Compliance in black patients with non-insulin-dependent diabetes mellitus receiving oral hypoglycaemic therapy

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Summary

Poor compliance with drug therapy is an important cause of therapeutic failure. Sixty-eight black patients with non-insulin-dependent diabetes mellitus receiving oral hypoglycaemic agents were interviewed and various factors, such as age, sex, degree of control and type of therapy, were recorded by means of a questionnaire. Compliance was determined by qualitatively assessing urine for the presence of the drugs. An alarmingly high incidence of non-compliance of 65% was found, which could still be an under-estimation because of the long half-life of one of the drugs involved — chlorpropamide. Although interesting trends were noted, no statistically significant differences between compliant and non-compliant patients were found. In the light of the high incidence of non-compliance, a larger and more detailed study seems to be warranted to identify problem areas and to plan appropriate interventions.

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Treatment compliance is often a major problem in the management of diabetes mellitus. The extent to which serum glucose levels can be controlled does not depend solely on the physician's skill, but also on the patients' adherence to the treatment regimen. The fact that non-compliance is often associated with irregular visits to clinics does not preclude other reasons for non-compliance. It is known that many non-compliant patients, although attending clinics regularly, are still finishing the supply of drugs of the previous month.[1]

Two other almost equally important reasons for non-compliance are unwanted side-effects and patients' forgetfulness. Yet the other, undoubtedly important, general reasons for non-compliance in pharmacotherapy, according to Haynes,[2] should also be considered seriously in diabetes mellitus (Table I). The determination of compliance is also confounded by the fact that serum glucose determinations do not always correspond with the exact date of measuring compliance and the fact that no definite correlation exists between fasting serum glucose levels and compliance.[3]

The present study was intended to establish the extent of poor compliance in black type II diabetic patients receiving oral hypoglycaemic drugs, and to compare this with various factors, e.g. age, number of drugs taken, and degree of control. We hoped to establish the major factors associated with poor compliance in an attempt to identify contributing factors to see whether compliance could be improved.

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TABLE I. REASONS FOR NON-COMPLIANCE*

Category	Specific reasons for non-compliance
Disease	Psychiatric illnesses
Regimen	Complexity, degree of behavioural change, duration
Therapeutic facilities	Inconvenient and inefficient clinics
Doctor-patient relationship	Inadequate supervision, patient dissatisfaction
Patient	Inappropriate health beliefs, previous or present non-compliance with other regimens, family instability

*After Haynes.[2]

Patients and methods

Sixty-eight black patients attending the Diabetic Clinic at Ga-Rankuwa Hospital, near Pretoria, were randomly selected to participate in the study. The patients were assessed by means of a questionnaire, which provided information regarding age, sex, height, body mass, drugs received (including those other than for the treatment of diabetes mellitus), time since last dose, and frequency of administration. The questionnaire was completed by the medical officer serving the clinic. Additional information regarding the last three measurements of serum glucose concentrations and qualitative determinations of glucose in the last three urine samples was obtained from each patient's clinical file. Evaluation and analysis of the last three serum glucose concentrations and of the last three urine samples (to determine the presence of glucose) were carried out to assess the degree of control. Metformin and chlorpropamide compliance were assessed by quantitative determinations of these two drugs in urine samples by means of high-pressure liquid chromatography (HPLC).[4,5] If no chlorpropamide or metformin were detectable in the urine of a patient receiving the drug(s), this was regarded as non-compliance. The information gathered from the questionnaire, as well as additional information, was analysed statistically by the Institute of Biostatistics of the South African Medical Research Council using univariate analysis, descriptive statistics and the Mann-Whitney *U*-test.

Results

Sixty-eight patients were interviewed; their mean (± SD) age was 55,6 ± 11,5 years. There were 26 men and 42 women in the study; the average duration of diabetes mellitus was 5,2 years, and 73% of the patients were obese. Among this group of patients receiving oral hypoglycaemic therapy chlorpropamide was used by 57 patients and metformin by 53. A total of 42 patients received both drugs, whereas 15 received chlorpropamide only and 11 metformin only.

Compliant v. non-compliant patients

We were unable to detect one or more of the drugs taken in the urine of 44 (65%) of the 68 patients interviewed. These 44 patients are compared with the rest of the patients in Table II.

TABLE II. COMPARATIVE CHARACTERISTICS OF COMPLIANT AND NON-COMPLIANT GROUPS

	Compliant	Non-compliant
Age (yrs)	**54,6 ± 10,6**	**56,7 ± 12,6**
Men (%)	**43,5**	**56,5**
Women (%)	**35**	**65**
Duration of diabetes mellitus (yrs)	**6,5 ± 5,5**	**4,5 ±3,1**
Chlorpropamide (mg/d)	**314,7 ± 189,4**	**379,7 ± 205,3**
Metformin (mg/d)	**1 470,6 ± 528,6**	**1 381,3 ± 561,6**
Time since last dose (h)	**5,4 ±4,5**	**9,3 ± 8,9**
Serum glucose values (mg/l)*	**9,2 ± 4,5**	**9,1 ± 4,1**

* Average values of last 3 serum glucose values. None of these differences were statistically significant.

Patients receiving chlorpropamide only ($N = 15$)

Subjects meeting this criterion were non-compliant in 50% of cases according to negative urine sample determinations for chlorpropamide. The mean (± SD) serum glucose level for these patients was 9,68 ± 5,1 mmol/1. The concordant values for the compliant and non-compliant patients were 9,1 ± 5,36 mmol/l and 10,39 ± 5,76 mmol/l, respectively ($P = 0,05$). Fifty-eight per cent of the non-compliant group were women, and the average duration of the illness was 2 years less than that of the compliant group. A significant increase in body mass was found in the compliant patients compared with non-compliant patients (73,7 ± 10,4 kg v. 66,1 ± 8,6 kg ($P = 0,0313$)).

Patients receiving metformin only ($N = 11$)

In this group 36% of patients were non-compliant. The mean (± SD) serum glucose level was 6,96 ± 2,60 mmol/l. A slightly lower value for non-compliant than for compliant patients (6,8 ± 3,1 mmol/l v. 6,94 ± 2,35 mmol/l) was found ($P = 0,05$). Ninety-two per cent of the non-compliant patients were women, and the average duration of the illness was 2,3 years less than that of the compliant group. Although statistically insignificant, there was a trend for the mean body mass to be lower among compliant patients (81,04 ± 6,04 kg v. 84,85 ± 9,4 kg).

Patients receiving both chlorpropamide and metformin ($N = 42$)

The patients receiving both chlorpropamide and metformin were non-compliant in 78% of cases. They were compliant for chlorpropamide in 45,2% of cases and for metformin in 66,7% of cases. Eighty-six per cent in the non-compliant group for chlorpropamide, also receiving metformin, were compliant for metformin. Among the non-compliant group for metformin 72,7% of patients, who also received chlorpropamide, were compliant for chlorpropamide. The mean (± SD) serum glucose level was 9,24 ± 4,01 mmol/l and the average duration of diabetes was 5,55 ± 4,36 years.

Discussion

This pilot study had many limitations, e.g. the fact that the 68 patients were assessed once only, and that the only contact with the patient consisted of a single interview (with the only aim being to gather information for completing a questionnaire). The method employed in this study differs to a significant extent from the more elegant design of the study conducted by Buchanan *et al.*[1]

It must be remembered that there is no infallible method for the measurement of compliance. Even direct measurements, e.g urinary excretion of drugs, have certain limitations. One should consider the fact that chlorpropamide is excreted very slowly in the urine; the elimination half-life of chlorpropamide is 35 hours.[6,7] After therapy for 16 days, 20 additional days may be required for clearance of the drug from the blood; therefore many patients, appearing to be compliant, might actually be non-compliant (i.e. taking drugs irregularly). A non-compliance figure of 65% (the present study) is therefore still very conservative and might well be much higher.

Despite the shortcomings, some interesting observations were made. It was found that compliance had no influence on mean serum glucose levels; for example no differences in mean serum glucose levels between compliant and non-compliant patients receiving chlorpropamide only were found. This is in accordance with the findings of Eshelman.[3] Although the mean serum glucose levels of patients receiving metformin were marginally lower for the non-compliant than for the compliant patients, the standard deviation was greater (3,11 v. 2,35) in the non-compliant group; this indicates a wider distribution of individual serum glucose levels among the patients who were non-compliant for metformin.

Gordis[7] stated that there is no correlation between compliance and age, sex, educational status, occupation, income or population group. We found some differences in compliance regarding age, sex, duration of illness, drug dosages, time since last dose and serum glucose levels (Table II), but these differences were not statistically significant. This calls for more elaborate studies, which should include more patients.

The only statistically significant difference in the present study, viz. a difference in mean body mass, was found between chlorpropamide-compliant and chlorpropamide-non-compliant groups; a likely explanation for this finding is the fact that chlorpropamide is known to stimulate the appetite and to cause an increase in body mass, probably because it (as well as the other sulphonylureas) causes degranulation of the β-cells in the endocrine pancreas, increasing the rate of secretion of insulin, and also an increase in the number of insulin receptors.[8] This study should be seen as exploratory, and the results, although interesting, should be seen in this light. Since the incidence of non-compliance is high, further more elaborate and methodologically more refined studies addressing this problem in black patients with type II diabetes mellitus receiving oral hypoglycaemic drugs are indicated.

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