

Quality of life and polysensitization in young men with intermittent asthma

Ignazio Cirillo, MD*; Andrea Vizzaccaro, MD*; Catherine Klersy, MD†; Ilaria Baiardini, BS‡; Gian Luigi Marseglia, MD§; G. Walter Canonica, MD¶; Maria Angela Tosca, MD||; and Giorgio Ciprandi, MD||

Background: Health-related quality of life (HRQoL) represents an important variable in asthma management. To date, to our knowledge, no study has explored the relationship between HRQoL and sensitization in patients with asthma.

Objective: To evaluate the relationships among HRQoL and sensitization, pulmonary function, and bronchial hyperreactivity in a group of young men with intermittent asthma.

Methods: We studied 185 conscripts with intermittent asthma and bronchial hyperreactivity. The Asthma Quality of Life Questionnaire was used. Skin prick testing, spirometry, and methacholine challenge were performed in all participants.

Results: The Asthma Quality of Life Questionnaire median scores were greater than 4, indicating suboptimal HRQoL. Polysensitization was significantly associated with the worst HRQoL, whereas pulmonary function and bronchial hyperreactivity category were not.

Conclusions: This study provides the first evidence that HRQoL is associated with polysensitization in intermittent asthma and underlines the importance of evaluating this issue when managing young patients with slight respiratory symptoms.

Ann Allergy Asthma Immunol. 2005;94:640–643.

INTRODUCTION

Asthma represents a global health problem because it substantially affects medical costs and socioeconomic outcomes and because it interferes with psychological well-being and the capacity to function in activities of daily living, as has recently been well documented in the literature.¹ To obtain a complete evaluation of the impact of asthma from a subjective point of view, health-related quality of life (HRQoL) is currently evaluated along with traditional biomedical variables.² Whereas symptoms, pulmonary function, and the effects of treatment on the HRQoL of patients with asthma have received great attention, few articles have investigated the relationship between bronchial hyperreactivity (BHR) and HRQoL by means of a specific tool.^{3,4} Furthermore, no study has been conducted, to our knowledge, to relate sensitization to HRQoL in patients with asthma. Thus, the primary aim of this study was to evaluate the possible association between HRQoL, measured using the Asthma Quality of Life Questionnaire (AQLQ),⁵ and sensitization, evaluated by skin prick testing, in a population of Italian conscripts with intermittent asthma. Furthermore, this study aimed to verify the relation-

ship of HRQoL with pulmonary function and BHR, evaluated by methacholine challenge.

MATERIALS AND METHODS

Study Patients and Design

A total of 185 young men with a mean (SD) age of 21.3 (3.7) years and referred as conscripts for a medical visit were enrolled in the study. A detailed clinical history and a complete physical examination were performed for each patient. All the patients had a diagnosis of intermittent asthma by clinical and functional features, according to the Global Initiative for Asthma guidelines.⁶

The study was conducted as a cross-sectional observational study. Only patients who met all the following criteria were eligible for inclusion in the study: a diagnosis of intermittent asthma, forced expiratory volume in 1 second (FEV₁) values of 80% of predicted or greater, and positive methacholine challenge results. Informed consent was obtained before study entry. The exclusion criteria were allergic rhinitis, acute and chronic upper and lower respiratory tract infections in the 30 days before the study, previous or current specific immunotherapy, the use of inhaled or oral corticosteroids during the previous 4 weeks, and the use of antileukotrienes and long-acting β_2 -agonists in the previous week. Skin prick testing, spirometry, methacholine challenge, and HRQoL evaluation were performed in all participants. The study was approved by the Navy Hospital Review Board.

Procedures

Sensitization was evaluated by skin prick testing, performed as stated by the European Academy of Allergology and Clinical Immunology.⁷ The allergen panel consisted of house

* Dipartimento di Medicina, Ospedale Marina Militare, La Spezia, Italy.

† Servizio di Biometria ed Epidemiologia Clinica–Direzione Scientifica, IRCCS Policlinico San Matteo, Pavia, Italy.

‡ Dipartimento di Medicina Interna, Università di Genova, Genova, Italy.

§ Clinica Pediatrica, IRCCS Policlinico San Matteo, Pavia, Italy.

¶ Pneumologia, Istituto Giannina Gaslini, Genoa, Italy.

|| Dipartimento Testa Collo, Azienda Ospedaliera Universitaria San Martino, Genoa, Italy.

Received for publication November 3, 2004.

Accepted for publication in revised form January 17, 2005.

Table 1. Clinical Characteristics of the 185 Male Subjects Enrolled in the Study

Characteristic	Value
Age, mean (SD), y	21.3 (3.7)
Smoker, No. (%)	13 (7)
Skin prick test result, No. (%)	
Negative	7 (3.8)
Monosensitivity	42 (22.7)
Polysensitivity	136 (73.5)
FVC, median (25th-75th percentile), % of predicted	96 (90.00-104.00)
FEV ₁ , median (25th-75th percentile), % of predicted	99.00 (90.00-109.00)
FEF ₂₅₋₇₅ , mean (SD)	93.1 (7.0)
PD ₂₀ /FEV ₁ , median (25th-75th percentile)	180 (70-320)
BHR, No. (%)	
Very mild	36 (19.5)
Mild	45 (24.3)
Moderate	46 (24.9)
Severe	58 (31.3)
AQLQ domain score, median (25th-75th percentile)	4.13 (3.34-5.29)
Symptoms	3.83 (3.08-5.09)
Emotional function	4.60 (3.50-6.20)
Environmental stimuli	4.25 (3.50-5.50)
Activity limitation	4.18 (3.55-5.36)

Abbreviations: AQLQ, Asthma Quality of Life Questionnaire; BHR, bronchial hyperreactivity; FEF₂₅₋₇₅, forced expiratory flow between 25% and 75%; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; PD₂₀, provocation dose of methacholine sufficient to induce BHR.

dust mites (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), cat, dog, grass mix, *Compositae* mix, *Parietaria judaica*, birch, hazel tree, olive tree, *Alternaria tenuis*, *Cladosporium*, and aspergilli mix; the concentration of allergen extracts was 100 IR/mL (Stallergenes, Milan, Italy).

Spirometry was performed using a computer-assisted spirometer (Pulmolab 435-Spiro 235; Pulmolab, Morgan, England) and according to the European Respiratory Society guidelines using the European Community for Steel and Coal reference equations.⁸ Four categories of BHR were considered: very mild (provocation dose of methacholine sufficient to induce BHR [PD₂₀]/FEV₁ >800 μ g/mL), mild (PD₂₀/FEV₁ of 401–800 μ g/mL), moderate (PD₂₀/FEV₁ of 101–400 μ g/mL), and severe (PD₂₀/FEV₁ $\leq$ 100 μ g/mL), as previously reported.⁹ Methacholine was administered using a computerized dosimeter (Mefar MB3; Mefar, Marcos, Italy) activated by the inhalator effort. Participants inhaled progressively increasing doses of methacholine, starting at 30 μ g/mL and progressing to 1,200 μ g/mL in 11 steps. The procedure was discontinued when FEV₁ decreased by more than 20% from baseline. A computerized algorithm provided the PD₂₀ value. If no response was obtained with the maximal cumulative dose of 1,200 μ g/mL, the test result was considered negative.

Measuring HRQoL

The AQLQ is a 32-item disease-specific questionnaire that has been well validated to measure the problems that adult patients with asthma experience in their daily lives.⁵ Patients are asked to indicate on a 7-point scale (1 indicating maximum impairment and 7 indicating no impairment) how they

have been during the previous 2 weeks. The items are grouped into 4 domains: activity limitation (11 items), symptoms (12 items), emotional function (5 items), and environmental stimuli (4 items). Global and domain scores result from summing across equally weighted items. Higher scores indicate better QoL. A score of 0.5 (global and in each domain) has been demonstrated to correspond to the minimal important difference of QoL, and a score of 1 corresponds to a moderate change.¹⁰ In this study, we used the validated Italian version of the questionnaire.

Statistical Analysis

Descriptive statistics were computed as mean and standard deviation for continuous variables, or as median and 25th and 75th percentiles if the distribution was skewed, and as absolute frequency and percentage for categorical variables. For the primary end point, QoL scores in patients with no sensitivity or monosensitivity vs polysensitivity on skin prick testing were compared using the Mann-Whitney *U* test. The mean differences in scores between the 2 groups were computed, together with their 95% confidence intervals. For secondary end points, the Spearman *R* was computed to measure the strength of the association of pulmonary function or PD₂₀ with QoL. Nonparametric analysis of variance (the Kruskal-Wallis *U* test) was used to compare QoL scores across BHR categories. A statistical software program (Stata 8; StataCorp, College Station, TX) was used for computation. A 2-sided *P* < .05 was considered statistically significant. Bonferroni correction for multiple end points was used. The Spearman correlation coefficient between AQLQ and number of sensitivities was computed.

Table 2. AQLQ Scores According to Polysensitivity at Skin Prick Testing*

AQLQ	No sensitivity or monosensitivity (n = 49)	Polysensitivity (n = 136)	Mann-Whitney U test P value
Global	4.76 (3.72-6.03)	3.98 (3.28-5.10)	.003
Symptoms score	4.50 (3.50-5.92)	3.75 (2.92-4.78)	.007
Emotional function score	5.60 (3.80-6.80)	4.40 (3.37-5.80)	.002
Environmental stimuli score	5.00 (3.75-7.00)	4.00 (3.25-5.50)	.002
Activity limitation score	4.67 (3.73-6.00)	4.05 (3.45-4.87)	.005

Abbreviation: AQLQ, Asthma Quality of Life Questionnaire.

*Data are given as median (25th-75th percentile).

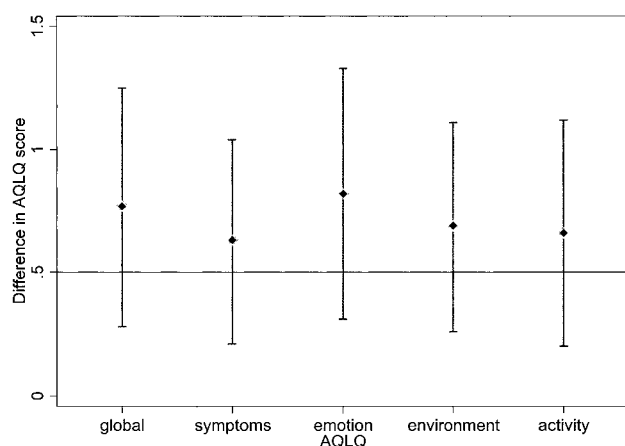


Figure 1. Mean differences in Asthma Quality of Life Questionnaire (AQLQ) scores in patients with no sensitivity or monosensitivity vs polysensitivity on skin prick testing. The horizontal line at 0.5 indicates the minimal important difference. Error bars represent 95% confidence intervals.

RESULTS

Demographic Data

The presenting characteristics of the participants are summarized in Table 1. Thirteen participants reported smoking habits. Only 7 patients with asthma had negative findings on skin prick testing, and almost 75% of the participants showed polysensitivity. Pulmonary function indices were within the reference ranges. More than half of the patients showed moderate-to-severe BHR. The AQLQ scores were comparable in the emotional function, environmental stimuli, and activity limitation domains but were lower in the symptoms domain. Median scores greater than 4 indicated a sufficiently good, although not optimal, HRQoL.

Quality-of-Life Assessment

The AQLQ scores, overall and in the 4 explored domains, were significantly lower in patients with polysensitivity vs those without sensitivity or with 1 sensitivity (Table 2). Furthermore, the size of the difference in scores between the 2 groups was of clinical interest (from minimal importance to moderate change in QoL) for the global score and for each domain (Fig 1). A median of 3 sensitivities per patient were

recorded (range, 0–8). We observed a significant, although weak, inverse correlation between the number of sensitivities and the AQLQ score overall and for each domain (Spearman R , 16%–20%; $P \leq .01$ for all).

The association between pulmonary function, as measured by forced vital capacity, FEV₁, and forced expiratory flow between 25% and 75%, and AQLQ score is summarized in Table 3. Correlation coefficients (Spearman R) were in all cases irrelevant, with maximum values of approximately 17%, pointing to a lack of association, although occasionally some statistical significance is obtained (but it disappeared after Bonferroni correction for multiple end points). The relationship between BHR and AQLQ scores was also of modest relevance (Table 3). Furthermore, when considering the 4 categories of BHR, patients with increasing reactivity seemed to have similar AQLQ scores.

DISCUSSION

Health-related QoL has become one of the most relevant outcome measures in patients with asthma because many clinical studies and trials include an HRQoL evaluation.¹¹ Specific questionnaires have been considered appropriate in asthma, including the AQLQ developed by Juniper et al,^{5,10,12} which showed great responsiveness in several studies.

In the present study, we evaluated the relationships among HRQoL and sensitization, respiratory function, and BHR in a group of young men with intermittent asthma. The fact that all the participants were young men might partially reduce the global value of the results, although the sample was sufficiently large. Also, we considered only patients with intermittent asthma because a secondary outcome was to evaluate the relationship between HRQoL and BHR. Thus, we had to enroll only individuals suitable for methacholine challenge, ie, those with normal pulmonary function.

The present findings suggest some considerations. First, almost all the patients were allergic, confirming previous results in children and young adults.¹³ Second, AQLQ scores showed suboptimal HRQoL, mainly concerning symptoms, despite normal pulmonary function. In fact, although these individuals had a diagnosis of intermittent asthma and underwent symptomatic therapy only, they showed impaired HRQoL. This aspect highlights the importance of HRQoL

Table 3. Association of Pulmonary Function and Bronchial Hyperreactivity With AQLQ Scores

	Global score		Symptoms score		Emotional function score		Environmental stimuli score		Activity limitation score	
	Spearman R, %	P value	Spearman R, %	P value	Spearman R, %	P value	Spearman R, %	P value	Spearman R, %	P value
FVC	9.0	.22	8.6	.25	11.1	.13	9.3	2.1	9.9	.18
FEV ₁	9.4	.02	10.9	.14	10.0	.18	10.0	.18	7.1	.34
FEF ₂₅₋₇₅	14.7	.046	16.4	.03	14.1	.06	13.3	.07	9.4	.20
PD ₂₀	15.0	.04	17.6	.02	16.6	.02	17.3	.02	4.5	.54

Abbreviations: AQLQ, Asthma Quality of Life Questionnaire; FEF₂₅₋₇₅, forced expiratory flow between 25% and 75%; FEV₁, forced expiratory volumes in 1 second; FVC, forced vital capacity; PD₂₀, provocation dose of methacholine sufficient to induce bronchial hyperreactivity.

evaluation in patients with normal spirometric values who manifest few symptoms.

Furthermore, sensitization to multiple allergens is significantly associated with worse HRQoL. This issue may be explained by the concept that polysensitized individuals are continuously exposed to the causal allergen. Allergic inflammation is strictly related to allergen exposure, as demonstrated by the concept of minimal persistent inflammation.¹⁴ Thus, it is reasonable to hypothesize that polysensitized patients with asthma are more inflamed than monosensitized patients, who are less exposed to allergen throughout the year. Therefore, the present findings provide the first evidence that HRQoL also depends on polysensitization in intermittent asthma. On the other hand, we did not find evidence of a significant relationship between pulmonary function or BHR and HRQoL. Note that our patients were mildly asthmatic because all of them had normal pulmonary function and underwent symptomatic treatment only. Furthermore, BHR is independent of allergic inflammation.¹⁵ Thus, it seems that HRQoL may be associated with polysensitization only in intermittent asthma. In conclusion, this study provides the first evidence that HRQoL is associated with polysensitization in intermittent asthma and underlines the importance of evaluating this issue when managing young patients with slight respiratory symptoms.

ACKNOWLEDGMENTS

We thank Professor E. F. Juniper for her kind and fruitful cooperation and for permission to use the AQLQ.

REFERENCES

1. Van Cauwenberg P. Advances in allergy management. *Allergy*. 2002;57:29–36.
2. Gerth van Wijk R. Allergy: a global problem: quality of life. *Allergy*. 2002;57:1097–1110.
3. Orr LC, Fowler SJ, Lipworth BJ. Relationship between changes in quality of life of lung function and bronchial hyperresponsiveness during high-dose inhaled corticosteroid treatment. *Am J Respir Med*. 2003;2:433–438.
4. Riccioni G, D'Orazio N, Di Ilio C, et al. Bronchial hyperresponsiveness and quality of life in asthmatics. *Respiration*. 2003;70:496–499.
5. Juniper EF, Guyatt GH, Ferrie PJ, Griffith LE. Measuring quality of life in asthma. *Am Rev Respir Dis*. 1993;147:832–838.
6. Global Initiative for Asthma. *Pocket Guide for Asthma Management and Prevention*. Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health; 1997. NIH publication 96–3659B.
7. EAACI Subcommittee on Skin Tests. Skin tests used in type I allergy testing. *Allergy*. 1989;44(suppl 10):22–31.
8. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault J-C. Standardized lung function testing. *Eur Respir J*. 1993;6:1–99.
9. Ciprandi G, Cirillo I, Tosca MA, Vizzaccaro A. Bronchial hyperreactivity and spirometric impairment in patients with seasonal allergic rhinitis. *Respir Med*. 2004;98:826–831.
10. Juniper EF, Guyatt GH, Willan A, Griffith LE. Determining a minimal important change in a disease specific quality of life questionnaire. *J Clin Epidemiol*. 1994;47:81–87.
11. Blaiss MS. Outcomes analysis in asthma. *JAMA*. 1997;278:1874–1880.
12. Juniper EF, Guyatt GH, Epstein RS, Ferrie PJ, Jaeschke R, Hiller TK. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trial. *Thorax*. 1992;47:76–83.
13. Ciprandi G, Vizzaccaro A, Cirillo A, Tosca MA, Passalacqua G, Canonica GW. Underdiagnosis and undertreatment of asthma: a nine-year study on Italian conscripts. *Int Arch Allergy Immunol*. 2001;125:211–215.
14. Ciprandi G, Buscaglia S, Pesce GP, et al. Minimal persistent inflammation is present at mucosal level in asymptomatic rhinitic patients with allergy due to mites. *J Allergy Clin Immunol*. 1995;96:971–979.
15. Crimi E, Spanevello A, Neri M, Ind PW, Rossi GA, Brusasco V. Dissociation between airway inflammation and airway hyperresponsiveness in allergic asthma. *Am J Respir Crit Care Med*. 1998;157:4–9.

Requests for reprints should be addressed to:

Giorgio Ciprandi, MD
Allergologia - U.O. ORL
Dipartimento Regionale Testa-Collo
Padiglione Specialità (piano terzo)
Ospedale San Martino
Largo R. Benzi 10
16132 Genoa, Italy
E-mail: gio.cip@libero.it