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ORIGINAL RESEARCH

What lies behind relief and worsening of asthma symptoms? A register-based study of adults with asthma and other chronic obstructive pulmonary diseases in Finland

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Received 23 January 2006; accepted 17 July 2006

KEYWORDS

Asthma symptoms;
Chronic obstructive
pulmonary disease;
Daily life;
Life changes;
Psychosocial factors

Summary

Aims: To examine how subjects with relief or worsening of asthma symptoms differ in terms of gender, age, severity and duration of asthma, comorbidity, and difficulties with medication and daily life.

Methods: A postal inquiry among a sample of 6000 adults with clinically diagnosed asthma and/or other chronic obstructive pulmonary diseases.

Results: Relief of asthma symptoms over a 12-month period was associated with a recent asthma diagnosis, within five years, in both sexes. Lack of current smoking and lack of problems in using anti-asthmatic treatment were associated with a positive outcome in men, and mild asthma and living alone associated with a positive outcome in women. Severe and moderate asthma predicted worse symptoms in both sexes, as did other obstructive pulmonary diseases, living alone, and medication problems amongst men.

Conclusions: Patients with asthma should be cared for comprehensively, requiring consideration of both clinical and psychosocial factors that can modify the course of the disease.

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Introduction

The aims of asthma treatment are to achieve complete recovery in as many patients as possible, particularly those showing early symptoms of the disease, and to prevent later worsening [1]. Inhaled corticosteroids play a major part in this [1,2], but environmental circumstances [3,4], smoking [5,6] and psychosocial and emotional factors [7–9] may also have an effect on the frequency of symptoms.

For most asthma patients the symptoms remain unchanged, but some experience relief and some a worsening of their symptoms [2]. We set out to assess by means of a questionnaire how the two groups of patients – those who experience relief vs. those who experience worsening of their symptoms – differ in terms of the duration of their asthma, comorbidity, smoking, medication problems and difficulties in daily life. Our aim was to help clinicians assess changes in patients' symptoms from a wider perspective than simply the response to medical therapy alone.

Materials and methods

Setting

The Finnish Social Insurance Institution (SII) maintains a nation-wide register of patients with certain chronic diseases who are entitled to a special refund on medication-related expenses. This register provides a good database for surveys and epidemiological studies. Inclusion presupposes that the patient's condition meets certain diagnostic and severity criteria as verified by a physician. The criteria for a special refund for anti-asthma medicines are:

- the need for regular anti-asthmatic medication for over six months, combined with
- an increase of $\geq 15\%$ in peak expiratory flow (PEF) or forced expiratory volume in 1 second (FEV1) in a bronchodilation test (≥ 50 l/min or ≥ 0.15 l in adults); or
- a decrease of $\geq 15\%$ in PEF or FEV1 during a physical strain test (≥ 50 l/min or ≥ 0.15 l in adults); or
- fluctuation of $>20\%$ from the peak value in 24-hour PEF monitoring (≥ 50 l/min in adults).

In addition to asthma, subjects with other chronic obstructive pulmonary diseases such as chronic bronchitis, COPD, and emphysema, may be entitled to a special refund if bronchodilator medication increases their PEF or FEV1 by approximately the same extent as in asthma.

For severe obstructive diseases there are specific inclusion criteria:

- FEV1 $<40\%$ predicted; or
- arterial blood CO₂ pressure permanently >6.5 kPa.

A total of 156 755 subjects aged 16 years or over were entitled to the special 75% refund on medicines for chronic asthma and similar chronic obstructive pulmonary diseases in the year 2000. A nationally representative systematic sample of 6000 subjects was drawn from this population, excluding patients in permanent institutional care. The sampling procedure has been described in detail earlier [2].

Questionnaire

A self-administered questionnaire was sent to the sample subjects in May 2000. From the 16 items of the form analysed here nine originated from previous Finnish studies [7,10,11].

The subjects were asked to report their clinical pulmonary diagnoses (alternatives: bronchial asthma/chronic bronchitis/COPD/emphysema) and the year in which asthma had been diagnosed. In addition they were asked to estimate the severity of their symptoms (mild/moderate/severe) and to report changes in the frequency of their symptoms over the past 12 months (considerably increased/moderately increased/no change/moderately decreased/considerably decreased). In the final analyses the alternatives "considerably" and "moderately" were combined.

The subjects were asked whether they had any other chronic illness besides pulmonary diseases, such as clinically diagnosed allergies, cardiovascular or mental disorders, and whether they had recently had any long-lasting feelings of melancholy or depression.

The subjects were asked about their smoking, the alternatives being: "I have never smoked"; "I smoked regularly, but stopped"; "I smoke occasionally"; and "I smoke regularly". The latter two groups were classified as "current smokers". They were also asked to report passive smoking and to say whether they had been exposed to any other substances or factors likely to aggravate their respiratory symptoms (yes/no/can't say) – see Table 1. Exposure was recorded if at least one of the substances or factors was reported. The subjects also indicated whether they lived alone or with someone, and whether they had any domestic pets.

The subjects estimated how well they coped with five defined aspects of anti-asthmatic

Table 1 Subjects, characteristics of their asthma and prevalence of other chronic diseases and exposures, by changes in asthma symptoms

	Asthma symptoms			p values [#]
	Relieved Number of subjects (%)	Stable Number of subjects (%)	Worse Number of subjects (%)	
Sex				<0.001
Men	396 (22.9)	1035 (59.9)	298 (17.2)	
Women	855 (30.3)	1420 (50.3)	546 (19.4)	
Age, years				0.002
16–44	379 (29.6)	711 (55.5)	191 (14.9)	
45–64	473 (26.5)	964 (54.0)	348 (19.5)	
≥65	398 (26.8)	780 (52.6)	306 (20.6)	
Severity of asthma				<0.001
Mild	929 (36.4)	1460 (57.1)	166 (6.5)	
Moderate	288 (17.3)	878 (52.8)	497 (29.9)	
Severe	22 (7.6)	94 (32.4)	174 (60.0)	
Years since asthma clinically diagnosed				<0.001
<2	218 (52.8)	130 (31.5)	65 (15.7)	
2–5	286 (31.3)	457 (50.1)	170 (18.6)	
6–19	435 (22.6)	1112 (57.9)	375 (19.5)	
≥20	236 (25.1)	546 (58.0)	159 (16.9)	
Other chronic obstructive pulmonary diseases in addition to asthma [*]				<0.001
No	1069 (28.8)	2058 (55.5)	580 (15.6)	
Yes	160 (21.1)	355 (46.8)	244 (32.1)	
Clinically diagnosed allergies				0.006
No	423 (28.7)	745 (50.5)	307 (20.8)	
Yes	744 (27.0)	1525 (55.3)	487 (17.7)	
Cardiovascular disorders				<0.001
No	847 (29.1)	1587 (54.6)	472 (16.2)	
Yes	474 (24.6)	868 (52.8)	373 (22.7)	
Mental disorders				<0.001
No	1199 (27.7)	2352 (54.3)	781 (18.0)	
Yes	52 (23.7)	103 (47.0)	64 (29.2)	
Self-expressed depression				<0.001
No	771 (28.7)	1494 (55.6)	424 (15.8)	
Yes	402 (25.0)	823 (51.1)	385 (23.9)	
Smoking status				<0.001
Never	658 (28.7)	1261 (55.1)	371 (16.2)	
Former smoker	307 (25.6)	619 (51.7)	271 (22.6)	
Current smoker	255 (26.2)	525 (54.0)	193 (19.8)	
Environmental exposures				0.026
No	106 (27.9)	225 (59.2)	49 (12.9)	
Tobacco smoke	347 (27.8)	689 (55.1)	214 (17.1)	
Other substances/factors [§]	111 (23.6)	261 (55.5)	98 (20.9)	
Domestic pets				0.413
No	971 (26.9)	1950 (54.1)	686 (19.0)	
Yes	248 (28.9)	460 (53.6)	151 (17.6)	

[#] Statistical significance calculated for the distribution with Pearson Chi-squared test.

^{*} Chronic bronchitis/chronic obstructive pulmonary disease (COPD)/emphysema.

⁺ Hypertension/coronary heart disease.

[§] Dust/solvent vapours or gasses/cold air or frost/physically strenuous work/mentally strenuous work.

Table 2 Difficulties in anti-asthmatic medication and in daily life in subjects with changes in asthma symptoms

Difficulties in anti-asthmatic medication	Change in asthma symptoms in the past 12 months		
	Relieved Number of subjects (%)	Worse Number of subjects (%)	95% Confidence Intervals for the difference %-points
Taking of anti-asthmatics out of doors	212 (22.2)	225 (32.2)	5.6–14.4
Inhaling anti-asthmatics correctly	81 (8.2)	104 (14.5)	3.2–9.4
Use of inhalation devices	28 (3.1)	59 (8.9)	3.4–8.3
Understanding medication instructions	41 (4.1)	63 (9.2)	2.6–7.6
Taking anti-asthmatic medicines regularly	280 (26.8)	217 (29.7)	–1.4–7.2
Difficulties in daily life	Change in asthma symptoms in the past 12 months		
	Relieved Number of subjects (%)	Worse Number of subjects (%)	95% Confidence Intervals for the difference %-points
Participating in public events	517 (52.4)	550 (79.4)	22.7–31.3
Travelling by public transport	470 (47.8)	478 (72.0)	19.6–28.8
Visiting and going to parties, or formal celebrations	593 (62.0)	508 (81.7)	15.4–24.0
Hotel accommodation	340 (39.4)	294 (57.9)	13.1–23.9
Dining in cafeterias and restaurants	186 (23.3)	174 (36.6)	8.1–18.5

95% Confidence Intervals for the differences (%-points) between worsened and relieved asthma symptoms.

medical therapy – as listed in Table 2 (major problems/minor problems/no problems/no experiences). In the final analyses a ‘difficulty’ was considered to be present if subjects reported major or minor problems in any of these aspects and the total numbers of such cases of difficulties were counted.

The self-estimated impact of asthma on daily life and managing life in defined life situations, as in Table 2, was assessed by means of a separate question. The items ‘‘visiting and going to parties’’ and ‘‘formal celebrations’’ were evaluated separately in the questionnaire, and the responses were combined in the final analyses. Of the alternatives ‘‘very’’, ‘‘rather’’, ‘‘not at all difficult’’ and ‘‘no experiences’’, a difficulty was considered to be present in the first two cases.

The self-estimated impact of defined life situations on the therapeutic equilibrium of asthma, irrespective of when they occurred, were ascertained in a separate series of questions (alternatives: relieved/worsened/no impact or indifferent/no experiences) – see Figure 1. Only the subjects that experienced these were included in the analyses.

Statistical methods

The data were analysed using the SPSS 12.0 software package. Statistical significances were calculated with the Pearson Chi-squared test and a *p*-value <0.05 was considered significant.

Binary logistic regression analyses were performed to determine the influence of various

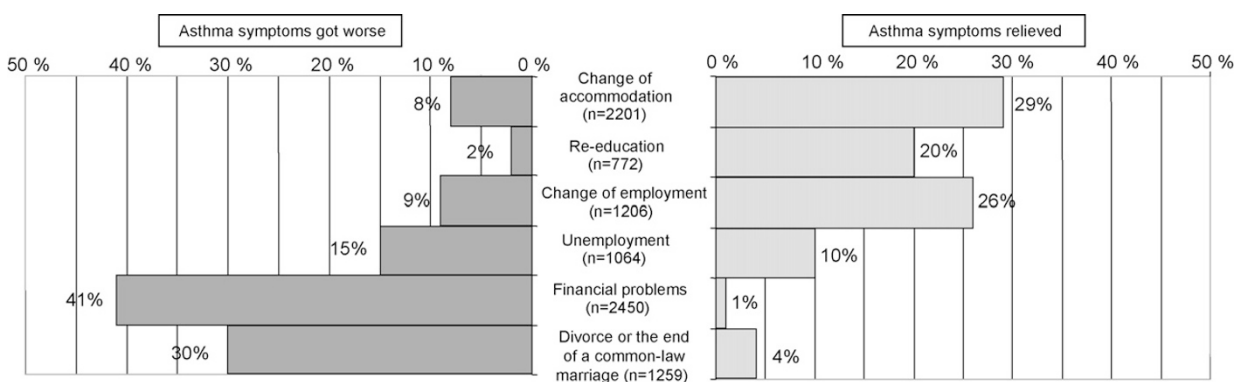


Figure 1 Impact of given life situations on asthma symptoms. Percentages (%) of subjects with relieved or worsened asthma symptoms among those concerned (n).

Table 3 Independent predictors of changes in asthma symptoms among men and women, determined in a multivariate model created by means of logistic regression analysis (method = forward)

	Asthma symptoms relieved		Asthma symptoms worse	
	Men (n = 777)	Women (n = 1306)	Men (n = 731)	Women (n = 1127)
	Odds Ratio and 95% Confidence Intervals	Odds Ratio and 95% Confidence Intervals	Odds Ratio and 95% Confidence Intervals	Odds Ratio and 95% Confidence Intervals
Age, years				
16–44				1.00
45–64				0.73 (0.52–1.03)
≥65				0.48 (0.32–0.74)
Living status				
Lives with someone		1.00	1.00	
Lives alone		1.45 (1.11–1.90)	1.80 (1.11–2.90)	
Years since asthma diagnosis				
<2	5.00 (2.78–8.99)	6.39 (4.01–10.18)		
2–5	1.80 (1.08–2.99)	2.10 (1.44–3.05)		
6–19	1.02 (0.65–1.60)	1.23 (0.87–1.75)		
≥20	1.00	1.00		
Other chronic obstructive pulmonary diseases in addition to asthma [#]				
No			1.00	
Yes			1.84 (1.17–2.92)	
Severity of asthma				
Mild		4.49 (1.44–14.08)	1.00	1.00
Moderate		2.81 (0.89–8.93)	4.39 (3.12–7.62)	5.15 (3.73–7.11)
Severe		1.00	13.77 (7.08–26.80)	18.11 (10.13–32.35)
Self-estimated problems in anti-asthmatic medication				
No	1.71 (1.19–2.45)		1.00	
At least one problem	1.00		1.55 (1.06–2.28)	
Clinically diagnosed allergies				
No				1.00
Yes				0.64 (0.46–0.87)
Self-expressed depression				
No	1.00			1.00
Yes	1.48 (1.03–2.13)			1.56 (1.17–2.08)
Smoking status				
Never	1.83 (1.17–2.87)		1.00	
Former smoker	1.71 (1.10–2.66)		1.23 (0.77–1.99)	
Current smoker	1.00		0.55 (0.32–0.95)	

Adjusted Odds Ratios and 95% Confidence Intervals using age, living status, years since asthma diagnosis, other chronic obstructive respiratory diseases in addition to asthma, self-estimated severity of asthma, problems in anti-asthmatic medication, clinically diagnosed allergies, cardiovascular disorders, mental disorders, self-expressed depression, and smoking status as covariates.

[#] Chronic bronchitis/chronic obstructive pulmonary disease (COPD)/emphysema.

covariates separately in relieving or worsening asthma symptoms. Subjects reporting either of these changes, men and women separately, were compared with those reporting a stable condition. The covariates included in the final forward stepwise analysis are listed in Table 3. The other variables tested, such as environmental exposures and inhaled corticosteroid therapy, were not statistically significant and were excluded from the final series.

Statistically significant factors are presented as adjusted Odds Ratios (OR), together with their 95% Confidence Intervals (95% CI).

Analysis of non-response

Altogether 4956 subjects (82.6%), 85.1% of the women and 78.5% of the men, responded to the questionnaire. Subjects aged 45 years or over were slightly over-represented in the final material. The

frequency of special refunds for medication for major chronic diseases other than asthma in the SII register was of the same magnitude among the respondents and non-respondents.

The proportion of missing answers to the questions on self-estimated difficulties in anti-asthmatic medication was fairly high ($n=1628$, 34.7%), especially among persons aged 65 years or over ($n=750$, 48.4%), most of the non-respondents being men of advanced age. However, there was no significant statistical difference between respondents and non-respondents with respect to self-estimated asthma severity or the progress of asthma symptoms.

Ethical requirements

The study was approved by the Ethical Committee of the Faculty of Medicine, University of Oulu, Finland.

Results

The final series comprised 4691 people (78.2%) who had asthma as at least one of their diagnoses, 1786 men (38.1%) and 2905 women. Of these, 369 men (21.0%) and 414 women (14.5%) had at least one other obstructive pulmonary disease in addition to asthma. The mean age was 55 years (SD 18) for the men and 54 years (SD 17) for the women, and the mean post-diagnosis times were 14 (SD 12) and 13 years (SD 11), respectively.

Of the subjects, 1251 (27.5%) reported relieved symptoms by comparison with the situation 12 months earlier, whereas 844 (18.5%) reported worsened symptoms (Table 1). Altogether 2597 subjects (56.9%) estimated their disease to be mild, 1672 (36.6%) moderate, and 294 (6.4%) severe.

Those with mild asthma most commonly reported stable ($n=1460$, 57.1%) or relieved ($n=929$, 36.4%) symptoms, whereas the majority of those with severe disease reported worsened symptoms ($n=174$, 60.0%). Of those with asthma diagnosed within two years, 218 (52.8%) reported relieved symptoms. The subjects with any comorbidity, except clinically diagnosed allergies, more commonly reported worsened asthma than those without such conditions (Table 1).

A fifth of the subjects ($n=995$, 21.7%) were current smokers. The proportion was 26.3% for the men and 18.9% for the women. Of current and previous smokers ($n=2227$), as many as 1232 (55.3%) had stopped, 726 men (61.2%) and 506 (48.6%) women. Relieved asthma was more common

among those who had never smoked than among the former or current smokers (Table 1).

Worsened asthma was more common among those who were exposed to environmental tobacco smoke or other substances or factors defined in Table 1.

Difficulties in anti-asthma medication were reported by 1255 subjects (41.0%). Difficulties were more common among the subjects with deteriorating asthma symptoms ($n=300$, 49.4%) than among those with stable ($n=612$, 38.1%) or relieved symptoms ($n=330$, 40.0%). Each of the problems, except taking anti-asthmatic medication regularly, was more common among the subjects with worsening asthma than among those with relieved symptoms (Table 2). As many as 435 (9.3%) subjects felt very worried and 2531 (53.9%) felt worried to some extent about the adverse effects of anti-asthma medicines.

A very large proportion ($n=2353$, 74.8%) of the asthma patients felt that participating in public events, travelling by public transport and/or going to parties were problematic. The subjects with worsened asthma had difficulties more often ($n=314$, 86.7%) than those with symptom relief ($n=471$, 69.6%) ($p<0.001$) (Table 2).

Logistic regression analysis showed relieved asthma to be associated with diagnosis within the last five years, equally so among the men and women (Table 3). Other such factors among the men were taking anti-asthma medication without problems, 'never' and 'former' smoking and self-expressed depression, and amongst women, mild asthma and living alone.

Worsened asthma was associated with moderate or severe disease in both sexes. Other such factors among the men were concurrent chronic obstructive pulmonary diseases, living alone, and having problems with anti-asthmatic medication; and among women, self-expressed depression. Among men, the likelihood of worsened asthma was reduced by current smoking in comparison with never smoking. Among women such factors were age 65 years or over and clinically diagnosed allergies.

In a sub-analysis among subjects aged 16–44 years the risk factors for relieved or worsened symptoms were much the same as those obtained among the whole study population. However, the occurrence of COPD in this age group was very low and its separate association was not statistically significant.

Another sub-analysis amongst those aged 16–64 years in the active labour force showed that exposure to predisposing substances at work or in hobbies was not connected with either relief (OR

0.75, 95% CI 0.51–1.11) or worsening of asthma symptoms (OR 1.07, 95% CI 0.63–1.81).

An analysis of the impacts of certain life situations on asthma symptoms showed that a change of accommodation, a new job, or re-education, had a beneficial effect on asthma in nearly all those concerned, whereas financial problems, divorce, or the end of a common law marriage, had worsened asthma equally among men and women (Figure 1). Unemployment could have either a beneficial or deleterious effect.

Discussion

At the time of inclusion in the Finnish register of special reimbursement, subjects represent mainly moderate or severe asthma or other chronic obstructive pulmonary disease. Our study revealed that more than half of the subjects derived from this register considered their disease to be mild. Irrespective of the length of time they were on the register, symptoms had been relieved in 27.5% of subjects in comparison with 12 months earlier, but this was more likely the shorter the time that had elapsed since diagnosis. Symptoms can be expected to be alleviated after commencing adequate medication. We have shown previously that the rate of use of inhaled corticosteroids in our subjects was as high as 83% [2]. However, patients may have technical or practical problems or fears related to the medication, thus interfering with the therapeutic response.

Worsening of symptoms, reported by 18.5% of the present patients, could be attributed in severe cases to concurrent chronic bronchitis, COPD or emphysema. Although similar drugs are used to treat both asthma and COPD [12], the two diseases have different courses [13].

The greater alleviation of asthma symptoms among non-smokers is understandable, since smoking directly affects asthmatic symptoms [5,6] and the development of COPD [14]. Tobacco smoke can also affect symptoms by altering the response to inhaled corticosteroids [15]. The crucial question is how patients who are less susceptible to bronchial symptoms caused by tobacco smoke can be induced to give up smoking. A quarter of the smokers reported symptom relief, but current smoking appeared to protect men against a worsening of asthma. One explanation may be that individuals with a less sensitive bronchial tract emerge as smokers in the long term [5].

We found that clinically diagnosed allergies protected asthmatic patients from worsening

symptoms – for instance, through avoidance of symptom-provoking contacts. Appropriate treatment for allergic inflammation in the upper airways has been shown to reduce susceptibility to symptoms in the lower airways [16].

An asthmatic patient may have to pay careful attention to his/her disease in everyday life situations. Patients commonly found that public transport, public events, hotel accommodation, going to parties, and formal celebrations, worsened their symptoms. While the prevalence of asthma and allergies is rising, environmental exposure should be taken into account in community planning. The health care system should be aware of these factors and should consider them when a patient's symptoms are not controlled.

We also found that major lifetime events such as cessation of employment, financial worries and divorce, or ending of a long-term relationship, can also affect later control over asthma. The effect may sometimes be two-dimensional. Cessation of employment, for instance, can reduce harmful exposure, but the financial worries and social stress connected with unemployment can affect control over asthma. In such situations alterations in medical therapy or clinical evaluation may not be sufficient, but the asthmatic patient may benefit from a comprehensive range of health and social services.

Feelings of melancholy and depression are fairly common among asthma patients and seem to be linked to worsening asthma among women, although surprisingly, depression was associated with alleviated asthma symptoms among men. Inaccuracies may occur in identification and reporting of depression and mental symptoms, and this finding among men needs further research. It is nevertheless important in clinical work to take account of the patient's state of mind, since depression can undermine compliance with treatment and thereby affect control over asthma [17,18].

One strength of this cross-sectional survey lies in its nationally representative register-based sample of adults who suffer from chronic obstructive pulmonary diseases and who fulfil certain consistent diagnostic criteria. The questionnaire method itself has been shown to be fairly reliable in measuring chronic morbidity [10,19] including respiratory diseases [20,21]. The response rate was high, with no major response bias, although some of the questions were only partly responded to, especially among elderly men. It seems that latent COPD did not significantly interfere with the results. Our results give support to earlier reports [5–9].

General practitioners (GPs) are in a key position regarding the clinical treatment of asthma [1,2]. Similarly, the role of asthma nurses in providing patient support should be strengthened [2]. Knowledge of the patient's psychosocial situation can help a doctor to treat the patient's asthma [22]. GPs should take a holistic view of the treatment of asthma patients and should pay attention to those psychosocial background factors which can greatly affect control over the disease and which can influence the use of medical services.

Acknowledgements

The study has been supported by the Finnish Social Insurance Institution (SII).

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