

Original article

Rhinasthma: a new specific QoL questionnaire for patients with rhinitis and asthma

Introduction: To date we have available specific instruments assessing health-related quality of life (HRQL) in rhinoconjunctivitis or in asthma, but not instruments evaluating rhinitis and asthma together, although they often coexist. The aim of our study was to develop and validate a specific quality of life (QoL) questionnaire for adult patients with rhinoconjunctivitis, asthma or both.

Materials and methods: A pool of 42 items covering the main symptoms and problems related to respiratory allergy, was generated based on literature review and clinical experience. The items were randomly listed and presented to 148 consecutive outpatients 46 suffering from asthma (age 32.9 ± 14.3 years), 53 suffering from rhinoconjunctivitis (age 32.6 ± 11.5 years) and 49 from asthma and rhinoconjunctivitis (age 35.6 ± 12.2 years). The patients were asked to indicate which item they had directly experienced and for each of them, its importance on a four-point scale (1 = not important; 4 = very important). Twelve items were cancelled from the list, because of low importance or redundancy. In the instrument validation phase, 104 patients (42 with rhinoconjunctivitis alone and 62 with asthma and rhinoconjunctivitis) were evaluated with the generic instrument SF-36 and the new questionnaire (RHINASTHMA).

Results: RHINASTHMA was able to differentiate patients with rhinitis from those with both rhinitis and asthma. In stable condition, RHINASTHMA showed good reliability. The factor analysis extracted three factors with a good reliability (0.93, 0.87, 0.76).

Discussion: RHINASTHMA is the first tool aimed at evaluating HRQL impairment in patients with rhinitis and/or asthma. It provides a short and simple assessment, and has overall psychometric properties. This is of relevance because of the frequent asthma–rhinitis comorbidity.

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A global evaluation of patients and therapies must include, together with clinical and instrumental parameters, the measurement of health-related quality of life (HRQL). Assessing the patient's subjective point of view, offers a more comprehensive description of the impact of the disease and its therapy on everyday life (1). This is of particular relevance in patients suffering from chronic diseases, when the primary goal of treatment is to improve their functioning in daily life and to achieve the highest level of well-being. Quality of life (QoL) is presently recognized as a primary outcome in clinical trials, population studies and public health. Also physicians and researchers are aware that HRQL is a need, rather than a simple option (2).

While health status is defined by physicians, the impact of a disease on HRQL is assessed by the patient himself by means of validated instruments (3, 4). Two types of tools are used. Generic questionnaires are applicable to

all health conditions, therefore they allow to compare patients suffering from different diseases as well as ill and healthy subjects. Specific questionnaires are restricted to a particular disease, to a selected population (e.g. adults, children and elderly), or to a specific function (e.g. sexuality) or problem (e.g. pain). These tools are more sensitive than the generic ones, but they do not allow comparison between different diseases.

The history of HRQL in the field of respiratory allergy is chronologically brief but the literature is rich, thus testifying the interest in this topic (5). During the last years, several questionnaires were validated and standardized for measuring HRQL in children, adolescents and adults with rhinitis or asthma (6–11). In parallel, clinical trials have documented the impact of allergic diseases and therapy on the HRQL of patients (12–21).

Asthmatic patients are bothered by their symptoms (i.e. shortness of breath, wheezing, cough, chest tightness,

sleep disturbances) and they invariantly report limitations in physical activities and social life. In addition, the impact of the disease on emotional aspects of life is not negligible. In rhinitis, the most troublesome problems are runny and stuffy nose, sneezing or itchy eyes. These symptoms cause an impairment in diurnal activities as well as sleep disorders, so that patients are often frustrated and irritable.

Recent clinical and epidemiologic studies suggested that a strict relationship between rhinitis and asthma exists (22–24). Up to 80% of asthmatic patients also have rhinitis, and rhinitic patients frequently have asthma or nonspecific bronchial hyper-responsiveness. These observations suggested the hypothesis of the unity of upper and lower respiratory tract and that a common pathogenic mechanism underlies rhinitis and asthma, but in previous studies asthma and rhinitis have been kept separated in evaluating HRQL. Indeed the assessment of HRQL in patients with respiratory allergy should consider both upper and lower respiratory tract. At present, this could be performed by using simultaneously two different questionnaires, one for rhinitis and one for asthma. This approach has several limits: (a) filling two questionnaires requires much time, (b) many items are the same in the two questionnaires (i.e. limitation in daily life, practical problems, mood, anxiety) and (c) it is not realistic to describe a unique disease separating it in different components.

The aim of our study was to develop and validate a HRQL questionnaire for adult patients suffering from rhinitis and/or asthma. The questionnaire considers asthma and rhinitis as different aspects of the same disease, so that the patient is not asked to attribute specific symptoms or problems to asthma or rhinitis separately. The new instrument takes into account functional, physical and emotional problems experienced by adult patients with respiratory allergy. This questionnaire was intended to be (1) short, simple and user-friendly, (2) psychometrically sound with good validity and reliability, and (3) useful both in research and clinical practice. The new questionnaire has been named RHIN-ASTHMA.

Materials and methods

The development and testing of the new tool required two separate procedures which were carried out in different groups of patients. The methods used for the two steps are described in detail below.

Patients

All adult patients involved in the development and validation of the questionnaire were seen at our Department. They suffered from respiratory allergy, ascertained through the routine diagnostic procedure. In detail, all patients underwent an interview for clinical and family history, clinical visit and skin prick test for the common allergens (a RAST assay was also performed in selected cases). Rhinitis was clinically diagnosed, following international guidelines.

The diagnosis of asthma was made based on clinical history and the results of pulmonary function test. In particular, a reversible bronchial obstruction (FEV1 <80% predicted with at least 12% increase after inhaled salbutamol 400 mcg) or either positive methacholine challenge were required as diagnostic criteria.

RHINASTHMA development procedure

The first task was to identify all those symptoms and problems, which are perceived as relevant and troublesome by patients with rhinoconjunctivitis, asthma or both.

First, a pool of 42 items was generated based on the following sources: (a) recent literature review of the available HRQL questionnaires and symptom score scales for rhinitis and asthma, (b) discussion with expert allergists and pulmonologists and (c) preliminary unstructured interviews to more than 200 adult outpatients with respiratory allergy. The items concerned both the burden of symptoms and the limitations/problems related to rhinoconjunctivitis and asthma. The items were randomly listed and administered to patients who had to indicate which of the 42 items selected they had directly experienced and the importance of each selected item on a four-point scale (1 = not important; 4 = very important). Patients were also asked to indicate other possible aspects on which the allergic disease might impact and whatever they consider worthy to be added or changed in the questionnaire.

This first phase was carried out in a sample of 150 outpatients, consecutively seen at our Department over a 2-month period. We subsequently calculated: (a) the percentage of patients who indicated each item as a consequence of their disease (frequency range: 0–100), (b) the importance (mean value) attributed from the patient to each item indicated as a problem (range: 0–4) and (c) the overall importance score of the item, defined as the product of the frequency and the mean importance divided by 100 (range: 0–4). The result of this first phase generated a 30-item questionnaire where patients had to indicate, on a Likert scale with multiple options (1 = not at all, 5 = very much), how much they were been troubled by each problem. The questionnaire was then administered to a different patients' population for validation.

RHINASTHMA validation procedure

The questionnaire obtained from the first phase was tested and validated, in accordance with current guidelines, through the following steps:

- (a) *Criterion validity.* It refers to the degree to which the test proves to measure what it is supposed to measure. This was tested by comparing RHINASTHMA scores of rhinitic patients and, patients with asthma and rhinitis, with the aim to identify the burden of rhinitis in respiratory allergy. The Mann–Whitney (MW) nonparametric test was used, because of the sample characteristics.
- (b) *Test–retest reliability.* It is the ability of a questionnaire to provide the same results when used repeatedly in stable conditions. A randomized group of 31 stable patients were assessed at baseline and after 1 week. Data were analyzed by *t*-test for paired samples as recommended in statistical literature (25)
- (c) *Construct validity.* It refers to the degree to which a test measures the theoretical ideas underpinning a particular topic. Factorial analysis was performed on RHINASTHMA scores; the principal component method with Varimax rotation was adopted. The concordance between SF-36 and RHINASTHMA was evaluated in order to verify the ability of the new instrument

to differentiate rhinitic patients and patients with rhinoconjunctivitis and asthma. In fact, SF-36 is a generic tool widely used to assess HRQL in both asthmatic and rhinitic patients. SF-36 scores were compared by using MW test. The *P* values were estimated by using the Bonferroni correction.

- (d) *Internal reliability*. It measures the homogeneity of a scale. It was established calculating Cronbach's α correlation coefficient on the whole test and on factorial scores. Good correlation was assumed to exist if the coefficients were 0.70 or higher.
- (e) *Responsiveness*. It refers to the ability of the questionnaire to detect clinically significant within-subject changes. We determined whether the RHINASTHMA is able to detect differences in QoL scores in a group of 27 patients with respiratory allergy (persistent rhinitis and intermittent asthma) evaluated at baseline and after 3 weeks of treatment with cetirizine. RHINASTHMA score were compared by using a nonparametric test (Wilcoxon).

In this testing phase, 120 consecutive outpatients, diagnosed as having respiratory allergy, were asked to fill-in the generated RHINASTHMA questionnaire and the generic questionnaire SF-36.

Results

RHINASTHMA development procedure

Of 150 patients, two declined to participate, therefore 148 preliminary questionnaires were suitable for the analysis. These patients had a mean age of 33.7 ± 12.7 years (age range 16–73); 46 (31.08%) of them suffered from asthma alone, 53 (35.81%) from rhinoconjunctivitis alone and 49 (33.11%) from asthma and rhinoconjunctivitis. No other significant impact of allergy on life aspects were indicated by patients. The demographics of this population is summarized in Table 1. Based on the patients' answers, 12 of the proposed items were excluded, because of their low importance or redundancy. Table 2 summarizes the results of the first phase.

RHINASTHMA validation procedure

Of 120 patients, six refused to fill-in the questionnaire, two were excluded because of severe visual impairment and eight were excluded for concomitant severe illness that may have had an impact on HRQL. The characteristics of the 104 eligible patients are shown in Table 3.

- (a) *Criterion validity*. Table 4 lists the RHINASTHMA average scores which was significantly different in the comparison between the two groups (rhinitis vs. asthma and rhinitis).
- (b) *Test-retest reliability*. All items showed a good reproducibility. In fact, the Pearson coefficient ranged between 0.70 and 0.92 for 25 items and between 0.61 and 0.69 for the remaining five items. The lowest were the following (need for medical controls, night awakenings, to clear one's throat, difficulty in concentrating on problems, having to carry drugs with them).

Table 1. Development phase: sample characteristics (*n* = 148)

	%
Gender	
Male	46.62
Female	53.38
Age	
33.7 ± 12.7	
Marital status	
Single	54.5
Married	45.5
Years of education	
0–5	2.03
6–8	27.70
9–13	39.86
More than 13	30.40
Employment status	
Employed	61.49
Unemployed	2.70
Housewife	9.46
Retired	3.38
Student	22.97
Disease	
Asthma	31.08
Rhinoconjunctivitis	35.81
Rhinoconjunctivitis and asthma	33.11

- (c) *Construct validity*. The unlimited factor analysis with eigenvalue > 1 extracted seven factors; by reducing the factors to three, 52% of variance was explained. Items belonging to each factor are listed in Table 5. All the SF-36 subscales significantly differentiated the two groups of patients. SF-36 scores of the two groups are shown in Table 6.
- (d) *Internal reliability*. Cronbach's α coefficient indicated highly satisfactory levels of internal consistency reliability. In fact, all α coefficients were higher than 0.07, the minimum recommended level, and more precisely were 0.93, 0.87 and 0.76 for the three factors extracted. Table 7 details the reliability analysis of the three-factor solution. The postulated distinction among problems and symptoms pertaining to rhinitis, asthma or both seems to be confirmed.
- (e) *Responsiveness*. Table 8 shows that RHINASTHMA is able to detect the within-subject changes with a good degree of significance.

Discussion

The HRQL measurement has been successfully applied to respiratory allergy, showing that both rhinitis and asthma have a significant impact on patient's life. Nevertheless, in all the available studies rhinitis and asthma has been considered as distinct diseases; in fact, specific questionnaires addressed to one disease or the other have been developed and validated during the last 10 years. Presently, based on the experimental evidence, it is generally

Table 2. Results of the evaluation of the preliminary version of the questionnaire

Item	Frequency (%)	Mean importance	Total importance
To clear one's throat	60.59	2.63	1.59
Having to take drugs	85.81	3.24	2.78
Having to spend money	76.72	2.84	2.18
Chest-tightness	70.27	3.04	2.14
Loss of taste*	39.19	3.03	1.19
Dyspnea	89.19	3.48	3.10
Itchy eyes	73.65	2.84	2.09
Loss of working days*	39.86	3.03	1.21
Having to carry drugs with them	66.22	2.70	1.79
Social relationship limitations*	42.57	3.11	1.32
Runny nose	83.11	3.10	2.58
Wake up in the night	68.92	2.34	1.61
Sneezing	83.11	3.02	2.51
Leisure time activities limitations	54.05	3.12	1.69
Sexual activity impairment	25.00	2.54	0.63
Difficulty in falling asleep	64.19	3.14	2.01
Sport activities impairment	63.51	2.95	1.87
Always having to carry tissues	77.03	2.67	2.06
Limitations in everyday's activity	62.84	3.00	1.88
Having to stay at home*	39.86	2.97	1.18
To trouble people*	53.38	2.78	1.48
Difficulty in concentrating on problems	63.51	3.03	1.92
Having to take drugs everyday*	70.27	2.98	2.09
Shortness of breath	75.68	3.31	2.50
Having to avoid certain environments	69.59	3.02	2.10
Stuffy nose	81.08	3.12	2.53
Feeling 'different'*	23.65	2.11	0.49
Loss of smell	53.38	2.83	1.51
Worried of not having drugs	50.68	3.21	1.63
Itchy nose	75.00	2.81	2.11
Eyes redness	72.97	2.78	2.03
Necessity of medical controls	60.81	2.89	1.76
Cough	66.89	2.86	1.91
Feeling ill*	41.22	2.72	1.12
Not being able to do whatever is desired	50.68	3.08	1.56
Drugs' side-effects	57.43	3.10	1.78
Having to breathe through the mouth*	83.11	3.17	2.63
Sore eyes	66.22	2.79	1.85
Troubled by certain smells*	34.46	2.70	0.93
Wheeze	62.84	3.05	1.92
Watery eyes	68.24	2.67	1.82
Having to take drugs everyday*	79.73	3	2.39

* Redundant/low important items.

Table 3. Validation phase: sample characteristics ($n = 104$)

	%
Gender	
Male	46.15
Female	53.85
Age	
35.1 ± 10.3	
Marital status	
Single	51.31
Married	48.69
Years of education	
0–5	1.9
6–8	29.8
9–13	40.4
More than 13	29.8
Employment status	
Employed	74
Unemployed	2.9
Housewife	7.7
Retired	3.8
Student	11.5
Disease	
Asthma and rhinoconjunctivitis	59.61
Rhinoconjunctivitis	40.38

Table 4. RHINASTHMA items with significantly different scores between patients with rhinoconjunctivitis and patients with rhinoconjunctivitis and asthma

Items	P-value
Cough	0.0001
Wheezing	0.0001
To clear one's throat	0.001
Shortness of breath	0.0001
Dyspnea	0.0001
Chest-tightness	0.0001
Sport activities impairment	0.007
Having to avoid certain environments	0.002
Wake up in the night	0.0001
Leisure time activities limitations	0.001
Having to spend money	0.004
Having to take drugs	0.0001
Not being able to do whatever desired	0.0001
Limitations in everyday's activity	0.001

believed that rhinitis and asthma represent two aspects of a single disorder of the respiratory tract. This hypothesis is supported by epidemiologic, clinical and pathophysiologic data, most of them suggesting that a common pathogenic mechanism underlies respiratory allergic diseases. For these reasons we attempted to develop and validate a specific HRQL questionnaire, suitable for patients suffering from respiratory allergy, independent of their disease (rhinitis or asthma).

The RHINASTHMA questionnaire was generated and tested following procedures well-established and applied to other similar instruments.

The RHINASTHMA seemed to have good psychometric properties and it is capable of differentiating patients with rhinitis from those with both asthma and rhinitis. Its added value stems from its ability in detecting both quantitative and qualitative differences between the impact of rhinitis alone vs the impact of rhinitis and asthma, and in defining the specific role of rhinitis in impairing patients' daily life. The RHINASTHMA is the first specific questionnaire aimed at assessing at the same time either rhinitis or asthma impact on daily life. This could have important effects on clinical practice as well as on clinical trials. In fact, there

Table 5. Factors identified using principal components analysis on full data set (bold typeface shows the component upon which each item loaded most highly)

Item	Factors		
	1	2	3
Difficulty in concentrating on problems	0.414	8.350×10^{-2}	-3.891×10^{-2}
Sport activities impairment	0.693	0.140	0.135
Itchy nose	9.294×10^{-3}	0.803	-6.317×10^{-2}
Necessity of medical controls	0.202	-7.619×10^{-2}	0.645
Stuffy nose	0.183	0.586	-0.269
Cough	0.488	0.150	0.312
Having to avoid certain environments	0.304	0.194	0.307
Watery eyes	-0.116	0.705	0.231
Leisure time activities limitations	0.779	0.105	0.143
Shortness of breath	0.716	-0.110	0.411
Wake up in the night	0.660	-1.984×10^{-2}	9.847×10^{-2}
Sore eyes	0.145	0.693	0.238
Dyspnoea	0.788	-0.106	0.252
Eyes redness	4.076×10^{-2}	0.710	8.806×10^{-2}
Drugs' side effects	0.116	-0.6030×10^{-2}	0.360
Chest-tightness	0.650	-0.211	0.305
Itchy eyes	5.442×10^{-2}	0.815	0.175
Wheeze	0.793	-0.126	0.295
Worried of not having drugs	0.541	-9.703×10^{-2}	0.352
Runny nose	-4.852×10^{-2}	0.690	-1.953×10^2
Having to spend money	0.206	2.588×10^{-2}	0.667
Sneezing	-6.222×10^{-2}	0.705	4.831×10^{-2}
Having to take drugs	0.213	1.994×10^{-2}	0.663
Limitations in everyday's activity	0.821	0.146	8.274×10^{-2}
Having to carry drugs with me	0.125	9.894×10^{-2}	0.750
To clear one's throat	0.320	0.100	0.435
Loss of smell	0.217	0.217	0.493
Always having to carry tissues	-1.852×10^{-2}	0.496	0.199
Difficulty in falling asleep	0.667	-1.010×10^{-2}	0.113
Not being able to do whatever desired	0.811	4.178×10^{-2}	0.251

Table 6. SF-36 domains with significantly different scores between patients with rhinoconjunctivitis and patients with rhinoconjunctivitis and asthma. Values are given as mean $\pm$ SD

SF-36 domains	Patients with rhinoconjunctivitis	Patients with rhinoconjunctivitis and asthma	P-value
Physical functioning	94.51 $\pm$ 9.06	86.23 $\pm$ 16.52	0.0001
Role physical	85.48 $\pm$ 23.96	68.51 $\pm$ 36.14	0.001
Bodily pain	94.81 $\pm$ 13.73	81.84 $\pm$ 26.60	0.0001
General health	68.71 $\pm$ 20.48	59.00 $\pm$ 20.38	0.0001
Vitality	64.03 $\pm$ 20.26	49.67 $\pm$ 22.69	0.005
Social functioning	82.26 $\pm$ 17.61	63.58 $\pm$ 22.95	0.0001
Role emotional	87.09 $\pm$ 22.24	57.25 $\pm$ 36.29	0.0001
Mental Health	70.06 $\pm$ 15.96	60.52 $\pm$ 18.83	0.033

is the need to '...ensure that the impairment in QoL attributed to asthma could not result from the concomitant allergic rhinitis' (25). And, on the other hand, because of the minor clinical relevance of rhinitis compared with asthma, 'Symptoms of allergic rhinitis are likely to be neglected, particularly in patients with

Table 7. Cronbach α correlation coefficient on factorial scores

Factor	Items	α Coefficient
Factor 1	Difficulty in concentrating on problems	0.9286
	Sport activities impairment	0.9212
	Cough	0.9259
	Leisure time activities limitations	0.9182
	Shortness of breath	0.9139
	Wake up in the night	0.9236
	Dyspnea	0.9148
	Chest-tightness	0.9180
	Wheezing	0.9150
	Worried of not having drugs	0.9239
	Limitations in everyday's activity	0.9169
	Difficulty in falling asleep	0.9224
	Not being able to do whatever desired	0.9159
Factor 2	Itchy nose	0.8463
	Stuffy nose	0.8754
	Watery eyes	0.8579
	Sore eyes	0.8546
	Eyes redness	0.8623
	Itchy eyes	0.8450
	Runny nose	0.8537
	Sneezing	0.8492
	Always having to carry tissues	0.8813
Factor 3	Necessity of medical controls	0.7322
	Having to avoid certain environments	0.7444
	Drugs' side-effects	0.7720
	Having to spend money	0.7084
	Having to take drugs	0.7237
	Having to carry drugs with me	0.7208
	To clear one's throat	0.7283
	Loss of smell	0.7421

Table 8. RHINASTHMA items with a significant difference after a 3-week treatment with cetirizine

Difficulty in concentrating on problems	0.034
Sport activities impairment	0.003
Itchy nose	0.0001
Stuffy nose	0.001
Cough	0.004
Having to avoid certain environments	0.004
Watery eyes	0.001
Sore eyes	0.002
Eyes redness	0.0001
Drugs' side-effects	0.034
Itchy eyes	0.0001
Wheezing	0.014
Worried of not having drugs	0.046
Runny nose	0.0001
Sneezing	0.0001
Limitations in everyday's activity	0.034
To clear one's throat	0.025
Always having to carry tissues	0.021

asthma' (26), both by physicians and by patients themselves. Therefore, the RHINASTHMA could to be useful in helping the physician in his diagnostic

procedures, in his decision-making processes and in properly evaluating the clinical outcomes.

Our results, supported by a rigorous statistical analysis, make us confident that it can be a useful and reliable clinical tool to be used in any clinical situation.

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