

Adherence to Antihypertensive Therapy in General Hospital of Penang: Does Daily Dose Frequency Matter?

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ABSTRACT

A number of factors have been identified that contribute to non-adherence to medications in hypertension, one of which is the drug regimen complexity. The purpose of this study was to identify patients with poor adherence to antihypertensive therapy and compare the levels of adherence with daily dose frequency of antihypertensive therapy [Single Daily Dose (SDD), Twice-Daily Dose (BID), and doses of more than twice daily (> BID)]. A cross sectional study was conducted on a convenience sampling of 518 patients with antihypertensive therapy at the Clinic of General Hospital of Penang, Malaysia. Adherence was assessed using the Morisky Medication Adherence Scale (MMAS). The one-way Analysis of Variance (ANOVA) was used to compare the means of three categorical independent variable (SDD, BID and > BID), and one continuous dependent variable scores ranging from 1 (adherence) to 5 (poor adherence). Our results show that, the MORISKY scale items were summed that 195 patients had poor adherence to hypertensive medication. According to this result, 51.3% of our total sample was taking their medicines irregularly. Also we found a significant relationship between daily dose frequency groups and adherence at level $p < 0.001$. It shows that hypertension patients groups, who have more daily dose frequency, will show higher level of adherence towards antihypertensive medications.

Keywords: Adherence, Antihypertensive therapy, Daily dose frequency, MMAS, Malaysia.

INTRODUCTION

Poor adherence to medications is a major public health problem and remains one of the main unresolved issues in the management of hypertension⁽¹⁾. Adherence to medication has been defined as the extent to which a person's behaviour coincides with medical or health advice⁽²⁾. In Malaysia, essential hypertension is one of the most common chronic diseases. Last national survey, which sampled more than 16,000 Malaysians, reported that the prevalence of hypertension amongst those aged 30 years and above has increased from 32.9% in 1996 to

40.5% in 2004 and to 42.6% in 2006, in time, levels of awareness, treatment and control are low⁽³⁾. With a growing worry on the increasing prevalence of hypertension among its population, health officers are thinking about the dreadful consequences of current and future Malaysians burdened with chronic ailments, which can otherwise be avoided.

As for the seriousness of poor adherence to medical regimens in Malaysia was projecting in 2006, the publishing results of a study by Hassan et al. (2006) which showed that 55.8% of drugs prescribed by physicians were not taken as directed⁽⁴⁾. As far as hypertension is concerned, adhering to prescribed medication is critically important for controlling blood pressure and reducing the associated risk of

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cardiovascular complications such as stroke⁽⁵⁾. This has been proved by studies which show that patients who take at least 80% of their medications have significantly better control over their blood pressure levels compared with those who take less than 50% of their prescribed medications⁽⁶⁾.

Previous studies found that there are many factors associated with poor adherence to antihypertensive therapy. Some studies have compiled more than 250 factors that could affect patient adherence in general such as age, gender, race and number of daily doses frequency⁽⁷⁾. The first factor age does not seem to play a major role on adherence to medication; most studies have failed to show an association between age and adherence^(8, 9). There are also contradictory reports on the influence of gender and race on adherence. Most studies have not found any association between gender, race and adherence⁽¹⁰⁾. Regarding income, the association between adherence and income is not clear. One study conducted on hypertensive patients in the United States did not find an association between adherence and family income⁽⁹⁾.

Complexity of the drug regimen is one of these factors, which consists of two major components: the number of medications prescribed and daily dose frequency⁽¹¹⁾. Previous research carried out on this topic has shown that dose frequency is an inconsistent variable. A study by Claxton et al. has found that adherence rates decreased as the number of daily dose increased⁽¹²⁾, whereas, in contrast, a study by Hashmi et al. has found that adherence rates increased as the number of daily dose increased⁽¹³⁾. Some latest studies, however, have identified no relation between increasing number of daily doses and poor adherence⁽¹⁴⁾, including one such study in an Asian population⁽⁴⁾.

This uncertainty highlights the urgency and the need for more investigation and research to explore the relationship between dose frequency and adherence, where the findings of previous researches are not necessarily applicable in Malaysia. It is clear that the findings of research conducted in other countries such as in the US cannot be blindly applied to Malaysia or to other cultures. Culture can also influence the outcomes of

the research⁽¹⁵⁾.

This study will attempt to identify patients with poor adherence among hypertension patients, and compare levels of adherence to antihypertensive therapy by patients with different daily dosing frequency groups.

METHDODLOGY

The study design is a non experimental cross-sectional study, which deals with adherence to antihypertensive medication. The plan for this study was to determine poor adherence to anti-hypertensive therapy in outpatient hypertension department at the Hospital Pulau Pinang (General Penang Hospital), the biggest government hospital in Penang, located at Jalan Residensi. The survey method is a quantitative design that uses structured questionnaires (Morisky Scale) as the primary method for data collection. In the mid-1980s, Morisky and colleagues developed a brief questionnaire four items' (see Table - 1) to aid practitioners in prospectively predicting adherence with antihypertensive medications⁽¹⁶⁾. Subsequently, the instrument was validated in a number of studies and demonstrated to have good psychometric properties (13, 17, and 18). The advantages of this over other methods of measurement include its simplicity, speed, cheap and viability of use. Several studies highlighted the usefulness of the self-report as an adherence measurement tool. A five-point Likert scale was used throughout the questionnaire for stating the required scaling to keep the mind of the respondents more focused on the statement. According to Shelly et al.,⁽¹⁷⁾ patients are considered adherent to the treatment if they answered (1 = never or 2 = rarely) for all Morisky scale, except those patients who are considered poorly adherent⁽¹⁷⁾.

Because the study was conducted in Malaysia, the questionnaire required translation to Malay language (Bahasa). Back-translation was used to assure the accuracy of the translation. The final translated questionnaire was then pre-tested with a panel of ten Malaysian citizens who had obtained Master degrees in the United States. Members of this pre-test group were asked for any comments on the questionnaire, pertaining

to ambiguity or awkwardness in the wording of the questions. In addition, pilot study was planned as a part of the scale development methodology to ensure a comprehensive analysis for a range of perspectives, to

detect any possible problems associated with the format, wording, and measurement, and to make sure that the respondents comprehended the instructions, questions.

Table 1: MORISKY Simplified Self-Report Measure of Adherence Scale

Morisky Items	Never	Rarely	Sometimes	Often	Always
1- Do you ever forget to take your medicine?	1	2	3	4	5
2- Are you careless at times about taking your medicine?	1	2	3	4	5
3- When you feel better do you sometimes stop taking your medicine?	1	2	3	4	5
4- Sometimes if you feel worse when you take the medicine, do you stop taking it?	1	2	3	4	5

Due to the time constraint and impossibility of treating our sample rigorously, meaning that we have no clear details about the schedule list of the respondents (patients), it was decided to conduct convenience sampling technique for this research. In clinical practice, we used patients who are available to us as our sample, we sample simply by asking for volunteers, as the name implies, the sampling refers to the collection of information from members of the population who are conveniently available. As a secondary data method, patients' medical records were used to know the patients daily dose frequency. Daily doses are the determination and regulation of the total doses per day for hypertension medications which have three categorical independent, Single Daily Dose (SDD), Twice Daily Dose (BID), or more than two times daily (>BID).

With regard to the size of the sample, 518 questionnaires were distributed to the patients while they were waiting for their turn to meet the doctor at the waiting area of the clinic. Once the data were collected from patients, only useable medical records that met our sample frame were selected and matched with the questionnaire data. In addition, a number of other inclusion and exclusion criteria were used to define our sample frame. The period of data collection was from 15th June 2007 to 10th February 2008. The Clinical Research Center (CRC) at the General Hospital in Penang

and Malaysian Ministry of Health granted approval for accessing the patients' medical records and distributing the questionnaire.

Inclusion Criteria

(Aged ≥ 18 and ≤ 60 years, diagnosed with essential hypertension, received at least one anti-hypertensive medication, duration of hypertension from 2 to 5 years)

Exclusion Criteria

Secondary hypertension states such as chronic renal disease, reno-vascular disease, Cushing's syndrome, patients diagnosed with other co-morbid diseases such as diabetes mellitus, dyslipidemia, heart failure, hepatic dysfunction, psychiatric disorder, pregnant women, finally, cancer patients.

The data collected was analyzed using SPSS® Version 15.0 (19) Data distributions were normal and therefore parametric analysis was conducted, while the one-way ANOVA is used to compare the independent variable (daily doses frequency) that has three different levels (SDD, BID and > BID), and one continuous dependent variable scores ranging from 1 to a 5-point scale version: never = 1; rarely = 2; sometimes = 3; often = 4; always = 5.

RESULTS

The final response rate from 518 patients was 73.36%

($n = 380$). From Table 2 we can infer the following: Overall, 218 (57.4%) of the respondents were male and 162 (42.6%) were female. The respondents' ages fall between 51 years and 60 years, 200 with 52.6%, and ages fall between 40-50 years old, with 45.3% of the respondents. The highest number of the respondents were Malay ($n = 146$; 38.4%), followed by Chinese (33.9%) and Indian (27.6%). Most of the respondents had poor adherence ($n = 195$; 51.3%), whereas 48.7% ($n = 185$) had good adherence. The level of the education shows

that the highest number of the respondents hold high school (330, 86.4%), which is approximately most of the sample. The result shows the highest income is more than 2000 Malaysian Ringgit (Malaysian currency) 69.6%. The survey shows that the highest number of the respondents are single daily dose (209, 55.0%), which is approximately half of the sample. 38.9% are twice-daily dose, while 6.1% are more than twice daily. The respondents' ages are between 36 years old and 45 years, 271 with 70.9% of the respondents.

Table 2: Analyzing results of demographic variables

Variables	Valid	Frequency	Percentage (%)
Gender	Male	218	57.4
	Female	162	42.6
Age	18 - 28	0	0
	29 - 39	8	2.1
	40 - 50	172	45.3
	51 - 60	200	52.6
Race	Malay	146	38.4
	Chinese	129	33.9
	Indian	105	27.6
Adherence	Good	185	48.7
	Poor	195	51.3
Dose Frequency	Single daily dose	209	55.0
	Twice-daily dose	148	38.9
	More than twice daily	23	6.1
Income	Below 500 RM	9	2.6
	500-1000 RM	38	9.9
	1000-2000 RM	67	17.6
	More than 2000 RM	266	69.9
Education	High school	330	86.4
	Bachelor Degree	50	13.6
	Master Degree	0	0
	Doctoral Degree	0	0

*(RM) Malaysian currency .

As mentioned earlier, data distributions were normal and therefore parametric analysis was conducted. Table (3) shows descriptive statistics for each category of daily dose frequency. Single daily doses group was the poorest

adherence had 209 patients, and their average adherence score was 3.37. A total of 23 patients found more than two times daily dose had an average adherence of 1.42.

Table 3: Descriptive Statistics of the Categorical Independent versus Adherence.

Categorical independent	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean	
					Upper Bound	Lower Bound
SDD	209	3.3732	1.38981	0.09613	3.1837	3.5627
BID	148	2.3953	1.44573	0.11884	2.1604	2.6301
>BID	23	1.4239	1.16580	0.05542	1.3090	1.5389
Total	380	2.8743	1.49311	0.07660	2.7237	3.0249

* SDD: single daily dose; * BID: twice daily dose; * >BID: more than two times daily

There are some adherences differences across daily doses groups. Thus, one-way ANOVA is used to determine if any of these groups reliably differ from each other on adherence level. The one-way analysis of variance (ANOVA) shown in Table 4 is used to compare the means of three categorical groups of independent variable “daily doses groups” and one continuous dependent variable with scores ranging from 1 (adherence) to 5 (poor adherence).

Table (4) shows that a significant relationship exists between the dose frequency groups and poor adherence at level $p < 0.001$, the mean of the (SDD = 3.3732 and BID = 2.3953), which associated with poor adherence. As the mean of (>BID = 1.4239), it is associated with adherence. The summary of the results states a relationship between daily dose frequency groups and levels of adherence.

Table 4: The One-Way Analysis of Variance (ANOVA) result

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	134.366	2	67.183	35.645	0.000
Within Groups	710.571	377	1.885		
Total	844.937	379			

*Dependent Variable: Poor Adherence.

At the second stage of the analysis of variance (ANOVA), post-hoc test is needed after we complete an ANOVA in order to determine which groups differ from

each other. Table (5) shows the significantly different mean between all the independent variables using post-hoc comparison tests.

Table 5: Post hoc test of dose groups

DOSE (I)	(J) DOSE	Mean Difference (I-J)	Std. Error	Sig.
SDD	BID	.97794(*)	.14749	0.000
	>BID	1.94929(*)	.30161	0.000
BID	SDD	-.97794(*)	.14749	0.000
	>BID	.97136(*)	.30771	0.005
>BID	SDD	-1.94929(*)	.30161	0.000
	BID	-.97136(*)	.30771	0.005

* SDD: single daily dose; * BID : twice daily dose; * >BID: more than two times daily.

For additional explanation regarding the relationship between the dosages in the adherence, we run a cross tabulation analysis between those three categories. As shown in Table (5), 30.6% of the SDD group show good adherence, whereas 66.2% of the BID dosages are within

the good adherence range. Regarding >BID, 100.0% are within good adherence, which is the best category to obtain better adherence.

Table 5: Daily Dose groups * Adherence “Crosstabulation”

Cross tabulation		Adherence		Total	
		Good Adherence	Poor Adherence		
DAILY DOSE GROUPS	SDD	Count	64	145	209
		% within Dose	30.6%	69.4%	100.0%
		% within adherence	34.6%	74.4%	55.0%
		% of Total	16.8%	38.2%	55.0%
	BID	Count	98	50	148
		% within Dose	66.2%	33.8%	100.0%
		% within adherence	53.0%	25.6%	38.9%
		% of Total	25.8%	13.2%	38.9%
	>BID	Count	23	0	23
		% within Dose	100.0%	0	100.0%
		% within adherence	12.4%	.0%	6.1%
		% of Total	6.1%	.0%	6.1%
Total	Count	185	195	380	
	% within adherence	100.0%	100.0%	100.0%	
	% of Total	48.7%	51.3%	100.0%	

* SDD : single daily dose ; * BID : twice daily dose; * >BID : more than two times daily

DISCUSSION

A- Identification of patients with poor adherence

In relation to the first objective, one of the main findings of this study was the identification of patients with poor adherence. The MORISKY scale items were summed, and the descriptive statistics presented in Table 1, showed that 195 patients had poor adherence to hypertensive medication. According to this result, 51.3% of our total sample was taking their medicines irregularly. This finding concurs with the finding by Hassan et al. (4). The rate of adherence is low compared with the rate that is prevalent in western population such as in Scotland where a 91% rate of adherence has been reported (14), and in Pakistan where a 77% rate of adherence has been

reported (13).

Poor adherence is related to the way in which a patient judges personal need for a medication against a variety of competing needs, wants, and concerns (adverse effects, stigma, cultural beliefs, cost, etc.). In fact, patients are not the only factor that affects adherence, with respect to the demographic variables, no statistically significant associations were found between the change in adherent patients' level and demographic variables in this study. Healthcare providers, complex medication regimens, and accessing and navigating the healthcare delivery system can contribute to the problem of non-adherence.

There are many factors that effect adherence; it could be because of the disease itself, given that hypertension is

a deadly condition that possesses no warning signs (asymptomatic) and is often dubbed as the 'silent killer'. In fact, while the questionnaire was distributed, it was noted that, most patients had not discovered that their blood pressure elevated until they had some degree of trouble. In 2008, Paul S. found that most chronic hypertensive patients have difficulty adhering to a prescribed regimen (20). In fact, the lack of awareness of hypertension and lack of adequate control with treatment could also be reasons for poor adherence to therapy (3).

Furthermore, poor adherence may also occur because patients do not believe that they have a disease or that the medication will be effective in reducing complications associated with their disease.

B- Daily dose frequency and poor adherence

Daily dose frequency is a factor that can affect poor adherence (11, 12, 21). Previous research carried out on this topic has shown that the relationship between dose frequency and poor adherence is an inconsistent variable. A study by Claxton and his colleagues had found that adherence rates decreased as the number of daily dose increased by using Morisky scale and electronic monitoring⁽¹²⁾, whereas, in contrast, a study by Hashmi et al. had found that adherence rates increased as the number of daily dose increased⁽¹³⁾.

Another study done by Inkster et al., investigating the relationship between daily doses and adherence toward antihypertensive therapy using one way ANOVA, found non-significant differences between level of adherence

and daily dose frequency, it concludes that changing from twice to once-daily dose does not have relationship with adherence or improve it⁽¹⁴⁾.

A significant relationship exists between daily dose frequency and poor adherence as supported by empirical data. It shows that hypertension patients groups, who have more daily dose frequency, will show higher level of adherence towards antihypertensive medication.

This could be attributed to the following: patients on single daily dose took their treatment lightly and those taking multiple doses understood the severity of their disease and hence the latter were more cautious with respect to their treatment regimen. In addition, the forgetfulness factor was less pronounced in patients under multiple medications than their counterparts who took only one daily dose. Some patients also had phobias regarding their multiple medications (22); patients who took more number of doses thought that they had a serious illness and following the prescribed prescription was strictly warranted.

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