THE MENTAKAB HYPERTENSION STUDY PROJECT PART V - DRUG COMPLIANCE IN HYPERTENSIVE PATIENTS

T O Lim, B A Ngah, R A Rahman, A Suppiah, F Ismail, P Chako, H H Na

ABSTRACT

Poor compliance with drug treatment is a barrier to effective management of hypertension. Drug compliance behaviour of 168 patients were studied, their drug compliance was measured by the pill-counting method. The prevalence of non-compliance with medication was 26%. Thirteen variables were examined for their association with compliance; these were age, sex, duration of hypertension since diagnosis, adequacy of blood pressure control, complexity of drug regimen and side-effect of drug, history of previous admission for hypertension related reason, patient's knowledge of hypertensive complications, patient's belief that drug was 'panas' or 'san', previous use of traditional treatment for hypertension, patient's fatalistic attitude, their social support and satisfaction with the health services. None of these variables were significantly related to compliance ($p>0.05$) except adequacy of blood pressure control. The performance of patient self-report was compared with pill-count as a measure of drug compliance; it was poorly predictive of non-compliance (sensitivity = 71%, specificity = 50%). An inverse relationship was found between non-compliance with medication and patient subsequent drop-out rate. Patients who were compliant were more likely to remain on treatment and vice versa. As a measure of drug compliance, detection of drop-out compared well with pill-count (sensitivity 97%, specificity 66%, positive predictive value 89%, negative predictive value 88%).

Keywords: Drug compliance, hypertension, drop-out, patient self report.

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INTRODUCTION

Patient non-compliance includes 2 elements: one is drop out of treatment which has been shown to be an important reason for ineffective blood pressure control[1], the other element is failure to consume the medications as prescribed. This has also been widely shown to be another major barrier to the control of hypertension[2, 3]. This problem, however, has not previously been studied in this country.

The objectives of this study were therefore

(1) to estimate the extent of non-compliance with drug among hypertensive patients.
(2) to identify characteristics of hypertensive patients as well as their drug treatment which are associated with non-compliance. To the extent these patients can be identified, efforts can be made to improve their compliance.
(3) to assess the performance of verbal self-report as a measure of drug compliance. Self-report has previously been found to perform reasonably well when compared with pill-count as a method of measuring drug compliance[4]. Performance of verbal tests, however, may vary widely among populations, and thus it is necessary to determine if this simple and useful test is applicable for our hypertensive population.
(4) to examine the relationship between the 2 elements of patient compliance : drug compliance and drop-out.

METHODS

Study subjects were selected from consecutive patients attending the out-patient department of Mentakab District Hospital in May 1989. Subjects were all known hypertensive patients, and on treatment with one or more antihypertensive drugs as follows : Metoprolol, Chlorthiazide and Prazosin.

The pill-counting method is the traditional 'gold standard' for measuring drug compliance[3] and was the method used in this study. At their visits to the hospital in May 1989, study subjects were routinely seen and examined by medical officers and instead of collecting their medication at the dispensary, patients were dispensed their medication in a plastic container for the ostensible purpose of trying out a new and more convenient method of dispensing. Each container contained a fixed number of tablets of a particular medication and in more than sufficient number required for 4 weeks treatment at any dose within the usual dosage range of that medication. All patients were told to return after 4 weeks and reminded to bring back

Medical Unit
Mentakab District Hospital
28400 Mentakab
Pahang, Malaysia

T O Lim, MBCHB (Glas), MRCP (UK)
Physician

B A Ngah, MBBS (Malaya)
Medical Officer

R A Rahman, MD (UKM)
Medical Officer

A Suppiah, MBBS (Malaya)
Medical Officer

F Ismail, MD (UKM)
Medical Officer

Pharmacy Department
Mentakab District Hospital
28400 Mentakab
Pahang, Malaysia

P Chako, BSc (Pharm)
Pharmacist

H H Na, BSc (Pharm)
Pharmacist Assistant

Correspondence to : Dr T O Lim
Clinical Specialist
Jabatan Nefrologi
Institut Urologi dan Nefrologi
Hospital Besar
Jalan Pahang 50586
Kuala Lumpur, Malaysia

the container with any residual tablet in it. They were not informed that their compliant behaviour were under observation. The known fixed number of tablets dispensed minus the residual number of tablets in the container after 4 weeks equals the number of tablets that have been removed from the container and presumably consumed. The number of tablets thus consumed by the patient divided by the number of tablets which should have been consumed for a particular dose and regimen of the medication over the 4-week-period gives the 'compliance ratio'. The selection of a ratio to distinguish the compliant from the non-compliant is entirely arbitrary; nevertheless, according to Sackett[5], 80% compliance with medication is required to achieve blood pressure reduction and thus a ratio of 0.8 (80%) or more is usually taken as the criteria for adequate drug compliance. We adopted the same criteria in this study.

On the day when study subjects returned to the hospital with the medication container, they were interviewed by trained interviewers. The structured interview aimed at eliciting patient self-report of compliance: their beliefs concerning drugs, their use of traditional medication for treatment of hypertension, self-report of any side-effects from drug therapy, patient's knowledge of the complications of uncontrolled hypertension, their general philosophical beliefs, their social support and their satisfaction with the service provided by the hospital for the treatment of hypertension. The composition of some of the questionnaires and the definitions of some of the terms used are shown in Table I. Data on age and sex of patients were also obtained.

The medical records of study subjects were retrieved and the following data obtained : blood pressure recordings at each visit after the first six months of follow up at the hospital, type, dose and regime of anti-hypertensive drug, duration of hypertension since diagnosis, previous admission into hospital for hypertension related reason. A patient's blood pressure control is considered adequate if the mean of blood pressure recordings obtained as above was equal to or less than diastolic 90 mmHg and systolic 160mmHg. The diastolic standard is as recommended by WHO/ISH [6].

Table I - Composition of Questionnaire and Definition of Terms

(1) Most people have trouble remembering to take their medication. Do you have trouble remembering to take yours?
Study subject who answered No was considered compliant by self-report.

(2) Do you believe that the medication prescribed is 'panas' (for Malay and Indian patients), or 'san' (Chinese patients)?
The words 'panas' and 'san' are commonly used by Malay/ Indian and Chinese patients respectively to describe their perceived ill-effects of 'western medicine' in contrast to the natural goodness of 'traditional herbal medicine'.

(3) Do you agree with the following statements :
(for Malay/Indian) : If something were to happen to me, it is the will of God,
(for Chinese) : If something were to happen to me, it is a matter of fate.
Patient who agreed with the above statement was considered 'fatalistic' in attitude for the purpose of this study.

(4) Who do you stay with now?
Patients who live by themselves were considered socially isolated.

(5) Do you have any complaints concerning the service provided by the hospital?
Patient who stated one or more complaints was considered dissatisfied with the service provided.

The attendance of all study subjects at the out-patient department for hypertension treatment was subsequently followed-up for one year to determine their drop-out rate. Drop-out was defined as failure to attend a scheduled appointment, and if the patient returned, the interval between drop-out and return was more than one month.

Results were analysed using x^2 test with yates correction or student t test where appropriate, relationships were considered significant at the 5% level.

RESULTS

A total of 191 hypertensive patients on treatment and follow up at Mentakab District Hospital were selected for the study. However, 23 patients failed to attend their scheduled appointment or failed to return their medication container and they were excluded from analysis.

Of the remaining 168 patients included in this analysis, there were 98 (58%) male and 70 (42%) female patients. Their mean age was 52 years (range 30 - 75 years) and their mean duration of hypertension since diagnosis was 6.1 years.

Using previously described definition of drug compliance, 124 (74%) of these 168 patients were compliant and the rest of 44 (26%) patients were non-compliant.

The characteristics and drug treatment of those who were compliant were analysed and compared with those who were not (Table II). Altogether, 13 variables were tested for their relationship with compliance. These included age, sex, duration of hypertension, nature of drug treatment, side-effects of drug therapy, history of previous admission for hypertension related reason, patient's knowledge of complication of hypertension, patient's beliefs concerning drugs, previous use of traditional medication, patient's fatalistic attitude, social isolation, satisfaction with health services and adequacy of blood pressure control. There was no significant difference ($p>0.05$) between complier and non-complier with respect to all the above variables mentioned except adequacy of blood pressure control.

In so far as antihypertensive drug is effective, compliance should be related to better blood pressure control. Thus, of 124

Table II: Comparison of Complier and Non-Complier

Variable	Complier	Non-Complier	P Value
Number of patients.	124	44	-
mean age (years).	51.2	54.1	NS
No (%) of men.	72 (58)	26 (59)	NS
No (%) with adequate blood pressure control.	34 (27)	2 (5)	$p < 0.01$
mean duration of hypertension since diagnosis (years).	6.5	4.8	NS
Drug treatment:			
No (%) on :			
- one drug	93 (75)	34 (77)	NS
- more than one drug	31 (25)	10 (23)	NS
- once daily regime	9 (7)	8 (18)	NS
- bd or tds regime	115 (93)	36 (82)	NS
No (%) reported at least one side-effect of drug.	74 (60)	29 (66)	NS
No (%) with previous admission into hospital for hypertension related reason.	46 (37)	9 (20)	NS
No (%) who knew the complications of hypertension.	58 (47)	23 (52)	NS
No (%) who believed that drug is 'san or 'panas'.	53 (43)	18 (42)	NS
No (%) who have fatalistic attitude.	74 (60)	31 (71)	NS
No (%) who had previous traditional treatment for hypertension.	36 (29)	14 (32)	NS
No (%) who were socially isolated.	2 (2)	2 (5)	NS
No (%) who expressed dissatisfaction with service provided for hypertension treatment.	38 (31)	41 (33)	NS

Relationship is significant at the 0.05 level.
NS: denotes x^2 test or student t test not significant with $p > 0.05$.

patients who were compliant, 34 (27%) had achieved adequate blood pressure control whereas only 5% of those who were non-compliant had well controlled blood pressure. ($x^2 = 8.779$. $p < 0.01$), however, the blood pressure of the vast majority of patients (73%) remained inadequately controlled inspite of their adequate compliance with drug therapy.

The performance of patient self-report as a measure of patient compliance is compared with pill-count. As shown on Table III only 65% of the patients were correctly classified using self-reports. The sensitivity of self-report as a measure of compliance was only 71% and its specificity 50%. 80% of patients who reported compliance were found to be so on pill count. However, only 38% of patients who admitted to non-compliance were found non-compliant by pill-count. Thus, self report was neither sensitive nor predictive of non-compliance.

Table III - Compliance Detection by Patient Self Report Compared with Pill Count.

Compliance by patient self report	Compliance by pill count		Total
	Compliant (> 0.8)	non-compliant (< 0.8)	
reported compliant.	88	22	110
reported non-compliant	36	22	58
Total	124	44	168

Sensitivity = $\frac{88}{124} = 71\%$

Specificity = $\frac{22}{44} = 50\%$

+ ve predictive value = $\frac{88}{110} = 80\%$

- ve predictive value = $\frac{22}{58} = 38\%$

Accuracy or predictive value = $\frac{110}{168} = 65\%$

There was an inverse relationship between compliance and subsequent drop-out rate, as shown in Table IV, patients who were compliant were more likely to remain on treatment ($x^2 = 70.787$, $p < 0.001$). Conversely of the 135 patients who had remained on treatment after one year, 120 (89%) had been compliant with their medication; of the 33 patients who had dropped out after one year, only 4 (12%) had been compliant. The difference is significant ($x^2 = 76.9$, $p < 0.001$). To assess the predictive value of drop-out as a measure of non-compliance with medication, its performance is compared with pill-count as shown in Table V. The accuracy of drop-out as a test is 88%. Its sensitivity is 97% and specificity 66%. Its positive and negative predictive values were also high, at 89% and 88% respectively. Thus, detection of drop-out appears to be a 'good' measure of drug compliance with high sensitivity and positive predictive value, reasonably specific but highly predictive of non-compliance.

Table IV - Relationship Between Drug Compliance and Subsequent Drop-Out Rate

Compliance ratio	Less than 0.6 n = 8	0.6 - 0.8 n = 36	more than 0.8 n = 124
Drop-Out rate at one year No (%)	8 (100)	21 (58)	4 (3)

Table V - Measure of Drug Compliance by Detection of Drop-Out Compared with Pill-Count.

Compliance by detection of drop-out.	Compliance by pill count		Total
	Compliant (> 0.8)	non-compliant (< 0.8)	
remain on treatment	120	15	135
Drop-out of treatment	4	29	33
Total	124	44	168

Sensitivity = 120/124 = 97%
Specificity = 29/44 = 66%
Positive predictive value = 120/135 = 89%
Negative predictive value = 29/33 = 88%

Accuracy = $\frac{120 + 29}{168}$ = 88%

DISCUSSION

In this study, the prevalence of non-compliance with medication among hypertensive patients was 26%. This can be considered relatively low, the usual reported range of non-compliance with medication is 25-50%[2, 7]. This confirmed clinician's impression in this country that most hypertensive patients comply with treatment[8]. However, that it exists as a barrier to effective blood pressure control can no longer be doubted. As a first step to improve drug compliance among patients, clinicians need to be aware of this problem and to pay attention to its occurrence among their patients.

There are two basic strategies for the management of non-compliance, and both have received much attention in the past 2 decades. One is preventive in approach; this requires that patients at risk of non-compliance be identified early so that preventive measures can be applied. The second strategy is curative; this requires that non-compliant patients be identified so that compliance improving intervention can be efficiently applied.

To be able to identify patients at high risk of non-compliance early, it is necessary to identify factors associated with non-compliance. In this study, we examined 13 factors, only blood pressure control was found to be significantly related to compliance, this is expected as blood pressure control is an outcome indicator of treatment and compliance is one measure among others, of the process of hypertension management. Indeed, the significant relationship between the two serves to validate the method of detection and definition of compliance used in this study. It is however disappointing that none of the other 12 factors studied were related to compliance. This seems surprising at first look. It was expected that complexity of treatment in terms of number of drug and regimen, side effect of drug, patient's previous experience with hypertension morbidity such as to result in admission into hospital, patient's knowledge of hypertensive complications, patient's belief that drug was 'panas' or 'san' and their 'fatalistic' attitude, patient's satisfaction with the health services and the social support provided by their family would all significantly influence compliance. However, all these hypothesized relationships failed

to materialize. We compared our experience with that of others in this regard. More than 200 variables have been studied to assess the determinants of compliant behaviour [9]; most, like this study, have concentrated on disease factors[10], patient characteristics[11, 12], treatment regimen[13], and process of care [14] as these are easy to measure. Results are however conflicting and inconsistent[7, 15]; there are no readily observable factors that correlate consistently with non-compliance to permit the early identification of patients at risk of non-compliance. This is so considering that there are well over 200 candidates for the determinants of compliance and the potential for their interactions is great. Further, compliance is a dynamic, not static phenomenon and patient's regimen and degree of compliance will vary over time. And finally, studies varied with respect to study populations, doctors and delivery system such that results may be conflicting and certainly have limited generalizability. In the light of these, our non-findings may not be that surprising after all. In recent years, the focus has shifted away from studying specific patient or provider or health system characteristics towards their interactions with one another, in other words, the doctor/provider-patient relationship within the health care delivery system as the determinant of compliance[16, 17]. This is more difficult to study though it has proven more fruitful.

To be able to identify non-compliant patients, it is necessary to have adequate methods of measuring compliance. Many methods are available, these include pill-count and measurement of drug or drug marker levels in body fluids. Both, however, are tedious or expensive and are not feasible in routine clinical practice. Clinicians' intuitive judgement is simple and probably the commonest method used to detect non-compliance; it is however unreliable[18, 19] even when clinicians feel confident of their predictions[18, 20]. Patient self-report is an attractive, easy-to-use method in routine practice and has previously been found to be highly predictive of non-compliance[4]. In our hypertensive patients however, as shown in this study, its performance is poor with low sensitivity and predictive value.

The inverse relationship as shown in this study between drug compliance and drop-out may be clinically useful. In the absence of other clinically applicable methods to measure compliance directly as discussed above, detection of drop-out is simple as patient is no longer there and can be used as an indirect indicator or non-compliance with medication. Thus, while every effort should be made to improve patient compliance and prevent drop-out, strenous efforts should also be made to recall patients who have dropped out. Compliance improving measures can then be targeted on this group of drop-outs. For those who subsequently are persuaded to remain for long term treatment, drug compliance can safely be assumed.

Of the two elements in patient compliance, drop-out and drug compliance, the former is undoubtedly the more critical one. Not only is it related to and highly predictive of drug compliance, the majority of complicated hypertensives admitted into hospital have been shown to be drop-out[1]. Detection and recall of drop-out and the subsequent management to improve their compliance is likely to be crucial to the success of any hypertension control programme.

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