Medication Noncompliance - A Thriving Problem

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Summary

A study was conducted among out-patients attending the Melaka Tengah Health Clinic to determine their compliance status towards antihypertensive, antidiabetic and antiasthmatic drugs. A total of 585 patients were enrolled in this study. Assessment of compliance was carried out using pill-counting and house-to-house interviews 14 days from the date of medication dispensed at the counter. The noncompliance rate among the 464 successfully interviewed patients was 56%. The mean noncompliance percentage was 78.0±43.1% (range: -10.0 - 314.3%). Among the four variables of compliance studied, race was not seen as a determinant of compliance. The older age group and those taking two or more drugs were statistically significant to be a noncomplier. Females were highly likely not to comply with drug therapy. Patients who conform to their refill dates were not really drug compliers. Forgetting to take their drugs and inability to read instructions on drug labels were the main reasons given. Underdosing was more common than overdosing, with an estimated cost of RM20,261.00 of unused medications per year.

Key Words: Medication compliance, Pill-counts, Questionnaires, Drug wastage

Introduction

Drugs are therapeutic agents to treat and to prevent diseases. In many cases, however, the desired effect is not reached, because drugs are not used adequately. Effectiveness of treatment of a disease depends mainly on two factors: the efficacy of the treatment prescribed and the rate of compliance of the patient with the treatment. Pharmacists and pharmacy assistants supplement the management by reinforcing the proper manner to take the drugs at the Out-patient Pharmacy Counter. The response of the patient taking the said drugs will be reviewed during follow-up appointments by the doctor where changes to drug therapy may be made if deemed necessary. During such visits, the doctor should enquire about side effects of the drugs prescribed as patients may not be compliant if they experience untoward reactions affecting their well being or daily life. It is very important then that patients should convey to doctors about any complaints during treatment[1].

Experience by pharmacists handling dispensing and counselling revealed a high percentage of patients who do not comply to their drug instructions. Patient compliance with physician's medication instructions has been a growing concern since the problem was highlighted in the early 1970s[2]. Some researchers estimate that as many as 50% of prescriptions fail to produce the desired results because of improper use[3]. Improper use of medications happens for a variety of reasons, such as confusion concerning correct dosage, lack of instructions by the physician or pharmacist, failure to purchase the prescription due to financial inability, side effects from drugs or often intentional noncompliance. Papers have been published in the pharmaceutical and medical journals local and abroad, about an alarmingly high level of noncompliance

especially those with chronic diseases such as hypertension, ishaemic heart disease, diabetes and bronchial asthma. In a review paper the percentage quoted was 20 to 82% noncompliance[4]. Noncompliance either in the form of underdosing or overdosing results in deterioration of the patients disease and drug wastage[1,5]. Due to these problems a study was carried out with the following objectives: a) to determine the prevalence of patient compliance with oral medications prescribed for hypertension, diabetes mellitus and bronchial asthma; b) to identify factors influencing compliance and to formulate proposals to improve medication compliance. In this study, patient variables were studied for their relationship with compliance. These include gender, age, race and number of drugs taken.

Materials and Methods

The study design was a cross-sectional survey. The study population was out-patients with hypertension, diabetes mellitus and bronchial asthma on oral medications attending the Klinik Kesihatan Melaka Tengah of Hospital Melaka. Patients excluded in this study were those with mental illness, speech and hearing disabilities and patients dependent on others for their daily activities. The sample size was based on a desired standardised difference of 0.30 with alpha value of 0.05 and a power of 0.85.

A preliminary survey was conducted to identify drugs used for treating hypertension, diabetes mellitus and bronchial asthma. The drugs chosen to be studied are shown in Table I. Study subjects were selected from consecutive patients with part supply prescriptions ('pharmacy refills') who presented themselves at the pharmacy counter from 29 April 1997 until 19 September 1997. Stratified sampling was then done for patients who were prescribed any one or more of those drugs. Upon selection, consent was verbally obtained from the patient to participate in the study. After the usual dispensing, prescription details was recorded in a register complete with the patient's address, telephone number and a rough sketch of the location of their house. The number of tablets were counted and verified by a second pharmacy assistant and

Table I
List of oral drugs included in the study

a) **Antihypertensives**
1. Methyldopa
2. Prazosin
3. Captopril
4. Metoprolol
5. Atenolol
6. Propranolol
7. Frusemide
8. Chlorothiazide
9. Nifedipine
10. Diltiazem

b) **Antiasthmatics**
1. Theophylline
2. Salbutamol
3. Terbutaline

c) **Antidiabetics**
1. Glibenclamide
2. Metformin
3. Chlorpropamide
4. Gliclazide

recorded in the data collection form. The patients were told verbally and supplemented with a small note to remind them not to mix the medications dispensed with those at home. Patients who presented within seven days (inclusive of earlier or later than) of the appointment date written on the prescriptions were classified as conformers and placed in Group A[6]. Non-conformers (Group B) were those patients who presented exceeding the seven days of the date.

Compliance was determined by pill-counting method. In this survey compliance was defined as exhibiting pill counts of 80-120% of actual number of tablets taken versus the number that should be taken[7]. If two or more drugs were given, a patient was regarded as noncompliant if any drug was found to be in the noncompliant range[3].

House-to-house interviews were conducted on the 14th day from the initial encounter at the pharmacy counter by trained pharmacy personnel. Each patient was asked to show all drugs taken from the pharmacy previously. The remaining tablets kept by patients were counted to ascertain the compliance status. The REMEDI Pharmaceuticals (M) Sdn Bhd pricing was used to cost all drugs in Table I. This was done by multiplying the cost of each drug by the total number of pills left over during the interview day. A pretested structured questionnaire was used to gain information on drug-taking behaviour. Questions were asked about the name and purpose of each drug and the number/timing of doses taken each day. The patient was also asked to read the label instructions (with spectacles when required). Enquiry was made about any difficulties encountered in taking those drugs and reasons for not complying to physician's instructions. Other patient comments and suggestions on possible improvements in their drug administration were sought. A pilot study was carried out involving twenty patients to test the workflow of the research prior to starting the real study.

Statistical analyses were performed using either the chi-square test or Fisher's exact test, where appropriate. EPI-INFO software version 6.02 was used for analysis. Statistical significance is accepted at p value less than .05.

Results

Patient characteristics

A total of 585 patients were initially enrolled into the study. Their characteristics were tabulated and shown in Table II. Four hundred and sixty four (79.3%) patients were successfully investigated to determine their compliance status. The remainder 121 (20.7%) patients were unable to be studied due to several reasons such as mixing with old drugs or failure to conduct house surveys for pill-counting. The fate of events of patients in the study is summarised in a flowchart shown in Figure 1.

Two hundred and four patients (44.0%) were found to be compliant towards their medications, while 260(56.0%) were noncompliant. The compliant group showed a mean percentage compliance of 98.05±8.89% (range: 80.0 - 120.0%, median 100.0%) while the noncompliant group

Table II
Characteristics of respondents enrolled in study
(n=585)

Characteristic	Respondents No. (%)
Gender	
Male	275 (47.0)
Female	310 (53.0)
Age	
31-40	17 (2.9)
41-50	123 (21.0)
51-60	253 (43.3)
61-70	162 (27.7)
71-80	30 (5.1)
Race	
Malay	325 (55.6)
Chinese	192 (32.8)
Indian	58 (9.9)
Others	10 (1.7)
No. of Drugs Taken	
1	144 (24.6)
2	315 (53.9)
3	105 (18.0)
4	19 (3.2)
5	2 (0.3)

had a mean of 77.98±43.09% (range: -10.0 to 314.3%, median 76.67%). Among the noncompliant patients, there were 318 out of 412(77.2%) incidences whereby patients had underdosed their medication and 94(22.8%) incidences of overdosing. A summary of the patient characteristics of both compliant and noncompliant patients is shown in Table III.

Drug characteristics

After the interview stage, only 963 drug records were fully completed (which fulfills the criteria for calculation). Of these records 512(53.2%) were for diabetes mellitus, 434(45.5%) for antihypertensives and 17(1.8%) for antiasthmatics. Nifedipine 10mg, metoprolol 100mg, prazosin 1mg tablets were the main

Patient interview

Four hundred and eighty five out of 585 patients (82.9%) were successfully interviewed either at their homes or offices. Four hundred and ten (84.5%) were patients from Group A and the remaining 75(15.5%) from Group B.

From the interview sessions, the main reasons for not complying to drug instructions for noncompliant and compliant patients respectively were forgetfulness (32.2% and 24.6%), unable to read instructions on drug containers (11.4% and 7.7%) and other miscellaneous reasons (22.8% and 14.8%).

Discussion

Noncompliance

The noncompliance among out-patients in Melaka Tengah District was found to be 56% based on the criteria of compliance set earlier. If the criteria was set at 80 - 100% then the rate of noncompliance would be even greater than 56%[3,8]. The authors acknowledge the risks of adverse effects of less than or more than 100% compliance for treating hypertension, diabetes and asthma. To capture a reasonable sample size for a study one should allow for an acceptable deviation. In a local study done in 1989 using pill-counting to measure compliance, the authors found the noncompliance rate among hypertensive patients was 26%[9]. They chose 80% as the criteria for adequate compliance but the prevalence of overdosing was not mentioned in that paper. Hypertensive patients were recruited at the out-patient department, and instead of making home-visits as in this study, the researchers performed pill-counting and interviewed the patients at the clinic after a period of 4 weeks. The approach taken in our study was to overcome the phenomenon of "pill-dumping" among patients prior to coming to the counter. Home-visits was thought to be a better method to interview patient rather than at the counter. Thus having said that, the noncompliance towards medications in Malaysia in general is still a prevalent and thriving problem.

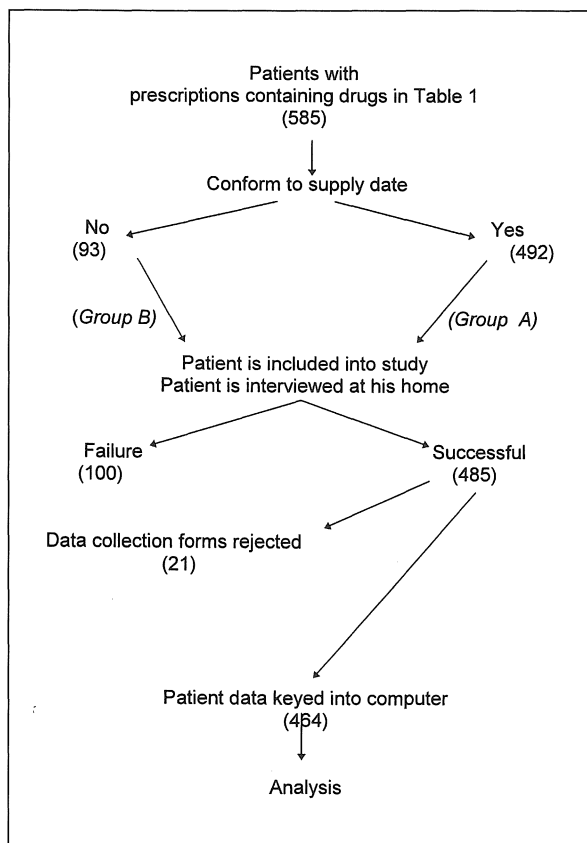This study supports a paper to demonstrate females have the preponderance to be noncompliant towards

Fig. 1:   Flow chart of patients included in the study.

drugs used to treat hypertension, while glibenclamide 5mg and metformin 500mg for diabetes mellitus and tablet theophylline 125mg for bronchial asthma. A sum of RM728.80 worth of drugs was omitted by underdosed patients with a corresponding RM115.40 value of drugs overdosed during the study period. Compliant patients took RM825.60 worth of drugs.

Conformance and compliance

Two hundred and nineteen (55.2%) out of 397 Group A patients were seen to be noncompliant as compared to 41(63.1%) out of 65 Group B patients. Performing a chi-square test, the p-value was not significant (p=233) meaning the test statistic used had failed to prove the null hypothesis that conformers to the appointment dates are compliers is true.

Table III
Summary of characteristics of compliant and noncompliant patients

Characteristic	Compliant n=204 No. (%)	Non-compliant n=260 No. (%)	P value
Gender			
Male	103 (50.5)	106 (40.8)	0.037 (S)
Female	101 (49.5)	154 (59.2)	
Age			
31-40	6 (2.9)	6 (2.3)	0.000 (S)
41-50	41 (20.1)	56 (21.5)	
51-60	88 (43.1)	113 (43.5)	
61-70	62 (30.4)	68 (26.2)	
71-80	7 (3.4)	17 (6.5)	
Race			
Malay	116 (56.9)	154 (59.2)	0.869 (NS)
Chinese	65 (31.9)	82 (31.5)	
Indian	19 (9.3)	19 (7.3)	
Others	4 (1.9)	5 (1.9)	
No. of Drugs Taken			
1	68 (33.3)	43 (16.5)	0.000 (S)
2	107 (52.4)	144 (55.4)	
3	25 (12.3)	60 (23.1)	
4	4 (2.0)	13 (5.0)	

Key: S=significant   NS=not significant

medications (see Table III)[10]. How gender can predispose to the act of noncompliance perhaps may only be answered in further research. At the moment this finding would add to the current knowledge about patient's drug-taking behaviour. Looking at the trend of noncompliance behaviour among patients in Table III, patients in the 71 - 80 years age group were more likely than the other groups to not complying with their drug regimens (70.8% noncompliant versus 29.2% compliant). This finding supports our initial presumption that the elderly have greater difficulty in complying with their medication treatment due to factors such as multiple chronic diseases, taking

multiple drugs, decreased mobility and isolated living conditions[10]. While it is reasonable to assume that the elderly are more likely to exhibit noncompliance behaviour than younger patients, there is little convincing evidence to support that belief. In a review of 36 studies that examined the relationship between age and compliance, researchers found that only six such studies showed poor compliance in the elderly[11].

The authors wish to highlight another determinant of compliance, namely the therapeutic regime used. There was strong evidence that as the number of drugs prescribed increases, the noncompliance increases (see

Table III)[10]. Even with only three groups of drugs studied, there were 17 patients who took 4 drugs in the study list. Analysing by percentage, patients taking the 4 drugs are more likely than those taking 1, 2 or 3 drugs to not comply with their drug regimen. This finding is in accordance with published literature[11]. They are candidates that warrants close supervision by doctors and pharmacists[7]. In the light of such occurrence, pharmaceutical manufacturers are beginning to pack medications in convenient "calendar packs" and blister packing to facilitate compliance by patients. Doctors will be able to assess drug-taking behaviour especially among patients suffering from hypertension, diabetes mellitus who may have to take other drugs due to complications such as coronary artery disease, nephropathy due to hypertension or diabetes mellitus. There were 5(1.1%) patients who claimed to suffer from side effects during the study. With such a low incidence, side effects was not seen as a determinant of compliance in this study.

The initial belief that patients who faithfully conform to their appointment dates are compliers was proven otherwise.

This report also showed noncompliance has no boundaries on race. Additionally, other research have shown that there is no consistent relationship between compliance and educational level, socio-economic status, occupation or marital status. The author also noted having a nonresponder rate of 17.1% for those who failed to be interviewed to be in the acceptable margin as reported by other surveys.

Reasons for Noncompliance

Col and colleagues in their paper on the role of medication noncompliance and adverse drug reactions in hospitalizations of the elderly found that forgetfulness was the most common cause of noncompliance attributed to 39.6% of respondents, a finding consistent with this paper[10]. The percentage may differ slightly, but it was a documented main reason. While being forgetful is acceptable in society, but to forget to take one's medication may endanger a person's life. Thus, doctors and pharmacist have an important role to reinforce compliance and drug instructions[1,12]. Drug counselling was proven in the literature to improve medication compliance[13,14,15]. Patients prefer individualised rather than standard drug information which augments verbal advice informed by the pharmacist[1]. Pharmacists in Leeds, UK used medicine reminder charts to increase compliance, specially designed to tackle 'ignorance, confusion and forgetfulness' was shown to achieve more than 85% compliance as compared to only 63% among patients without one. In their practice, the researchers link drug-taking to routine daily activities, of which these events acted as cues to remind patients[16].

Overdosing, underdosing and wastage

Underdosing was more prevalent (71.2%) than those who take extra doses[3,12,17]. Underdosing was reported at the rate of 81% by another article[10]. If this situation is discussed along the lines of reasons for noncompliance, the author may expect that since 75.3% patients studied were 50 years and above, then 'forgetfulness' and 'unable to read drug instructions' may be accepted as why underdosing was common.

The house-to-house surveys conducted in this study revealed certain behaviours of drugs consumers. 4.3% of the data collection forms had to be rejected due to, amongst other reasons drugs supplied during the study period were mixed with those at home, or patients had ignored taking them altogether, instead took their own stock of similar drugs kept at home.

Underdosing may subsequently result in an accumulation of drugs, an overaccumulation leads to overstoking at home which in turn may lead to wastage and even poisoning[1]. This finding was discovered elsewhere in a community project in Pulau Pinang[18]. (Unpublished observations). Researchers conducted visits to households in selected residential areas to collect medicines stored at home. They found that respondents tend to keep the drugs longer than necessary and have the tendency to reuse them again. After keeping those drugs, respondents were not fully aware of the types of medicines and how to use them properly. This situation is unhealthy in view of the heavy burden on the government to subsidise the cost of medications in the country. One should be more wary of the cost implications of hoarding drugs at home. It may even lead to self medication. It is known here that the

cost of noncompliance (underdosing) was RM728.80 during the 14 day period. If this figure is extrapolated for the whole year, it is estimated that RM20,261.00 worth of antihypertensive, antidiabetic and antiasthmatic drugs will not be used, and ultimately wasted. The underuse of drugs deprive patients of anticipated therapeutic benefits, often leading to new consultations and new prescriptions, thus increasing drug costs and resources. Noncompliance may lead to the progressive deterioration of the clinical condition of the patients.

Methods of Assessing Compliance

There are two main methods to measure compliance namely direct and indirect methods. Direct methods include observation, use of markers and biological assays. Pill-counts, interviews and medication monitors are examples of indirect methods. In this study, compliance was assessed by pill-counting. The advantages are this method is cheap, requires no instrumentation and is easily carried out by a trained personnel. Pill-counting does not involve blood samples as required in serum drug concentration studies. Medication monitoring system is costly as it requires the investigator to purchase electronic tablet containers and computer software to analyse the results. In pill counting however, the actual consumption of the remaining pills remains doubtful. Neither does the technique indicate which days a patient took the appropriate, more, or fewer pills than were prescribed, nor could investigators be certain the pills were not discarded before counting to portray an image of having complied with the regime[17,19]. It was mentioned in the literature that about 13% of pills has been removed from the container before coming to the pharmacy for refills[19]. By adopting home-visits to patient's residences, we had attempted to minimise the latter problem. Overdosing, erratic drug use and drug holidays require the electronic medication monitoring system which is able to detect taking and timing compliance. To minimise possible errors from the above argument, the author had used pill-counting in combination with qualitative assessment in the form of questionnaires with the intention of increasing the validity of the response. Each of these methods has its own advantages and limitations and none is totally reliable[3,19].

Based on the experience from this study, the following recommendations to improve compliance is therefore timely: a) doctors and pharmacists check the remainder of the previous supply of medications during follow-up visits; b) intensified and structured counselling sessions involving a multi-disciplinary approach; c) to have blister-packed drugs commonly used in treating hypertension, diabetes and bronchial asthma; d) to introduce compliance aids especially for geriatrics and known noncompliant patients; e) to improve the current labelling standards to aid in comprehension; and f) better communication skills for counter personnel.

Conclusion

The noncompliance towards antihypertensive, antidiabetic and antiasthmatic drugs shown by this study was 56% involving a sample size of 464 patients. Noncompliance was demonstrated by patients of female gender, in the elderly age group and who were prescribed two or more drugs. Race was not associated with compliance behaviour. Among the noncompliant patients, underdosing was commoner than overdosing of drug dosages, a finding in coherence with published papers reviewed.

Acknowledgements

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