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Quality of life of patients undergoing hymenoptera venom immunotherapy

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Abstract : Hymenoptera stings are one of the main causes of anaphylaxis in Europe [1] . Clinical observation shows that the most dangerous effects are those that develop immediately after the sting[2] . Most often, allergic symptoms occur within 5 to 20 minutes. There are reactions starting after 2 hours and sometimes even after 72 hours. The group of patients at risk of more severe reactions are atopic patients, patients with skin mastocytosis , the elderly, burdened with additional diseases. The highest mortality rate is observed in people over 50 years of age [3] .

Aim : The aim of this study is to evaluate and compare parameters of quality of life, anxiety and anxiety among patients who have undergone immunotherapy for Hymenoptera venoms.

Material and Methods : The research was conducted at the turn of January and February 2019. The study involved 100 patients desensitized to hymenoptera venoms in the Department of Allergology and Lung Diseases of the Provincial Specialist Hospital named after of Stefan Cardinal Wyszyński in Lublin. The diagnostic method that was used in the study was the

diagnostic survey. The research tool used was the questionnaire: The World Health Organization Quality Of Life (WHOQOL) -BREF (short version of the questionnaire assessing the quality of life) extended by the author's questionnaire. The database was created and statistical analyzes were carried out based on Statistica 9.1 computer software. (StatSoft, Poland).

Rezults : The vast majority of respondents said that their quality of life is good or very good. As much as 82% gave such an answer. Only seven of the respondents rated their quality of life as bad or very bad. 11% of respondents could not determine the level of quality of their lives. The respondents gave similar satisfaction to their health condition. As many as 74% of respondents declare that they are satisfied or very happy with their health. A quarter of the respondents could not determine whether they were satisfied or not about their health.

Conclusion : In allergy to hymenoptera insects, a significant impact of the disease on the emotional, professional, social and implemented sphere is observed. The previous experience of anaphylaxis symptoms plays a significant role here, but more importantly anxiety associated with their reoccurrence, which is usually the cause of a deterioration in comfort of life, a sense of security risk. That is why proper education conducted simultaneously with patients' immunotherapy is so important. This has a significant impact on the quality of life of patients allergic and immunotherapy to Hymenoptera venoms.

Key words: quality of life; immunotherapy; patient

Introduction

In different countries, depending on the climate, 56.6 - 94.5% of inhabitants declare that they were stung by Hymenoptera insects at least once in their life. Hymenoptera sting is one of the main causes of anaphylaxis in Europe [4]. In Poland, in ECAP research [5], 2-3% of respondents declared hypersensitivity to insect venom. In Nittner-Marszalska's research, as much as 8.9% of the inhabitants of Lower Silesia declared that they had undergone a systemic anaphylactic reaction after the sting. It is believed that in such people the risk of systemic reaction at the next sting is 25 - 75%. This risk decreases in subsequent years, if the patient is not stung, in order not to exceed 20% after several years [6].

Among other allergic diseases, hymenoptera venom allergy is distinguished by a high risk of developing anaphylaxis and even death. To quote Niitner - Marszalska, "such a threat creates the temptation to widely use venom immunotherapy as the only guarantee of protection against the occurrence of life-threatening symptoms of venom hypersensitivity. The qualification for venom vaccination understood in this way would, however, be irrational, because it would disregard at least three important factors: the probability of spontaneous extinction of venom hypersensitivity, the risk of re-sting and the calculated risk of complications occurring during venom immunotherapy. "[7]

Specific immunotherapy with stinging venom vaccines (insect venom immunotherapy) is the choice of the most effective form of causal treatment for patients with Hymenoptera allergy[8].

The effectiveness of immunotherapy is well documented. In most patients with Hymenoptera venom allergy, you can safely achieve tolerance through insect venom immunotherapy. However, some patients still fail to be protected against life-threatening anaphylaxis after stings. [9]

Anaphylactic shock after stinging in "field" conditions is often the cause of death. Many such cases have been described after the stings of persons who were not provided with professional medical assistance on time [10].

Insect venom allergy is diagnosed in patients with at least one systemic reaction after an insect sting and an immunoglobulin-dependent mechanism of hypersensitivity to venom allergens has been demonstrated. Any patient with a severe generalized allergic reaction after a wasp or bee sting should be referred to an allergist specialist to qualify for venom desensitization of these insects. Desensitization, or specific immunotherapy - VIT (Venom immunotherapy) [11], is the only therapeutic method with high effectiveness preventing a serious, life-threatening anaphylactic reaction[12].

Essence of allergy to hymenoptera venom .

The insects whose venom allergic reactions comes almost exclusively from the order Hymenoptera (Hymenoptera) [13].

The venom injected is responsible for causing an allergic reaction after a bee and wasp sting. It is a multi-component substance stored in insect venom tanks, containing a number of ingredients with strong toxic and allergenic properties . Man only shows toxic symptoms when the dose of venom is very high. The insect venom allergens known to date are proteins or peptides. It has been shown that the venom contains both antigens common to a particular insect family, as well as separate antigens characteristic only for specific species [14].

From the allergology point of view, the most important are the Apidea (bee) and Vespidea (wasp) families.

The genus Apis includes 4 species: the giant bee, the dwarf bee, the eastern bee and the honey bee (Apis mellifera). All species belonging to the genus Apis live in organized societies.

The wasp family is represented by three types: wasp (Vespula), Dolichovespula and hornet (Vespa).

During a sting, a bee can introduce about 0.012 mg of venom into the victim's body, including 50 ug to 140ug of protein, despite the fact that the venom bag contains even over 300ug of venom. Wasps that have the ability to repeatedly sting (do not lose the sting apparatus), release a smaller dose of venom during a single sting (about 1.7-17ug of venom) [15]. Information on the composition of venoms and allergens contained therein are the basis for the correct diagnosis and treatment of hymenoptera venom allergies[16].

Insect venom hypersensitivity usually has an IgE- dependent immune mechanism , less often an IgE- independent immune mechanism or a non - immune mechanism[17].

Epidemiology of hymenoptera venom allergies.

The individual risk of sting is about 30% in life. In European studies on the causes of anaphylaxis in adults, insect stings rank third after food and drugs[18].

Positive IgE for insect venom allergens in vivo skin tests or in vitro serum tests is found in 15-30% of the population; more often in children and in people with multiple stings. Clinical manifestations of allergies after stings are much less common [19].

Generalized (anaphylactic) sting reactions are relatively rare and, according to the vast majority of studies, occur more than ten times more frequently in adults (up to 7.5%) than in children (0.5-6.5%). Ethnic factors can also affect the frequency of reactions [20]. The death rate caused by anaphylactic shock after hymenoptera stings is in Central Europe 0.246 deaths per 1 million inhabitants per year [21]. In Poland, up to a dozen or so people die each year due to insect stings. In beekeepers and those professionally exposed to Hymenoptera stings, local and generalized reactions are more common than in the general population [22].

Immunotherapy with hymenoptera venom.

Allergen-specific immunotherapy is a widely accepted, highly effective treatment for inhalation and hymenoptera venom allergies [23].

The history of subcutaneous immunotherapy for insect venom covers approximately 50 years. In the initial phase, an extract of the whole body of insects was used. Over time, it turned out that this method has low effectiveness and the dose of allergen has negligible repeatability. Over time, aqueous solutions of venom extract began to be used, using studies on the widespread availability of recombinants [24].

The success of hymenoptera venom-specific immunotherapy depends on careful diagnostic procedures. The basis is an interview and confirmation of venom allergy in skin tests and determinations of specific IgE antibodies in serum. The final diagnosis is based on a critical assessment of all results and the qualification should follow generally accepted principles of immunotherapy [25].

In general, immunotherapy is indicated for all patients with an immediate IgE-mediated immediate - type sting reaction . It is obligatory for patients after severe life-threatening reactions (III and IV grade according to Mueller classification) and after milder reactions with comorbid risk factors (beekeepers, their family members and neighbors; special professional groups, e.g. farmers, gardeners, fruit sellers, firemen active leisure in the fresh air; motorcyclists)[26].

Beekeepers are a special group of people most exposed to stings and allergies to bee venom due to their work. Positive skin test results or the presence of bee-specific IgE venom are observed in up to 60% of the tested beekeepers, and bee venom allergy occurs much more frequently than in the general population. However, the reaction after the sting is mild in most beekeepers, which is the result of creating natural tolerance to bee venom [27].

Material and methods

The method by which these tests were performed is a diagnostic survey. According to T. Plich: "The diagnostic survey method is a way of gathering knowledge about the features of the structure and function of social phenomena and their dynamics, as well as about the opinions and views of selected social groups. Through the diagnostic survey you can also gain knowledge about the severity and development directions of some phenomena. "

Following the choice of method, detailed preparation of research techniques follows. The research technique and tool helpful in obtaining information to present this research was the questionnaire: The World Health Organization Quality Of Life (WHOQOL) -BREF (short version of the survey assessing the quality of life) extended by the author's questionnaire.

The author's survey contains a metric that includes questions about age, education, whether the occupation is related to the presence of stinging insects, the place of residence and the length of the desensitization process. In addition, the survey contains three questions to check the patient's level of knowledge on how to avoid exposure to stings, symptoms that may occur after sting, and how to behave after hymenoptera stings. These questions are closed-ended questions that contain both correct and incorrect answers, which is intended to more accurately verify the knowledge of desensitized patients.

The obtained test results were subjected to statistical analysis. The values of the measurable parameters analyzed were presented with the mean value, median and standard deviation, and for the unmeasurable with the help of count and percentage.

For qualitative features, the Chi ² test was used to detect the existence of relationships between the analyzed variables . To test the differences between the two groups, the Student's t-test was used , and if the requirements for its application were not met, the Mann-Whitney U test . Comparison of three groups was performed using ANOVA analysis of variance, and in the event of failure to meet the requirements, the Krusk ala-Wallis test was used for its application . Spearman rank correlation was also used to check the relationship between some variables. A level of significance of p <0.05 indicating the existence of statistically significant differences or dependencies was adopted. The database and statistical research were based on the computer software Statistica 9. 1 (StatSoft , Poland).

Results

Assessment of the quality of life of patients undergoing immunotherapy for hymenoptera venoms in the aspect of various spheres of life . An assessment of the quality of life of the respondents in various spheres of life (somatic, psychological, social and environmental) was presented, and the quality of life due to independent variables (age, gender, education, as well as the length of desensitization period) will be analyzed.

Subjective assessment of the quality of your life	Ν	%
Very angry	1	1.00
Bad	6	6.00
neither good nor bad	11	11.00
Okay	43	43.00
very good	39	39.00
altogether	100	100.00

Table 1. Subjective assessment of the quality of life of the patients studied.

The subjective assessment of the quality of life is at a very high level in all four spheres of life. Satisfaction with their state of health is declared by more than three quarters of patients surveyed.

Table 2. Satisfaction with one's health due to the age of respondents in four spheres oflife.

Analyzed	under 35 years old			35–49 years old			50 years and more			F ^A / H ^B	р
variable	Μ	Me	SD	M	Me	SD	Μ	Me SD			
Satisfaction with the quality of your life	3.91	4	1.03	4.19	4	0.86	4.28	4	0.81	2.587 ^B	0.274
Satisfaction with your health	3.94	4	0.88	4.25	4	0.76	4.19	4	0.89	2,409 ^B	0,300
The somatic sphere	80.56	81	13.69	78.69	81	14.07	75.64	81	15.63	0.999 _{A.}	0.372
Psychological sphere	78.91	81	16.08	80.63	81	15.50	79,42	81	12.04	0.118 A	0.889
Social sphere	82.44	81	14.79	76.16	75	14.70	77.14	81	19.65	1.327 A	0,270
Environmental sphere	78.19	81	16.31	81.81	84.5	12.17	79.64	81	13.97	0.526 A	0.593

A - ANOVA variance analysis

B - Kruskal-Wallis test

The noticed statistically significant difference only in the field of the environmental (F = 3.685, p = 0.015). The difference concerns the comparison of the quality of life in the

environmental sphere of subjects with desensitization up to one year (average M = 72.95) and subjects with desensitization 4-5 years (the average in this group is M = 85.15). There were no statistically significant differences between the other groups in the environmental sphere.

In the remaining cases, there were no statistically significant differences in the quality of life between the compared groups.

				_						_				
Analyzed	I) 1		II) 2			III) 3			IV) 4-5		F ^A / H ^B	р		
variable	Μ	Me	SD	Μ	Me	SD	Μ	Me	SD	Μ	Me	SD		
Satisfaction with the quality of your life	3.62	4	1.28	4.17	4	0.87	4.23	4	0.61	4.41	4	0.64	5,243 ^в	0.15 5
Satisfaction with your health	3.90	4	0.77	4.17	4	0.91	4.18	4	0.91	4.22	4	0.80	2,419 ^B	0.49 0
The somatic sphere	73.8 6	81	15.0 3	77.2 7	81	13.6 5	79.9 5	81	14.3 6	81.1 5	88	15.1 1	1.148 A	0.33 4
Psychological sphere	74,2 9	81	18.0 5	79.9 7	81	12.5 6	77.8 6	81	16.4 2	84.8 9	88	9.61	2,369 A	0,07 5
Social sphere	78.8 6	81	15,1 3	79.4 0	81	16.0 0	75.5 9	75	15.8 4	79.6 7	81	19.8 2	0.291 A	0.83 2
Environmenta l sphere	72.9 5	75	15.1 1	81.9 7	81	14.2 1	77.1 4	78	14.9 8	85.1 5	88	10.1 8	3.685 _{A.}	0.01 5 I-IV

Table 3. Satisfaction with the quality of life depending on the length of desensitization period.

A - ANOVA variance analysis

B - Kruskal-Wallis test

The relationship between education, work in the profession related to the presence of hymenoptera insects and the length of desensitization, and knowledge of ways to avoid exposure to staphylococci. The vast majority of respondents gave the correct answer to the question asked about ways to avoid exposure to staphylococci regardless of education, work in the profession associated with the occurrence of membranes or the length of desensitization.

			Answer to a question	Chi ²		
Analyz	ed variable		to avoid wasp / b	р		
		-	incorrect correct			
	basic /	N	12	19		
	professional	%	38.71%	61.29%	Chi ² =	
	1.	Ν	13	twenty	1.293	
Education	medium	%	39.39%	60.61%	df = 2	
	1	Ν	10	26	p = 0, 524	
	nigner	%	27.78%	72.22%		
	37	Ν	5	11	Chi ² =	
Work in a profession related to bees	Yes	%	31.25%	68.75%	0.003	
		Ν	thirty	54	df = 1	
	no	%	35.71%	64.29%	p = 0, 954	
Length of desensitization	1	Ν	9	12		
	1 year	%	42.86%	57.14%	Chi ² =	
		Ν	9	21		
	2 years	%	30.00%	70.00%	0.950	
	3 years	Ν	8	14	df = 3	
		%	36.36%	63.64%	p = 0,813	
	4.5	Ν	9	18		
	4-5 years	%	33.33%	66.67%		
1.		N	35	65		
altogether		%	35.00%	65.00%	1 -	

Table 4. Relationship between education, occupation related to Hymenoptera insects and duration of desensitization, and knowledge of how to avoid exposure to Hymenoptera sting.

DISCUSSION

The problem of the quality of life of patients desensitized to hymenoptera venoms has been raised many times in allergy literature in Poland and in the world. This is an important problem, especially since the decision to desensitize and undergo immunotherapy patients is already assumed to reduce their anxiety and thus improve their quality of life.

According to research by Allergology Clinic, University Hospital Groningen and Department of Clinical Epidemiology and Biostatistics, University of McMaster, in Hamilton , immunotherapy for Hymenoptera venom resulted in a clinically significant improvement in quality of life of patients allergic to the venom of wasps , and the treatment was well tolerated and had high patient acceptance. The improvement was not affected by age, gender, general anxiety, and the time interval between the last sting and visit to the VIT center. Patients' quality of life was also not affected by anaphylaxis after repeated stings. The quality of life of desensitized patients was assessed at a high level [28].

Therefore, a similarity is noted between the results of the above-mentioned studies and the results presented in this paper. In both cases, the respondents highly rated the quality of their lives regardless of the designated variables. Both the research conducted by the McMaster University in Hamilton and the results of the research presented in this paper indicate that the respondents highly evaluate the effectiveness of desensitization, indicate the great usefulness of desensitization and improve the quality of life.

Other studies conducted in 2016 by the Student Scientific Association of Immunology and Allergology at the Clinic of Immunology, Rheumatology and Allergy, Medical University of Lodz give the following conclusions: failure to undertake immunotherapy in patients with Hymenoptera venom allergy is associated with a lower quality of life and a higher level of anxiety [29].

The results presented in the author's paper do not compare the quality of life of patients who for various reasons did not undergo immunotherapy with desensitized subjects. In contrast, respondents answered the question about whether the level of anxiety in the aspect of sting by hymenoptera stings decreased during immunotherapy. As many as 80% of respondents declared a reduction in anxiety levels, and only every tenth respondent gave a negative answer, while 11% of respondents did not have a specific opinion on this topic. Over 90% of patients surveyed believe that desensitization is needed. Therefore, an analogy can be seen in the case of original research and research cited in the literature.

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