Health-related quality of life predicts onset of asthma in a longitudinal population study

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Summary
Background: Health-related quality of life (HRQL) has been increasingly used as an outcome measure in asthma, but less is known about the prognostic implication of low health-related quality of life. The purpose of this study was to investigate if a set of quality of life measures could predict onset of asthma.

Methods: In the baseline study 391 subjects without asthma answered a respiratory questionnaire and the Gothenburg Quality of Life (GQL) instrument in 1990. The GQL questionnaire included two parts: (1) the prevalence of HRQL-related symptoms and (2) well-being scores for physical, mental and social dimensions. The participants were also investigated with spirometry and allergy testing. In 2003, the same respiratory questionnaire that had been used in 1990 was sent. There were 290 responders, of whom 22 subjects had developed asthma.

Results: Participants who had developed asthma by the follow-up had a higher prevalence of sleep disturbances (30% vs. 10%), problems with chest pain (16% vs. 2%), depression (40% vs. 20%) difficulty relaxing (40% vs. 13%) and constipation (25% vs. 2%) at baseline than participants who did not develop asthma (p < 0.05). Subjects who developed asthma also scored significantly lower on well-being variables as sleep, energy, mood, patience, memory, appetite, fitness and sense of appreciation outside home. These differences remained after adjusting for age, sex, smoking habits, asthma heredity, socioeconomic groups and building dampness.

Conclusion: Participants with low health-related quality of life at baseline were more likely to report having developed asthma 12 years later.

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HRQL predicts onset of asthma

Introduction

Health-related quality of life (HRQL) assessment as a measure of clinical and therapeutic outcome has been increasingly used as an outcome measure in chronic respiratory disease, especially in asthma. In contrast to conventional indicators of the disease and its objective outcomes, HRQL focuses on the patients’ own assessments. Both disease-specific and generic measures of HRQL have been developed to quantify the experience individuals have with their health.

The prevalence of asthma has increased worldwide and with the increased prevalence of asthma in the western world, it is of great importance to describe factors that contribute to the onset of the disease in order to make it possible to identify assessments to promote health and accordingly minimize the human suffering due to asthma.

Furthermore, finding risk factors that may be influential could lead to reducing the financial burden that the disease accounts for in today’s society.

A longitudinal study on asthma prevalence and incidence was performed in two counties of Sweden in 1990–2003. The Gothenburg Quality of Life Instrument (GQL) was included in the 1990 measurement. The GQL is a generic measure that has been used in previous studies when, for example, estimating the impact of different health-related risk factors on the onset of cardiovascular disease, diabetes, and Sjögren’s syndrome. Several studies have shown that a low HRQL is related to increased risk of mortality, hospitalization and emergency department utilization in patients with asthma and chronic obstructive pulmonary disease. In the present study the hypothesis was that a low health-related quality of life is related to asthma onset.

Material and methods

This is a longitudinal study with an epidemiological design including a baseline measure in 1990 and a follow-up in 2003.

Study area

This study includes participants from two counties in Sweden, Jämtland and Gävleborg. The total area of Jämtland is approximately 30,000 km². The western part, bordering Norway, is mountainous, while the central and eastern parts contain more farming areas, forests and watercourses. Jämtland’s climate is cold, with a mean January temperature of −8 to −15 °C in January and a mean July temperature varying from 12 to 15 °C. Gävleborg is situated on the Baltic coast at low altitude and covers 4200 km². The mean temperature in January is −5 °C and the mean July temperature 17 °C.

Study sample

In the 1990 baseline study, subjects were selected from the responders to a postal respiratory questionnaire sent to three different age groups: all individuals aged 16 years, and a random selection of the age groups of 30–39 years and 60–69 years, aiming at reaching 13% of each group. In Jämtland 6149 and in Gävleborg 6583 individuals were included. A total of 11294 subjects (89%) answered the questionnaire.

In a second phase all subjects who reported a history of asthma, chronic bronchitis or respiratory symptoms were invited for a clinical investigation including spirometry, allergy testing and assessment of HRQL using the GQL questionnaire. In addition a random selection of 600 subjects without a history of respiratory diseases and respiratory symptoms were also invited to this phase of the investigation. The present analysis is based on the 391 subjects without respiratory symptoms that completed the GQL questionnaire (Fig. 1). Of these 86 were excluded as the clinical investigation indicated a presence of asthma or other lung disease.

In 2003, 290 of the 391 subjects without respiratory diseases or symptoms at baseline completed a postal respiratory questionnaire with similar questions as in 1990 (Fig. 1). In addition, there was a question on occupation in 2003, that was used for socioeconomic grouping.

Measurements

Respiratory questionnaire 1990 and 2003

The respiratory questionnaire used was based on the British Medical Research Council questionnaire, later modified and used in earlier studies in northern Sweden. The questionnaire consists of 22 items including questions on: previous history of asthma or chronic bronchitis; use of anti-asthmatic medication; physician’s diagnosis of asthma, chronic bronchitis, or emphysema; attacks of dyspnoea, shortness of breath or breathlessness; wheezing in the chest; and prolonged productive cough and smoking.

Health-related quality of life 1990

To assess subjective well being, the Gothenburg Quality of Life instrument (GQL) was used. The instrument was constructed as early as 1972 and is based on the definition of health by WHO. Part one of the instrument covers 30 common symptoms answered by ‘yes’ or ‘no’ to questions on whether the respondents had experienced any of the symptoms during the last 3 months. Part two of the instrument includes 18 items covering subjective physical, mental and social well being. The respondent is to answer each item on a seven-step Likert scale ranging from ‘very bad’ (=1) to ‘excellent/could not be better’ (=7) thus a high score indicates a better HRQL. GQL has been validated using a Swedish sample.

Clinical measurements 1990

The clinical measurement consists of spirometry, allergy testing and recording of PEF variability.

Lung function was tested with pneumotachographs (Vitalograph Alpha, London, England). Vital capacity (VC) and forced expiratory volume in 1 s (FEV₁) were tested. The ATS (American Thoracic Society 1987) recommendations for spirometric testing were followed, except that the Vitalographs were calibrated once daily with a 1-L syringe, as suggested by the ATS. Diagnoses were based on the criteria suggested by the ATS.

A skin prick test was performed using Phazet (Pharmacia Diagnostics, Uppsala, Sweden), which are stainless lancets.
pre-coated with allergen extracts from the Nordic panel of 10 common allergens. Lancets with allergen were applied on the skin inside the forearm. A skin test was said to be positive if the mean wheal diameter was greater than 3 mm.

**Socioeconomic grouping 2003**
Reports of the respondents’ current occupations were divided into five socioeconomic groups: (1) managers and professionals (i.e. legislators, senior officials, managers and professionals); (2) other non-manual (i.e. technicians and associate professionals, clerks, service workers and market sales workers); (3) skilled manual (i.e. skilled agricultural and fishery workers and craft and related trades workers); (4) semi-skilled or unskilled manual (i.e. plant and machine operators and assemblers and elementary occupations); and (5) unclassifiable or unknown (i.e. housewife, student, not classifiable job, unemployed, not working because of poor health, and retired). A Swedish classification of occupations based on the International Standard Classification of Occupations (ISCO-88) and the European Union variant of ISCO-88 was used.

**Definitions**

**Definition of asthma**
From the respiratory questionnaire in the follow-up 2003 four questions were chosen in order to estimate onset of asthma. These are: Have you had or do you have asthma? Has your doctor diagnosed asthma? Do you use any asthma medicine? and Do you have or have you had asthma symptoms (attack of difficulty breathing or breathlessness, with or without cough, with or without wheeze in the chest). The respondents were judged to have had an onset of asthma if they answered yes to one or more of these questions concerning asthma.

**Definition asthma heredity**
Participants answering "yes" to the question: "Do your parents, sibling or children have asthma?" in 1990 are referred to as having asthma heredity.

**Statistical analysis**
The SPSS 14.0 software program was used for statistical analyses. The Chi-squared test was used to compare the prevalence of GQL symptoms, and the Mann–Whitney U-test to compare GQL symptom scores in participants who developed or did not develop asthma during the follow-up period. The association between asthma onset and clinical measures was tested for with an unpaired t-test. Multivariate logistic regression was used to test if the association between GQL symptoms and asthma onset remained statistically significant after adjusting for potential confounders: age, sex, smoking habits, asthma heredity, and socioeconomic groups and building dampness in home.
Ethical approval

The study was approved by Ethics Committee at the University of Umeå (x222, 1989-12-12) and the Ethics Committee, Faculty of Medicine, Uppsala (Dnr. 01-313).

Results

Twenty-two subjects had developed asthma during the follow-up period (Fig. 1). Subjects who had developed asthma had more asthma in the family compared to non-asthmatic subjects, but otherwise no significant differences were found between the groups regarding baseline characteristics (Table 1).

The prevalence of HRQL symptoms in subjects who developed or did not develop asthma is presented in the polar diagram (Fig. 2). Participants who had developed asthma by the follow-up study had a higher prevalence of most of the HRQL symptoms. A statistically significant difference between those who developed asthma and those who did not was found for sleep disturbances, chest pain, difficulty relaxing, depression and constipation. This difference remained statistically significant after adjusting for age, sex, smoking habits, asthma heredity, socioeconomic groups and building dampness.

Analysis of the non-responders

Non-responders (n = 68) were more likely to belong to the youngest age group (56% vs. 30%, p < 0.001) than subjects who answered the follow-up questionnaire. No significant differences were found regarding sex, smoking habits, asthma heredity, atopy, respiratory symptoms and spirometry results. Non-responders reported significantly less general fatigue (21% vs. 35%, p < 0.05) than responders were as no significant differences were found regarding the GQL well-being scale.

Discussion

In this longitudinal study of quality of life, several symptoms such as sleep disturbances, difficulty to relax and chest pain were significantly increased in subjects who subsequently developed asthma. The subjects who developed asthma during the study period also scored significantly lower on several well-being variables at baseline. This indicates that early undiagnosed or pre-clinical asthma affects quality of life or that poor quality of life makes it more likely that a diagnosis of asthma is made. An alternative explanation is that low quality of life is an independent predictor of asthma onset.
Sleep disturbances were significantly more common in subjects who developed asthma during the study period. Previous studies have shown that sleep disturbances, awakenings and daytime sleepiness are common among patients with asthma.22 This is also in line with findings that inadequately controlled allergic rhinitis18 is related to impaired sleep since asthma and rhinitis often coexists. Another possible explanation may be that nocturnal gastroesophageal reflux which is common in asthma23 is a predictor of low quality of sleep.24 It has also been proposed that occult obstructive sleep apnoea is a more common cause of sleepiness in asthmatics than asthma itself.22 Poor sleep has a detrimental impact on daily functioning and quality of life even in healthy people. Sleep disturbances make people more susceptible to cognitive impairment such as poor memory decreased learning abilities and weakened concentration. Also, psychological consequences such as fatigue, irritability, anxiety and depression are present in such situations.27

Symptoms including depression, difficult to relax, difficult in passing urine, constipation, and loss of weight was also significantly more prevalent in subjects who developed asthma. There are several studies showing relationships between depression, anxiety and insomnia.25 These results are also in accordance with other studies showing that depressive symptoms are common in adults with asthma and are associated with poorer health outcome.27 Furthermore, there appears to be a high comorbidity of anxiety disorders in patients with asthma.26,33,34 Whether these psychological aspects precede onset of asthma or are a consequence of living with asthma, the main objectives of health care should be to give support aimed at preserving a satisfactory level of HRQL. Further HRQL should be taken into account as part of the clinical evaluation in asthmatics.

Individuals who developed asthma scored significantly lower on several well-being variables, than subjects who remained free of asthma. This negative effect on well being may be consequence of living with undiagnosed asthma. Alternatively these well-being variables might be related to stress. Environmental stressors may impact asthma morbidity through neuro-immunological mechanisms, which are adversely impacted and/or buffered by social network, social support and psychological functioning.29 The impact of stress on airflow in asthmatics is, however, unclear.30 The use of coping and differences coping style may be a valuable tool in handling stress and asthma.28,31 In the Lazarus transactional model of stress, when facing a stressful situation each individual sets up specific adjustment strategies called coping styles.32 This includes a meaningful pattern of cognitive, behavioural, emotional and physical responses. The use of active coping styles can perhaps be valuable in handling stress and asthma. This hypothesis remains to be tested. Nevertheless, with individuals at risk for asthma, health care providers can teach and support them in health behaviours, stress management and coping in order to improve health.
The strengths of this study are the longitudinal design, the selection of subject and the validated instrument used in several studies. It is also strength in that the criteria for new cases of asthma were carefully defined. The usefulness of the GQL assessment is determined by the predictive powers of the variables. Further, the GQL instrument has been used in several studies exploring HRQL in a variety of health conditions such as diabetes, cardiovascular disease and Sjögren’s syndrome. The weakness of this study is that the group with asthma onset was rather small and that the GQL measurement was performed only at baseline. Furthermore asthma onset was only assessed by questionnaire with no clinical validation. The optimal situation would have been a follow-up with both a clinical examination and the GQL instrument also in 2003.

Generic measures on health-related quality of life have been used in a variety of studies to investigate possible predictive factors. There is evidence that a generic measure may be more valuable/valid measure than, for example, an asthma-specific health-related quality of life measure in the search for predictive factors. On the other hand, asthma-specific measures are more likely to reflect small changes in asthma status, providing greater responsiveness over time. Generic instruments are broader and reflect the impact of asthma on more global aspects of functioning and well being. Generic instrument has also been used as a predictive tool in respiratory obstructive disease.

In conclusion, subjects who developed asthma had a higher prevalence of HRQL-related symptoms such as sleep disturbances, depression, difficulty relaxing and chest pain and scored significantly lower on several well-being variables at baseline. This indicates that early undiagnosed or pre-clinical asthma affects quality of life or that poor quality of life makes it more likely that a diagnosis of asthma is made. An alternative explanation is that low quality of life is an independent predictor of asthma onset.

**Conflict of interest statement**

These data will not be submitted elsewhere during the review process and they have not previously been published elsewhere. There is no conflict of interest in connection with this paper.

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**Reference**


