

## **Cat and dog specific immunotherapy impact on quality of life and self-reported satisfaction in a real-world setting**

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To the Editor,

Cat and dog respiratory allergy represents a growing health problem and its negative repercussions in quality of life (QoL) is an important aspect to be considered (1). In addition to avoidance measures and symptomatic medication, allergen-specific immunotherapy (AIT) is an accepted treatment option and is the only that targets the underlying pathophysiology and thus shows disease modifying effects (2). Previous studies of cat and/or dog AIT focused on safety (3–5) and efficacy (4–8), but the evidence of its impact on QoL after cat or dog AIT is limited (5,9).

In this prospective, single arm, single center, longitudinal pilot study, we assessed the impact on QoL of cat and dog AIT in real-world conditions. Patients included were allergic to cat and/or dog and had indication of AIT according to standard clinical practice. Subcutaneous immunotherapy (SCIT) with native cat or dog extracts was prescribed. Immunotherapy doses and schedules were performed according to manufactures' recommendations. The following parameters were analyzed at baseline and after one year: clinical characteristics, medication, asthma exacerbations (AE), total Immunoglobulin E (tIgE), specific IgE (sIgE) to the whole cat and dog extract and to allergen components (Fel d1, Fel d2, Can f1, Can f2, Can f3 and Can f5) by CAP System (Thermo Fisher Scientific; Waltham, Massachusetts, USA), IgG4, spirometry, rhinitis classification according to the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines (10), Asthma Control Test (ACT) and, to assess patients QoL, the validated versions in Spanish for the Allergic Rhinitis Quality of Life Questionnaire (ESPRINT-15) (11) and the Asthma Quality of Life

Questionnaire (AQLQ) (12) were used. In addition, patients assessed their nasal symptoms (congestion, rhinorrhea, sneezing) and ocular symptoms (itching, tearing, conjunctival hyperemia and eye swelling) using a numerical rating scale (NRS) from 0 to 10, with 0 points being no symptom, and 10 points being the most severe symptom. Finally, patients completed a visual analogue scale (VAS) of satisfaction with the AIT. Statistical analysis was performed using Wilcoxon and McNemar tests. The study was approved by the ethics committee of Hospital Universitario La Paz (HULP-PI 3443) and the participants signed an informed consent document.

Thirteen patients were included (7 women and 6 men) with a mean age of 32 years old. Of these, 46.1% were allergic to cat only, 30.7% to dog only and 23% to both cat and dog. We summarized baseline characteristics in Table I.

After one year of AIT, the severity of rhinitis decreased significantly according to ARIA classification: 77% reported moderate/severe rhinitis at baseline and 100% had mild rhinitis after one year. Concordantly, there is a significant improvement in the NRS for ocular and nasal symptoms ( $p=0.001$  and  $p=0.002$  respectively). Furthermore, there is a statistically significant improvement in mean ACT score one year after AIT ( $p=0.011$ ) and 50% of patients had an increase greater than the minimal clinical important difference (MCID):  $ACT \geq 3$  (13).

Regarding to QoL, AIT contributed significantly to the improvement of rhinitis according to the ESPRINT-15 questionnaire ( $p=0.003$ ); as for QoL in asthma there were no significant differences ( $p=0.139$ ). Based on MCID for questionnaires responses, 69.2% of the patients had an increase  $>0.9$  (MCID) in ESPRINT-15 (11) and 70% had an increase of  $>0.5$  (MCID) in AQLQ (12) after one year of AIT. Otherwise, it was recorded that 88.3% patients had an increase of MCDI in both ESPRINT-15 and AQLQ.

As to medication use, patients were asked yes or no whether they needed medication in relation to direct contact with cat or dogs at baseline and after one year of AIT. There was a marked decrease in the use of

antihistamines (from 92.3% to 61.5%) and in the inhaled short-acting  $\beta$ 2-agonists (SABAs) (from 46.2% to 15.4%). No changes were observed in the use of the treatment step for asthma, 3 or 4 according to the Global Initiative for Asthma Management and Prevention (GINA) guidelines (14), being treated with a combination of low doses of inhaled corticosteroids (ICS) and long-acting beta agonists (LABA), remaining on the same therapeutic step. Regarding AE, it was observed that 30% of patients had at least one AE the year before AIT, requiring rescue medication with SABAs and oral corticosteroids, and after one year of AIT only 15.3% reported AE.

During the first year of AIT, a good overall adherence and tolerance was observed; only 30.8% of the patients had local adverse reactions that were controlled with antihistamines and no systemic reaction were recorded. Moreover, patient satisfaction with AIT was 7.8 in the VAS. No significant differences were observed in other parameters such as IgE, sIgE, IgG4 and spirometry values. Results of the outcomes analyzed after one year of AIT are shown in Table II.

Based on our results, patients receiving AIT improve their RC symptoms, and therefore, a significant improvement on QoL according to ESPRINT-15 was demonstrated. For asthma, AIT was effective since we found a decrease in use of SABAs that corresponded with significant increase in ACT score. However, although a 70% of patients improved in QoL, no significant changes were found in AQLQ, probably due to the small size of the included cohort. Previous studies in the literature described similar positive findings in terms of quality of life after cat or dog AIT (5,9). Inside the allergological study, unfortunately, we could not assess the SPT after one-year, although in previous studies (8,9,15) AIT was succeeded in reducing the surface of the wheal, demonstrating the efficacy of AIT.

Although this is a pilot study and the interpretation of the results should considerate its limitations as the small sample, the absence of a defined control group, the lack of randomization, the different extracts used and the possible variability in exposure to allergens over the study, we were able to demonstrate the positive impact of dog and cat AIT on the RC QoL, a safety profile in a real-world setting along with a high

satisfaction rate. Even so, we believe that further studies with larger samples should be conducted to reinforce our findings.

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**Table I. Baseline characteristics.**

<b>Variables</b>	<b>Patients (N=13)</b>	<b>Missing data (%)</b>
Sex ( <i>n, %</i> )		0
Women	7 (53.8)	0
Men	6 (46.2)	0
Age (mean years $\pm$ SD)	32,31 $\pm$ 9,0	0
Exposure to cat or dog ( <i>n, %</i> )		0
Permanent	7 (53.8)	0
Sporadic	6 (46.2)	0
Allergic comorbidities ( <i>n, %</i> )		0
Urticaria	3 (23.1)	0
Atopic dermatitis	3 (23.1)	0
Food allergies	1 (7.7)	0
Drug allergies	0	0
Sensitization to aeroallergens ( <i>n, %</i> )		
Cat	13 (100)	0
Dog	8 (61.5)	0
Grasses	9 (69.2)	0
Reed grass	6 (46.2)	0
Olive tree	5 (38.5)	0
Shade plantain	3 (23.1)	0
Mite	6 (46.2)	0
Alternaria	1 (7.7)	0
Clinical allergy ( <i>n, %</i> )		0
Cat only	6 (46.1)	0
RC	2 (15.3)	0
RC and asthma	4 (30.7)	0
Dog only	4 (30.7)	0
RC	0	0
RC and asthma	4 (30.7)	0
Cat and dog allergy	3 (23.0)	0
RC only	1 (7.7)	0
RC and asthma	2 (15.3)	0

Abbreviations: SD, standard deviation; RC, rhinoconjunctivitis.

**Table II. Result of the outcomes analyzed after one year of AIT.**

Variable	Baseline	After one year	p-value	Missing data
<b>Rhinitis severity (ARIA) (n, %)</b>				
Mild	3 (22.9)	13 (100)	NA	0
Intermittent	2 (15.3)	11 (84.6)	NA	0
Persistent	1 (7.6)	2 (15.3)	NA	0
Moderate/severe	8 (77)	0	NA	0
Intermittent	4 (30.8)	0	NA	0
Persistent	6 (46.2)	0	NA	0
ACT (mean ± SD)	17.1 ± 5.1	22.1 ± 2.02	0.011	0
<b>NRS (mean ± SD)</b>				
Ocular	19.5 ± 10.2	4.8 ± 5.7	0.001	0
Nasal	20.8 ± 8.4	9.5 ± 7.6	0.002	0
<b>Allergologic study (mean ± SD)</b>				
<b>Skin Prick Test (mm<sup>2</sup>)</b>				
Cat	7.5 ± 2.5	NA	NA	0
Dog	4.7 ± 3.2	NA	NA	0
Total IgE (kU/L)	547,7 ± 562,9	697.3 ± 739,5	0.13	0
Total Cat IgE (kU/L)	56,1 ± 43,8	55,1 ± 40,2	0.91	0
Fel d 1 (kU/L)	51,9 ± 37,7	45,9 ± 37,50	0.88	0
Fel d 2 (kU/L)	2,6 ± 4,3	2,3 ± 3,9	1.0	2 (15.38)
Total Dog IgE (kU/L)	75,5 ± 104,3	99,6 ± 150,5	0.46	0
Can f 1 (kU/L)	20,7 ± 39,1	29,7 ± 47,1	0.28	0
Can f 2 (kU/L)	19,0 ± 9,5	21,0 ± 33,7	0.14	0
Can f 3 (kU/L)	11,9 ± 8,4	12,1 ± 18,9	0.65	1 (7.69)
Can f 5 (kU/L)	13,4 ± 26,6	4,6 ± 2,9	0.68	0
IgG4 (mg/dL)	66,7 ± 25,1	71,0 ± 31,0	0.81	1 (7.69)
<b>Spirometry</b>				
FEV <sub>1</sub> (L)	3,6 ± 1.0	2.6 ± 0.6	0.71	3 (23.0)
FVC (L)	4,5 ± 0.9	3.6 ± 0.7	0.71	3 (23.0)
FEV <sub>1</sub> /FVC (%)	88.6 ± 9.1	89.2 ± 10.2	0.68	3 (23.0)
<b>Treatment characteristics</b>				
Antihistamines	12 (92.3)	8 (61.5)	0.125	0
Nasal corticosteroids	1 (7.7)	1 (7.7)	-	0
Oral corticosteroids	0	0	-	0
Inhaled corticosteroids (ICS)	0	0	-	0
SABA	6 (46.2)	2 (15.4)	0.125	0
ICS with LABA	6 (46.2)	5 (38.4)	1.0	0
<b>QoL questionnaires</b>				
ESPRINT-15 (mean ± SD)	2.56 ± 1,56	1.07 ± 0.88	0.003	0



AQLQ (mean $\pm$ SD)	5.16 $\pm$ 1,7	6.06 $\pm$ 0.98	0.139	0
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Abbreviations: SD, standard deviation; NA, non-analyzed; RC, rhinoconjunctivitis; ARIA, Allergic Rhinitis and its Impact on Asthma; ACT, Asthma Control Test, NRS, numerical rating scale, IgE, Immunoglobulin E; IgG4, Immunoglobulin G4; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; ICS, inhaled corticosteroids; SABA, short-acting  $\beta$ 2-agonists; LABA, long-acting beta agonists; QoL, quality of life; ESPRINT, Allergic Rhinitis Quality of Life Questionnaire; AQLQ, Asthma Quality of Life Questionnaire.

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