

Relationship between regimen complexity and medication adherence behavior in Thai elderly with hypertension

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- Background** : Only 22 - 25 percent of Thai elderly with hypertension can control their blood pressure. Such failure has been largely ascribed to poor adherence with antihypertensive medication. The regimen complexity is an important factor that influences medication adherence in the elderly.
- Objectives** : To examine the relationship between regimen complexity and medication adherence behavior in Thai elderly with hypertension.
- Setting** : Out-patient department of five general hospitals in Thailand.
- Research design** : Cross-sectional study.
- Patients** : There were 422 elderly with hypertension who participated in this study.
- Methods** : The samples were selected based on multi-stage sampling. Data were collected using Medication Regimen Complexity Index and Morisky Medication Adherence Scale. The data were analyzed using descriptive statistics and Pearson's product moment correlation coefficient.

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Results : *Regimen complexity had negative correlation with medication adherence behavior ($r = -.25, p < .01$). More complex prescription such as variety of dosage forms, multiple daily dosing frequencies, and additional instructions for drug administration were related to poor medication adherence behavior ($r = -.12, -.21$ and $-.26, p < .01$, respectively).*

Conclusions : *The data revealed that the elderly who have more complexity of medication regimen are less likely to be adherence. Nurses should take an active role in assessment the regimen complexity and promote medication adherence behavior in Thai elderly with hypertension especially the high risk groups by educating them to overcome the complexities of medication therapy.*

Keywords : *Regimen complexity, medication adherence, elderly.*

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ความสัมพันธ์ระหว่างความซับซ้อนของแผนกำหนดการใช้ยาและพฤติกรรมความสม่ำเสมอ
ในการรับประทานยาของผู้สูงอายุไทยโรคความดันโลหิตสูง. จุฬาลงกรณ์เวชสาร 2554
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- บทนำ** : มีผู้สูงอายุไทยโรคความดันโลหิตสูงจำนวนเพียง 22 - 25 เปอร์เซ็นต์ที่สามารถควบคุมระดับความดันโลหิตได้ ความล้มเหลวนี้เนื่องจากมีพฤติกรรมการรับประทานยารักษาโรคความดันโลหิตสูงที่ไม่สม่ำเสมอ ความซับซ้อนของแผนกำหนดการใช้ยาเป็นสาเหตุหลักอย่างหนึ่งที่มีผลต่อพฤติกรรมความสม่ำเสมอในการรับประทานยาของผู้สูงอายุ
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- ผลการศึกษา** : ความซับซ้อนของแผนกำหนดการใช้ยามีความสัมพันธ์ทางลบกับพฤติกรรม ความสม่ำเสมอในการรับประทานยาของผู้สูงอายุโรคความดันโลหิตสูง ($r = -.25; p < .01$) ความซับซ้อนของแผนกำหนดการใช้ยาที่เพิ่มขึ้น ได้แก่ความหลากหลายของรูปแบบยาที่ใช้ การรับประทานหลายครั้ง และคำแนะนำการใช้ยาเพิ่มเติม มีความสัมพันธ์กับพฤติกรรมความไม่สม่ำเสมอในการรับประทานยาของผู้สูงอายุโรคความดันโลหิตสูง ($r = -.12, -.21$ และ $-.26, p < .01$, ตามลำดับ)

- วิจารณ์และสรุป** : ผลการวิจัยพบว่าผู้สูงอายุที่มีความซับซ้อนของแผนกำหนดการใช้ยาเพิ่มขึ้นจะมีพฤติกรรมความสม่ำเสมอในการรับประทานยาลดลงพยาบาลควรให้ความสำคัญกับการประเมินความซับซ้อนของแผนกำหนดการใช้ยา และส่งเสริมพฤติกรรมความสม่ำเสมอในการรับประทานยาของผู้สูงอายุไทยโรคความดันโลหิตสูง โดยเฉพาะกลุ่มเสี่ยง โดยการให้ความรู้เกี่ยวกับความซับซ้อนของแผนกำหนดการใช้ยา
- คำสำคัญ** : ความซับซ้อนของแผนกำหนดการใช้ยา, พฤติกรรมความสม่ำเสมอในการรับประทานยา, ผู้สูงอายุ.

Hypertension is a chronic disease typically found in the elderly. Data from the fourth report of Thai population health examination survey revealed that 38 - 47% of the elderly were affected by hypertension; and hypertension was the top of chronic diseases in the elderly.⁽¹⁾ Moreover, hypertension is the first leading cause of hospital admission in Thai elderly.⁽²⁾ The prevalence of hypertension rises sharply not only with age but also with the incidence of heart failure, stroke, and coronary heart disease.⁽³⁻⁵⁾

Antihypertensive medications have been reported as a highly effective treatment in reducing blood pressure level and in reducing the adverse outcomes.^(6,7) However, only 22-25% in Thai elderly can control their blood pressure⁽¹⁾ (<140/90 mmHg or <130/80 mmHg for patients with diabetes or chronic kidney disease).⁽⁸⁾ Such failure has been largely ascribed to poor adherence with antihypertensive medication.^(9,10)

Hypertensive elderly often suffer from many coexisting illness in addition to the primary disease, often referred to as co-morbidity, for which they simultaneously need to take various medications. Assantachai et al⁽¹¹⁾ found that Thai elderly with hypertension also suffered from associated co-morbidity such as hyperuricemia (33.3%), diabetes mellitus (22.9%), heart disease (18.0%) and hyperlipidemia (13.9%). Therefore, they often have multiple medical conditions to manage, with a high number of concurrent medications. More medication demands more daily dosing and a complex regimen to prescribe.

In the adherence literature for the elderly and chronic illness, regimen complexity is an important

barrier to medication adherence.⁽¹²⁻¹⁴⁾ Regimen complexity consists of multiple different characteristics of the prescribed regimen. These include the dosage forms, dosage frequency, and additional instruction for drug administration.⁽¹⁵⁾

Information about regimen complexity which is important to medication adherence is needed. The purpose of this study is to examine the relationship between regimen complexity and medication adherence behavior in Thai elderly with hypertension.

Materials and Methods

Study population

A cross-sectional study was conducted in general hospital in Thailand. The samples included elderly persons, aged 60 years old and over, being diagnosed with hypertension, having been treated with at least one antihypertensive medication, having normal cognitive function, no problems with deafness, blindness or dementia, and willing to participate in this study. A multi-stage sampling technique was used to identify the sample; there were 422 elderly in 5 general hospitals including Lumphun Hospital, Phatthalung Hospital, Umnatcharoen Hospital, Phra Phutthabat Hospital, and Samutsakhon Hospital.

Measurements

Chula Mental Test (CMT)⁽¹⁶⁾ was used to assess cognitive function in the elderly. There are 13 items listing cognitive functions, including age, time, registration of three things, month, person, rice, do follow, proverb, speak follow, judgment, count 10 to 20, naming objects, and subtraction. The possible summation of all items to represent cognitive function ranged from 0-19. Elderly who had the score lower

than 15 had impaired cognitive function and scores 15-19 had normal cognitive function. The results of the CMT reliability using a test-retest kappa coefficient and an internal consistency coefficient were 0.65 and 0.81.

Regimen complexity was measured by Medication Regimen Complexity Index (MRCI).⁽¹⁵⁾ The MRCI is divided in three sections: A, B and C. Section A corresponds to the information on dosage forms, section B corresponds to the information on dose frequency and Section C corresponds to additional instructions relevant to the administration of the drug, such as drug specific time and concomitant use with food, among others. The MRCI consisted of 65 items. Each section is scored based on the analysis of the patient's pharmacotherapy and the complexity index is obtained by adding the points (scores) of the three sections. Higher score means higher complexity of the regimen. In this study the English-Thai language translation was established and the inter-rater reliability for the total score on the MRCI between the 2 raters was 0.997.

Medication adherence behavior was measured by Morisky Medication Adherence Scale (MMAS).⁽¹⁷⁾ The MMAS is an 8-item questionnaire. Response categories are yes/no for each item with a dichotomous response and a 5-point Likert response for the last item. The total score was calculated by the summation for the scores of the 8 items. Highly adherent patients were identified with the score of 8 on the scale, medium adherers with a score of 6 to less than 8, and low adherers with a score less than 6. The MMAS had already been translated into Thai and used in diabetes patients.⁽¹⁸⁾ The Cronbach's alpha for MMAS was 0.61 and test-retest reliability

was 0.83. In this study, Cronbach's alpha was 0.81.

Data collection

Data collection included demographic characteristics, regimen complexity and medication adherence behaviors. The interview technique was used for the elderly including demographic characteristics and MMAS questionnaire. Regimen complexity was recorded by the researcher from the medication records at the hospital. The study has been approved by the Ethical Committee of the hospital settings. Before data collection, the participants received information regarding the study and signed consent forms.

Statistical analysis

Descriptive statistics such as frequency, percentage, mean, and standard deviation were used to describe sample characteristics, regimen complexity and medication adherence behavior. Pearson's product moment correlation coefficient was performed to explore the relationship between regimen complexity and medication adherence behaviors.

Results

The 422 elderly with hypertension participated in the study. Their ages ranged from 60 to 85 years old with a mean of 69.54 years old (SD = 6.61). Most of them were age 60-69 years (51.9%). The majority of the elderly were female (77.5%), 55.5% of them were married, 81.0% received primary school education, and their family incomes were under 10,000 baht (59.7%) per month. About 64.4% of them were unemployed and had co-

morbidity (77%). The average duration of hypertensive was 7.66 years. Most of them were able to control their blood pressure (60.4%), whereas 39.6% could

not control their blood pressure. They had sources of medical payment from the universal coverage health care scheme (71.6%) (Table 1).

Table 1. Demographic characteristics of the sample (n = 422).

Demographic characteristics	Number	Percentage
Age (Mean = 69.54, SD = 6.61)		
Young-old (60-69 years)	219	51.9
Old-old (70-79 years)	165	39.1
Oldest-old (80 years and over)	38	9.0
Gender		
Male	95	22.5
Female	327	77.5
Marital status		
Single	8	1.9
Married	234	55.5
Widowed	174	41.2
Separated, Divorced	6	1.4
Education level		
No formal education	46	10.9
Elementary education	342	81.0
Secondary education	29	6.9
Vocational education	1	0.2
Bachelor degree	4	0.9
Duration of illness Min= 3 month, Max = 35 years, Mean =7.66, SD = 6.92		
Employment status		
Employment	150	35.6
Unemployment	272	64.4
Family income (baht/month)		
≤ 10,000	252	59.7
> 10,001-20,000	70	16.6
> 20,001-30,000	56	13.3
> 30,001	44	10.4
Sources of medical payment		
Medical welfare for government officer	115	27.3
Universal Coverage	302	71.6
Social Security Insurance	4	0.9
Self	1	0.2

Table 1. Demographic characteristics of the sample (n = 422). (continued)

Demographic characteristics	Number	Percentage
Blood pressure control*		
Controlled	225	60.4
Uncontrolled	167	39.6
Comorbidity**		
No	97	23.0
Yes	325	77.0
Diabetes mellitus	186	44.1
Hyperlipidemia	129	30.6
Heart disease	63	14.9
Musculoskeletal disease	49	11.6
Kidney disease	24	5.7

* Blood pressure control (<140/90 mmHg or <130/80 mmHg for patients with diabetes or chronic kidney disease) and blood pressure uncontrol (\geq 140/90 mmHg or \geq 130/80 mmHg for patients with diabetes or chronic kidney disease) defined by the Seventh Report of the Joint National Committee (JNC 7) on Prevention, Detection, Evaluation, and Treatment of High Blood pressure

** Some patients had multiple diseases

Majority (96.9%) of the elderly were taking more than one medication a day. Fifty-two percent of the elderly were taking two to five medications. Their medication ranged from 1 to 16 drugs with a mean of 5.47 drugs (SD = 2.54). In term of antihypertensive drugs, more than half of them (56.4%) were receiving more than one antihypertensive drug. By types of antihypertensive drug, nearly half of the elderly (46.2%) received calcium channel blocker, followed by diuretic (37.9%), beta adrenergic blocker (36.0%), and angiotensin converting enzyme inhibitor (35.1%).

With regard to dosage forms, it was found that majority of the drugs prescribed were tablets or capsules (100%) followed by cream (16.5%) and injection (7.8%). Most medications were taken three times per day (39.3%) followed by once daily (29.9%)

and twice daily (23.9%). The most common additional instructions for drug administration was taking medication in relation to food (100%), followed by taking medication or use them at specified times (99.5%) and required breaking or crushing of the tablets (65.4%) (Table 2).

The elderly had complexity score ranged from 11 to 49.50 with a mean of 24.09 (SD=9.61). The dosage forms score ranged from 1 to 11 with a mean of 2.47 (SD=2.35). The medication frequency score ranged from 3 to 23.50 with a mean of 9.12 (SD=4.37). And the additional instructions score ranged from 5 to 27 with a mean of 12.49 (SD=4.39).

Medication adherence behavior scores range from 1.50 to 8.00 with a mean of 6.17 (SD= 1.81). About 31.5% had high adherence

behavior, 40.8% had medium adherence behavior, whereas 27.7% had low adherence behavior. In each adherence category, elderly who could control their blood pressure in high adherence group was 70.0%, medium adherence group was 66.3.0%, and low

adherence group was 41.0%. The elderly who could not control their blood pressure in high adherence group was 30.0%, medium adherence group was 33.7%, and low adherence group was 59.0% (Table 3).

Table 2. Medication regimen of the sample (n = 422).

Information of medication	Frequency	Percentage
Types of antihypertensive drug**		
Diuretic	160	37.9
Alpha adrenergic blocker	11	2.6
Beta adrenergic blocker	152	36.0
Calcium channel blocker	195	46.2
Angiotensin receptor blocker	52	12.3
Angiotensin converting enzyme inhibitor	148	35.1
Vasodilator	23	5.5
Number of antihypertensive drugs (Mean = 1.76, SD = 0.82)		
1	184	43.6
2	175	41.5
3	48	11.4
4	12	2.8
5	3	0.7
Number of total drugs (Mean = 5.47, SD = 2.54)		
1	13	3.1
2-5	220	52.1
6-9	157	37.2
10-13	29	6.9
14-16	3	0.7
Dosage forms of total drugs**		
Capsules/Tablets	422	100
Liquids	18	4.3
Powders	2	0.2
Cream	70	16.5
Dressing	19	4.5
Eye drops	25	5.9
Eye jells/ointments	6	1.4
Inhalation	9	2.1
Injection	33	7.8

**Some patients received multiple medications

Table 2. Medication regimen of the sample (n = 422). (continued)

Information of medication	Frequency	Percentage
Dosing frequency of hypertensive drugs**		
Once daily	398	94.3
Twice daily	81	19.2
Three times daily	12	2.8
Four times daily	3	0.7
Dosing frequency of total drugs**		
Once daily	126	29.9
Twice daily	101	23.9
Three times daily	166	39.3
Four times daily	29	6.9
Additional instructions for drug administration of hypertensive drugs**		
Break or crush tablet	206	49.0
Multiple units at one time	49	11.6
Take/use at specified times	422	100
Relation to food	419	99.3
Alternating dose	3	0.7
Additional instructions for drug administration of total drugs**		
Break or crush tablet	279	65.4
Dissolve tablet/powder	2	0.2
Multiple units at one time	194	46.0
Variable dose	26	6.2
Take/use at specified times	420	99.5
Relation to food	422	100
Alternating dose	3	0.7

**Some patients received multiple medications

Table 3. Morisky Medication Adherence Scale (MMAS) category and blood pressure control of the sample (n = 422).

Blood pressure control*	Morisky Medication Adherence Scale (MMAS) category		
	High adherence (MMAS=8) (n=133, 31.5%)	Medium adherence (MMAS 6 to less than 8) (n=172, 40.8%)	Low adherence (MMAS<6) (n=117, 27.7%)
Controlled	93 (70.0%)	114 (66.3%)	48 (41.0%)
Uncontrolled	40 (30.0%)	58 (33.7%)	69 (59.0%)

* Blood pressure control (<140/90 mmHg or <130/80 mmHg for patients with diabetes or chronic kidney disease) and blood pressure uncontrol (\geq 140/90 mmHg or \geq 130/80 mmHg for patients with diabetes or chronic kidney disease) defined by the Seventh Report of the Joint National Committee (JNC 7) on Prevention, Detection, Evaluation, and Treatment of High Blood pressure

Regimen complexity had negative correlation with medication adherence behavior ($r = -.25, p < .01$). Dosage forms, dosing frequencies, and additional instruction had negative correlation with medication adherence behavior ($r = -.12, -.21$ and $-.26, p < .01$, respectively).

Discussion

It was found that most of elderly with hypertension adhered to taking medication at a moderate (40.8%) to high level (27.7%). The reason may possibly be because the treatment was covered by the universal coverage health care scheme (71.6%); thus it could help the subjects achieve better medication adherence. Most of samples (51.9%) were young elderly who had the ability to take medication and had normal cognitive function. The research suggests that the young old (ages 60 to 75) tend to have relatively high rates of medication adherence.⁽¹⁹⁾ Moreover, the elderly who had adequate cognitive functioning and received information about their medication could understand the illness, its treatment,

and the purpose of taking the medication. They also comprehended, organized and remember the medication regimen requirements, when to take the medication, what kind of side effects could be expected, and how to deal with them,⁽²⁰⁾ then they can adhere to the medication regimen.

In each medication adherence category, the elderly who could control their blood pressure in high adherence group was 70.0%, medium adherence group was 66.3.0%, and low adherence group was 41.0%. Conversely, the elderly who could not control their blood pressure in high adherence group was 30.0%, medium adherence group was 33.7%, and low adherence group was 59.0%. The data indicated that highly adherent elderly were more likely to achieve blood pressure control than elderly with medium or low adherence to medication. The results were consistent with the study of Bramley et al,⁽²¹⁾ showed that patients in high adherence group were had high rate of blood pressure control (43%) compared with medium (34%) and low group (33%). Level of adherence has been positively correlated with blood

pressure control.⁽²²⁾ Low adherence has been cited in the literature as the primary cause of unsatisfactory control of hypertension.⁽⁸⁾

The data revealed that the elderly who have more complexity of medication regimen are less likely to be adherence ($r = -.25, p < .01$). The complexity of prescribed regimens varied with dosage forms, dosage frequency, and additional instructions for drug administration.⁽¹⁵⁾ In this study, more than half of them were receiving more than one antihypertensive drug. The average hypertensive drug taken per day was 1.76. Adherence behavior is also affected by use of numerous concomitant medications^(23, 24) which is common among the elderly patients, who often have multiple chronic illnesses. In this study, most of the hypertensive elderly had co-morbidity (77%), and they consequently have multiple medications to take; these come with the complexity of the medication prescribed. More than half of them were taking two to five medications daily. The average drug taken per day was 5.47. The elderly prescribed multiple drugs often have to take medications at several different times of the day: some before meals, some after meals, sometimes needed to halve the tablets, often use multiple dose forms and multiple routes of administration.⁽²⁵⁾ Studies have shown that the greater number of medications prescribed for elderly patients causes the greater medication non-adherence.^(13, 26, 27)

The dosage form plays a very important role in patient adherence. Variety of dosage forms were related to poor medication adherence behavior ($r = -.12, p < .01$). In this study, dosage forms that the hypertensive elderly frequently used were tablets or capsules. The oral route still represents the preferred

route of administration, owing to its several advantages and high patient adherence compared to many other routes.⁽²⁸⁾ However, the nature of the dosage form, such as the size of the pills or a liquid preparation, can negatively affect adherence if it is inconvenient to take or unpalatable.⁽²⁹⁾ A review of the factors found that the route of drug administration, the appearance, color, test of medication, and the tablet size all these influence adherences.⁽³⁰⁾ These can create confusion among patients using multiple medications.⁽³¹⁾ Moreover, difficulty in swallowing pills can be a cause for elderly patients failing to adhere to treatment.⁽³²⁾ A study reported that 19% of the elderly aged 70 years and older had difficulties in swallowing the tablets.⁽³³⁾ There are also studies that have looked into ease of swallowing of different tablets, where one study showed that people usually prefer to swallow smaller tablets and oval rather than round when the tablets are of larger size.⁽³⁴⁾ This was repeated when a group of researchers found that patients preferred gelatin capsules over tablets, and, again, oval tablets rather than circular.⁽³⁵⁾ Other dosage form such as injection is necessary in cases like insulin (7.8%). Some elderly are uncomfortable with injection devices that appear too technical or complex and some conditions such as poor eyesight or manual difficulties may pose physical obstacles to the use of most injection devices.⁽³⁶⁾ The likelihood of arthritis or tremors increases with advancing age⁽³⁷⁾, adding to the difficulty of manually operating handheld devices.

Multiple daily dosing frequencies were related to poor medication adherence behavior ($r = -.21, p < .01$). In this study, hypertensive drugs were taking once daily (94.3%) and most medications were taken three times per day (39.3%). A recent meta-analysis

of eight studies reports that the average adherence for single daily dosing was significantly higher than multiple daily dosing (91.4% versus 83.2%, respectively $P < 0.001$).⁽³⁸⁾ Increase in dose frequency was related to poorer adherence.^(14, 39, 40) Reduction of prescribed medication dosing from 3 and 4 times daily to once daily significantly improved medication adherence ($P = .008$ and $P < .001$, respectively).⁽²³⁾ Similar to hypertension study, reducing the number of daily doses was effective in increasing adherence with antihypertensive medication from 8% to 19.6%.⁽¹⁰⁾ Once-daily dosing was also associated with higher adherence to antihypertensive medication than was twice-daily dosing.⁽³⁸⁾

Variety of additional instructions for drug administration was related to poor medication adherence behavior ($r = -.26$, $p < .01$). In this study, all of hypertensive elderly had to schedule their medications related to meals followed by taking or use medication at specified times and more than half of them required breaking or crushing of the tablets. These activities impact daily life, require judgment, and can impact adherence.⁽⁴¹⁾ Frequently, adhering to medications is not just ingesting the drugs themselves but includes adjustment to daily routines and this may include complex timing of doses in conjunction with eating. Moreover, Lam et al,⁽⁴²⁾ studied the prevalence of drug non-adherence among Chinese elderly people and its associated risk factors, and found that the necessity to cut tablets was associated with a 5-fold increase in the risk of drug non-adherence (OR=4.8; 95% CI, 2.1-10.7; $P < 0.001$). Although this problem has not been addressed before, they suggested that it might be related to the inconvenience of halving a tablet, or that patient might

not realize that the pills needed to be cut before intake. Older patients experiencing reduced hand dexterity might be another reason. Further studies are needed to explore this observation.

Conclusion

The data revealed that the elderly who have more complexity of medication regimen are less likely to be adherence. Poor medication adherence in hypertensive elderly can be a significant barrier to attaining blood pressure control. Comprehensive treatment plans that can reduce treatment complexity should be considered. Nurses should take an active role in assessment regimen complexity and promote medication adherence behavior in Thai elderly with hypertension especially high risk group by educating about the complexities of medication therapy.

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