Assessing the quality of prescribing in general practice

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Chapter 7

Guideline adherence for the treatment of asthma in general practice is associated with a higher quality of life

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Submitted

Background: Guidelines are intended to help healthcare professionals to optimise the quality of patient care. While optimal therapy focuses on the patient, traditionally assessment of the effectiveness of guidelines has focused on physicians and little attention has been given to the effect of guidelines on patient outcomes. In this study we compare QOL in asthma patients treated according to the 1997 National Institute of Health International (NIH) asthma guideline and those receiving non-guideline recommended treatment.
Methods: We determined the asthma severity of 146 asthmatics during a clinical research appointment based on a combination of symptom, lung function and medication use data. The appropriateness of each patient's medication regime was determined according to the NIH asthma guideline. QOL was assessed on a 7-point scale using the validated Asthma Quality of Life questionnaire (AQLQ).
Results: Patients treated according to the guideline had a significantly higher QOL than patients with non-guideline treatment (5.7 vs. 5.3, p=0.019).
Conclusions: This study supports the role of evidence-based guidelines in daily practice. We observed an association between non-guideline treatment and a poorer QOL. Further studies are warranted to determine if guideline treatment is responsible for the increase in asthma related QOL observed in this work.

Introduction

Asthma is a chronic inflammatory airway condition affecting more than 8% of adults in Western European[1]. Like most chronic conditions, the majority of asthma patients are managed in general practice[2]. International consensus regarding optimal treatment for asthma has existed since the early 1990s, as evident in the international guidelines first published in 1992[3]. These guidelines aimed to help health care professionals bridge the gap between current knowledge and daily practice, and to standardise and improve the quality of asthma care provided. Over the past decade these guidelines have been reviewed and up-dated[4]. The most recent international asthma guideline was published in 1997, by the National Institute of Health (NIH)[5]. Pharmacotherapy is an important element in the optimal management of asthma as recommended in the guidelines. Common to all versions of the guidelines, the goals of asthma therapy are to improve the patient's quality of life (QOL) by preventing chronic and troublesome symptoms, maintaining "normal" lung function, maintaining normal activity levels, preventing recurrent exacerbations and providing optimal pharmacotherapy with minimal adverse effects.

While the goals of asthma therapy focus on the patient, assessment of the guidelines and their effectiveness has focused on physicians. Little attention has been given to the effect of guidelines on patient outcomes such as mortality, morbidity or QOL in asthma. Prescriber adherence to the asthma guidelines with respect to diagnostic procedures, drug therapy and patient self-management counselling has been investigated[2,6-8]. While explicit guidelines have been shown to improve physician clinical practice, it is not known if such improvement has similar positive effects on patient outcomes[9,10]. Earlier work on the effect of guidelines on patient outcomes concluded that there was little evidence that clinical guidelines are effective in improving patient outcomes, although the poor quality of the guidelines investigated was believed to have had a major influence on this finding[11]. More recent work has indicated that asthma patients receiving guideline recommended drug therapies have less hospital admissions[12] and better lung function[13] than patients not treated according to the guidelines. What remains unknown is the effect of guidelines on the patient's day-to-day QOL. In this study, we compare QOL in asthma patients managed in general practice who are treated according to the NIH asthma guideline with QOL in those not receiving guideline recommended treatment.

Patients and Methods

Study population

The *Registratie Netwerk Groningen* (RNG) is a general practice database from the Northern Netherlands. At the time of the study, the RNG included 30486 patients registered with 16 general practitioners (GPs). All participating GPs use the database in place of paper medical records.

All patients aged 18-49 years with an anti-asthma medication (Anatomical Therapeutic Chemical classification-ATC group R03[14]) or an asthma contact (International Classification of primary Care-ICPC code R96[15]) during 1997 were included in the study. Data from 1997 was used for recruitment to ensure that patients had chronic asthma. Patients no longer registered with an RNG doctor or receiving anti-asthma medications for non-asthma indications were ineligible. GPs invited eligible patients to attend a clinical appointment with a research assistant. A reminder letter was sent to non-respondents within 3 months of the initial invitation. Anonymous data for non-responding patients were obtained from the database to enable comparison between non-responders and patients participating in the study with respect to age, sex and medication use. The local medical ethics committee approved the study and informed consent was obtained from each participant.

Participating patients attended a single research appointment (May 2000-December 2000) where FEV_1 was measured and a questionnaire regarding recent asthma symptoms, medication use and asthma related QOL completed by each participant. FEV_1 was assessed by an experienced research assistant trained in spirometry according to the standards of the American Thoracic society using a Microlab 3300 spirometer (Micro Medical Ltd, Rochester, Kent UK). For each participant the best of 3 readings was used.

Guideline adherence

For this study we used the most recent international asthma guideline, the National Institute of Health: Expert Panel Report 2 Guidelines for the Diagnosis and Management of Asthma (NIH)[5]. Adherence to the guideline was defined as any drug or drug combination recommended in the international asthma guideline for the relevant asthma severity (Table 1). Since improving lung function and reducing symptoms are important treatment aims, drug combinations from higher asthma severity classifications were also considered adherent when prescribed for patients with a lower severity classification. Self-reported medication use, by patient interview, has been shown to be a reliable method of obtaining information regarding current medication use[16,17]. The accuracy of self-reported medication use was further improved by having patients bring all their

current asthma medications to the clinical appointment. As well, the research assistant questioned patients using both brand and generic names, during the clinical appointment about their current asthma medications. Each patient's regime was classified as adherent or non-adherent using a computer algorithm based on the recommendations in the guideline (Table 1).

Severity classification

In order to classify asthma treatment regimes, the severity of each participant's asthma was determined using a second computer algorithm based on the severity classification criteria presented in Table 1. Since no objective severity classification for treated asthma patients is known, the severity classification from the international guideline for untreated patients was used[5]. This classification uses a combination of both daytime and night-time symptoms and lung function (FEV_1) to determine asthma severity rather than relying on a single component. A higher severity class indicates more severe asthma.

Quality of life assessment

QOL was assessed using The Adult Asthma Quality of Life Questionnaire (AQLQ)[18]. The AQLQ is a validated disease specific QOL questionnaire consisting of 32 items measuring 4 dimensions of asthma related health: 12 items assess symptoms, 5 measure emotional function, 4 assess exposure to environmental stimuli and 11 determine activity limitations due to asthma. The AQLQ uses a 7-point scale where a higher score corresponds to a better QOL. Each participant completed the self administered, Dutch language version of this instrument during the research appointment.

Sample size

In earlier studies using the AQLQ, the mean QOL for asthma patients treated in general practice ranged from 4.6 to 6.0[19]. In order to detect a difference in QOL of 0.5, at least 63 patients with adherent and 63 with non-adherent treatment regimes were required. Previous work clinically assessing asthma treatment reported that 60% of patients were treated with pharmacotherapy not recommended in the guidelines[2,7]. Thus, we aimed to recruit 160 patients in order to achieve a power of 0.80 with an alpha of 0.05.

Analysis

Student's t-test was used to assess the difference in QOL between the asthmatics treated according to the guidelines and those with non-guideline treatment.

Table 1: Severity classification and pharmacotherapy recommendations from the 1997 NIH asthma guideline.

Asthma severity Class	Criteria for classifying asthma severity*	Main pharmacotherapy recommendations
Class 1 *Mild intermittent*	Symptoms: Symptoms ≤ 2 times a week Asymptomatic and normal PEF between exacerbations Exacerbations brief Night time symptoms: ≤ 2 times a month Lung function: FEV_1 or PEF≥ 80% predicted	Short-acting inhaled β-agonist as needed
Class 2 *Mild persistent*	Symptoms: > 2 times a week but < 1 time a day Exacerbations may affect activity Night time symptoms: > 2 times a month Lung function: FEV_1 or PEF ≥ 80% predicted	Short-acting inhaled β-agonist as needed AND Low† dose inhaled
Class 3 *Moderate persistent*	Symptoms: daily Daily inhaled short-acting β-agonist use Exacerbations affect activity Exacerbations ≥ 2 a week Night time symptoms: > 1 a week Lung function: FEV1 or PEF >60% and <80% predicted	Short-acting inhaled β-agonist as needed AND Medium†† dose inhaled corticosteroid OR Low dose inhaled corticosteroid AND inhaled long acting β-agonist
Class 4 *Severe persistent*	Symptoms: continual Limited physical activity Frequent exacerbations Night time symptoms: frequent Lung function: FEV1 or PEF ≤ 60% predicted	Short-acting inhaled β-agonist as needed AND High††† dose inhaled corticosteroid AND Inhaled long acting β-agonist AND/OR Ipratropium bromide

*The presence of one of the features of severity is sufficient to place a patient in that category. An individual should be assigned to the most severe grade in which any feature occurs

† low dose inhaled corticosteroid is 200-400mcg budesonide (or equivalent) daily

†† medium dose inhaled corticosteroid is 400-600mcg budesonide (or equivalent) daily

††† high dose inhaled corticosteroid is >600mcg budesonide (or equivalent) daily

Results

Study Population

In total, 369 eligible patients were invited to attend a clinical appointment, of which 152 patients were willing to participate. After initial contact by the researchers, 6 patients were unable to attend an interview during the study period, leaving a final study population of 146 (response rate 39.6%).

Patient characteristics

Patient characteristics and current asthma medication use are shown in Table 2. Six patients (4.1%) reported using no current asthma medications. Of the 45 patients not using a short acting β-agonist, 9 were using ipratropium and 10 a long acting β-agonist. Salbutamol was the most commonly used short acting β-agonist used by 88.1% (89/101) of patients reporting use of a short acting β-agonist. Of the remaining short acting β-agonist users 12 used terbutaline and 1 each rimiterol and fenoterol. One patient was using both salbutamol and terbutaline and one patient both salbutamol and rimiterol.

Table 2: Patient characteristics (n = 146)

General	
mean age in years (SD)	39.8 (8.3)
% female	58.2
mean FEV1 (SD)	83.5 (17.9)
mean QOL* (SD)	5.49 (0.96)
Severity	**% patients**
class 1	34.9
class 2	6.2
class 3	47.9
class 4	11.0
Medication	**% patients**
inhaled short acting β-agonist	69.2
inhaled corticosteroid	65.8
inhaled long acting β-agonist	15.8
inhaled cromoglycates	5.5
inhaled ipratropium bromide	13.0

*on a 7-point scale

The most commonly used inhaled corticosteroid was budesonide (40.0%, n=59/146). Twenty-three patients used beclomethasone and 14 patients fluticasone. Long acting β-agonists were used by 22 patients. Salmeterol was used by 13 patients and formoterol by 9 patients. While almost 70% of patients were using an inhaled short-acting β-agonist and 66% of patients an inhaled corticosteroid, only 43.2% (n=63/146) used an inhaled short acting β-agonist and an inhaled corticosteroid.

Non-respondent characteristics

There was no significant difference with respect to gender (58.2% and 57.8% female respectively, difference=0.5, 95% confidence interval: -8.7 to 9.6) between non-respondents (n=223) and participating patients (n=146). Participating patients were slightly older (39.8 years vs 35.8 years, $p<0.05$). There were no significant differences between participating and non-responding patients in the mean volume prescribed per patient for inhaled short-acting β-agonists, inhaled corticosteroids, inhaled anticholinergics, and oral salbutamol.

Relationship between QOL and treatment according to the guideline

After stratifying for severity, a large clinically relevant difference in QOL between asthma severity class 4 patients receiving guideline (5.6) and non-guideline treatment (4.6) was observed. No difference was seen for the lower severity classes (Table 3).

Table 3: Relationship between QOL and treatment adhering to the guideline.

	Mean QOL ± SD			
	All patients	***Adherent***	***Non-adherent***	***Significance***
All severities	**5.5 ± 1.0 (n = 146)**	**5.7 ± 0.8 (n = 73)**	**5.3 ± 1.0 (n = 73)**	**p = 0.019**
Severity 1	6.1 ± 0.7 (n = 51)	6.1 ± 0.6 (n = 35)	6.0 ± 0.8 (n = 16)	
Severity 2	5.5 ± 0.4 (n = 9)	5.7 ± 0.4 (n = 5)	5.3 ± 0.3 (n = 4)	
Severity 3	5.2 ± 0.9 (n = 70)	5.1 ± 0.8 (n = 30)	5.2 ± 0.9 (n = 40)	
Severity 4	4.8 ± 1.2 (n = 16)	5.6 ± 1.0 (n = 3)	4.6 ± 1.2 (n = 13)	

As seen in Table 3, Patients treated according to the guideline had a significantly higher QOL (5.7) than those with non-guideline regimes (5.3). In general, a trend towards decreasing QOL with increasing asthma severity was observed.

Non-guideline treatment regimes

A number of different non-guideline prescribing patterns emerged. Of the 16 patients in severity class 1 not using a short acting β-agonist, none were using ipratropium and 2 were using a long acting β-agonist. The majority of these patients (n=12) were using inhaled corticosteroids.

The main reason for non-adherent therapy among class 2 patients (n=4) was the lack of anti-inflammatory treatment (n=3). One patient was not using a short acting β-agonist or any other bronchodilator.

Lack of anti-inflammatory treatment was also the major factor contributing to non-adherent treatment for patients in asthma severity class 3. Of the 40 patients with a treatment regime not recommended in the guideline, 27 were not currently using any anti-inflammatory medication and 1 was using cromoglycate in place of the inhaled corticosteroid recommended in the guideline. Eighteen class 3 patients were not using a short acting β agonist, however from these 18, 6 were using ipratropium and 4 a long acting β-agonist. There were 6 patients in this severity class with neither a short acting β-agonist nor an inhaled corticosteroid.

In severity class 4, the most severe class, there were 13 patients without a guideline recommended treatment regime. Of the ten patients with no short acting β-agonist, one had ipratropium and 4 a long acting β-agonist. Three patients had no anti-inflammatory medication and 1 was using cromoglycate in place of an inhaled corticosteroid. There were 6 patients without either a long acting β-agonist or ipratropium

Discussion

This study showed that asthma patients treated according to the NIH guideline have a significantly better QOL than patients not treated according to the NIH guideline. A difference of 0.5 points on the AQLQ has been determined to represent a clinically relevant difference in QOL[20] indicating that not only was the difference observed in this study statistically significant but more importantly it was borderline clinically relevant. In terms of QOL, it has been argued that clinical relevance is of more importance to the prescriber than statistical significance[21].

In general, the QOL among the patients participating in the study was relatively high (5.49). Other studies have also found that the average QOL in mild to moderate asthma patients is close to that of the general population[22]. A strong link between asthma-related QOL and disease severity[19,23] has been reported and this relationship was also observed in our study. Overall for all patients irrespective of asthma severity, QOL decreased from 6.1 for severity class 1 patients to 4.8 for the most severe patients, which is similar to that seen in other studies[19]. The decrease in QOL was more marked in patients with non-guideline treatment regimes: from 6.0 for severity class 1 patients to 4.6 for class 4 patients. It is most likely that the relationship between QOL

and asthma severity is due to the relationship between QOL and asthma symptoms[24,25].

Since no objective severity classification for treated asthma patients exists, we used the severity classification presented in the international guideline. This classification uses a combination of symptoms, both daytime and nocturnal, and lung function (FEV_1) to determine asthma severity rather than relying on a single component. Previous studies have shown a severity classification based FEV_1, symptoms and medication use to be valid[26]. Since treatment may improve both symptoms and lung function, using this classification in treated asthma patients may lead to under-estimation of the actual asthma severity. Prescribing recommendations in almost all asthma guidelines follow a step-wise progression. Treatment for a higher severity is always in addition to treatment from a lower severity either with respect to increasing the dose of an existing medication or the addition of a new medication. Thus, optimal treatment according to the guideline for a particular severity class implies that the treatment will also be optimal for a lower severity class. Under-estimation of an individual patient's severity classification should have no effect on whether their treatment is considered adherent to the guideline, however it may have affect the relationship between quality and life and asthma severity.

While the response rate in this study was low (39.6%) there was no difference between participants and non-respondents in terms of age or sex. The low response rate may be related to the age group (18-49 years) targeted by this study since this age group comprises a large proportion of the workforce and may have been unable to attend the research appointment due to work commitments. A more aggressive recruitment strategy, including out-of-hours appointments, may be one manner of overcoming this problem.

To determine each patient's current asthma medication regime, we questioned each patient about their current asthma medications using both brand and generic names, as well as having each patient bring their current medications along to the clinical appointment. The limitation of using this method to look at adherence is that it is based on what the patient is currently using and not necessarily on what the doctor has prescribed. It has been reported that specific patient groups do not redeem as many as 27% of prescriptions[27], thus a doctor may have prescribed a guideline-based regime that a patient has chosen not to have dispensed. This would indicate that from a GPs perspective this study could underestimate the proportion of patients treated according to the guidelines.

In this study we found a number of prescribing patterns not recommended in the NIH guideline. Almost 30% of patients participating in this study were

not currently using a short acting β-agonist. A small number of these patients were using ipratropium which while not recommended in the guideline as a bronchodilator has traditionally been used in this role. A larger number of patients without a short acting β-agonist were using a long acting β-agonist. While the pharmacokinetics of formoterol may support its use as a bronchodilator, the majority of patients in this study were prescribed salmeterol. Salmeterol does not share the same pharmacokinetic profile as formoterol and may not be suitable for rapid relief of symptoms in an acute situation. Under-use of inhaled corticosteroids was also evident in our study population. Whether these patients had ever been prescribed a corticosteroid is not known and further investigation in needed to discover if this is a prescriber or patient problem. For the most severe patients, the major problem identified was lack of a long acting β-agonist as recommended in the guideline. Disturbingly, 62.3% of severity class 4 patients were not currently using a short acting β-agonist and half of these patients had no other possible bronchodilator.

We observed an association between guideline treatment and a higher QOL. Further studies are needed to determine if treatment adhering to that recommended in the guidelines is responsible for the observed increase in asthma related QOL observed in this work. For doctors and other health care professionals this study emphasises the role of evidence-based guidelines in daily practice.

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