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ADRIAN GILLISSEN

PATIENTS' ADHERENCE IN ASTHMA

St. George Medical Center, Robert-Koch-Hospital, Leipzig, Germany

Nonadherence in asthma treatment results in increasing mortality, morbidity, and it is associated with increasing treatment costs. In asthma, adherence rates are often below 50%. Understanding of the needs and behaviors of asthma patients as well as treatment barriers to comply with asthma guidelines is important in developing programs to promote adherence. This article presents information on common types of nonadherence in asthma patients, the causes, and it reviews the literature on interventions to overcome these factors to maximize adherence rates. Although several interventions are effective in improving medication adherence in asthma, only few significantly enhance adherence rates and clinical outcomes of these patients. An improvement in treatment adherence is a complex task, requiring asthma self-management, education programs coupled with educational reinforcements, simplifying treatment planes and applications forms. Good communications skills among clinicians and patient education are also central for improving adherence. Methods to overcoming physician barriers ensure consistency in implementing guideline recommendations in practice.

Keywords: *asthma, adherence, compliance*

INTRODUCTION

The control of asthma symptomatology requires a complex treatment plan that changes as presenting symptoms wax and wane (1). In this setting, patient adherence may easily frail, and its maintenance requires exceptional alertness. A pervasive and intractable obstacle to effective treatment, patient nonadherence to a prescribed treatment regimen, contributes significantly to poor outcomes in asthma management. Maintaining adherence is particularly important as well as

challenging in children with asthma, a group that is especially vulnerable to irreversible airway narrowing under insufficient inhaled cortiosteroid therapy (2).

Low patient adherence with prescribed inhaled therapy may result in overdosage, but mostly underdosage, and is directly related

a) to enhanced morbidity and mortality in asthma, and

b) to enhanced treatment cost (3-5).

In real life, compliance affects many aspects of the management of chronic conditions, such as avoidance of aggravating factors, monitoring, appointment keeping, prevention or applying an emergency plan of action when needed. Compliance as well as adherence issues are only in part related to the patient but also to social factors, and the quality of primary and secondary medical care (6). Patient adherence is directly dependent on the quality of the health care system, e.g., the accessibility to health care resources, the theoretical and practical knowledge of the physician, the physician's willingness to follow the latest recommendations in guidelines, and a good relationship between the patient and the doctor (7-9).

This report describes the major barriers to adherence in asthma treatment and suggests strategies for promoting adherence.

Definition of terms

The terms "compliance", "adherence", and "concordance" are frequently used in the literature to describe agreement between prescribed medication and patient practice. In general these terms mean *"the extent to which a person's behavior – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider"* (10). However, the meaning of these terms often differs between authors. The following definitions are adapted in the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) (11):

- Compliance: "following doctors orders". The extent to which a patient's behavior matches the prescribers advice. This term was criticized, as it was thought to convey a negative image of the relationship between patient and prescriber, in which the role of the prescriber was to issue the instructions and the patient's role was to follow the doctor's orders. Consequently, noncompliance was interpreted as patient incompetence to follow clear instructions.
- Adherence: "the extent to which a person's behavior corresponds with recommendations from a health care provider". The extent to which the patient's behavior matches *agreed* recommendations from the prescriber. The patient is free to decide whether to adhere to the doctor's recommendations. Adherence develops the definition of complicance by emphasizing the need for agreement.

- Concordance: “shared decision-making, a coming to an agreement that respects the patients beliefs and wishes”. This term is predominantly used in the United Kingdom. It emphasizes the patient/prescriber relationship and the degree to which the prescription represents a shared decision, in which the beliefs and preferences of the patient have been taken into consideration (12). In this review, the concordance is not discussed in further detail.

Generally, nonadherence can be classified into intentional or unintentional (not followed). Failing to understand correct use of an inhaler or lack of sufficient demonstration of a device by the physician or nurse exemplifies unintentional nonadherence, while refusing to take medication from whatever reason constitutes intentional nonadherence.

Main causes of nonadherence

Many reasons for intentional and unintentional nonadherence exist. The main reasons for largely intentional nonadherence are:

- Anxiety regarding side-effects, dependence and overdosage (13)
- Awkwardness of taking medication via a large volume spacer
- Denial of being asthmatic or of the severity of the illness, specially in children, youth and young adults. In general, juveniles are less adherent than adults. In children, adherence rate is strongly depended on active parental involvement.
- Inconvenience of treatment: In general, nonadherence is higher with inhalation therapy than with pills or tablets, and it increases as more doses of single medicine are prescribed per day (14-16).
- Forgetfulness, laziness, and/or carelessness (17)
- Struggle with the authority
- Unwillingness to adapt lifestyle, e.g. to quit smoking. One third of asthmatics smoke regardless of their disease (*Fig. 1*) (18)

Examples of reasons of largely unintentional nonadherence are:

- Treatment that is too complex or too time-consuming
- Inadequate training in the inhalation technique
- Lack of understanding about the need for long-term preventive treatment, e.g., when preventive medication does not produce immediate symptom relief
- Inability to coordinate inhalation and actuation of metered dose inhaler (MDI). Inability to inhale forcefully with dry powder inhaler (DPI) (19)

Further negatively influencing factors are (20):

- Large family size
- History of recreational drug intake
- Cultural pressures; sociocultural, psychological and various other individual barriers
- Chaotic home environment
- Adherence worsens over treatment time in chronic treatment

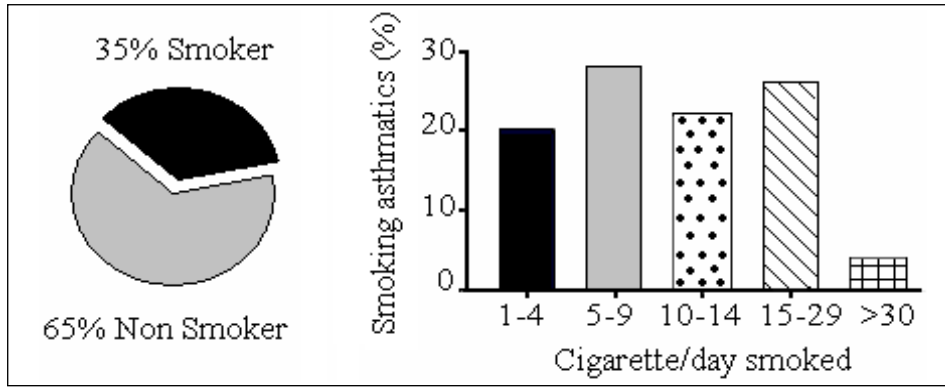

Fig. 1. Regardless of their disease, 1/3 of all asthmatics smoke cigarettes (left) which matches the average smoking population (18). On averange, most asthmatic smokers consume 5 to 29 cigarettes/day (right)

Fact or myth?

Noncompliance is only weakly or not at all associated with various factors commonly thought to be important. Following aspects have only in part or no impact on patient adherence:

- Type or severity of disease do not significantly relate to adherence rate (21)
- No clear relationship to sociodemographic variables and nonadherence, e.g., gender, age in adults
- In general, the socioeconomic status is no clear predictor for adhesion rates. Adherence is only positively correlated with income when the patient is paying for the treatment, and can be increased offering patients from lower income families adequate care for free (22).
- Low-income and high-income families as well as minority patients do not cite different concerns and barriers that included cost, difficulty of obtaining medication, daily life hassles, and a general distrust of the medical establishment (23).
- Drug cost-sharing policies within the same population do not enhance adherence rates. In contrast, co-payment and co-insurance plus deductible policies were associated with significant reductions in use of inhaled medications, mostly due to decreased initiation and increased cessation rates (24).
- The notion of a typical nonadherent patient is a myth: most of us are nonadherent some of the time (12).

Epidemiology of nonadherence

A World Health Organization (WHO) report estimates that 50% of patients with chronic diseases in developed countries do not use their medications as recommended. When taken together with poor access to health care, lack of appropriate diagnosis, and limited access to medicines, poor adherence seriously

threatens any effort to tackle chronic illness (10). In asthma, adherence rates are particularly challenging and ranges from less than 30% to 70-80% with <50% in children adhering to their prescribed inhaled medication regimens (25-29). This greatly concerning, given the fact that noncompliance is strongly related to disease instability as well as poor outcome on the long term (4, 28, 30, 31).

Persistent asthma symptoms, delayed and insufficient anti-inflammatory treatment is associated with amplified deterioration of lung function in asthma, reduced bronchodilator response, enhanced exacerbation rates, all of which might eventually lead to a COPD-like disease (19, 32, 33).

The adherence of asthma patients (all severity stages) who had received a medical prescription was found to be 40% in USA and ranging from 60% to 70% in France, UK, Germany, and Italy (34). A major problem seems to be the undertreatment with anti-inflammatory preventative medication, particularly in patients with severe persistent asthma, which ranges from 17%-26% in Western Europe to merely 9% in Japan, as well as incoherent use of objective lung function testing in these patients (35, 36).

METHODS TO ASSESS ADHERENCE

Adherence is usually lower than measured and lower than anticipated. Patient adherence is difficult to quantify, because an absolute reliable technology is not available. The following methods have been frequently used: direct observation of patient, biochemical monitoring, electronic or mechanical device monitors, medical or pharmacy records, counting remaining doses, clinician judgment, and patient self-report or diaries (*Table 1*). In daily practice weighing a metered dose inhaler, checking the date of issue or counting remaining tablets could enable the physician to gain insight into treatment adherence. However, confronting the patient with approaches like these may stigmatize the patient and eventually undermine a good patient-physician relationship. Further, in studies where tablets were counted or medication was weighed the results were only 50% accurate in reflecting compliance (37-39). Treatment can also be monitored directly by quantifying drug levels in blood, but in practical terms this applies only to theophylline and cyclosporin, which are medication of third choice or seldom used in current practice respectively. Electronic devices have been tested for metered dose inhaler as well as for oral medications. These chip equipped devices which are only available for research purposes, record the exact time, frequency and dosage (14, 15). Besides of ethical concerns when patients are not properly informed about the monitoring of a "bugged inhaler", these devices cannot monitor if the medication is indeed taken by the patient instead of simply actuated into the air (40).

The patient's perception

Improvement of adherence rates demands a trustworthy relationship between the patient and his or her doctor, who must understand the patient's likes and

Table 1. Methods to quantify patient adherence and/or compliance. MDI, metered-dosed inhaler, DPI, dry powder inhaler (adapted from (83-85)).

Method	Technique	Strengths	Limits
Biochemical measures	Drug levels in blood, urine or other body fluids	Accurate, objective	Expensive, intrusive, limited drug tests available, limited to recent drug therapy
Electronic device monitors	Exact date, time and dosage recordable	Accurate, objective	No control if patient actually took the medication, expensive, possible alteration of patient habits in trials? Methodology only for compliance trials suitable.
Observation of patients device technique	Direct review of patient performance with aerosol device by a nurse or doctor	Accurate with training of observer, simple, objectively based	Observations will only be occasionally performed (not for dosing schedule), requires staff time
Medical/pharmacy records	Retrospective review of patient records or refills	Objective, relatively simple to obtain and therefore often used in compliance trials	Time required to obtain patient data, limited to detecting non-refills, cannot tell if patient actually took the drug.
Monitoring remaining dose counts or medication	Doses/solution packages left, MDI canister weighting, DPI doses left	Simple and easy, objective, low cost	Patient may waste doses instead of taking medication, no information on actual dosing schedule
Clinical judgement of provider	Global judgement of health-care provider during clinical visit	Quick, low cost, only in part objective	Overestimating adherence rates
Patient self-report	Periodic recall survey, patient interview, patient diary	Fast for health-care provider, low cost, easy, no objectivity	Very unreliable because vulnerable to patient error and beliefs

dislikes (41). Patients understandably do not favor medication regimes that require regular diagnostic controls, frequent visits at the doctor's office, not even taken medication every morning and evening. Most studies further indicate a preference for oral over inhaled administration route (42, 43).

In our own study we asked 101 asthmatic children and 109 of their parents in an eye-to-eye interview regarding their personal beliefs regarding the disease and therapy using a validated and structured questionnaire. These results were compared with the judgment of pediatricians. High frequency of daily drug application, the fact that the children need to be remembered to take the medication regularly, and the inhalation procedure itself were the main answers given when asked what they dislike in the therapeutic management. Only a minority of the children and their parents feared possible side effects and poor efficacy of the drugs, which was to some extent in sharp contrast to the pediatricians (*Fig. 2*). Children and their parents were much alike in their judgments. Children and their parents preferred to obtain more information on the disease and the medication than the pediatricians anticipated. When asked what source of information they favored, the children stated a group teaching and computer based information including the Internet as their first choice, while their parents preferred the physician's advice first (18). In adults, physicians tend to

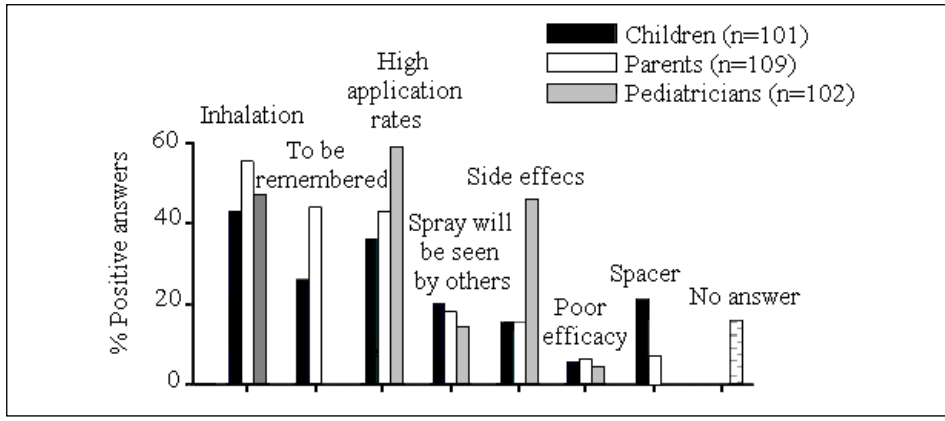

Fig. 2. Asthmatic children (n=101) and their parents (n= 109) were asked separately in an eye-to-eye interview what they dislike. Answers were given, more than one answer were optionally possible. The pediatricians (n=102) were asked what they think their patients would have answered (answers were given) (18).

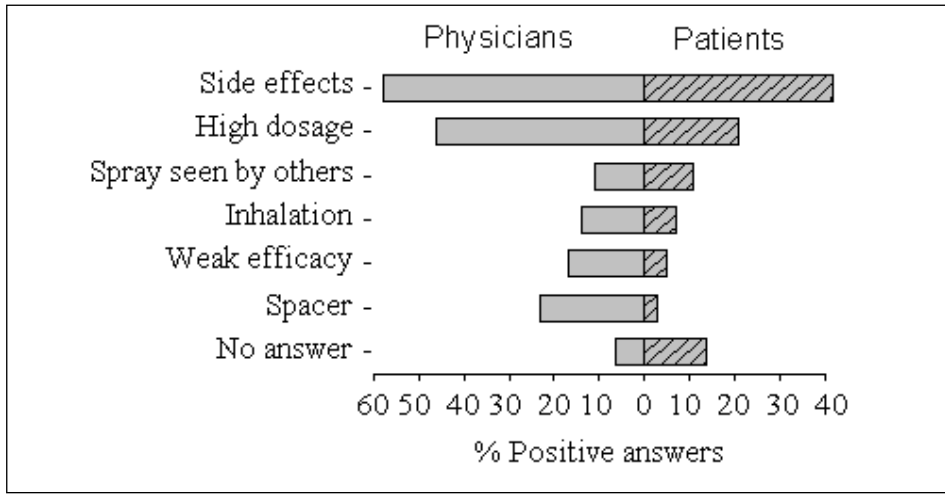

Fig. 3. Asthmatic patients (n=244) were asked in a structured telephone interview what they dislike. The physicians (n=205) were asked, what they think their patients would have answered. Answers were given, more than one answer were optionally possible (18).

underestimate the patient's fears of side effects and high daily dosage (*Fig. 3*), which is in concordance with other reports (44). In our study, patients did not express major concerns about inhaled corticosteroids (ICS). In another trial, approximately one third had marked concerns about adverse effects of ICS, although the patients acknowledged the necessity of ICS treatment (45-48). These concerns were not necessarily related to actual experience, but rather to beliefs

about the link between regular use and dependency or other perceived side effects. Further, we found out that particularly pediatricians, but also other doctors, seem to consider ICS more a foe than a friend even in asthma management, a belief they might convey to their patients as well (18). These findings suggest that the necessity/concerns framework identifies key perceptual barriers that must be addressed by interventions to facilitate uptake and persistence with asthma medications. Prescribers need to counter doubts about personal need and address treatment concerns of their patients. This, however, requires insight into the origins of these beliefs and the willingness to actively correct them if necessary.

METHODS TO IMPROVE ADHERENCE

Creating strategies for improving adherence must start with the identification of root causes of under- or overtreatment. New interventions must be simple, easily implemented, and applicable in many clinical settings:

- Better education of patients and care givers (see below (49))
- Simplifying treatment plans, reduction of doses (reduction from 3-times daily to once-daily regimen increased adherence from 59% to 83.6% (14, 50)). Combining two inhaled drugs into one formulation for inhalation halve the number of times needed for drug administration, and thereby reduce the complexity for drug inhalation. Stoloff et al (51) reported that with this approach adherence doubled (4.06 refills per 12-month period with the fixed combination and 2.35 refills with each compounds in a single inhaler respectively). With the fixed combination fluticasone/salmeterol adherence were almost identical to oral treatment with montelukast (4.51 refills per 12 month period (51)). In comparison with the inhaled administration form, the oral administration was always associated with better adherence rates (51-53).
- Improvement of communication links between doctors and patients. Asthma management seems more efficient when patients were supervised by specialists then solely by general practitioners, as shown in a French study (54). Unquestionably is the most important factor in promoting adherence: a good physician – patient relationship (8, 55).
- Moreover, the implication of innovative techniques, such as telemonitoring of patients are, among others, important interventions that promote better treatment adherence (56).

In the past a variety of interventions to improve patient adherence, ranging from simple adjustments in the medication regimen to complex multidisciplinary interventions that address health system barriers and communication between patients and care givers were tested not only in pulmonary medicine. Unfortunately, the overall quality of the published studies varies widely in terms of study design, outcome measures, and duration of follow-up. Just recently

Kripalani et al (57) published a systematic review in which the authors evaluated 38 out of 13061 trials with one ore more unconfounded interventions to enhance adherence with self-administered medications in the treatment of chronic medical conditions. To compare the outcome of those interventions a standardized measure of effect size (ES) was calculated. Several types of the interventions (including informational, behavioral, and combined information behavioral, and/or social investigations) are effective in improving medication adherence. However, only a few of these interventions significantly lead to an improvement of clinical outcome. Efforts to increase adherence are apparently promising in asthma patients and in contrast quite disappointing in COPD patients (57, 58).

Because studies testing methods to enhance patients compliance differ substantially in patient population, intervention, adherence measure, and the reported clinical outcome parameters, making a pooling of results impracticable, this review divided the publications into four intervention groups as suggested by Kripalani et al (57):

- *Informational interventions*: cognitive strategies designed to educate and motivate patients by instructional means. Examples are face-to-face oral, telephone, written, or audiovisual education, didactic group classes or mailed instructional material.
- *Behavioral interventions*: strategies to influence behavior through shaping, reminding, or rewarding desired behavior including reinforcement. Examples are skill building by health care professionals, pillboxes, calendars and other methods of reminder.
- *Family and social interventions*: social support strategies provided by family or another group. Examples are support groups and family counseling, group sessions.
- Combined interventions 2 or 3 of the preceding categories

Informational efforts

Cote et al (59) evaluated in asthma and COPD patients the effect of a limited education plan plus a structured educational program, which addressed beliefs, attitudes, knowledge, and social support, which was followed by a reinforcement arm. The control group received only limited education on inhaler technique and a peak-flow measurement based self-management plan. In contrast to the COPD group, in the asthma group the 6-month visit reduced urgent visits for asthma exacerbation from 34 within 6 months in the control group to 9 in the intervention group ($P<0.03$). Similarly, Gallefoss et al (60) compared an intervention group consisting of two 2-hour group sessions followed by one or two individual sessions of 40 minutes and a self-management plan with usual care. In the intervention group FEV1 increased by 112 ±386 ml while in the control group FEV1 fell -83 ±383 ml ($P<0.05$). Adherence was monitored using refill audits (prescribed doses of ICS). Again, COPD patients had no benefit. Other authors

found similar results using individual educations sessions, which were performed either by physicians and/or pharmacists or nurses, the provision of booklets to the patients, and the introduction of peak-flow measurement based self-management plans. While severe attacks and emergency visits or readmissions did not decline, the peak-flow increased, symptom scores and routine physician visits decreased ($P<0.001$) when intervention and control groups were comared. The lack of a reduction of severe asthma attacks is, however, somewhat contradictory to the reported positive results (61, 62). Another study evaluated the use of an experimental audiotape incorporating components of protection motivation theory and a standard asthma management booklet, separately or in conjuction, or no educational materials. Dose refill rates increased by 15% to 19% in the intervention groups (booklet alone or audiotape plus booklet) and declined 22% in the control group after 6 months, although scores in the asthma control questionnaire did not change (63). The discussion of self-management plan with pediatricians, individual education sessions by a nurse (4 sessions of 30 min each), followed by three group education sessions (90 min) had neither a significant effect on a self reported adherence 10-point scale nor on FEV1 improvement when compared with pediatrician visits every four months (64).

Behavioral interventions

The most common and effective from of behavioral intervention is the simplification of dosage combined with repeated assessment of medication use using feedback measures. If patients know that their medication use is being monitored, they are more likely to adherent. Stimulus-control techniques refer to using cues to prompt desired actions. Some have found that such prompts do improve adherence (65). Other trials tested specialized packaging, directly observed therapy and cognitive behavior therapy. None of these techniques significantly affected clinical outcomes (56, 66).

Family and social interventions

Heath care providers can advise patients together with family members to enhance adherence. They can help outside the clinical venues (e.g., national/district program, support groups) to consider how their efforts compliment the asthma education provided in treatment settings, focus on developing self-regulation skills of patients, and systematically develop the capacity of key individuals across the circles of influence to help patients attempt to control asthma. This might particularly of interest in children (67). However, scientific proof of clinical efficacy implementing these interventions is lacking (5).

Combined interventions

Most combined interventions included informational, behavioral components, as well as social support strategies. When compared with usual care consisting of

educational pamphlets, routine physician encouragement, the combined interventions using educational pamphlets, workbooks, tailored self-management plan, individual counseling sessions, support groups, as well as telephone follow-up and reinforcements resulted in a reduction of self reported severe symptoms score (P=0.002). Further, all actively treated patients reported about increased adherence rate to inhaler (P=0.001, compared with standard care) and to medications (P=0.005), and were rated being excellent compliant by the staff (P=0.001). Because the primary outcome parameters related mainly on patient self-reports, these positive results might be overstated (68). This is in concordance with Levy et al (62) who found an significant improvement of self-reported compliance, significantly higher peak-flow values, fewer symptoms at six months, fewer days off work, and fewer consultations with health professionals following a complex education program. In this group, the use of ICS and rescue medication in severe asthmatic attacks were significantly higher. But there was no difference between the groups for use of these medications for mild attacks. Ignacio-Garcia et al (69) coupled a self-management education program with education reinforcements, and, after 3 years, showed a significantly decrease in the number of days off work or school, consultations at general practitioners, admissions to emergency services, hospital admissions, nocturnal awakenings, and an improvement in FEV1 in patients of the intervention group. The number of patients using oral corticosteroids decreased significantly (69).

Complex interventions did not always improve adherence with medications and may not even result in an increase of asthma knowledge as Cote et al (70) showed. Faber et al (71) found in a small study (n=28 patients) that a single session of education and management intervention, consisting of basic asthma education, written self-management plan, training how to hold the aerosol chamber, and three brief follow-up phone calls were not sufficient to have a major positive impact on treatment outcomes. Regardless of this result, an improvement in asthma controller medication use was reported (dispensing events of controlling medication, mostly ICS; P=0.004 compared with usual care) (71). Individual self-treatment guidelines for exacerbations on top of a general self-management program did not improve clinical outcome in asthma (72). Also a pharmaceutical care program in which the patient received education materials, peak-flow training and monthly calls to elicit peak-flow meter values, was not positive. The purpose of this trial was to assess the efficacy of a pharmacist-based intervention monitoring peak-flow data in regard to patient adherence and health care utilization. There was no difference between the intervention group and the usual care group in terms of adherence to medication and health related quality of life after six months and at one year (73).

Adherence of physicians to asthma guidelines

Better adherence to asthma guidelines by health professionals is crucial in translating recommendations into improved outcomes. It is well known that,

despite wide promulgation, guidelines *per se* have little effect in changing physician behavior (49, 74, 75).

Barriers

Little is known about the process and factors responsible why physicians do not comply with current guidelines. In order to develop strategies to enhance physician adherence, the underlying barriers must be identified first. In this context the study from Cabana et al (49) is worthwhile to mention who reviewed the literature from 1966 to 1998 and selected 76 published studies describing at least one barrier to adherence to clinical practice guidelines, such as practice parameters, clinical policies, or national consensus statements. Among those, 293 barriers were found which can be separated in 3 general categories and 10 subcategories:

- Physician knowledge (76)
  - lack of familiarity: volume of information, time needed to stay informed, guideline accessibility
  - lack of awareness: volume of information, time needed to stay informed, guideline accessibility
- Attitudes
  - lack of agreement with specific guidelines: interpretation of evidence, applicability to patient not cost-beneficial, lack of confidence in guideline developer
  - lack of agreement with guidelines in general: to rigid to apply, challenge to autonomy, not practical (too voluminous, hard to understand for non-specialists), biased synthesis, too many guidelines for a general practitioner
  - lack of outcome expectancy: physicians disbelieve in efficacy of guideline recommendations
  - lack of self-efficacy: doubt to perform guideline recommendations properly
  - lack of motivation/inertia of previous practice: lack of consideration for other treatment options as well as selfishness in the efficiency of personal knowledge, year long habits and routine
- Behavior
  - External barriers
    - Patient factor: inability to reconcile, patient preferences interfere with guideline recommendations
    - Guideline factor (9): guideline characteristics (too long, difficult to read, didactic aspects), presence of contradictory or to many guidelines about the same topic
    - Age and employment status (77): younger physicians and self-employed physicians are more likely to adapt guideline recommendations and to attend educational programs.

- Environment factors: lack of time, lack of resources, organizational constraints, lack of reimbursement, concerns related to malpractice liabilities.

Other factors may also influence health care provider's quality to manage the patient disease such as physician discomfort with uncertainty and his/her personal perceptions, a compulsion to treat despite the lack of effective interventions, opinion leaders who may have nonevidence-based opinions, the persuasive stimulus of pharmaceutical representatives, and fear of standing out including the competitive pressure arising among colleagues. Strategies to successful improve guideline adherence must address these barriers prior to designing individualized intervention programs and/or step-by-step systematic training programs to initiate change in physician practices. Such change strategies may include both education and utilization of behavioral attitude change techniques. Dissemination of guidelines alone has little impact on physician behavior (78). A study in Israel revealed that one year after the national guideline for asthma treatment was published and distributed 75% of the primary care physicians had read it, but less than 25% had participated in educational programs on the management of asthma. Only 40% of the physicians who had read the guideline changed their management strategies accordingly (77). Thus, simply educating the physician is not enough. The education must be at all levels of care from the nurses to the office personnel for successful implementation of guidelines into everyday practice. Successful implementation of guidelines is imperative for patients to receive quality health care (9).

Methods to change physician prescribing patterns

After participating in a successful continuing medical education (CME) program, many but still not all participants are motivated to change their clinical practice behavior. Unfortunately, the most commonly used method of CME, the traditional lecture, has been proven to only partially efficient. The knowledge and change of prescribing patterns may unravel over time. A more effective model is the small-group interactive case discussion (e.g., problem-based learning) which has been shown to improve acceptance of and adherence to new guidelines eventually resulting in improvement of patient outcomes. Davis at al (79) demonstrated the success of three teleconferences during a 3-week period (each lasted one hour) in which a asthma case were discussed. Not only was the acceptance rate uniformly positive among the participants, but, most importantly, it lead to an increase of prescribed ICS use from an average of 2.54 to 7.76 refills per moths for the 6 months after the intervention ($P<0.001$).

In contrast to more interactive intervention programs, passive interventions, such as sending informative materials including patient-specific intervention packets to patient's prescribers and pharmacists had no clear effects on the prescription of appropriate long term controller treatment of asthma patients (80). Interestingly, also the participation in clinical trials (sponsored by pharmaceutical

companies) had no significant impact on physician's adherence to international treatment guidelines but increased the use of the trial sponsor's drugs (81).

As this review demonstrates, adherence is a very complex but important issue requiring a multidisciplinary approach. Critical analysis of the methods applied is necessary in order to prove that the particular intervention is efficient. With increased attention to these issues, asthma care consistent with current guidelines should increase with resulting decrease in morbidity and mortality.

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Author address: A. Gillissen, St. George Medical Center, Robert-Koch-Hospital, Nikolai-Rumjanzew-Str. 100, D-04207 Leipzig, Germany; phone: +49 341 4231201, facimile: +49 341 4231203, Internet: www.rkk-leipzig.de