Patient factors and compliance with asthma therapy

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Compliance by patients to prescribed treatment regimens can be considered as the interface between effective therapy and effective disease management. Compliance can be affected by the nature of the relationship between the practitioner and the patient, and their attitudes towards each other. It has also been suggested that practitioner behaviour can influence patient behaviour and health status. However, each individual patient is influenced in his or her attitudes, and reactions to disease and its management, by a wide variety of patient-related factors. These include psychological variables such as mood, beliefs, and the knowledge, motivation and ability of the patient. Social factors may also play a role: these include age, marital and socioeconomic status and level of education. Results from a range of studies in patients with pulmonary or other diseases show that the psychosocial determinants of compliance are only poorly understood, and suggest that compliance cannot be predicted from patients' health status and that social factors are weak indicators only. Furthermore, it appears from available data that patients' beliefs about health issues are not as useful as indicators of likely compliance as was previously believed.

Introduction

The use of a regular inhaled anti-inflammatory drug with a bronchodilator provides effective relief of symptoms for many asthmatics. However, despite the availability of a large number of well-tolerated treatments, non-compliance with asthma (and other) medications remains a problem (1). Studies available suggest that, although some patients do indeed manage their disease well, many do not take medication as prescribed (2–4). As non-compliance with treatment is a cause of mortality and morbidity in asthma (5,6), it is in the interests of both practitioners and their patients to understand why patients fail to follow medical advice.

A variety of different factors that relate directly to patients and their personal characteristics and backgrounds can influence compliance with asthma therapy, and many of these can be applied to compliance with therapy for other chronic diseases. These factors are complex and involve psychological, social and medical issues, all of which may alter patients' perceptions of the benefits of compliance with their recommended treatment regimen. Social and cultural factors, such as socioeconomic status, level of education and health belief issues may also influence the ways in which patients perceive their treatments, and may affect compliance with them. Attempts have been made to determine levels of compliance in patients with asthma and other diseases, and while accurate determination of compliance is difficult, the measurement of variables that affect compliance can be even more difficult. In most studies, compliance is reported, rather than objectively measured. The proportion of compliers in most studies appears to be low (approximately 50%). Notwithstanding these difficulties and complications, there are a number of studies of interest that have been conducted in a variety of therapeutic areas.

Compliance and the doctor–patient relationship

A report published by the Royal Pharmaceutical Society of Great Britain's working party on medicine-taking has recommended that 'concordance' should replace the term 'compliance' (7). This change in terminology reflects the change in the doctor–patient relationship. In modern society the doctor–patient relationship should be one that is based less on trust and more on openness and respect. The price for this loss of dependence on the doctor will be greater responsibility, in the doctor's case for the quality of the evidence, diagnosis, treatment and explanation, and in the patient's case for the consequences of his/her choices. At a consultation, for example, the patient should convey his/her health beliefs, the doctor should enable this to happen and use his/her expertise to make a diagnosis and to recommend the most appropriate intervention. Thus, the intention is to form a therapeutic alliance, which should allow the patient to make as informed a choice as possible about the diagnosis and treatment; the most important determinations, in terms of patient behaviour, are those that are made by the patients themselves.

Patient-related factors affecting compliance with asthma therapy

PSYCHOLOGICAL FACTORS

Increasing interest has been shown in recent years in the relationship between psychological and social factors and asthma, and these issues should be taken into account when plans for the management of patients are made. Psychological factors that can influence compliance with asthma and other treatments include cognitive impairment, especially in the elderly in whom memory or concentration may be affected, and a loss of the patient's capacity to understand the need for treatment. Psychopathology associated with the illness may also be involved, and may take the form of clinical depression, anxiety, denial or fatalism. Furthermore, poor interpersonal skills may affect the ability of the patient to interact effectively with the clinician and/or others who are key to achieving effective therapy. Functional illiteracy may also be seen, which affects the patient's ability to read and follow simple instructions.

Dew et al. (8) identified compliance problems in a group of 101 patients who had undergone heart and lung transplantation and were followed for 1 yr. This may be considered surprising in the light of the critical nature of the procedure involved; however, the investigators found that anger and hostility were four times as likely to be identified in patients with poor compliance than in those who complied with their treatment regimen. Such reactions may be related to patients' postoperative experiences and such factors as their perceptions of their own personal difficulties and lack of support from their families.

Few data are available to show the effect of psychological factors on the compliance of patients with asthma. However,

in a prospective study of 102 such patients, psychological assessment was performed using the Hospital Anxiety and Depression Scale and the Inventory of Interpersonal Problems, and compliance with inhaled medication was recorded using an electronic device, over a 12-week period (9). Of those patients who completed the study, 51% were defined as non-compliant (<70% of the prescribed dose, or doses omitted for at least 1 week). Non-compliant patients had a significantly higher mean score for depression than compliant patients (4·7 vs. 3·2, $P < 0.05$), and the depression score correlated with non-attendance at follow-up clinics. There was no significant difference in anxiety score between non-compliant and compliant patients (Fig. 1). Anxiety can have both positive and negative effects on compliance, as anxious patients may be highly motivated to take medication exactly as prescribed or be overwhelmed and unable to follow the prescriber's instructions.

PATIENT MOTIVATION, ABILITY AND BELIEFS

When individuals are faced with health advice from their doctor or another healthcare professional they will interpret and evaluate this advice and decide whether it should be incorporated into their behaviour. Patients make this evaluation in the light of their beliefs about the illness and the treatment. Thus, within the concordance model,
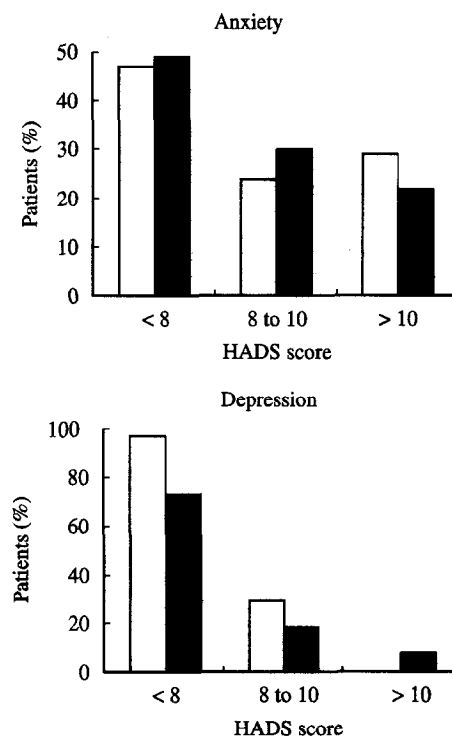

FIG. 1. Hospital Anxiety and Depression Scores (HADS) for compliant and non-compliant patients in patients with asthma. χ^2 test showed no significant difference between compliers and non-compliers for anxiety, but $P < 0.05$ for depression (9). □: compliant; ■: non-compliant.

there are two main areas the clinician can focus on in an attempt to achieve optimal patient compliance with therapy: firstly, the degree of motivation of the patient (which will predominantly affect intentional non-compliance), and secondly, the ability of the patient (which will affect unintentional non-compliance). In order to increase a patient's motivation for treatment, the clinician needs to focus on the patient's beliefs, and to improve a patient's ability the clinician needs to focus on a patient's skills (Fig. 2).

Compliance is thought to be heavily influenced by the knowledge and attitudes of the patient. These factors have been encompassed in a number of different psychological models, the best known of which is Becker's health belief model (10). This model postulates that the likelihood of patients following a healthcare or treatment regimen is related to their motivation and incentive to do so. Two main beliefs held by patients about their medications have emerged: the necessity of the medication (i.e. necessary for present and future maintenance of health) and concern about the medication (arising from beliefs about potential negative effects, such as dependence). Patients with stronger beliefs about the necessity of the particular treatment are likely to have higher compliance, while those with stronger concerns are likely to have lower compliance with treatment. Thus, patients engage in a risk–benefit analysis, balancing the necessity with the concerns of the medication, and non-compliance may be a logical attempt to moderate the perceived risks by taking less. It is important that the patients' perceived risks are not based on mistaken beliefs about the dangers of the medication, and this is where the doctor must allow the patient to make as informed a choice as possible. In addition, a patient's understanding of his or her disease is likely to be influenced by education and socioeconomic status. These are classified as social rather than psychological factors, and are therefore discussed later.

All factors relate to the degree of motivation and ability that the patient develops during treatment, and there is therefore a need for a combined approach to intervention that will be effective on the different causal factors. Thus, increasing concordance by focusing on beliefs and correcting misconceptions about treatment

FIG. 2. A simple model relating the factors that influence motivation and ability to intentional and unintentional compliance. Note the association of patient factors (highlighted) with patient motivation and ability.

might increase motivation to take medication, and increasing the convenience of a regimen might improve skills and hence ability to comply. These factors are also inter-related, as a patient who is unable to use a treatment will become demotivated, and one who thinks a treatment is unnecessary may not develop the skills to use the medication.

Notwithstanding the above, data of considerable interest are available from the southern U.S.A. which cast doubt on the hypothesis that health beliefs influence adherence to good health-related behaviour. Martin and Paniucci (11) studied 20 health beliefs (including dental visits, wearing of car seat belts, abstinence from tobacco and alcohol and checking of blood pressure) in Black women aged over 65 years who were recruited through local Baptist churches. As might be expected, the women studied believed that all these beneficial practices were important, and assigned to them a mean overall importance score of 9·36 (range 8·4 to 10·0) out of 10. However, self-reporting of adherence to these practices resulted in an overall adherence rate that was somewhat lower (85%) with a much wider range (28 to 100%). Most importantly, the investigators found no evidence of any correlation between health beliefs and an individual's adherence to those beliefs ($r = -0·01$; $P = 0·9$). This indicates that although patients may be aware of measures that are beneficial to their health, not all will comply with these measures.

MOTIVATION AND THE STAGES OF CHANGE MODEL FOR COMPLIANCE

The Stages of Change Model is a device for examining the structure of change associated with both self-mediated and treatment-facilitated modification of addictive and other problem behaviours (12,13). It integrates motivational and behavioural aspects and recognizes the process character and temporal dimension of behaviour change. It also shows how these changes occur and which mechanisms are important (14). However, it is important to note that none of these studies have used this model to test patient outcomes, such as health status and healthcare use, while few, if any, have focused on chronic illness. The main use of the model has been exercise compliance or participation. The model consists of five ordered categories that describe motivational readiness to change a problem behaviour. These five stages of change are:

Precontemplation: there is no intention to change behaviour in the foreseeable future. Many individuals at this stage are unaware or under aware of their problems, or are not yet ready to deal with a threatening illness and are not willing to adopt relevant strategies.

Contemplation: at this stage, the individual is aware that a problem exists and is thinking about overcoming it, but has yet to make a commitment to take action.

Preparation: intention and behavioural criteria are combined at this stage. Individuals intend to take action (usually within 30 days), and may have taken a first step towards action in the past year.

Action: this is where individuals modify their behaviour, experiences or environment to overcome their problems,
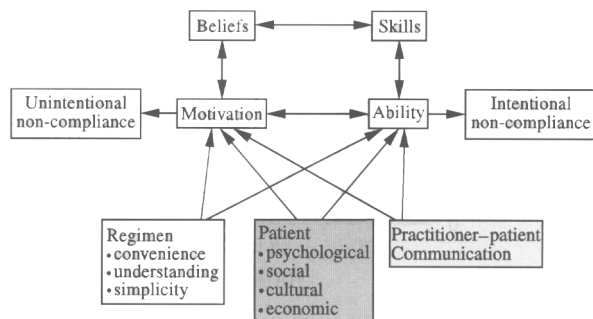
and involves the most overt behavioural changes. This stage involves expenditure of the most time and energy.

Maintenance: individuals work to prevent relapse and to consolidate gains made during the action stage. Maintenance is an active stage that can last from 6 months to 5 yr; for some behaviours, maintenance can be considered to last for life.

Transition between the stages of change is affected by a set of independent variables known as the processes of change. Knowledge of these processes, together with the characteristics of the individual and the current stage of change, should help healthcare professionals decide how to most effectively motivate the patient, and improve compliance with therapeutic regimens.

SOCIAL FACTORS

Various factors such as age, marital and socioeconomic status and level of education should be considered when promoting compliance. However, before each of these is examined in detail, none of these factors will guarantee that an individual will comply, hence it is recommended that clinicians treat every patient as a non-complier to ensure that all receive adequate education. High levels of unemployment, single-parenthood and the culture of poverty associated with low socioeconomic status can seriously affect the ability and motivation of an individual or family to manage chronic illness. Families that lack the social and structural support of financial resources and the presence of two parents to share household and childcare responsibilities carry significant additional burdens compared with others who possess these advantages. Compliance with treatment regimens may also be influenced by the patient's level of literacy. Financial, personal and structural barriers to compliance, such as difficulty in attending the clinic for repeat visits and prescriptions, and concomitant problems and stresses (e.g. poor housing and low levels of social support) that make compliance with therapy a low priority for the patient, are all likely to combine to cause considerable problems for healthcare professionals who are trying to provide effective treatment.

Schrott et al. (15) investigated 2763 post-menopausal women with heart disease in the U.S.A. who were receiving medication to improve their serum lipid profiles (defined as the achievement of 1988 and 1993 Adult Treatment Panel goals of a serum LDL-cholesterol level of below 3·4 mmol l^{-1} or 2·6 mmol l^{-1}, respectively). Although 47% of participants were taking lipid-lowering medication, 63% did not meet the 1988 treatment goal and 91% did not meet that for 1993. The status of being unmarried (adjusted odds ratio [OR] 0·47; $P = 0·002$) and education to graduate level (OR 0·69; $P = 0·02$), were shown by multiple logistic regression to be associated with failure to achieve the 1998 LDL-cholesterol target. Women who smoked (OR 1·90; $P < 0·001$), drank alcohol (OR 1·10; $P = 0·01$) or who were African Americans (OR 2·03; $P < 0·001$) were found to be more likely to fail to comply with lipid-lowering medication, whereas older women (OR 0·75; $P = 0·008$) and those

who had never married (OR 0·36; $P = 0·02$) were more likely to comply.

Increasing age and education to a higher level appeared to predict more consistent compliance in a study in patients requiring anti-arrhythmic therapy (16). Compliance over 1 yr was assessed by self-reporting and tablet counting in 930 of an original cohort of 1816 enrolled patients. However, unlike Schrott et al. (15), these investigators found that consistent compliance was predicted by the presence of a spouse, which indicates that the support provided by a partner may be a significant social factor affecting compliance with therapy. Good general and mental health and low levels of stress were also found (perhaps not surprisingly) to predict more consistent compliance over a 1-yr period.

Compliance data are also available from two large studies in patients with chronic obstructive pulmonary disease (COPD). In one trial, the compliance (based on average time of nebulizer use each day) of 985 patients on home nebulizer therapy was assessed by questionnaire (17). The best social predictors (by logistic regression) of good compliance were White race (almost certainly a socio-economic factor) and married status (adjusted OR 2·30 and 1·49, respectively). Other good predictors were increased age, history of higher education and stable lifestyle. Negative factors were also identified in these patients: these included smoking and drinking habits. However, although statistically significant, numerical differences between groups tended to be only small, which may call the clinical significance of these differences into question (Fig. 3).

Two-year follow-up data (analysed by multiple logistic regression) are available from the Lung Health Study, a double-blind, multicentre, randomized controlled trial of smoking intervention and bronchodilator therapy in which 3923 participants had their compliance measured by self-reporting and weighing of metered-dose inhaler canisters.
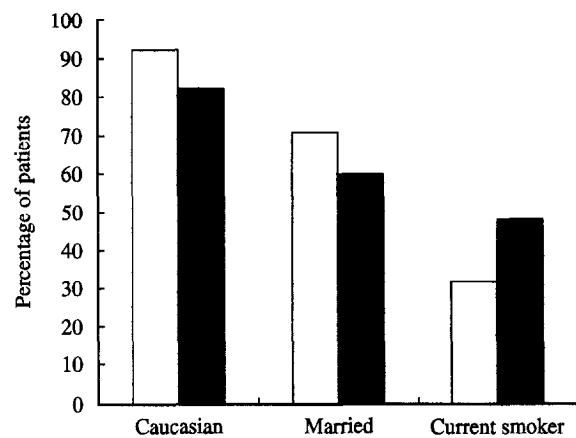

FIG. 3. Compliance with long-term nebulizer therapy for COPD in the IPPB trial. Differences between groups (compliant and non-compliant patients) for race, marital status and smoking status. Note small numerical differences between groups, although $P = 0·001$ for all these variables (17). □: compliant ($n = 498$); ■: non-compliant ($n = 487$).

One-year results (with adjusted ORs) for self-reported compliance confirmed by canister weights indicated that compliance was associated with marital status (1·461), age (1·055), race (1·859), shortness of breath (0·906), confinement to bed with a respiratory infection (0·788), days hospitalized (0·728) and poor respiratory function (0·863) (18). Moreover, the level of compliance was reported to have initially improved with the use of a structured programme, but to have declined over 2 yr. The self-reported rate of inhaler use exactly as prescribed declined from 52% at the first 4-month follow-up visit to 43% at year 1 and 38% at year 2.

There appear, to date, to be few studies evaluating predictors of compliance with treatment in patients with asthma. Preliminary results of a study in 45 female and 43 male patients are available (19), however, in which compliance with metered-dose inhaler therapy was measured with questionnaire answers and the Inhaler Adherence Scale (IAS), which ranges from 0 (compliant) to 6 (non-compliant). Compliance in this trial was found to be better in older patients ($r = -0.24$; $P < 0.05$) and those with lower peak flow rates ($r = 0.25$; $P < 0.05$). IAS scores were better (i.e. lower and hence more compliant) in female than male patients (Fig. 4), and occupational profile significantly influenced the IAS score with unemployed patients having a better score than professionals (Fig. 4). Conversely, level of education and number of work days missed because of asthma did not correlate with IAS scores.

COMPLIANCE PROBLEMS IN THE ELDERLY

It should be noted that, although increasing age was associated with improved compliance in all the trials reported above, problems can be encountered in elderly patients who may be taking a variety of medications for a number of medical conditions. Social isolation, often encountered in the elderly, is a significant predictor for a number of chronic health problems, disability and premature death (20). In addition to auditory and visual impairment, elderly patients may also have cognitive difficulties (including forgetfulness or dementia) which may make the understanding and following of treatment regimens difficult. Many elderly patients also care for elderly partners who may have chronic health problems of their own (which complicates the management of their own conditions), and may have diseases such as arthritis that make the use of metered-dose inhalers difficult or impossible.

Quality of life

As described earlier, Lurie et al. (19) found no correlation between quality of life and level of compliance in patients with asthma. This is surprising when viewed in the light of the simple hypothesis that the attainment of better health through effective treatment should lead to positive reinforcement of good compliance behaviours. Clinical papers that include comparisons of quality of life and compliance are unfortunately few, but there are nevertheless some data available from trials in patients with pulmonary or other diseases.

In general, compliance has not been shown to be related to quality of life or mood state, and only weakly related to disease severity, in a variety of studies. In a study in patients undergoing haemodialysis, compliance with treatment was found to be associated with severity of illness (as judged by attending clinicians), but not with Karnofsky performance status, level of social support or patients' perceptions of illness (21). It should be noted that the Karnofsky scale measures a patient's functional status, and is not a true quality-of-life measure; however, it may be argued that the use of markers such as this is made acceptable by the shortage of available data with which to investigate the present arguments. Results are also available from patients receiving immunosuppressive therapy after renal transplantation to show that compliance was unrelated to demographic variables (apart from better compliance with prednisone treatment for men than women, which may be a sampling issue because of the small sample assessed in this study), graft function or Nottingham Health Profile (a generic measure of impaired health) (22). However, compliance in these patients increased significantly after episodes of transplant rejection, which may explain the observation that compliance was better for immunosuppressive than for anti-hypertensive therapy ($P < 0.0001$).
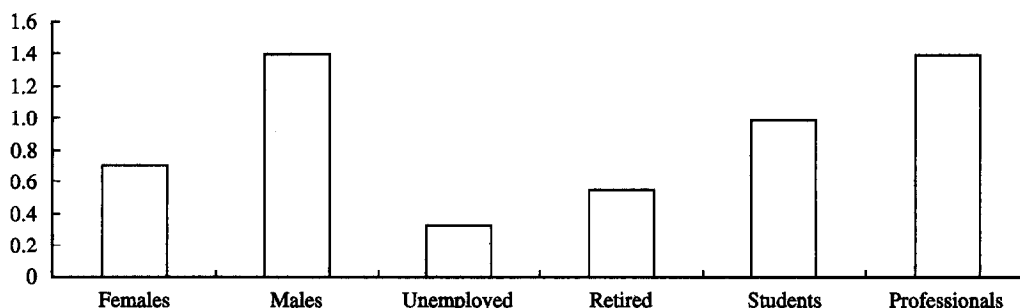

Fig. 4. Inhaler Adherence Scale (IAS) scores for patient gender and occupation in 88 ambulatory patients with asthma. $P < 0.05$ between males and females; $P < 0.0007$ for differences between occupations (unemployed, non-active, students, professionals) (19).

TABLE 1. Compliance with anti-retroviral therapy in patients with AIDS (adapted with permission (23) [Carfax Publishing Ltd, Abingdon, U.K.]

Variable	Results		P
	Compliant patients (n = 29)	Non-compliant patients (n = 17)	
Age (years)	39	42	n.s.
Depression score (Beck Depression Inventory)	14·1	19·5	n.s.
Overall mood score (Profiles of Mood State score)	43	65	n.s.
Karnofsky score	87	92	n.s.
Coping	8·2	11·6	0·03
Previous intravenous drug misuse (%)	21	59	0·01

Major predictors of compliance were described by Schron et al. (16) in a study in patients receiving anti-arrhythmic therapy. However, interpretation of the data from this study is complicated by the finding that patients with a history of angina or myocardial infarction and those with poor physical function were likely to be good compliers. This appears to conflict with another observation from these authors that patients with good general and mental health were more likely to adhere to treatment, and indicates that the relationship between health status and compliance is far from straightforward. However, results obtained by Singh et al. (23) were more concordant with those in other trials and indicated that depression (Beck Depression Inventory), overall mood (Profiles of Mood State scores) and Karnofsky scores did not correlate with compliance or non-compliance in patients with AIDS who were receiving anti-retroviral therapy (Table 1). Patients were assessed at baseline, and at 6 and 12 months, with those taking at least 80% of their medication being classed as compliant. The overall compliance rate was 63%, and the major predictor of non-compliance was a history of intravenous drug misuse.

In the COPD trial of Turner et al. (17), there were no statistically significant differences between compliers and non-compliers in terms of generic quality of life (as assessed by the Sickness Impact Profile) and mood (as assessed by the Profile of Mood Status scores) (P = 0·8 and 0·5, respectively). The need for caution when analysing data derived from patients' answers to questionnaires that relate to compliance were evident in this trial from the reasons patients gave for their use of nebulized therapy. Of the compliant patients, 82% said they adhered to their treatment because it made them feel better; however, as many as 67% of the non-compliant patients responded similarly. Reasons for missing nebulized therapy are less unexpected (Table 2), but the high numbers of non-compliant patients who felt too tired or busy to use their nebulized therapy concurs with the premise described earlier that patients apply value judgements to their treatments and are unlikely to adhere to the prescribed regimen if they perceive its benefits not to outweigh its inconvenience and other negative characteristics.

Conclusions

Clearly, there are very few assumptions that may be made on the basis of currently available evidence about the way in which a patient's psychological and social background will affect their likelihood to comply with medication for asthma (or any other condition). Although it appears that the behaviour of practitioners can influence patients' behaviour and therefore health outcomes (24,25), the effects of other factors are unclear. Each patient is uniquely shaped and affected by his or her background and psychological status, and may well respond to treatment instructions in a way that is entirely unexpected, as in cases where poor compliance is seen in patients with critical illnesses. Overall, it seems that there is still much to be learned about the psychosocial determinants of compliance in asthma. Although information gleaned from studies in patients with other diseases could be useful, data are currently too few and inconsistent to be able to draw solid conclusions, or to extrapolate from one disease state to another. Currently available results suggest that compliance cannot be predicted from a patient's health status, that social factors are weak determinants, if at all useful, and that an understanding of patients' beliefs may not be as useful as has been previously thought. Certainly, studies into the decision-making processes used by patients with asthma (and other conditions) are needed, and practitioners

TABLE 2. Reasons given by patients for missing nebulized drug therapy in the IPPB study (17)

Reason	Percentage of patients		P
	Compliant	Non-compliant	
No effect on breathing	21	42	0·001
Too tired	7	31	0·001
Too busy	20	45	0·001

should endeavour to relate to each patient as a unique individual.

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