPen auto-injector at follow-up.

The improvement in ARQOL after VIT is consistent with the findings of Oude Elberink *et al.*<sup>2,11</sup> In their work, VIT and information about SRs and future chances resulted in an improvement in health-related QOL in patients allergic to yellow jacket stings. This improvement could not be reached over time, when VIT was avoided and EpiPen and information were the only treatments. They speculated that providing VIT and information about its efficacy was sufficient to improve expectations about the outcome of future stings and to improve vespical ARQOL. The incremental contribution of the present study is in the actual measurement of changes in underlying handicapping thoughts and beliefs, *viz.*, debilitating beliefs and protracted preoccupation with the SR event. Our findings indicate that the increase in ARQOL covaried with the decrease in such cognitions, coupled with increased confidence from the treatment.

Nevertheless, in agreement with a similar observation by Oude Elberink and Dubois,<sup>2</sup> VIT improved ARQOL for some patients only. Furthermore, some patients still held debilitating beliefs and continued to be preoccupied with the SR event. Nearly one-third of the patients still had high scores on individual items of the respective scales. Their intrusive thoughts and images related to the SR event and their dysfunctional beliefs concerning the restrictions imposed by their medical status were found to be significantly associated with distress symptoms (somatic complaints, anxiety, and depression) and with impaired ARQOL and QOL in general. These findings suggest that VIT, even when coupled with professional reassurance, was not sufficient to dispel unfounded, self-imposed dysfunctional beliefs in this subgroup of patients where the association between ARQOL and QOL in general was somewhat higher (0.34), albeit not statistically significant.

Notwithstanding this later observation, an additional and very important finding was the lack of association between ARQOL and QOL in general. It would have been expected that the pronounced impact of the SR on different life domains, as outlined earlier, would have a negative impact on QOL in general, but such a generalization did not seem to occur for most patients. The impact was confined to allergy-specific QOL. Further supporting evidence for this assertion is that the beneficial effect of the VIT was manifested by an improvement in ARQOL only. In addition, the negative association between distress symptoms and AR-

QOL disappeared after VIT. The VIT positively affected ARQOL but had no effect on emotional distress symptoms.

No change after VIT was found in QOL in general. On the other hand, QOL in general was significantly and predictably associated with the emotional distress symptoms of anxiety and depression. There are at least two possible reasons for the absence of VIT effect on the later two outcomes. First, these outcomes may be affected by factors other than the reaction to the allergy, such as comorbidly or exposure to life stress, which have been shown to be associated with these outcomes. Second, the distress symptoms might reflect stable personality dispositions such as hypochondriasis and neuroticism, which have been shown to be related to exaggerated perception of symptoms in allergic patients.<sup>12</sup> Thus, nondisease features and personality traits contribute to elevated distress symptoms and impaired QOL in general not amenable to change by VIT, which is not designed to address these issues.

The present study has some limitations. It was conducted on a small group of patients. However, the fact that the association between patients' beliefs and expectations and ARQOL observed in our earlier cross-sectional study,<sup>3</sup> which was also observed in the present study conducted on a different sample, reinforces the generalizability of the findings. In addition, there was no reference group. Ethical considerations did not permit us to include a nonintervention group. One possible control group would be patients who refuse VIT, but as indicated earlier, we encountered only few such patients, which were not enough to constitute a control group. Another possible control group would be patients who receive EpiPen treatment only, as in the study performed by Oude Elberink *et al.*<sup>11</sup> These researchers have found that when patients choose EpiPen instead of VIT, no deterioration (or improvement) in health-related QOL was seen. However, when patients were randomized to the control group treated with EpiPen only a significant deterioration in health-related QOL was observed. For the former group, even though the treatment with EpiPen might not be desirable medically, this treatment might be suitable from an health-related QOL point of view. For the randomized patients, however, these results indicate that EpiPen only is unacceptable neither medically nor from a health-related QOL point of view. Consequently, we rejected the idea of forming such a possible control.

The present study has several advantages. First, it used a prospective design, thus overcoming the major limitation of our previous, cross-sectional study. This design enabled us to uncover the beneficial effect of VIT on all allergy-related variables, which we were unable to detect in the earlier study. Second, this study reconfirmed the identification of patients' underlying

cognitions related to ARQOL and this could be an additional focus of treatment as elaborated later. Third, this research contributed information to the limited amount of research that exists in this area.<sup>2</sup>

## CONCLUSIONS AND IMPLICATIONS

This prospective study showed that most of the patients with allergic reaction to stings who were guided by trained personnel and treated with VIT improved over a 1-year period, in all allergy-related variables that were measured, including ARQOL. However, nearly one-third of the patients continued to hold self-imposed, medically unfounded, debilitating beliefs. They continued to be preoccupied by the risk imposed by their allergy, resulting in emotional distress, leading to impairment in ARQOL.

Many clinicians are not aware that such long-lasting dysfunctional beliefs are held by some patients and their impact on QOL.<sup>13</sup> Thus, to facilitate improvement in the health-related QOL of such patients, these beliefs (detailed in the study by Confino-Cohen *et al.*<sup>3</sup>) should be diagnosed and disputed by the allergy specialists. The identification of such beliefs can be done by simply asking them to describe in what ways, if any, they feel their allergy is restricting them and if or how they are troubled because of this. The list in the study by Confino-Cohen *et al.*<sup>3</sup> may help to formulate specific questions if the patient finds it difficult to respond to an open-ended question. Such patients may be also offered a sting challenge and the (hopefully) negative result will be able to further challenge these debilitating beliefs. Only when these measures do not help, patients may be referred for external help such as that provided by cognitive behavioral therapy.<sup>13</sup>

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