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Treatment improves quality of life in patients with poor perception of asthma

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KEYWORDS
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Summary *Aim:* To find out whether symptom-free asthmatic patients with impaired lung function, improve with regard to quality of life after treatment adjustment.

Methods: Forty-two primary care asthma patients without symptoms were divided into two groups: (A) with normal lung function ($n = 22$); and (B) with impaired lung function ($n = 20$). Lung function, symptoms and quality of life were assessed before and after a 3-month interval. In group B (but not in group A), treatment was adjusted on the first visit.

Results: Quality of life was significantly worse in group B at visit 1 and was improved up to the same level as in group A after 3 months of treatment adjustment. Quality of life did not change in group A during the 3 months of observation. Lung function improved significantly only in group B but did not reach the same level as in group A.

Conclusion: Adjustment of therapy improves quality of life even in patients who do not experience symptoms. Asthma treatment should therefore be guided by both symptoms and lung function.

Introduction

In many subjects with asthma, the correlation between the experience of symptoms and lung function is poor [1—4]. A proportion of asthmatic subjects do not perceive increased symptoms, despite the fact that their asthma is worsening and their lung function is impaired. Those patients are usually called ''poor perceivers''. Guidelines on long-term treatment of asthma are mostly based on perception of day-and-night symptoms and regular PEF monitoring [5]. However, the adherence of patients to PEF monitoring is often bad [6—8], and therefore the need for increased treatment is most often based on the experience of symptoms. It is thus obviously a risk that patients, who do not experience symptoms, despite impaired and/or decreasing lung function, are not sufficiently treated. It is uncertain whether treatment adjustment based on lung function benefits patients in terms of lung function and quality of life. Furthermore, it is not clear whether or not poor perceivers are at higher risk of chronic lung function impairment than asthmatic subjects who more easily perceive symptoms. If so, alteration in treatment should always be guided by lung function measurement in combination with a registration of symptoms.

Undertreatment because of poor perception has been claimed to increase the risk of fatal asthma [9,10]. Little evidence is available as to whether or not poor perception of asthma symptoms really is a diminished experience of symptoms or just a temporal adaptation [11]. It would be of interest to find out whether asthmatic subjects with

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impaired lung function, who regard themselves to be symptom-free, improve in lung function and quality of life following therapy adjustment. If the clinical status in poor perceivers would improve, following increased therapy, our attitude towards treatment of so called mild asthma would change.

The aim of the present study was to identify asthma patients with poor perception of symptoms in primary care and to find out whether or not they would benefit from increased therapy in terms of lung function and quality of life.

Materials and methods

Patients

The study was based on a previous study [4] conducted at a health care centre in central Stockholm. In that study, 405 subjects within the area were diagnosed by a physician as having asthma. Of those, 285 patients were either not found, did not show up despite one notice to attend and one reminder or did not fulfil the inclusion criteria. Exclusion criteria were pregnancy and serious diseases including severe physician-diagnosed COPD [4]. Persons who had moved out of Stockholm and those who had a poor understanding of Swedish were also excluded. Finally, 120 patients with asthma, 18—65 years of age, were characterised with regard to symptoms on a visual analogue scale (VAS), health related quality of life [12] and lung function including a reversibility test. The non-responders were younger (30 years; range: 18—56 years) than the responders (38 years; range: 18—64 years) and it is thus difficult to corroborate that the sample fully represents the underlying population.

In the present study, only patients who considered themselves to be symptom-free, according to the visual analogue scale (VAS <2 cm), were included. On a 10 cm VAS, the patients indicated the severity of their asthma symptoms by answering the question: ''Have you experienced any asthma problems or breathing difficulties during the last 2 weeks?'' Each end of the scale indicates the range being considered: from ''No problems at all'' to ''Problems so bad that I had to be admitted to hospital''.

The Asthma Quality of Life Questionnaire by Juniper et al. was used [12]. The questionnaire has 32 items, divided into four domains: activity limitations (11 items); symptoms (12 items); emotional functions (5 items); and environmental stimuli (4 items). Five of the 11 items in the activity domain were individualised, and the patients were asked to identify 5 activities that were limited because of asthma. Twenty-six activities are offered as probes to aid recall, such as walking upstairs, hurrying, laughing or vacuuming. The patients were asked to indicate the extent to which they had been limited on a 7-point scale, where 1 indicates maximal impairment and 7 no impairment at all.

From the previous study, 20 patients with VAS <2 and impaired lung function defined as FEV1 $\leq$75% of predicted value (group B) were willing to attend the intervention study and 22 patients with VAS <2 and normal lung function defined as FEV1 $>$75% of predicted value (group A) served as a control group (Table 2).

In patients with FEV*1* $\geqslant$ 75% of predicted value, an intervention was undertaken according to a fixed schedule (Table 1). All patients came to the primary care centre every 4 weeks to receive new drugs. In patients with normal lung function (FEV1 $>$75% of predicted value), treatment was not altered. All patients returned 3 months later for a second visit with quality of life assessment and lung function measurements.

FEV1 and FVC were measured with a MicroLab 3300 Spirometer (Micro Medical Ltd., Rochester, Kent, UK) according to the standards of the American Thoracic Society. For reversibility tests, salbutamol (5.0 mg) and ipratropium bromide (0.5 mg) were mixed and inhaled using a jet nebuliser (Aiolos, Medicinsk Teknik AB, Karlstad, Sweden). Lung function was measured 20 min after inhalation.

Table 1 Treatment regimen.

	I	II	III
Current therapy	No treatment β-Agonist prn DSCG prn	400 μg BUD per day 400 μg BDP per day 200 μg FP per day	>400 μg BUD per day >400 μg BDP per day >200 μg FP per day
Intervention	200 μg BUD bid β-Agonist prn	Doubling of the steroid dose	Add salmeterol 50 μg bid

In patients with FEV*1* $\geqslant$ 75% of predicted value treatment (intervention) was added according to Table 1. BUD: budesonide; BDP: beclomethasone dipropionate; FP: fluticasone dipropionate; DSCG: disodium cromoglycate.

Reference values by Hedenstrom et al. [13,14] were used.

The study was approved by the Ethics Committee of Huddinge Hospital, Sweden.

Statistics

Results are given as mean values (S.E.M.). Regarding quality of life data, comparisons between groups were assessed by Mann–Whitney *U*-test, and within-group comparisons were assessed by Wilcoxon signed rank test. Lung function data was analysed by means of Student's *t*-test for paired and unpaired observations. A *P*-value <0.05 was considered significant.

Results

Patients in group A (asymptomatic, normal lung function) were younger, and the number of smokers was lower than in group B (asymptomatic, impaired lung function) (Table 2).

A majority of the patients was unable to name and specify activity limitations, according to the five ''individualised'' questions. Therefore, this part of the questionnaire was not analysed and thus not included in the calculation of ''activity limitation'' and ''overall assessment''. Prior to treatment, quality of life differed significantly for activity limitation ($P = 0.031$), symptoms ($P = 0.015$) and overall assessment ($P = 0.047$, Fig. 1). After 3 months, no change in quality of life assessed by the

Table 2 Patient characteristics.

Group	A	B	*P*-value
n	22	20	–
Sex (M/F)	10/12	10/10	–
Age (mean (range)) (years)	35 (21–61)	47 (26–64)	<0.01
FEV1 (mean (S.E.M.)) (% predicted)	88.9 (1.6)	66.3 (2.5)	<0.001
ΔFEV1 (mean (S.E.M.)) (% predicted)	4.0 (1.2)	12.2 (1.6)	<0.001
Smokers (*n*)	1	11	–
Ex-smokers (*n*)	7	6	–
Non-smokers (*n*)	14	3	–
I (*n*)	11	9	–
II (*n*)	9	3	–
III (*n*)	2	8	–

I–III represent treatment at study entry according to classification in Table 1. ΔFEV1 indicate the increase of FEV1 in percent of predicted value at the reversibility test on the first visit.

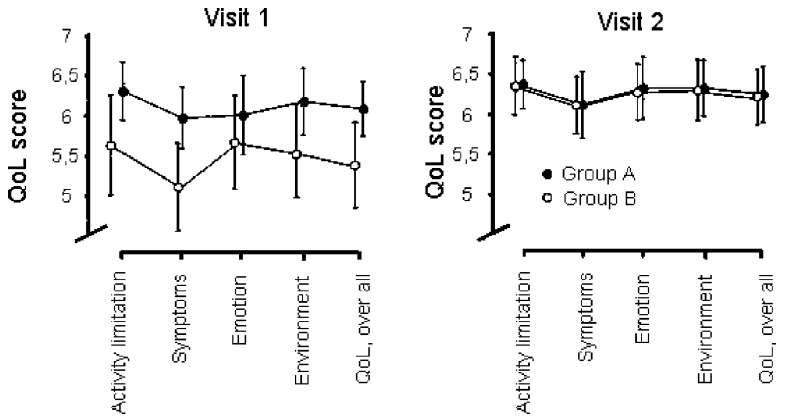

Figure 1 Quality of life in patients without asthma symptoms with normal (group A) and impaired lung function (group B). Visit 1 = study entry; visit 2 = data after 3 months of unaltered treatment (group A) or increased (group B) treatment. Comparisons between the groups: activity limitation ($P = 0.03$), symptoms ($P = 0.015$), emotion ($P = 0.32$), environment ($P = 0.089$), quality of life overall ($P = 0.047$). In group B, where treatment was increased a significant improvement was observed after 3 months for all domains and overall assessment ($P < 0.01$ for all domains and overall assessment). No difference with regard to quality of life was found between the groups at the second visit (right panel). Mean values and 95% confidence intervals.

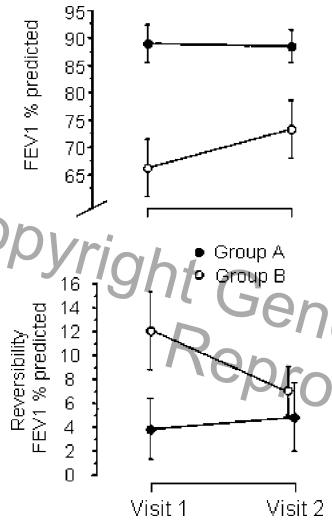

Figure 2 Lung function assessed by FEV1 before (visit 1) and after (visit 2) 3 months of unaltered treatment (group A) or increased treatment (group B). Upper panel shows FEV1 in percent of predicted value. FEV1 at visit 1 was 3.57 l (0.15 l) in group A and 2.39 l (0.14 l) in group B. Lower panel shows the increase in FEV1 following inhalation of salbutamol (5 mg) and ipratropium (0.5 mg) in percent of predicted value. Mean values and 95% confidence intervals.

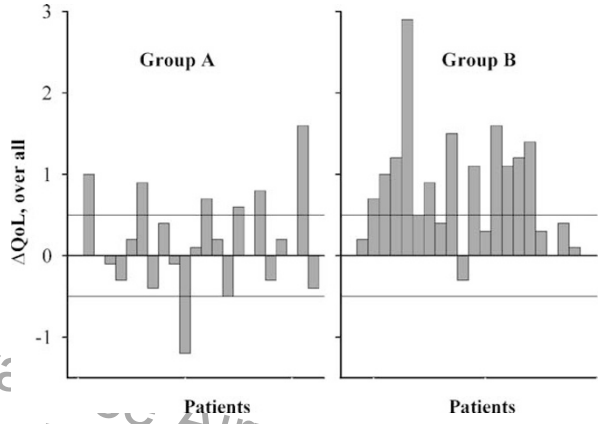

Figure 3 Change in quality of life overall in group A ($n = 22$) and group B ($n = 20$). Each bar represents one patient. Horizontal lines indicate a change of 0.5, i.e. the minimal important difference, that the patients perceive as beneficial [15].

AQLQ was found in group A (where no alteration in treatment had been done). In group B, where treatment was increased (according to Table 1), a significant improvement was observed for all domains and overall assessment ($P < 0.01$, Fig. 1). No difference with regard to quality of life was found between the groups at the second visit.

Lung function assessed by FEV1 increased significantly in group B (+0.26 l (0.06 l), $P = 0.0007$), but not in group A (−0.01 l (0.05 l), $P = 0.93$, Fig. 2). At visit 1, inhalation of 5 mg of salbutamol and 0.5 mg of ipratropium induced an increase of 4.0% (1.2%) of predicted value in group A and 12.3% (1.6%) of predicted value in group B. Corresponding values at visit 2 were 5.0 (1.4) in group A and 7.2 (1.0) in group B (Fig. 2).

According to previous studies, a within-subject score change of 0.5 represents the minimal important difference (MID) and 1.0 represents a moderate change which the patient perceives as beneficial [15]. In group A, the overall assessment of quality of life increased by ≥0.5 in 6 out of 22 patients, of whom 2 showed an increase >1.0. In group B, the overall score increased by ≥0.5 in 12 out of 20 patients, of whom 8 had an increase of ≥1.0 (Fig. 3). The overall score decreased in eight subjects in group A and in one subject in group B (Fig. 3). Improvement in quality of life was evenly distributed between the three treatment groups (I–III).

Discussion

In the present study, primary care patients with mild asthma, who regarded themselves as free of symptoms (assessed by one single question, VAS), were investigated. The VAS is validated with regard to dyspnoea [16] but has not been validated as a tool for assessment of ''overall'' asthma control. The idea in the present study was to get an impression about the patients' opinion about their asthma status in a situation that may be similar to the routines in a primary care unit. At the first visit, we found a lower health related quality of life in patients with impaired lung function (group B). Adjustment of treatment in that group resulted, after 3 months of therapy, in a substantial improvement of quality of life, up to the same level as the patients with initially normal lung function (group A). Also lung function improved during treatment, but not up to the same level as in group A. On an individual basis, a clinically relevant improvement of quality of life (total score improvement >0.5) was observed in more than half of the patients in group B, while the corresponding figure for group A was approximately 25%. All patients were included in the study, after having been invited by the investigator, and none came to primary care because of worsening of asthma or asthma symptoms. Thus, the expectation of a clinical improvement by the patients was probably low. The small, insignificant changes of quality of life observed in group A were probably related to increased attention to, or improved compliance with therapy. In order to improve compliance, the patients came to the primary care centre once a month to receive new drugs. Although a minor part of the improvement in group B may be explained

by increased awareness, we assume that the major effect was a result of the treatment adjustment.

One drawback of the present study is that groups A and B are not fully comparable. Patients with impaired lung function (group B) were more often smokers and were older than the patients with normal lung function (group A). Similar to the present study, others have found that poor perception increases in elderly patients [17,18]. It seems likely that smokers are more prone to deny airway symptoms, and there are findings supporting a higher prevalence of poor perception in smokers, compared with non-smoking asthmatics [19,20]. It could be argued that patients with COPD may have been included in the present study. However, only one patient had a FEV1/FVC ratio below 70% (thus fulfilling the basic criterion of COPD) after bronchodilation at visit 2. We are therefore confident that the patients in our study did not suffer from COPD. An objection thus could be that the study should have been conducted only on patients included in group B who should have been randomised into active or placebo. With this design, the treatment of subjects with impaired lung function would not have been adjusted according to current recommendations. Furthermore, the small number of patients found would have made such a design less favourable. On the other hand, we found it beneficial to find out that quality of life actually reached the same level after treatment in group B as in group A which justifies the inclusion of group A as a control group. In the present study, we included all patients within a primary care area who were willing to participate and the sample size was thus not based on power calculations. Therefore, these results should not be considered to be fully conclusive but rather hypothesis generating. A randomised, power calculated study on this issue is in progress.

The ability to perceive the severity of asthma varies between individuals, while the intra-individual variation over time seems to be small [21]. It has been suggested that some patients are not receiving sufficient asthma treatment because they are ''turning down their life thermostat'' [22]. Long periods of stimulation may result in a reduction of perceived symptoms, a process that usually is recognised as temporal adaptation [11]. In addition, long-term adaptation to breathlessness may change the frame of reference [23]. Reduced perception of bronchoconstriction has been reported in the elderly [17,18,24], in patients with chronic obstruction [11,25], in patients with frequent airflow variation [11] and long duration of the disease [20]. Patients in group B were older than those in group A and it is reasonable to assume that they had had their asthma for a longer time which may have contributed to a reduced perception of symptoms. Peiffer et al. found a circadian rhythm of dyspnoea that had a stronger correlation with lung function in the morning and evening than in the afternoon [26]. In that study, 83% had a circadian rhythm in peak expiratory flow, whereas only 40% fluctuated in dyspnoea score. However, they did not find a relationship between symptom perception on one hand, and age, sex, severity and duration of asthma on the other. In our study, all visits were conducted between 8 a.m. and 3 p.m. with no difference between the groups. In the present study, we found that asthmatic patients did not perceive symptoms in daily life, although they had impaired lung function and a clear room for clinical improvement. The reduced perception of symptoms thus may have resulted in undertreatment and it could not be excluded, that this may have contributed to irreversible lung function deterioration.

Our results indicate that adjustment of therapy cannot fully be based on the patients having experienced symptoms. This may be of particular importance in elderly and smoking asthmatic subjects. The present data strongly supports the use of a regular measurement of lung function in the long-term management of asthma, regardless of whether symptoms are experienced or not. According to international guidelines, treatment recommendations should be based on a combination of symptoms and lung function measurements [5]. It is reasonable to assume that lung function is not regularly measured in symptom-free subjects with mild asthma. Based on previous and present results, and in accordance with other studies [2,4,24], we found that more than 20% of the asthmatic subjects do not experience symptoms, despite a reversible lung function impairment.

Asthma patients seem to be more inclined to adjust treatment based on symptoms than on PEF monitoring [27]. In a number of studies, it has been demonstrated that many asthma patients are reluctant to measure PEF on a regular basis [7,28]. We conclude that a successful long-term management of asthma should include regular lung function measurement. Since self-monitoring of pulmonary function seems difficult to maintain, the responsibility of successful asthma management depends on regular visits to a physician or nurse managed facility. This is particularly important when realising that asthmatic subjects with poor perception of symptoms may be at risk of fatal and near fatal asthma attacks [24].

In conclusion, we have shown that patients with mild asthma, who regard themselves as free of symptoms, and impaired lung function experience a clinical relevant improvement of quality of life

following adjustment of therapy. This improvement of quality of life was not accompanied by a corresponding improvement of lung function. Asthma treatment should therefore be guided by monitoring of both symptoms and lung function. Further studies on early intervention and its consequences for long-term outcomes in mild asthma are needed.

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