Assessing and ensuring drug compliance in chronic respiratory disease.
SEPCR-ERS Workshop, Wiesbaden, 1990

Chairman - P. Vermeire*

CONTENTS

* University of Antwerpen (UIA), Antwerp.

Therapeutic compliance in asthma; its magnitude and implications

G.M. Cochrane**

Compliance with medical regimes has been claimed to be a major problem facing medical practice [1]. Despite the apparent importance of patient compliance, there is a paucity of studies which examine compliance in detail, and with close attention to the scientific method. SOUTTER and KENNEDY [2] in 1974 examined 768 studies published in the British Medical Journal and The Lancet between 1967 and December 1972 in which various aspects of

drugs were reported. Assessment of patient compliance was deemed possible and necessary by the authors in 324 of the studies but had actually been undertaken in only 61 (19%). Assessment of the magnitude of compliance as a problem in lung disease is difficult when little or no attempt has even been made to verify therapeutic compliance in the strict environment of clinical trials of new drugs, particularly in patients with asthma and chronic obstructive bronchitis. Compliance or adherence with medical advice remains, particularly in

** Consultant Physician, Guy's Hospital, London, UK.

patients with chronic illness, with variable symptoms over hours, days and months, a major problem which in thoracic medicine continues to be ignored.

Definition of compliance or adherence

The definition of compliance to medical advice is simple; total compliance is that the patient follows fully the medical advice given by the practitioner. Such a definition assumes that the medical practitioner has made the correct diagnosis, the medical advice is sound and any medication prescribed is both appropriate and has proven efficacy for the disease diagnosed. Total compliance over long periods of time at a 100% level is probably unrealistic and therefore any assessment of compliance needs to relate the level of compliance with the advice which will maintain the patient in good health. Failure to complete a course of antibiotics for otitis media or sinusitis may well be associated only with a further acute episode, the organism remaining sensitive. Minimal drug taking, particularly of one of a number of preparations as in non-compliant patients with tuberculosis, will lead to the development of resistant organism with far more sinister implications.

Differing patterns of poor compliance may occur in long term diseases such as asthma and chronic bronchitis. The 'on/off' noncomplier who takes all of the medications until 'cured' and then stops all medication, may with recurrence of symptoms reinstitute the full therapeutic programme. The "little bit each day" noncomplier with one or two 'puffs' of one or the other inhaler just to keep the doctor happy, may lead to a different end-point! Technical problems, which will be discussed over the next two days, have so far prevented a true analysis of the magnitude of the problem with inhaler therapy in asthma and chronic bronchitis and the extent to which either of these two extremes occur in practice. In patients prescribed two medications they may be fully compliant with one and not the other, as has been suggested in asthmatics compliant using bronchodilators but with only minimal adherence to prophylactic drugs.

In order to assess the magnitude, we have to start determining numerate values of non-compliance. Full compliance is probably within the range 80%–100% instructions followed. Numerical values do lead to problems if we model the biological implications of 50% compliance on the 'all or none' behaviour pattern compared to the 'little bit all the time'. Are they comparable? Until clear guidelines are developed, interpretations between these two patterns of 50% compliance with therapy will continue to be unsatisfactory.

Effects of poor compliance

The effects of poor compliance in some diseases are obvious; in adolescent diabetics the inevitable frustration with both medication and behavioural constraints leads to rapid deterioration and hospital admissions. In many epileptics, cessation of treatment is associated with a fit and the embarrassment of loss of licence or stature in the community [3]. The effects of poor compliance in asthma and bronchitis however can be far more varied. Patients with long standing mild asthma which is never fully controlled, do not appear to be aware of the potential improvement possible with treatment [4] and fail to even try new therapies, particularly if the word "steroid" is mentioned. Others may stop inhaled prophylactic therapy and have periods of nights, weeks or months with mild symptoms and then suddenly develop a life-threatening attack of asthma.

The effects of poor compliance are not just limited to increased morbidity. In patients on proven effective therapy poor compliance may well jeopardise the development of new therapies unless a more rigorous approach is taken to verify compliance with therapy offered.

Attitudes towards the verification of compliance

Attitudes towards the verification of compliance are complex. The physician assumes patient compliance and may fear verification as an audit of his clinical skills [5]. The patient's reactions are more poorly understood in lung disease but extend from anger at the doctor checking on his behaviour to the simple admission of "forgetting all of the time". Frequently patients justifiably suggest that the medical advice was poorly given and not reinforced with education of the need to take medication or even how to take it, particularly in the case of metered dose aerosol prescribing. Family interactions, particularly wives of patients with chronic obstructive bronchitis and parents of adolescent asthmatics, become confused between the desire for their loved one to be well and their loved one's addiction or reliance on medication. The attitude of the pharmaceutical industry to studies verifying compliance is probably the most confused. Most clinical studies are ruthless in excluding 'protocol violators' for minor variations in predicted peak flows or a minimally reduced haemoglobin but will include patients into studies assessing efficacy of new preparations purely on asking a patient whether they had taken the preparation, with no spot checks of biological fluid assays or longitudinal assessment in terms of therapeutic outcome or pill counts.

Finally, any author with original work investigating the magnitude of compliance is amazed at the ambiguity of the journals as he receives the reject letter full of praise for the study requesting an editorial when and if the study does get published.

The extent of poor compliance in lung disease

Verification of compliance with short term therapy in lung disease is virtually non-existent. Studies looking at the efficacy of antibiotics in acute exacerbations are many but assessment of compliance scarce, as is the case with short term course of oral steroids in moderately severe asthma. Chest physicians in the early 1950s were the leaders on therapeutic compliance in patients

Table 1. – Studies of compliance amongst adult asthmatic patients

Investigator	No.	In- or out-patients	Drug	Objective confirmation	Compliance
Chryssidis	114	30 in 84 out	Inhaled	weighing	103% 196% recent in-patients
Glanz		97 out	Prednisolone for acute attack	plasma	85% overall 9 of 10 plasma positive
James	142	out	ALL	none	50%
Kinsman	88	in	Inhal	none	61%
Kleiger	100	in	ALL	none	61%
Steenhoek	467	283 in 185 out	Theophylline	plasma	95% in-patients 67% out-patients
Harding	47	out	ALL	none	55%
Spector	19	out	SCG like "chronolog"		48%

SCG: sodium chromoglycate. ALL: all drugs prescribed to patients.

with tuberculosis but have only recently returned to this subject in the use of long term oxygen therapy in patients with respiratory failure and in asthmatics.

Recent studies investigating compliance in asthma are shown in table 1 highlighting the marked variation in adherence to medical advice [5]. Much of this variation may be accounted for by variations in the techniques used to assess compliance but many other factors are also implicated. Frequency of drug administration as seen in table 2 in patients taking anti-epileptic medication, demonstrates the difficulties in taking medication four times a day but shows minimal difference between once- and twice-daily medication. The effect of multiple drug prescribing and the potential role of continuous twice daily regimens are now accepted in the treatment of hypertension, but many feel academic and clinical purity would be affected if anti-asthma preparations were combined, despite the same clinicians regularly prescribing combined anti-tuberculous preparations.

Table 2. – Frequency of drug medication. Oral medication for epilepsy

Compliance	Regime
87%	once-daily
81%	twice-daily
77%	three times daily
39%	four times daily

"Aware" population using electrically timed prescription bottles. Cramer et al, JAMA, 1989, 261, 3273–3277.

Conclusions

The factors leading to poor compliance of medical advice in the treatment of lung disease, except tuberculosis, are poorly understood mainly through lack of appropriate investigations. Until studies determine these factors, the undoubted efficacy of much of the chest physician's advice and prescribing will be unavailable to the patient.

Summary

Failure to heed medical advice is common, but the precise extent is poorly understood and barely investigated. Factors leading to poor compliance are not known but claims of lack of education are frequently mentioned. However these have yet to be scientifically substantiated. The frequency of medication and social and economic factors, allied to poor communication, are probably involved but do not account for it entirely as non-compliance may vary between 20–80% of patient populations. Asthma mortality is not decreasing despite effective medication and increasingly there are worries that poor compliance may be a significant factor.

References

1. Glanz K, Fiel SB, Swartz MA, Francis ME. – Compliance with an experimental drug regimen for treatment of asthma; its magnitude importance and correlates. *J Chron Dis,* 1984, 11, 815–824.
2. Soutter BR, Kennedy K. – Patient compliance assessment in drug trials; usage and methods. *Aust NZ J Med,* 1984, 4, 360–364.
3. Cramer JA, Mattson RH, Prevey ML, Scheyer MDS, Ouellette RN. – How often is medication taken as prescribed? A novel assessment technique. *JAMA,* 1989, 22, 3273–3277.
4. Horn CR, Cochrane GM. – An audit or morbidity associated with chronic asthma in general practice. *Respiratory Medicine,* 1989, 83, 71–75.
5. Horn CR, Clark TJH, Cochrane GM. – Compliance with inhaled therapy and morbidity from asthma. *Respiratory Medicine,* 1990, 84, 67–70.