Determining factors of patient compliance to treatment in allergic rhinitis

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Summary

Background: **Compliance with prescribed treatment is essential for reducing costs of health care and improving efficacy of treatment in patients with allergic rhinitis.**

Objective: **To evaluate the extent of compliance and identify predictive factors and risk profiles for patient noncompliance with the therapeutic regiments of sublingual immunotherapy and H1-antihistamines.**

Methods: **In this retrospective study we analysed data from two non-interventional studies: one study with a total of 42,111 patients taking H1-antihistamines and one study with 354 patients receiving sublingual immunotherapy. Both studies were approved by the local ethics committees and competent authorities. By performing univariate and multivariate logistic regression analysis we calculated odds ratios with a 95% confidence interval for given characteristics.**

Results: **There was a compliance rate of 79.6% with the administration of sublingual immunotherapy. Factors associated with compliance were severe nasal, eye and airways symptoms, and strong impairment in social and work life. Compliance with the intake of H1-antihistamines was 98%. Patients with a concomitant disease, especially with a bronchial asthma or a psychiatric disorder had higher odds for being non-compliant.**

Conclusion: **Compliance with intake of sublingual immunotherapy and H1-antihistamines is high. However, our findings point out that patients with characteristics such as a comorbid bronchial asthma or mild symptoms have higher odds for noncompliance and require attentive monitoring to reduce healthcare costs and morbidity.** ***(Asian Pac J Allergy Immunol 2013;31:148-56)***

Key words: *Allergic rhinitis, allergic rhinoconjunctivitis, compliance, sublingual immunotherapy, H1-antihistamines*

Abbreviations

CI	=	Confidence interval
ND	=	No data
SCIT	=	Subcutaneous immunotherapy
SD	=	Standard deviation
SLIT	=	Sublingual immunotherapy
TNSS	=	Total nasal symptom score

Introduction

Allergic rhinoconjunctivitis is a major health issue, affecting more than 500 million people in their daily life around the world.[1] In the last decades, an increase in allergy prevalence especially in the industrialized countries was observed. Two large surveys conducted in the United States in 2006 and 2007 revealed that 14% of the adult population and 13% of children suffer from allergic rhinitis.[2-3] In Europe, the prevalence of allergic rhinitis is found to be 25% of the population with immense geographical variations.[4-5] Although allergic rhinitis is no direct cause of mortality, it escalates the risk of developing various secondary diseases such as asthma and allergic conjunctivitis. Moreover, asthma can be the cause of allergic rhinitis.[1,6] Thus, the economic impact of this chronic condition is substantial as a result of the high prevalence and the decrease in productivity during allergy season. From

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2000 to 2005, the costs of treating allergic rhinitis in the United States increased from $6.1 to $11.2 billion.[7] Compliance with the treatment of allergic rhinitis is highly relevant as noncompliance not only limits the effectiveness of treatment but also elevates the costs of healthcare. Compliance issues are of concern especially in chronic conditions, which require long-term or repetitive treatment. The term describes to which extent patients follow treatment instructions, but compliance can also be understood as a multidimensional concept which arises from the interaction of various factors such as patient-related, condition-related, socioeconomic, treatment-related and health system factors.[8]

During the last years, research in the field of nasal allergies showed inconsistent rates of compliance and multiple predictors of noncompliance. Rates of compliance with sublingual immunotherapy (SLIT) varied between 30 to 97% in clinical studies published since 2004, regardless of the duration of therapy and the method of measurement.[9-21] Costs, side effects, lack of efficacy and forgetfulness were identified as major reasons for noncompliance.[13,18-20, 22,23]

Comparable rates were detected with subcutaneous immunotherapy (SCIT). Within clinical trials of the last decade rates of compliance ranged between 60 and 78% after 1 to 5 years of treatment.[24-26] Socioeconomic factors found to be related to noncompliance were age and female sex as well as comorbidity. The inconvenience of SCIT and side effects were identified as treatment-related factors of noncompliance.[24-26]

It has to be kept in mind that the causal effect of allergen-specific immunotherapy needs a treatment duration over three years.[1] It has been shown that the treatment persistence for SLIT as well as for SCIT is comparable to that seen for other chronic diseases, but is decreasing in the consecutive years by half for SLIT and even by two thirds for SCIT which makes it evident that risk profiles for therapeutic non-compliance should be identified to enhance compliance and, in consequence, treatment effectiveness.[27]

Compliance with H1-antihistamines was hardly in focus of recent compliance research. Solely, Valero et al.[28] evaluated compliance with an H1-antihistamine in a phase IV study with 324 patients by carrying out pill counts. After 1-6 and 1-12 months, 90 and 83% of the patients were compliant with the medication intake. To date, there is no relevant study evaluating determinants of noncompliance with the administration of antihistamines.

The objective of the present analysis was therefore the assessment of predictive factors and risk profiles for therapeutic non-compliance in patients suffering from allergic rhinitis receiving SLIT or antihistamines.

Methods

In our analysis, we sought to identify predictors of compliance with the therapeutic regiments of SLIT and H1-antihistamines in order to develop a multivariate model, which predicts the compliance outcome. On a long-term basis, it should serve to integrate treatment-related characteristics of behaviour into the conception of guidelines.

First of all, we investigated the extent of compliance with antihistamines and sublingual immunotherapy. In a second step the single factors associated with compliance were identified and finally examined within a multistage model. We performed secondary data analyses using case reports of patients with allergic rhinitis from non-interventional studies on SLIT and antihistamines. Patients had to be included into the analyses if there was a proven diagnosis of allergic rhinitis, a clear statement of the therapeutic regimen and missing values less than 10% in the data base.

All patients or their guardians gave their written informed consent to participate in the two studies, which were conducted in accordance with the International Conference on Harmonization guidelines on good clinical practice and agreed to further (secondary) data analyses. Both studies were approved by the local ethics committees and competent authorities. Since this work is a secondary data analysis it is not necessary to obtain an additional ethical approval.

To give consideration to the multidimensional character of the compliance concept we used the following conceptual framework as a structure for possible determinants/influence factors (Figure 1). The basic concept of this framework is the Andersen's health service utilization model, which classifies variables that influence care as well as its utilization.[30] Because especially within the treatment of diseases, communicated as non-serious and trivial, characteristics of therapy and the treatment process will primarily influence the compliance behaviour, these two dimensions expanded the framework mentioned above. Statistical analyses were conducted within four steps:

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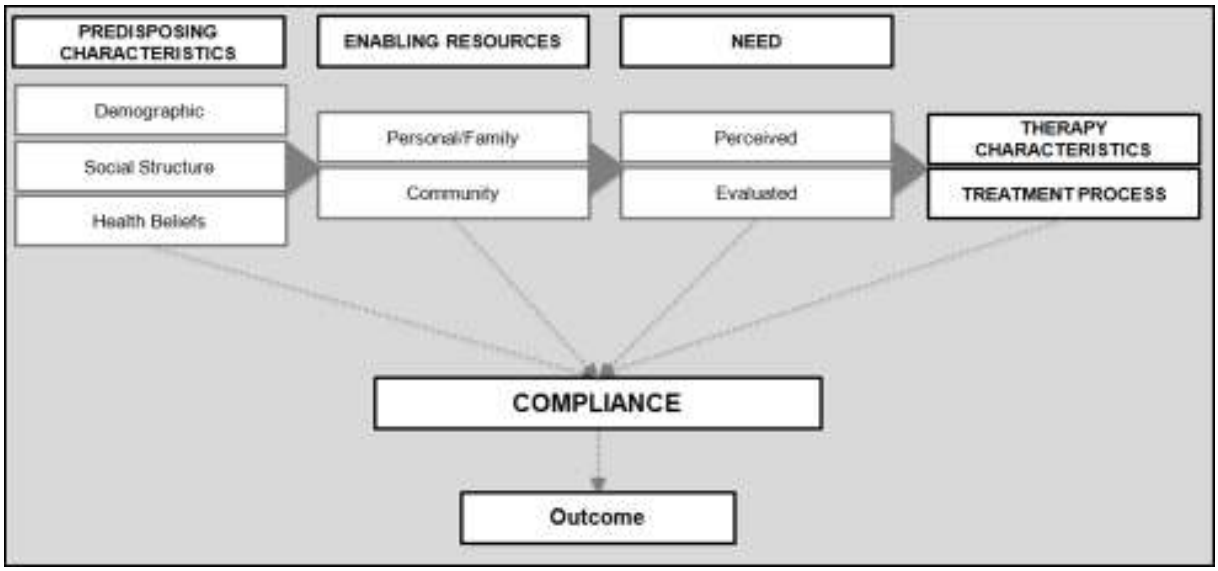

Figure 1. Framework to assess relevant influence factors for compliance and noncompliance

1. Screening of the raw data pool on predefined in- and exclusion criteria (see above)
2. Comparison of the raw and final screened data pool in terms of relevant differences in patient characteristics
3. Simple logistic regression (dependent variable: compliance; one independent variable)
4. Stepwise logistic regression (dependent variable: compliance):
   a. Model 1 variables: predisposing characteristics
   b. Model 2 variables: predisposing characteristics + need variables
   c. Model 3 variables: predisposing characteristics + need variables + therapy characteristics
   d. Model 4 variables: predisposing characteristics + need variables + therapy characteristics + treatment process

The following description presents further details of the used observational studies and special conditions of their analysis. Statistical analyses were performed with SPSS version 18 and STATA 11. P-values of p <0.05 were considered statistically significant.

Antihistamines

Data on antihistamine administration was collected in a multicentre post-marketing surveillance study with a total of 42,111 subjects receiving the H1-antihistamine Desloratadin (Aerius®) in a daily dosage of 5mg. The study was performed in Germany in 10,000 medical practices from February to September 2001 with the planned treatment duration of 4-6 weeks, including two visits for evaluation at the beginning and the end of treatment. At both visits, the severity of the following symptoms was assessed by the physician: nasal obstruction, rhinorrhoea, sneezing, itching, conjunctivitis and the reduction of quality of life in terms of sleep and daily life impairment. The physician graded compliance with following the instructions for medication intake, as well as efficacy and tolerance of treatment on a 4-point scale at visit 2 (1: "excellent", 2: "good", 3: "moderate", 4: "poor"). Compliance was rated by questioning the patient whether the medication had been taken as instructed. Therefore physicians assessed the adequacy of the consumed number of drugs as well as the continuity of drug intake. For example a dosage consumed according to physician's instructions and its use at regular intervals, respectively, determined an excellent grading. Per study site (n = 10,000) only one staff member (study investigator) participated in grading the compliance of patients.

Analysis of compliance

Compliance as the dependent variable was dichotomized. Participants who were graded as "excellent" or "good" in their medication intake were classified as compliant and patients with "moderate" and "poor" medication persistence were regarded as non-compliant. To evaluate this mode of dichotomization we verify our decision by a median split.

To evaluate the influence of socio-demographic, treatment-related and condition-related factors on the compliance, in a first step a univariate logistic regression analysis was carried out. To show

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reliability of the results data was divided into a model and a control group according to the start of treatment. 28,398 patients who began treatment before the 1st of May, 2001, were included into the model group and 13,713 patients who started therapy at May 1st, 2001 or later represented the control group. Odds ratios were estimated with a 95% confidence interval for the following independent variables of the model group: age, sex, duration of allergic rhinitis, severity of nasal obstruction, rhinorrhea, sneezing, itching, conjunctivitis as well as comorbidity (binary coded) and impairment of sleep and daily life. Furthermore, a multivariate logistic regression analysis was performed by stepwise inclusion of variables. Variables were added to the model if they had a reciprocal enhancing effect or improved model quality.

Sublingual Immunotherapy

This non-interventional study was performed to evaluate quality of life in patients with allergic rhinitis treated with sublingual immunotherapy. In the context of this study a smaller study population (n = 354) with seasonal and/or perennial allergic rhinitis and/or bronchial asthma received SLIT during January to September 2007. All patients were treated for their sensitization to grass-pollen, rye or wheat. There were three obligatory visits: at baseline (V1), at start of the treatment (V2) and a final visit (V5) as well as two more optional visits (V3, V4).

Initial sublingual immunotherapy (Staloral® allergen extract, 5-grasses, 4-wheat and rye) was either given as standard titration over 11 days or as ultra-rush titration within 2 hours. Maintenance dose was 8 puffs daily for seasonal treatment and 8 puffs 3 times a week or 4 puffs daily with a concentration of 300 I.R. /ml for perennial treatment.

Analysis of compliance

Compliance with following the instructions for administration of SLIT was graded by the physician in charge on a 4-point-scale ("never","seldom", "almost always", and "always") at V3, V4 and V5. In our analysis, compliance at V5 as the dependent variable was also dichotomized by median split. As a result we had two groups of patients. The first group comprised high compliant patients and the second one rarely or noncompliant patients.

In addition to socio-demographic factors study data allowed the analysis of treatment-related and condition-related factors measured at each visit by the quality of life questionnaire RHINASTHMA, which consists of 42 items.[31] For analysis we considered quality of life assessed at the beginning of treatment (V2). Furthermore the need of a patient was included into regression analysis. The extent (severity and frequency) of patient's (subjective) need was rated on a 5-point symptom scale by patients themselves for allergic rhinitis and conjunctivitis impairment.

Data was not divided into a model and control group as done for analysis of antihistamines due to the smaller size of the study population.

Results

The following results include rates of compliance and factors associated with noncompliance for treatment with SLIT and H1-antihistamines.

H1-antihistamines

The final data pool consisted of 42,111 out of 56,595 patients screened in raw data pool. 14,484 patients were not included as they did not match the above mentioned in- and exclusion criteria. Comparison of the raw and the final data pool did not show any significant differences within patient characteristics.

The final data set consisted of 11 to 101 year old patients (mean age: 38.1 years, SD ± 14.9), diagnosed with seasonal allergic rhinitis and a mean duration of disease of 7.7 years (SD ± 6.6) (see Table 1). During mean treatment duration of 41.6 days, 74.5% and 23.6% of the participants of the model group were "excellent" and "good" in terms of compliance with the intake of the H1-antihistamine. Only 1.6% and 0.3% had a "moderate" and "poor" compliance.

Univariate logistic regression analysis showed that patients without concomitant disease had 1.54 times higher odds for being compliant (95% CI: 1.28-1.85) (Table 2). Especially sufferers of allergic

Table 1. Characteristics of study populations

	H1-Antihistamines	SLIT
No. of patients	42111	354
Age (years)	38.1 ± 14.86	32.7 ± 12.62
Sex (% male)	42.9	45.8
Duration of allergic rhinitis (years)	7.7 ± 6.64	8.2 ± 9.16
TNSS at baseline	5.8 ± 1.89	4.36 ± 2.43
Patients with comorbidity (%)	23.5	ND
Patients with allergic conjunctivitis (%)	93.4	63.6

*Results for the patients in percentages or means ±SDs.

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rhinitis without an additional bronchial asthma (n=26,297/28,398), without another respiratory disease (n=27,599) or without a psychiatric disorder (n=28,092) had 1.75-times higher (95% CI: 1.32-2.32), 1.67-times higher (95% CI: 1.01-2.77) and 3.69-times higher (95% CI: 1.14-11.93) odds for being compliant. Non-compliance was 3.1% in asthmatics compared to 1.8% in non-asthmatics (p <0.001) and 6.5% in patients with a psychiatric disorder compared with 1.9% in patients without such a disease (p <0.05). The factors sex, age, duration of disease, Total Nasal Symptom Score (TNSS) and quality of life at the beginning of therapy were not found to be associated with increased noncompliance. Table 2 summarizes the findings of all other factors analysed in univariate analysis.

Moreover, the treatment was highly effective in reducing nasal symptoms from a mean baseline TNSS of 5.79 points to an average of 1.47 points after treatment (p <0.001). Antihistamines were significantly more efficient in compliant patients (p <0.001). Furthermore, patients with a comorbid disease experienced a significantly lower reduction of TNSS than patients without comorbidity (p <0.001).

On multivariate analysis, the following variables were finally included in the regression model 4: severity of allergic conjunctivitis, asthma and nasal symptoms (sneezing, itching, obstruction, and rhinorrhoea), absence of comorbidity and absence of a psychiatric disorder (Table 3). The Hosmer-Lemeshow Goodness-of-Fit test showed a chi-square-value of χ^2=2.678 with a significance of p =0.953. The area under the curve was 0.609. These results indicate that the model is sufficiently explaining all aspects contributing to the complex process in the development of compliance. For the control group, we attempted to show the reliability of the multivariate regression model. Therefore, we calculated the logistic regression equation, Hosmer-Lemeshow test and the area under the curve for the data of the control group. The area under the curve was 0.578. The Hosmer-Lemeshow test resulted in χ^2=5.084 with a significance of p=0.251. Thus, the results show reliability of the multivariate logistic regression model calculated for the model group.

Sublingual Immunotherapy

Patients were between 5 to 68 years old (mean: 32.69 years, SD ± 12.62) and had suffered from allergic rhinitis for a mean duration of 8.22 years (SD ± 9.16 years) (see Table I). Furthermore, 201

Table 2. Univariate logistic regression: Compliance with H1-antihistamine intake and SLIT

Characteristics	Compliance with H1-antihistamine intake	Compliance with SLIT
Age	0.997 (0.991-1.003)	0.996 (0.973-1.019)
Sex		
male	*reference*	*reference*
female	1.068 (0.896-1.273)	1.377 (0.752-2.521)
Total Nasal Symptom Score	1.057 (1.010-1.106)	-
Quality of Life Score	0.987 (0.943-1.033)	1.051 (0.582-1.896)
Concomitant disease		
no	1.540 (1.281-1.852)	-
yes	*reference*	
Duration of allergic rhinitis (years/months)	0.986 (0.975-0.999)	0.998 (0.995-1.001)
Bronchial asthma		
no	1.754 (1.323-2.324)	0.675 (0.327-1.393)
yes	*reference*	*reference*
Other respiratory disease		
no	1.672 (1.009-2.772)	-
yes	*reference*	
Psychiatric disorder		
no	3.688 (1.140-11.926)	-
yes	*reference*	
Endocrinological/ metabolic disease		
no	1.084 (0.535-2.195)	-
yes	*reference*	
Neurological disease		
no	1.239 (0.304-5.050)	-
yes	*reference*	
Disease of the cardio-vascular system		
no	1.103 (0.709-1.715)	-
yes	*reference*	
Gastrointestinal disorder		
no	1.197 (0.380-3.773)	-
yes	*reference*	
Ophthalmological disease		
no	0.864 (0.444-1.679)	-
yes	*reference*	
Dermatopathy		
no	1.273 (0.854-1.897)	-
yes	*reference*	
Financial burden of buying medication		
none	-	*reference*
little		2.364 (0.992-5.630)
fair		0.909 (0.393-2.106)
high		1.879 (0.628-5.620)
Affected by loss of working hours		
none	-	*reference*
mild		0.651 (0.332-1.278)
moderate		0.763 (0.293-1.985)
severe		2.563 (0.317-20.749)
Affected in personality by impairment of social contacts	-	
none		*reference*

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Table 2. (continue)

Characteristics	Compliance with H1-antihistamine intake	Compliance with SLIT
mild	-	0.748 (0.385-1.475)
moderate		1.476 (0.549-3.970)
severe		4.301 (0.541-34.183)
Affected in personality due to bothering others with nasal symptoms	-	
none		*reference*
mild		0.599 (0.310-1.156)
moderate		0.807 (0.291-2.237)
severe		2.737 (0.338-22.134)
Affected by conjunctivitis during previous week		
none	-	*reference*
mild		0.631 (0.319-1.249)
moderate		1.095 (0.432-2.778)
severe		1.578 (0.335-7.430)
Affected by coughing during previous week		
none	-	*reference*
mild		1.585 (0.781-3.216)
moderate		1.690 (0.745-3.836)
severe		5.282 (0.663-42.063)
Affected by gasping during previous week		
none	-	*reference*
mild		0.907 (0.478-1.721)
moderate		7.961 (1.038-61.031)
severe		1.990 (0.235-16.840)
Affected by dyspnea during previous week		
none	-	*reference*
mild		0.587 (0.308-1.122)
moderate		2.769 (0.617-12.435)
severe		2.077 (0.252-17.096)
Asthma symptoms		
none	2.271 (1.593-3.235)	
mild	2.464 (1.674-3.627)	-
moderate	1.485 (1.013-2.179)	
severe	*reference*	
Conjunctivitis symptoms		
none	*reference*	*reference*
mild	1.529 (1.117-2.093)	0.793 (0.318-1.977)
moderate	1.849 (1.376-2.486)	0.670 (0.320-1.403)
severe	1.713 (1.241-2.365)	1.081 (0.408-2.866)
Rhinorrhoea		
none	*reference*	*reference*
mild	0.945 (0.649-1.374)	2.030 (0.851-4.838)
moderate	1.478 (1.036-2.109)	1.313 (0.593-2.907)
severe	1.239 (0.852-1.800)	1.221 (0.488-3.052)
Obstruction		
none	*reference*	*reference*
mild	0.953 (0.668-1.309)	1.907 (0.845-4.306)
moderate	1.011 (0.745-1.373)	2.863 (1.201-6.823)
severe	1.150 (0.816-1.621)	2.238 (0.838-5.974)
Sneezing/ (Itching)		
none	*reference*	*reference*
mild	0.833 (0.517-1.343)	1.937 (0.842-4.457)
moderate	1.295 (0.816-2.054)	2.156 (0.941-4.942)
severe	1.162 (0.724-1.866)	2.879 (1.052-7.883)

participants were sensitized to more than one allergen and 112 were diagnosed with bronchial asthma.

Conventional titration was given to 82.5% of patients and 17.5% of them received ultra-rush titration. Compliance was not significantly different between those two groups of patients (p=0.768). After mean treatment duration of 23.36 weeks (SD ± 8.25) 79.6% of the patients were graded as high compliant and 20.4% of the patients were graded rarely non-compliant with the medication intake of SLIT. Compliance was not evaluated in 94 patients. The final and the raw data pool did not show any significant differences within patient characteristics.

On univariate logistic regression analysis, female sex led to 1.33-times higher odds (95% CI: 0.75-2.52) for being compliant. Patients who felt highly affected by loss of working hours had 2.56-higher odds (95% CI: 0.33-20.75) for compliance. Allergic rhinitis sufferers who felt strongly impaired in their social contacts by the disease had 4.30-times increased odds (95% CI: 0.54-34.18) and patients who felt strongly affected as they assumed to bother others with their nasal symptoms had 2.74-times higher odds (95% CI: 0.34-22.13) for being compliant.

Furthermore, severe nasal or airway symptoms at the beginning of treatment led to increased odds for compliance with SLIT. Table II depicts a selection of variables investigated on univariate analysis.

Additionally, we developed a multivariate regression model for predicting the compliance outcome (model 4 see Table 4). The model has a Hosmer-Lemeshow Goodness-of-Fit value of χ^2=3.284 with a significance of p =0.915 and an area under the curve value of 0.790. These results demonstrate the high quality of the model. The model itself highlights that mainly the severity of symptoms and interference with work and social life are crucial factors in the formation of compliance. Hence, the consideration of the mentioned determinants allows for a reliable prediction of the compliance outcome.

Discussion

The objective of this secondary data analysis was to identify rates and determinants of compliance with the intake of H1-antihistamines and SLIT. Our findings for the compliance with SLIT correspond with compliance rates of comparable studies of the last years.[9-21]

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Table 3. Multivariate logistic regression for the model group: Compliance with H1-antihistamine intake

Characteristics	Odds Ratio (95% Confidence Interval)
Concomitant disease	
no	1.286 (1.049-1.576)
yes	*reference*
Psychiatric disorder	
no	3.245 (0.988-10.657)
yes	*reference*
Asthma symptoms	
none	2.127 (1.462-3.094)
mild	2.286 (1.528-3.419)
moderate	1.445 (0.976-2.139)
severe	*reference*
Conjunctivitis symptoms	
none	*reference*
mild	1.361 (0.979-1.891)
moderate	1.545 (1.123-2.125)
severe	1.588 (1.106-2.279)
Rhinorrhoea	
none	*reference*
mild	0.937 (0.614-1.429)
moderate	1.196 (0.789-1.811)
severe	0.998 (0.632-1.576)
Obstruction	
none	*reference*
mild	1.007 (0.708-1.432)
moderate	0.923 (0.668-1.275)
severe	1.174 (0.810-1.703)
Sneezing/ Itching	
none	*reference*
mild	0.703 (0.410-1.205)
moderate	0.973 (0.566-1.673)
severe	0.865 (0.487-1.538)

Table 4. Multivariate logistic regression model: Compliance with SLIT

Characteristics	Odds Ratio (95% Confidence Interval)
Sex	
male	*reference*
female	1.193 (0.582-2.447)
Financial burden of buying medication	
none	*reference*
little	2.785 (1.016-7.639)
fair	0.878 (0.314-2.459)
high	1.197 (0.305-4.699)
Affected by loss of working hours	
none	*reference*
mild	0.424 (0.176-1.024)
moderate	0.648 (0.175-2.395)
severe	1.327 (0.066-26.811)
Affected in personality by impairment of social contacts	
none	*reference*
mild	1.331 (0.457-3.882)
moderate	2.358 (0.550-10.102)
severe	7.809 (0.569-107.164)
Affected in personality due to bothering others with nasal symptoms	
none	*reference*
mild	0.467 (0.171-1.276)
moderate	0.509 (0.099-2.627)
severe	0.976 (0.060-15.825)
Affected by sneezing during previous week	
none	*reference*
mild	1.603 (0.522-4.921)
moderate	2.370 (0.725-7.747)
severe	3.113 (0.634-15.277)
Affected by nasal obstruction during previous week	
none	*reference*
mild	1.879 (0.647-5.454)
moderate	1.605 (0.482-5.346)
severe	0.845 (0.185-3.851)
Affected by coughing during previous week	
none	*reference*
mild	2.453 (0.872-6.900)
moderate	3.756 (0.991-14.244)
severe	20.273 (1.375-298.870)
Affected by gasping during previous week	
none	*reference*
mild	0.834 (0.260-2.677)
moderate	5.410 (0.528-55.396)
severe	0.141 (0.003-7.930)
Affected by dyspnea during previous week	
none	*reference*
mild	0.272 (0.097-0.761)
moderate	0.608 (0.100-3.715)
severe	1.547 (0.037-64.917)

Patients in clinical studies are in an artificial situation and even in non-interventional studies, the tighter medical care by the investigators may lead to a better compliance compared to the situation in daily life. However, an analysis of unselected patient data from a German prescription database (Insight Health) showed a persistency rate of 71% for SLIT in the first year which was very close to the compliance rate which we have found in our patient group, but there was a remarkable reduction of the persistency over the treatment years.[27] Even if this reduction was comparable to that seen in other chronic diseases, it underlines the necessity to emphasize the monitoring of patients to improve the compliance and, hence, the efficacy of the treatment.

In our analysis on the intake of H1-antihistamines, compliance was higher than in the study by Valero et al.[28] A possible explanation for our result could be that a qualitative rather than a quantitative method was applied to measure patient compliance. This is the main limitation of our analysis as the method is more subjective to bias than direct methods of measuring compliance. Additionally, the short duration of treatment might

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contribute to the high rate of compliance. Nevertheless, we consider the investigated treatment period of approximately six weeks as clinically relevant as it has been shown that patients suffer from allergic symptoms on an average of 52.5 days a year.[29]

Analysis of predictors of compliance with H1-antihistamines revealed that patients with allergic rhinitis who suffered from a concomitant disease, especially patients with an additional psychiatric disorder or bronchial asthma were more likely to be non-compliant. Generally, multimorbidity often leads to polypharmacy, which can result in noncompliance as the patient is overburdened with multiple and complex medication schedules.[32-33] Compliance issues have been widely reported in the treatment of patients with psychiatric disorders as they often have difficulty following therapeutic regiments.[34] Due to the retrospective character of this analysis the data do not provide further information about the diagnosed psychiatric disorders. Furthermore, patients with a concomitant asthma might have a reduced compliance with the intake of H1-antihistamines as they might feel more affected by their asthmatic symptoms.

In case of SLIT, univariate logistic regression showed that the presence of a concomitant asthma was a predictor of compliance. These oppositional findings were possibly caused by the different indications of those two treatment regiments. SLIT is a validated treatment option for asthmatic patients as it has been proven to be effective in reducing asthmatic symptoms.[35] Oral H1-antihistamines on the other hand are not part of regular asthma therapy although they also have some effectiveness in reducing asthmatic symptoms.[1]

Further results of univariate analysis of SLIT mainly identified patient- and condition-related determinants of medication compliance. Thus, patients who suffer from moderate or severe nasal, eye or airway symptoms and those who felt extremely impaired by allergic rhinitis in their social and work life functioning were more likely compliant. Our multivariate compliance model incorporates multiple condition-related, patient-related and demographic factors and the Hosmer-Lemeshow Goodness-of-Fit test shows high model quality. In comparison, model quality of the multivariate compliance model for H1-antihistamines was rather deficient which indicates that relevant predictors of compliance were not available for analysis in the data of this non-interventional study. Nevertheless, comorbidity has to be considered as a relevant determinant of noncompliance.

The dichotomization of the compliance variable was performed to predict the compliance outcome in a binary form within a logistic regression model. Disadvantages of this method are its artificial character and the loss of information, which is possibly caused by the simplification of the 4-point classification.

On the basis of our results, we suggest the integration of treatment-related patient characteristics into the conception of future guidelines. In concrete terms, it has to be considered that specific groups of patients such as patients with a psychiatric disorder or bronchial asthma and those with less severe symptoms might profit from an intensified monitoring to enhance compliance and efficacy of treatment.

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