

Evaluation of adherence and attitudes of patients with allergic rhinitis to nasal steroid treatment

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Abstract

Background: Allergic rhinitis (AR) is defined as an inflammatory disease of the nose. Nasal corticosteroids (NCS) are one of the most effective drugs used in AR treatment.

Objective: One of the most important issues in the treatment of AR is patient adherence to NCS. We aimed to evaluate the adherence and attitude of patients with AR to NCS treatment.

Methods: One hundred four patients who were prescribed NCS for AR at any time and who used NCS during the study period were included in the study. Morisky Medical Adherence Scale-8 (MMAS-8) was performed on the patients to determine their treatment adherence.

Results: The scores of the MMAS-8 were below 6 in 55% of the patients, and the adherence of the patients to the NCS treatment was low. The adherence of the patients to NCS treatment was good in only 19% of the patients. As the duration of the disease increased, the adherence of the patients to the treatment decreased ($p = 0.001$). Patients who benefited from allergen immunotherapy had statistically significantly higher MMAS-8 scores than those who did not ($p = 0.015$). As expected, drug adherence was statistically significantly lower in patients with drug-related adverse effects ($p = 0.01$). Sixty percent of the patients had received NCS training, and MMAS-8 scores were significantly higher in those who received training ($p = 0.023$).

Conclusion: Inadequate drug adherence is a challenging problem in the treatment of AR. Frequent evaluation of patients' drug adherence and drug use techniques in daily practice is important for the follow-up and treatment of the disease.

Key words: adherence, allergic rhinitis, medication, Morisky scale, nasal corticosteroids

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Introduction

Rhinitis is defined as an inflammatory disease of the nose and presents with nasal symptoms such as anterior or posterior rhinorrhea, sneezing, congestion, and itching. These symptoms occur for two or more consecutive days and often for longer than an hour. Rhinitis is classified depending on its etiologies. Allergic rhinitis (AR), the seasonal type of which is called hay fever, occurs when the IgE-mediated immune system overreacts to allergens in the air and is the most common noninfectious form of rhinitis. Allergic rhinitis is estimated to affect approximately 20-40% of the population worldwide.^{1,2} The effect of AR on daily life can be examined separately in terms of its effects on sleep, learning, and working life, as well as its negative effect on the quality of life in general.^{3,4,5} Allergic rhinitis affects learning and other activities. The economic burden of AR is also significant, as is its social burden.

The Allergic Rhinitis and its Impact on Asthma (ARIA) consensus is a classification according to AR severity, which is divided into four classes: mild or moderate to severe intermittent, and mild or moderate to severe persistent.¹

Nasal corticosteroids (NCS) are one of the most effective drugs used in the treatment of AR^{6,7} and control the disease by suppressing inflammation. Today, for most people with persistent or severe AR, NCS are used as the first option. It is generally accepted that significant clinical efficacy of NCS can be achieved when used for days to weeks. Despite the differences in pharmacodynamic and pharmacokinetic properties between NCSs, they are not superior to each other in improving AR symptoms. Nasal steroids have some local and systemic adverse effects. The most common local adverse effects are dryness, pricking-burning sensation, and bleeding.^{5,6}

Nasal corticosteroid treatment requires regularity and adherence.⁸ Adherence is a proactive behavior that results in a lifestyle change by the patient, who must follow a daily regimen, such as taking NCS for AR during allergy season.⁹ One of the most important issues in the treatment of AR is patient adherence to NCS. Just as in the treatment of asthma, drug adherence is very important in the treatment of AR because AR and asthma are known as single airway diseases. Uncontrolled AR is a risk factor for the development of asthma.^{1,2} In addition, inadequately treated AR causes asthma exacerbations in people with asthma. As in patients with asthma, there are many factors affecting drug adherence in patients with AR. Steroid phobia is one of the factors.^{2,8} People with steroid phobia tend to be wary of using the drug. Elimination of the patient's concerns about steroid adverse effects before starting and during NCS use affects treatment success. Relieving anxiety and providing education on NCS drug use increase disease control.

Although there are many studies on asthma and drug adherence in the literature, there are few studies on NCS adherence in AR.¹⁰⁻¹³ This study aimed to evaluate the adherence and attitudes of patients with AR to NCS treatment.

Materials and methods

Study design

The study was conducted at the Immunology and Allergy Diseases clinic between January 2018 and January 2019. Adult patients who were prescribed NCS for AR at any time and who used NCS during the study period were included in the study. Patients aged younger than 18 years and those who were not prescribed NCS were not included in the study. All patients were prescribed NCS for the first 2 months, but oral and/or nasal antihistamines were added to the treatment of patients whose symptoms did not decrease with NCS. All patients received NCS treatment for at least 2 months. The local ethics committee of the medical school of Ankara University approved the study (Approval date and number: 11.06.2018/10-667-18). Informed consent was obtained from all patients.

Study parameters

Evaluation of treatment adherence

The Morisky Medical Adherence Scale (MMAS-8) is a commonly used, self-reported, medication-taking-behavior scale for different medical conditions.¹⁴⁻¹⁷ It was originally validated for the treatment of hypertension, and then it began to be used in asthma and many other chronic diseases.^{14,15,18} The scores of MMAS-8 range from 0 to 8. A score below 6 indicates low adherence, a score between 6 and 8 means medium adherence, and a score of 8 indicates high adherence (**Supplemental Table**). The Morisky 8-item medication adherence questionnaire for patients with asthma and chronic obstructive pulmonary disease has been validated in Turkish.¹⁸ The Turkish version of MMAS-8 was used in two studies from our country in patients with AR.^{16,17} Patients were evaluated for drug adherence using the Turkish version of MMAS-8 two months after NCS was started for AR. Treatment of patients with MMAS-8 scores was evaluated only while using NCS. In addition, we asked the patients whether they had received training on how to use NCS. It was inquired which healthcare professional provided the drug use training. A checklist was used by the physician to evaluate the patient's ability to use NCS correctly. Patients were asked questions about the reasons for poor drug adherence. These questions were as follows:

- 1- What are the reasons for your reduced drug adherence?
- 2- Do you have corticosteroid phobia?
- 3- Do you not have symptoms intense enough to require medication?
- 4- Has your physician adequately explained how to use the medicine?
- 5- Have you experienced any medication adverse effects (e.g. bleeding, dryness)? Is this why you don't use the medicine properly?

Based on the answers to these questions, reasons that reduced drug adherence were determined.

Evaluation of atopy and severity of AR

Skin-prick tests were performed using a common panel (Allergopharma, Stockholm, Sweden). In the skin prick test panel, we tested dust mites, grass pollen, cat, dog, tree pollen, mold fungi, grain pollen, and cockroach allergy. The positive and negative controls used were histamine (10 mg/mL) and phenolated glycerol saline. A mean wheal diameter of 3 mm or greater than that obtained with the control solution, was considered positive.¹⁹ Patients with positive skin prick tests were included in the study. All patients were evaluated for AR severity according to the ARIA guidelines.¹

Statistical Analysis

Data are summarized as mean \pm standard deviation and median (minimum-maximum) for continuous variables and frequencies (percentiles) for categorical variables. The Chi-square or Fisher's exact test was used to compare categorical variables, as appropriate. A logistic regression model was used to estimate the odds ratios (OR) and 95% confidence intervals (95% CI) of risk factors

for low MMAS-8 scores. Variables with $p < 0.10$ in the univariate analysis were evaluated using multiple logistic regression analysis to simultaneously identify independent risk factors of low MMAS-8 scores. Statistical significance was set at a value of $p < 0.05$. Data analysis was performed using the SPSS 11.5 for Windows software package (SPSS Inc., Chicago, IL, USA).

Results

The study comprised 87 women and 17 men (mean age: 34.7 ± 12.89 years). More than half of the patients were university graduates. Three-quarters of the patients were never smokers. Forty percent of the patients had a childhood-onset allergic disease. The most common allergic disease that started in childhood was AR. Forty-three percent of the patients had a family history of allergic disease and AR appeared most frequently in their families. The demographic characteristics are detailed in **Table 1**.

Table 1. The demographic characteristics of the study group.

		Number (n)	%
Age (years)	34.7 ± 12.89		
Sex	Female	87	83.7
	Male	17	16.3
Education	Uneducated	3	2.9
	Primary education	11	10.5
	High school	24	23.1
	University / college	66	63.5
Occupation	Unemployed	2	1.9
	Housewife	22	21.2
	Student	32	30.8
	Working at any job	45	43.2
	Retired	3	2.9
Smoking history	Never smoked	78	75
	Ex-smoker	12	11.5
	Smoker	14	13.5
Allergic disease history in childhood	Asthma	11	9
	Eczema	5	3
	Allergic rhinitis	34	32
	None	54	60
History of allergic disease in the family	Yes	44	43
	No	60	57

The most common symptoms among the patients were rhinorrhea (91.3%), nasal itching (98.1%), and sneezing (97.1%). The severity of rhinitis in the patients was 80% moderate-severe persistent, 13% mild persistent, 5% moderate-severe intermittent, and 2% mild intermittent, respectively. Sixty-two percent of the patients had seasonal allergen symptoms. Only 19% of patients had multiple allergen sensitivities (polysensitized). The clinical characteristics are presented in **Table 2**.

Table 2. The clinical characteristics of the study group.

Symptoms		n	%
Itchy nose		102	98.1
Sneezing		101	97.1
Watery rhinorrhea		95	91.3
Conjunctivitis		89	85.6
Post nasal drip		79	76.0
Nasal congestion		75	72.1
Headache		44	42.3
Anosmia		43	41.3
Clinical features			
Time (years)	< 1	21	20.2
	1 -< 3	27	26
	3 -< 5	24	23.1
	5 -< 10	20	19.2
> 10	12	11.5	
Severity of rhinitis	Mild intermittent	3	2
	Moderate-severe intermittent	5	5
	Mild persistent	13	13
	Moderate-severe persistent	83	80
Duration of symptoms	Perennial	40	38
	Seasonal	64	62
Atopy	Monosensitized	84	81
	Polysensitized	20	19

Morisky Medical Adherence Scale-8 was performed to evaluate patients' adherence to NCS. The scores of the MMAS-8 were below 6 in 55% of the patients, and the adherence of the patients to NCS treatment was low. The adherence of the patients to NCS treatment was good in only 19% of the patients (**Figure 1**). The most common reason for reducing drug adherence was corticosteroid phobia. The second most common reason was the failure to explain the use of drugs by the physician. For both reasons, it shows that drug adherence decreases in patients who are not well informed by the physician. The reasons for reducing drug adherence are shown in **Figure 2**.

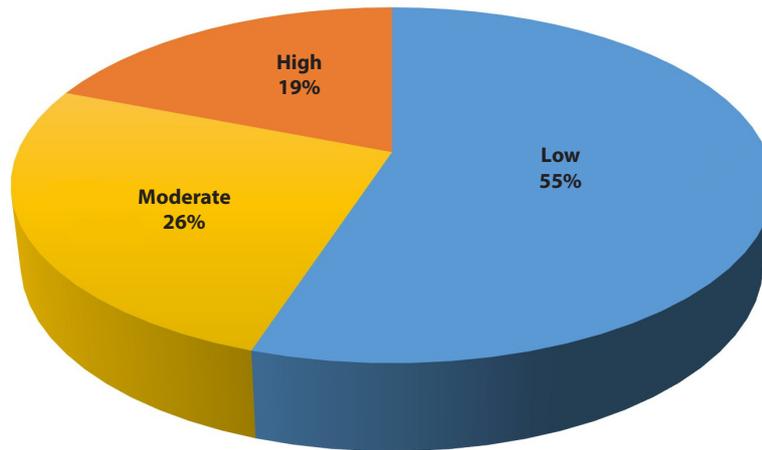


Figure 1. The patients' adherence to NCS treatment according to MMAS-8.

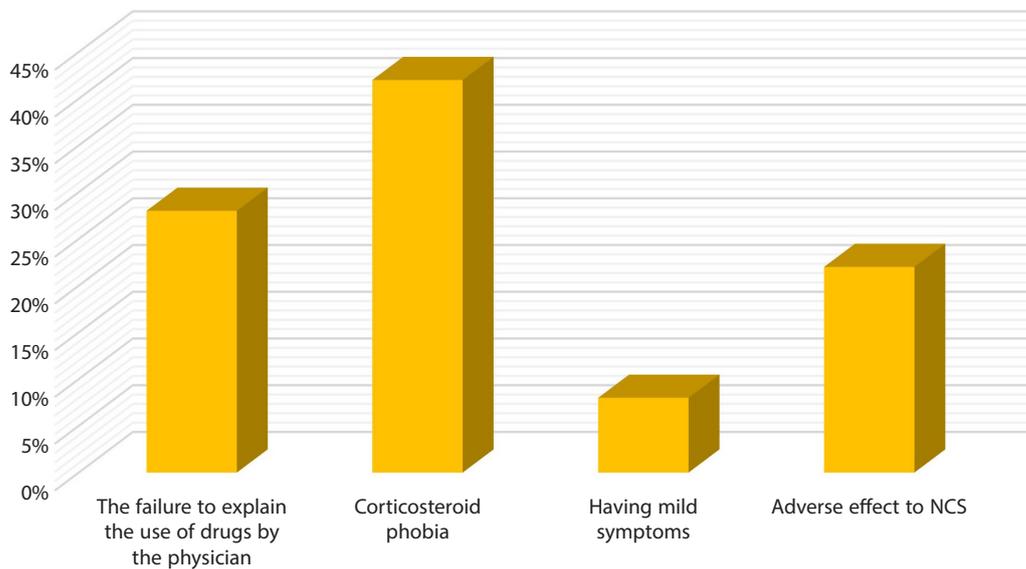


Figure 2. The reasons for reducing NCS adherence.

The scores of MMAS-8 were significantly higher in patients who had perennial allergen sensitivity ($p = 0.03$). Monosensitized patients' MMAS-8 scores were lower than polysensitized patients' scores. Monosensitized patients had less adherence to NCS than those who were polysensitized ($p = 0.028$). The scores of MMAS-8 increased as disease severity increased and symptoms became persistent; however, it was not statistically significant ($p = 0.26$). As the duration of the disease increased, the adherence of the patients to the treatment decreased ($p = 0.001$). Patients who benefited from allergen immunotherapy had statistically significantly higher MMAS-8 scores than those who did not ($p = 0.015$). MMAS-8 scores were lower in patients with more than two dependent children, but not statistically significant ($p = 0.17$). As expected, drug adherence was statistically significantly lower in patients with drug-related adverse effects ($p = 0.01$). A comparison of MMAS-8 scores according to the parameters is detailed in **Table 3**.

Sixty percent of the patients had received NCS training, and MMAS-8 scores were significantly higher in those who received training ($p = 0.023$) (**Table 3**). This training was given most frequently by physicians at a rate of 77.8%. Those who received training from physicians had better drug adherence, but it was not statistically significant ($p = 0.22$). Eighty percent of those who did not receive training learned about the use of drugs from the drug information forms. The results of the multiple logistic regression analysis revealed that time and adverse effects were significant predictors of low MMAS-8 scores ($p = 0.001$ and $p = 0.004$, respectively). The logistic regression model demonstrated good predictive accuracy, correctly classifying 71.2% of cases. More than 5 years of disease duration increases the risk of low NCS adherence by 6.40 times compared with less than 5 years. Having adverse effects increases the risk of low NCS adherence by 3.85 times (**Table 4**).

Table 3. Comparison of MMAS-8 scores according to the parameters.

Parameters		MMAS-8 (n)			P value
		Low	Moderate	High	
Allergens	Pollen	29	17	5	0.03*
	Perennial	28	10	15	
Atopy	Monosensitized	48	24	12	0.028*
	Polysensitized	9	3	8	
Severity of rhinitis	Mild intermittent	3	0	0	0.26
	Moderate-severe intermittent	1	2	2	
	Mild persistent	8	4	1	
	Moderate-severe persistent	45	21	17	
Number of dependent children	≤ 2	26	14	14	0.17
	> 2	31	13	6	
Time (years)	< 1	4	1	16	0.001*
	1 -< 3	11	13	3	
	3 -< 5	16	7	1	
	5 -< 10	17	3	0	
	> 10	9	3	0	
Immunotherapy	No	28	13	9	0.9
	Yes	29	14	11	
Benefit from immunotherapy	No	20	4	3	0.015*
	Yes	9	10	8	
Has the patient been trained to use NCS?	No	29	8	4	0.023*
	Yes	28	19	16	
From whom did the patient receive NCS training?	Physician	18	17	14	0.22
	Pharmacist	9	2	2	
	Nurse	1	0	0	
Adverse effects	No	28	19	17	0.01*
	Yes	29	8	3	

*P values lower than 0.05 were considered statistically significant.

Table 4. Univariate and multiple logistic regression for MMAS-8 scores.

Variable		Univariate Logistic Regression		Multiple Logistic Regression	
		OR [95% CI]	p value	OR [95% CI]	p value
Allergens	Pollen	1.78 [0.54-2.55]	0.680		
	Perennial	1 (Reference)			
Atopy	Monosensitized	1.63 [0.61-4.35]	0.329		
	Polysensitized	1 (Reference)			
Severity of rhinitis	Intermittent	1 (Reference)	0.776		
	Persistent	1.23 [0.29-5.22]			
Number of dependent children	≤ 2	1 (Reference)	0.158		
	> 2	1.76 [0.80-3.84]			
Time (year)	< 5	1 (Reference)	0.001	1 (Reference)	0.001
	≥ 5	5.73 [2.10-15.62]		6.40 [2.24-18.23]	
Immunotherapy	No	1.10 [0.51-2.38]	0.814		
	Yes	1 (Reference)			
Benefit from Immunotherapy	No	5.71 [1.76-18.51]	0.004		
	Yes	1 (Reference)			
Has the patient been trained to use NCS?	No	3.02 [1.31-6.97]	0.010		
	Yes	1 (Reference)			
From whom did the patient receive NCS training?	Doctor	1 (Reference)	0.027		
	Other	4.31 [1.18-15.75]			
Adverse effect	No	1 (Reference)	0.005	1 (Reference)	0.004
	Yes	3.39 [1.45-7.95]		3.85 [1.54-9.62]	

OR, odds ratio; CI, confidence interval

Discussion

In this cross-sectional study, we found NCS adherence to be low in half of the patients with AR. The adherence of the patients decreased in the monosensitized group and those with a long duration of disease. Drug-related adverse effects were found to be related to low drug adherence (Table 4). More than half of the patients who received NCS training had better adherence. This study highlights the adherence problems of NCS use in patients with AR in a tertiary care hospital.

For the treatment of all chronic diseases, it is necessary to use the drugs recommended by physicians regularly and completely. The MMAS is a simple questionnaire with proven reliability and validity used to determine drug adherence in many diseases such as hypertension and asthma.^{14,16,17} Treatment of AR requires regular drug therapy, like other chronic diseases. Nasal corticosteroid used in the treatment of AR are very effective drugs, suppressing nasal inflammation most effectively. Accordingly, effective symptom control is achieved in AR caused by both seasonal and perennial allergens, with regular daily use in the long term. Although the airway remodeling seen in chronic asthma is not directly demonstrated in AR,

minimal permanent effects of long-term inflammation on the nasal mucosa are detected and NCS prevent nasal mucosal changes.^{20,21} However, it may take several weeks for the effects of NCS to appear, which may reduce drug adherence.^{2,5,6} Patients should be informed about the mechanism of action and onset of effects of NCS.

There are few studies on adherence with NCS and they show low drug adherence.^{16,17} In the first study, 76 children with a mean age of 7.82 years were prescribed mometasone furoate nasal spray after the diagnosis of AR and were recommended to use it for 30 days. The mean MMAS-8 score at the end of 30 days was 2.80, and children being dependent on a single caregiver was associated with low adherence ($p = 0.011$). It has been shown that as the number of children increases, drug adherence decreases.¹⁶ In the second study, it was recommended that 59 adult patients use mometasone furoate nasal spray for 30 days after diagnosis. In the results of the study, the mean age was found as 32.5 years, and the mean MMAS-8 score was 3.64. The number of dependent children ($p = 0.001$) and inadequate drug use ($p = 0.001$) were associated with low adherence. In addition, patients with higher education levels had better medication

adherence than patients with lower education levels.¹⁷ When we compared the two studies conducted in adults with our study, the mean age of the patients was close to each other. In our study, different from the study of Ocak et al., a comparison was made according to the types of AR (e.g., perennial, seasonal persistent, polysensitized, monosensitized). However, Ocak et al. mostly studied the effect of socio-economic factors (marital status, multidrug use, comorbidities, daily working hours, number of dependent children, adverse effects, benefit from the drug, days abroad per month, education level) in NCS adherence. The parameters we evaluated jointly were the number of dependent children and adverse effects. Ocak et al. found that NCS-related adverse effects did not affect drug adherence, but we found that it reduced drug adherence. In addition, the number of dependent children affected NCS compliance in their study; no statistically significant effect was found in our study.¹⁷

Rhinitis is recognized as a risk factor for asthma. The onset of rhinitis and asthma differs according to the time of the onset of atopy. The prevalence of asthma in those with rhinitis ranges from 10-40%.^{2,12,22} Asthma was present in 37.5% of our patients by history. All of our patients with asthma were using inhaled corticosteroids and NCS adherence was higher. Regular use of inhaled steroids due to asthma may increase NCS adherence. In addition, in patients with AR and asthma, the need for medication may be higher because their symptoms are more frequent and intense.²

The most common triggering factors in AR are aeroallergens. Pollen is common in seasonal AR, and dust mites, mold spores, and pets are allergens in perennial AR.^{23,24} The allergen sensitivity profiles of patients with AR in our study were similar to current data. Drug adherence was worse in our patients with pollen sensitivity. The reason for this may be that patients do not care about the disease because their symptoms are temporary. Therefore, it may be that they are not using enough medication.

Drug adverse effects affect adherence with NCS drug use in AR, as in many other diseases.^{25,26} Drug adherence is lower in patients with adverse effects. The most common drug-related adverse effect is nose bleed, which has been associated with not using the drug with the correct technique. In patients who were taught the correct technique by the physician, adverse effects were found to be less and drug adherence was better. In the literature, there are many studies on adverse effects, drug use technique training, and drug adherence in asthma. Inadequate and incorrect use of asthma medications causes deterioration in asthma control and asthma attacks.²⁷⁻³⁰ Asthma and AR are single airway diseases, and regular and correct use of NCS in AR affects the control of both diseases.^{2,24,30} There are few studies on the relationship between intranasal corticosteroid technique training and patient adherence. In our study, we evaluated the drug use technique and from whom the patients learned the technique. We determined that the physician factor was very important in drug use education. More studies are needed to examine the effect of correct NCS use technique training on control of AR.

A systematic review of eight studies (882 participants) published in 2022 compared the regular use of NCS with the use of NCS as needed. In that review, it was found that nasal peak inspiratory flow, sneezing, nasal congestion, and quality of life scores were better with regular NCS use than with NCS as needed. There was no difference between regular and as-needed NCS use for ocular symptoms, symptom-free days, nasal itching, and runny nose scores.³¹ Unlike the work of Hoang et al., we aimed to determine how well the patients who were recommended to use NCS regularly by their physicians adhered to their medication. We did not compare the use of NCS as needed and regular NCS use.

This study has some limitations. First, the study population is small. Second, we evaluated drug adherence only with the MMAS-8. If we could evaluate patients with daily symptom scores, quality of life questionnaires, and various drug scores, we would have stronger data on low adherence to NCS. However, we could not evaluate patients' daily symptom scores and quality of life questionnaires in this study. In addition, we did not evaluate whether there was a difference between NCS types in terms of drug adherence. Previous studies have shown that the efficacy of different NCS types is similar to each other.^{32,33} However, in our country, it can be found in a different form of device, even if it is the same NCS agent. We think that even the ease of use of different devices may affect drug compliance. There is no study on this subject. In the present study, we did not collect any data on different device types. However, we plan to investigate this issue in future studies.

As a conclusion, inadequate drug adherence is a challenging problem in the treatment of AR, like in other chronic diseases. The benefits of using NCS according to the prescribed dose and frequency must be emphasized to patients with AR at each visit. Education of patients by physicians increases adherence to AR treatment. Frequent evaluation of patients' drug adherence and drug use techniques in daily practice is important for the follow-up and treatment of the disease.

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Author contributions

- BGA: made contributions to study design, collecting data, manuscript drafting and revision
- OA: made contributions to study design, collecting data, manuscript drafting and revision
- IK: made statistical analysis, manuscript drafting and revision
- All authors are involved in the collection of the data and the writing of the manuscript. All authors read and approved the final manuscript. Patients' data protection. This study was presented at the World Allergy Congress Istanbul in 2022.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Confidentiality of data

The authors declare that they have followed the protocols of their work center on the publication of patient data and that the patients included in the study received sufficient information and gave their informed consent in writing to participate in the study.

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Supplemental Table. Morisky Medical Adherence Scale (MMAS-8).

Do you sometimes forget to take your medicine?	Yes: 0	No: 1
Thinking over the past two weeks, were there any days when you did not take your medicine?	Yes: 0	No: 1
Have you ever cut back or stopped taking medicine without telling your doctor because you felt worse when you took it?	Yes: 0	No: 1
When you travel or leave home, do you sometimes forget to bring along your medicine?	Yes: 0	No: 1
Did you take all your medicine yesterday?	Yes: 1	No: 0
Do you sometimes stop taking your medicine when you feel like your symptoms are under control?	Yes: 0	No: 1
Do you ever feel hassled about sticking to your treatment plan?	Yes: 0	No: 1
How often do you feel difficulty remembering to take all your medicine?	Never/rarely Once in a while Sometimes Usually All the time	
Low Adherence < 6	Moderate Adherence: 6-7	High Adherence: 8