Case Report

Evolution of Quality of Life in Patients with Anaphylaxis Due to LTP Syndrome After 3 Years of Specific Immunotherapy and 1 Year after Treatment Completion

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Abstract

Severe food allergies caused by lipid-transporting proteins (LTP) are becoming increasingly prevalent in our environment, predominantly affecting a young population.

INTRODUCTION

The clinical presentation and related symptoms significantly diminish their quality of life. The Food Allergy Quality of Life Questionnaire – Adult form (FAQLQ-AF), developed and validated by Flokstra-de Blok et al. [1], is the first specific questionnaire designed to assess the health-related quality of life (HRQoL) in adult patients allergic to food. This questionnaire has been translated into various languages, including Spanish [2], and cross-validated in the EuropreVall study, a multicenter European food allergy research project with the objective of analyzing the impact of food allergies on the quality of life [3,4].

The LTP syndrome, or Lipid Transfer Protein syndrome, refers to an allergic reaction that can manifest in various ways within the human body. This allergic reaction may initially present as an Oral Allergy Syndrome (OAS) and, in more severe cases, progress to episodes of generalized urticaria affecting the respiratory, digestive, and vascular systems. In extreme situations, this reaction can lead to anaphylaxis, a potentially life-threatening allergic response. Another characteristic of these patients is that they often have rhinitis and/or asthma with pollen allergies.

OBJECTIVES

The primary goal of this study is to investigate the evolution of the quality of life in patients with anaphylaxis due to LTP syndrome after undergoing specific immunotherapy for 3 years and one year after completing the treatment, in comparison to a control group that did not receive immunotherapy.

MATERIAL AND METHODS

Study population: The active group of this study consisted of 21 patients who were over 18 years old and had been diagnosed with anaphylaxis due to LTP syndrome (SLTP). These patients underwent a 3-year treatment regimen involving ALK-Abello® peach-specific sublingual immunotherapy (SLIT), which effectively managed their condition. Consequently, they were able to reintroduce a diet that no longer required the exclusion of LTP allergens [5]. On the other hand, the control group included 13 patients with comparable clinical characteristics who made a personal decision not to initiate immunotherapy treatment.

Quality of life test: Patients in the active group underwent a quality of life assessment at the beginning of treatment, at the end of the treatment period, and one year after completing treatment. Patients in the control group underwent the same assessment at the beginning and at the end of the study. The assessment tool used was the S-FAQLQ-AF, which comprises 29 questions grouped into 4 domains for maintaining internal consistency (see Annex 1). Each question is scored from a minimum of 0 to a maximum of 6, resulting in a total score of 174 points (1). The domains or blocks in which the test is structured are: A.- Allergen Avoidance + Dietary Restriction (AADR or Allergen Avoidance and Dietary Restrictions): 11 items: 1, 2, 3, 4, 6, 8, 9, 10, 11, 12, 20. B.- Emotional Impact (EI or Emotional Impact): 7 items: 5, 24, 25, 26, 27, 28, 29. C.- Risk of Accidental Exposure (RAE or Risk of Accidental Exposure): 8 items: 7, 13, 14, 15, 16, 17, 18,

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21. D. Food Allergy Related Health (FAH or Food Allergy Related Health): 3 items: 19, 22, 23.

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B.- Emotional Impact (EI or Emotional Impact): 7 items: 5, 24, 25, 26, 27, 28, 29.

C.- Risk of Accidental Exposure (RAE or Risk of Accidental Exposure): 8 items: 7, 13, 14, 15, 16, 17, 18, 21.

D.- Food Allergy Related Health (FAH or Food Allergy Related Health): 3 items: 19, 22, 23.

Statistical analysis: Statistical analysis was conducted using R (version 4.0.5). Continuous variables were summarized using measures of central tendency and dispersion, including mean, standard deviation, median, quartiles (25% - Q1 and 75% - Q3), minimum, and maximum values. Normality of continuous variables was assessed using the Shapiro-Wilks test. Independent samples were compared using the independent Student's T-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. For dependent samples, the dependent Student's T-test was used for normally distributed data, and the Wilcoxon signed-rank test was used for non-normally distributed data. A p-value threshold of < 0.05 was considered statistically significant. The ggplot2 package [6] was employed for generating the graphs presented in this study (Tables 1,2).

RESULTS

Table 2 displays the individual results of each patient's responses to the FAQLQ-AF questionnaire, which is divided into domains (A, B, C, D) and provides a total score (T) at three different time points: at the beginning (time 1), after 3 years of treatment (time 2), and 1 year after discontinuing immunotherapy (time 3).

Tables 3 and 4 present the statistical results, comparing the scores of the different domains and the total score of the questionnaire at the three time points within the active group. Additionally, these tables compare the results of the active group with those of the control group. The findings reveal statistically significant differences in all domains and the total score of the questionnaire. Moreover, statistically significant distinctions are evident when comparing the results with the control group.

DISCUSSION

Health-related quality of life (HRQoL) is a term that encompasses various aspects of a person's well-being, including

Table 1: Patient demographics

	Patients with treatment	Patients without treatment
Total no-missing, n	21	13
Missing, n	0	0
Gender		
Men, n (%)	7 (33.3%)	4 (30.8%)
Women, n (%)	14 (66.7%)	9 (69.2%)
Age		
Mean (SD)	40.1 (11.2)	40.3 (12.7)
Median (Q1, Q3)	42.0 (29.0, 49.0)	39.0 (30.0, 46.0)
Min, Max	22.0, 61.0	26.0, 65.0
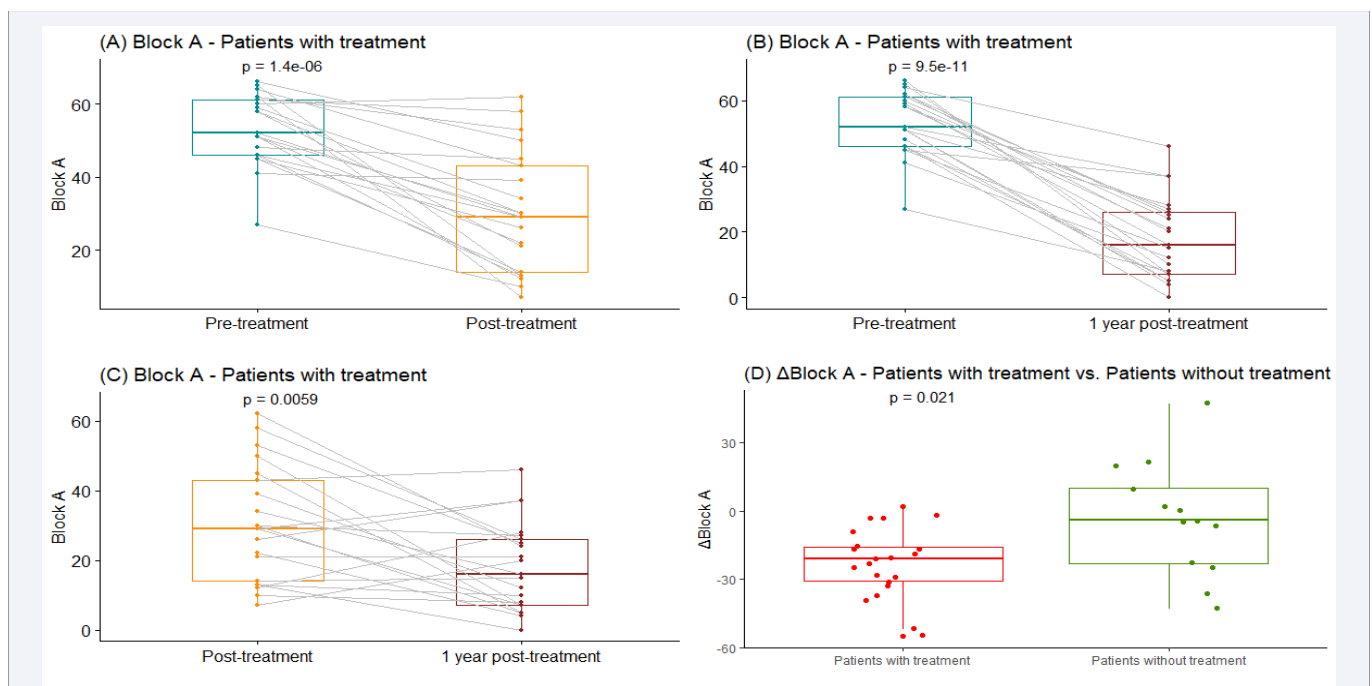
Graph 1 Block results A

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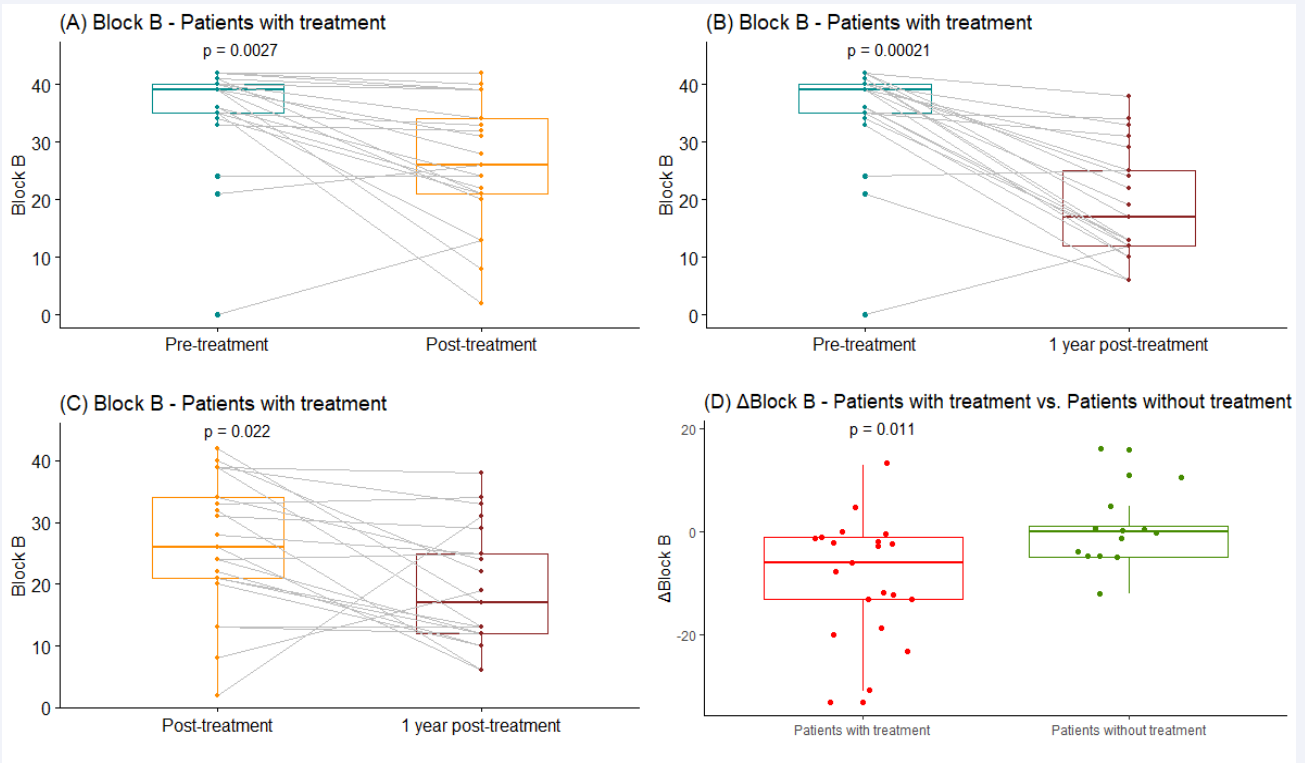
Graph 2 Block results B
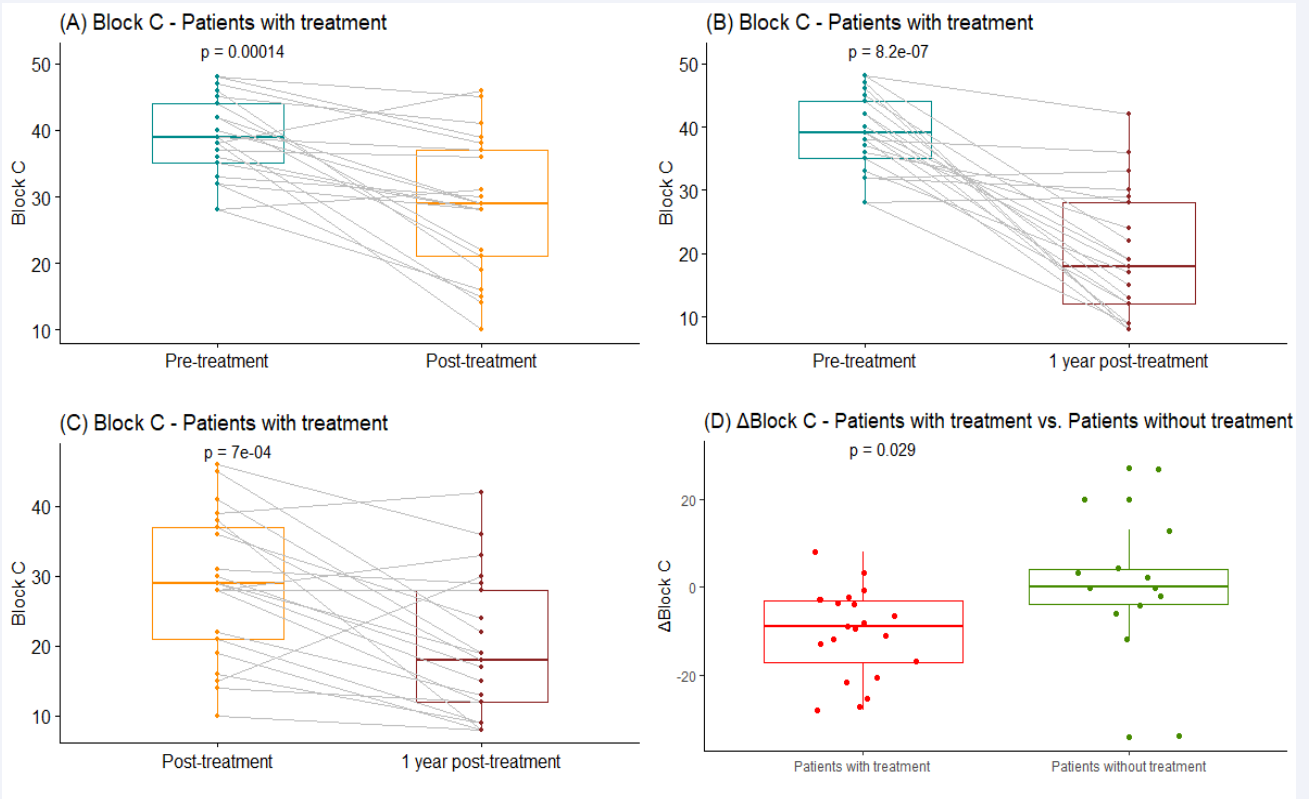
Graph 3 Block results C

Graph 4 Block results D

Graph 5 Block results Total.

Table 2: Results of each patient's responses

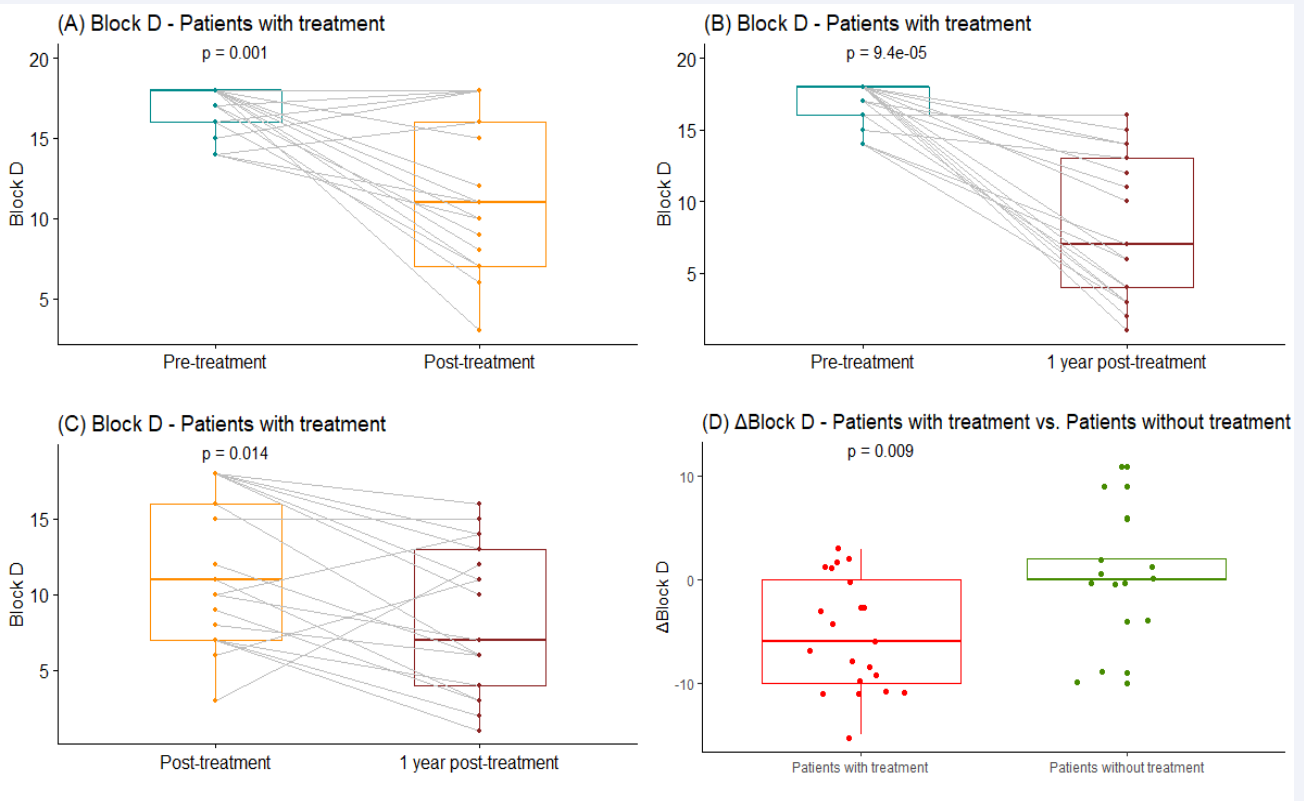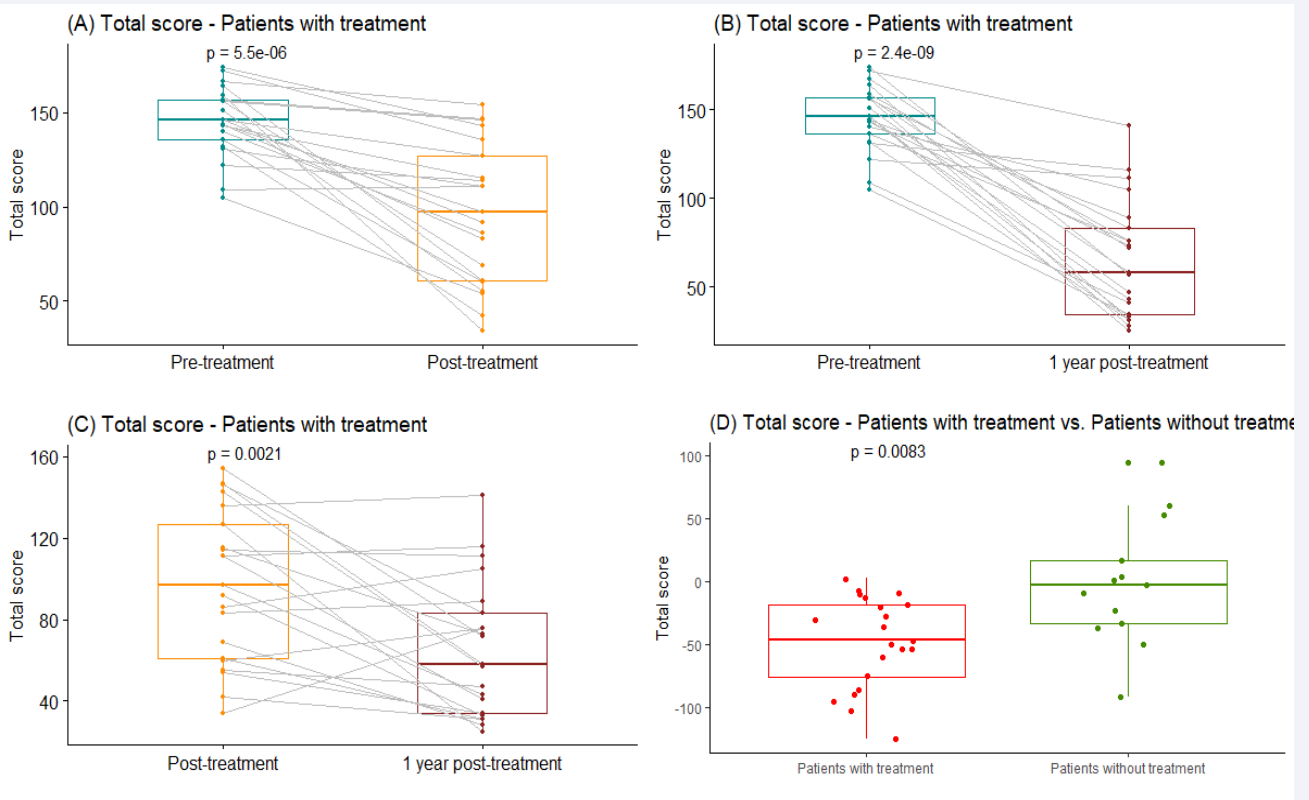| Age	Sex	Group	Block A			Block B			Block C			Bloc D			Total		
			A1	A2	A3	B1	B2	B3	C1	C2	C3	D1	D2	D3	T1	T2	T3
42	W	Active	45	26	37	24	24	25	38	46	36	15	18	13	122	114	111
29	W	Active	65	13	10	39	20	10	42	21	9	18	7	2	164	61	31
25	W	Active	51	12	28	39	31	29	32	28	33	18	15	15	140	86	105
41	W	Active	27	10	8	34	21	13	28	16	9	16	7	4	105	54	34
22	M	Active	62	7	20	35	2	31	44	22	13	18	3	12	159	34	76
38	W	Active	48	45	5	33	32	6	47	38	8	18	12	6	146	127	25
28	M	Active	58	30	27	40	28	25	32	15	30	14	10	7	144	83	89
50	W	Active	66	50	7	42	40	22	48	45	22	18	8	6	174	143	57
50	W	Active	46	13	0	0	13	12	38	10	8	17	6	11	132	42	31
42	M	Active	51	22	4	41	21	12	46	19	8	18	7	4	156	69	28
61	W	Active	58	21	21	36	13	13	39	14	12	18	7	1	151	55	47
26	M	Active	41	39	12	21	26	6	33	30	17	14	16	6	109	111	41
47	W	Active	61	58	26	40	34	24	37	36	24	18	18	10	156	146	83
54	W	Active	64	43	46	42	39	38	48	39	42	18	15	15	172	136	141
37	W	Active	51	30	5	35	22	10	42	29	15	18	11	3	146	92	33
48	W	Active	52	29	37	35	33	34	28	31	29	16	18	16	131	111	116
26	M	Active	60	62	24	41	39	13	39	37	18	17	9	3	157	147	58
31	W	Active	46	29	7	40	39	33	40	29	19	17	18	14	143	115	73
44	M	Active	59	34	16	36	24	12	35	28	12	14	11	3	144	97	43
49	W	Active	45	14	15	39	8	19	36	28	28	18	10	14	136	60	76
52	M	Active	62	53	25	42	42	17	45	41	19	17	18	11	167	154	72
26	W	Control	65	58	-	36	36	-	42	45	-	15	16	-	158	155	-
27	W	Control	45	47	-	32	31	-	29	31	-	16	17	-	122	126	-
36	W	Control	61	61	-	41	41	-	47	47	-	18	18	-	167	167	-
30	M	Control	53	49	-	35	23	-	39	35	-	15	11	-	142	118	-
65	W	Control	52	62	-	38	38	-	40	44	-	13	15	-	143	159	-
46	W	Control	20	15	-	20	16	-	12	12	-	9	9	-	61	52	-
39	M	Control	62	39	-	42	37	-	44	38	-	18	18	-	166	132	-
42	W	Control	10	57	-	7	18	-	8	35	-	3	12	-	28	122	-
27	M	Control	17	37	-	18	34	-	19	32	-	3	14	-	57	117	-
33	W	Control	66	30	-	36	37	-	43	41	-	18	18	-	163	126	-
43	W	Control	36	58	-	36	41	-	27	47	-	12	18	-	111	164	-
62	M	Control	66	23	-	42	37	-	48	14	-	18	8	-	174	82	-
48	W	Control	65	40	-	42	37	-	43	31	-	18	9	-	168	117	-

M->Men; W->Woman.

the impact of disease and its treatment on disability, daily functioning, and overall quality of life. It also reflects how perceived health affects a person's ability to lead a fulfilling life. Specifically, HRQoL measures the value a person places on their life span, considering impairments, functional states, perceptions, and opportunities influenced by factors such as disease, injury, treatment, and policy [7].

Two primary types of tools are used to assess the impact of different diseases on patients' quality of life: generic and disease-specific questionnaires. Generic questionnaires allow researchers to compare various clinical conditions, while disease-specific questionnaires focus on problems associated with a particular disease. Disease-specific questionnaires are better equipped to detect small changes in HRQoL following treatment [8].

According to the 2005 National Allergological Survey of Spain, patients with food allergies, assessed using the SF-12 Generic Questionnaire (physical and mental scales), perceived their quality of life as worse than that of 75% of the Spanish population of similar age and sex [9].

Currently, there is a growing body of research on the quality of life of patients with food allergies [8-10]. Additionally, numerous trials on sublingual immunotherapy (SLIT) in food allergies explore different approaches to managing this clinical condition, including peanut and peach immunotherapy. However, most studies do not specifically examine changes in quality of life after peach or peanut immunotherapy [11,12]. Therefore, it is essential to recognize that lipid-transfer protein syndrome (LTLS) can be severe in many cases and profoundly affect patients' HRQoL. Thus, it becomes crucial to assess not only the safety and efficacy of SLIT-peach® immunotherapy but also the improvements in HRQoL following long-term SLIT administration and the sustainability of these positive effects after treatment cessation. The significant enhancement in the quality of life observed in our patients following a 3-year course of SLIT-peach® suggests further evidence of the treatment's beneficial effects.

With this study, our aim was to track the evolution of the questionnaire over the four-year follow-up period of our patients. We have confirmed that the S-FAQLQ-AF (2) is a valuable and indispensable tool for monitoring this patient population.

Table 3: Results of the active group at the beginning of treatment, after 3 years of treatment, and 1 year after completing treatment

	Mean (SD)	Median (Q1, Q3)	Min, Max	p. value
Block A				
Pre-treatment vs. Post treatment				
Pre-treatment	53.2 (9.7)	52.0 (46.0, 61.0)	27.0, 66.0	**1.4e-06**
Post-treatment	30.5 (16.5)	29.0 (14.0, 43.0)	7.0, 62.0	
Pre-treatment vs. 1 year post-treatment				
Pre-treatment	53.2 (9.7)	52.0 (46.0, 61.0)	27.0, 66.0	**9.5e-11**
1 year post-treatment	18.1 (12.6)	16.0 (7.0, 26.0)	0.0, 46.0	
Post-treatment vs. 1 year post-treatment				
Post-treatment	30.5 (16.5)	29.0 (14.0, 43.0)	7.0, 62.0	**0.006**
1 year post-treatment	18.1 (12.6)	16.0 (7.0, 26.0)	0.0, 46.0	
Block B				
Pre-treatment vs. Post treatment				
Pre-treatment	35.0 (9.7)	39.0 (35.0, 40.0)	0.0 42.0	**0.003**
Post-treatment	26.2 (11.1)	26.0 (21.0, 34.0)	2.0, 42.0	
Pre-treatment vs. 1 year post-treatment				
Pre-treatment	35.0 (9.7)	39.0 (35.0, 40.0)	0.0 42.0	**0.0002**
1 year post-treatment	19.2 (9.7)	17.0 (12.0, 25.0)	6.0, 38.0	
Post-treatment vs. 1 year post-treatment				
Post-treatment	26.2 (11.1)	26.0 (21.0, 34.0)	2.0, 42.0	**0.022**
1 year post-treatment	19.2 (9.7)	17.0 (12.0, 25.0)	6.0, 38.0	
Block C				
Pre-treatment vs. Post treatment				
Pre-treatment	38.9 (6.2)	39.0 (35.0, 44.0)	28.0, 48.0	**0.00014**
Post-treatment	28.7 (10.4)	29.0 (21.0, 37.0)	10.0, 46.0	
Pre-treatment vs. 1 year post-treatment				
Pre-treatment	38.9 (6.2)	39.0 (35.0, 44.0)	28.0, 48.0	**8.2e-07**
1 year post-treatment	19.6 (10.2)	18.0 (12.0, 28.0)	8.0, 42.0	
Post-treatment vs. 1 year post-treatment				
Post-treatment	28.7 (10.4)	29.0 (21.0, 37.0)	10.0, 46.0	**7e-04**
1 year post-treatment	19.6 (10.2)	18.0 (12.0, 28.0)	8.0, 42.0	
Block D				
Pre-treatment vs. Post treatment				
Pre-treatment	16.9 (1.5)	18.0 (16.0, 18.0)	14.0, 18.0	**0.001**
Post-treatment	11.6 (4.8)	11.0 (7.0, 16.0)	3.0, 18.0	
Pre-treatment vs. 1 year post-treatment				
Pre-treatment	16.9 (1.5)	18.0 (16.0, 18.0)	14.0, 18.0	**9.4e-05**
1 year post-treatment	8.4 (5.0)	7.0 (4.0, 13.0)	1.0, 16.0	
Post-treatment vs. 1 year post-treatment				
Post-treatment	11.6 (4.8)	11.0 (7.0, 16.0)	3.0, 18.0	**0.014**
1 year post-treatment	8.4 (5.0)	7.0 (4.0, 13.0)	1.0, 16.0	
Total score				
Pre-treatment vs. Post treatment				
Pre-treatment	145.4 (18.6)	146.0 (136.0, 157.0)	105.0, 174.0	**5.5e-06**
Post-treatment	97.0 (37.5)	97.0 (61.0, 127.0)	34.0, 154.0	
Pre-treatment vs. 1 year post-treatment				
Pre-treatment	145.4 (18.6)	146.0 (136.0, 157.0)	105.0, 174.0	**2.4e-09**
1 year post-treatment	65.2 (33.2)	58.0 (34.0, 83.0)	25.0, 141.0	
Post-treatment vs. 1 year post-treatment				
Post-treatment	97.0 (37.5)	97.0 (61.0, 127.0)	34.0, 154.0	**0.002**
1 year post-treatment	65.2 (33.2)	58.0 (34.0, 83.0)	25.0, 141.0	

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Table 4: Comparison of results between the active group and the control group

	Mean (SD)	Median (Q1, Q3)	Min, Max	p. value
Block A				
Patient with treatment	-22.8 (15.4)	-21.0 (-31.0, -16.0)	-55.0, 2.0	**0.021**
Patient without treatment	-3.2 (24.9)	-4.0 (-23.0, 10.0)	-43.0, 47.0	
BlockB				
Patient with treatment	-8.7 (11.6)	-6.0 (-13.0, -1.0)	-33.0, 13.0	**0.011**
Patient without treatment	0.1 (7.3)	0.0 (-5.0, 1.0)	-12.0, 16.0	
BlockC				
Patient with treatment	-10.2 (10.0)	-9.0 (-17.0, -3.0)	-28.0, 8.0	**0.029**
Patient without treatment	0.8 (14.9)	0.0 (-4.0, 4.0)	-34.0, 27.0	
BlockD				
Patient with treatment	-5.3 (5.4)	-6.0 (-10.0, 0.0)	-15.0, 3.0	**0.009**
Patient without treatment	0.5 (6.0)	0.0 (0.0, 2.0)	-10.0, 11.0	
Total score				
Patient with treatment	-48.4 (36.2)	-47.0 (-76.0, -19.0)	-125.0, 2.0	**0.008**
Patient without treatment	-1.8 (49.8)	-3.0 (-34.0, 16.0)	-92.0, 94.0	

Box plots and whiskers (1, 2, 3, 4, 5) (boxplot) have been used to represent the results (Graphs 1-5).

We believe that this study is groundbreaking in terms of collecting a significant number of patients with LTP syndrome and conducting a four-year follow-up. Based on our findings, we can conclude that patients with anaphylaxis due to LTP syndrome, who underwent treatment with SLIT-peach®, experienced a substantial improvement in their quality of life from the beginning of treatment to its completion (3 years). Furthermore, this enhanced quality of life continued to improve globally up to one year after discontinuing immunotherapy.

CONCLUSIONS

Treatment with SLIT-peach® improves the quality of life of patients, and this improvement is sustained after its completion. This is currently the first 4-year follow-up on anaphylactic diseases in patients with LTP syndrome.

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