Original Article

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Medication Use and Adherence in Patients with Hypertension: A Prospective Study in Vietnam

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Abstract:

Objective: to document patients' antihypertensive agents, determine their medication adherence, and identify factors associated with the adherence.

Material and Methods: A prospective study was performed on a group of hypertensive outpatients, with social health insurance, in Can Tho, Vietnam. The study included 330 patients over 18 years old, who agreed to participate and could listen, speak and answer questions in Vietnamese. The data collection method was based on prescriptions and patient interviews. Data were analyzed using descriptive statistics, and Generalized Estimating Equations with Poisson-log linear distribution.

Results: Among the drug use characteristics, 76.1% were prescribed beta-blockers, 91.5% polytherapy, and 63.0% changed drugs at the third follow-up visit. The percentage of patients who adhered to medication ranged from 70.0% to 91.2%. Factors that improved drug adherence included: the academic level at high school or higher (39.0% increase), living in urban areas (15.0% increase), having a job related to social interaction (11.2%), and having a family history of hypertension (9.0% increase). Factors that reduced adherence included: advanced age (22.0% decrease), prolonged disease duration (16.0% decrease), prolonged treatment duration (11.0% decrease), and changes in at least one type of antihypertensive drug (8.0% decrease).

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Conclusion: The highlight of this study is the demonstration of an inverse relationship between the adherence rate and the number of follow-up visits: the higher the number of visits, the lower the adherence rate. The 3rd follow-up adherence rate was 70.0%, and the decreased adherence rate is related to older age, higher education levels, and a longer duration of treatment.

Keywords: hypertension, medication adherence, related factors, Vietnam

Introduction

Hypertension is a chronic disease, with an increasing incidence that is becoming a leading concern in world medicine[1]. Globally, there are 1 billion people with hypertension, and this is expected to increase to 1.5 billion by 2025[2]. The prevalence of hypertension in adults in low and middle-income countries is higher than in high-income countries: 31.5% and 28.5%, respectively[3].

Hypertension is the leading cause of disability and death in developing countries[4], with the World Health Organization estimating that 9.4 million people die annually due to hypertension[5]. On the contrary, well-controlled blood pressure prevents illness complications and improves longevity and quality of life[6–8]. If not properly and adequately treated, hypertension will cause dangerous manifold complications, which may lead to death or leave severe sequelae; thus, becoming a burden to both families and society. Over the past decades, numerous clinical studies have shown that effective treatment of hypertension reduces the risk of cardiovascular disease and death[9–11]. Hence, medication adherence in hypertensive patients is crucial to treatment success. According to the research results of the author: Nguyen Tran Phuong Thao, the adherence rate in using antihypertensive agents was 77%[12].

In Vietnam, the number of participants in social health insurance increased from 7.1 million people in 1995, to 88.8 million people in 2021; reaching a coverage rate of 91.01% of the population. This is an average annual increase of more than three million people[13]. According to results in the first six months of 2022, the number of participants in social health insurance in Can Tho city was 1,041,337 people; reaching 91.6%. This study was aimed at patients with social health insurance. Patients with chronic diseases; such as high blood pressure, are covered by social health insurance; thus, they tend to return for follow-up visits. Consequently, the number is higher than those who do not have insurance due to the treatment cost.

Stemming from that fact, this study was conducted with the objectives of: (1) to determine the characteristics of antihypertensive drugs, (2) to determine the percentage of patients adhering to the use of antihypertensive drugs, and (3) to identify some factors related to the adherence of antihypertensive medication use.

Material and Methods

Study population

This study included patients diagnosed with hypertension were being examined and treated as outpatients in a General Medicine department of a hospital in Can Tho, Viet Nam, and had social health insurance coverage; from June 1st, 2020 to December 31st, 2020.

Inclusion criteria: Patients over 18 years of age that agreed to participate in the study (1) could hear and speak and answer the questions being examined in Vietnamese, (2) were being treated as outpatients for hypertension, and (3) were participating in the social health insurance at Can Tho City.

Exclusion criteria: Patients that were pregnant or lactating, and patients with abnormal consciousness or abnormal mental status.

Methods

Study design: this was a prospective study, conducted from June to the end of December 2020, evaluating patient adherence to drug use at the following time points: one month, three months, and six months after the start of the study. This study's duration was conducted over a long time, with follow-ups, and frequent meetings with the patients to learn more about patients with hypertension.

The formula for estimating the precision of a proportion was applied to calculate the required sample size. Using an expected proportion of adherence of 0.77 and a margin of error (95% confidence interval) of ±0.05, 273 patients were required[12]. To avoid unsatisfactory study samples, 20% more patients were added to the sample (54 patients). Therefore, the sample size to be collected was 330 patients. Sampling was performed randomly from a list of hypertensive patients being managed at a provincial hospital in Can Tho. Patients were explained the study's significance and agreed to participate. Each patient was interviewed and collected prescriptions four times; including: at the beginning of the study, at the time of the 1st (after one month), the 2nd (after 3 months), and the 3rd (after six months) follow-up.

The data were collected from June 1st, 2020 to December 31st, 2020, using the following steps: (1) collecting age, gender, place of residence, education level, occupation, BMI, duration of hypertension, duration of hypertension treatment, marital status, family history, comorbidities, diagnosis, prescription, phone number, address information: via in-person interviews and (2) face-to-face interviews, and collection of prescriptions for follow-up visits. Assessment of adherence to antihypertensive drug use was made according to the Morisky Medication Adherence Scale (MMAS-8); including eight questions. Questions 1-4 and 6-8: an answer of: "NO" scored 1 point, and an answer of: "YES" scored 0 points. Particularly for question 5: answering "YES" scored 1 point, and answering "NO" scored 0 points[14]. Evaluation of the summed scores was divided into two levels: adherence (from 6-8 points) and poor adherence (less than 6 points), based on the results of three follow-up visits (after one month, three months, and six months after the start of the study). The questionnaire was translated and adjusted for Vietnamese people[15].

At the time of T0, data collectors recorded patient information regarding the patient's phone number or relatives and addresses, conducted face-to-face interviews, and collected prescriptions.

Time to follow-up T1, T3, T6: if the patient was not re-examined within three days after the appointed time, the data collector would make a phone call (phone interview), and collect prescriptions once the patient was re-examined. If a telephone was unavailable, the data collector visited the patient's home to conduct a face-to-face interview and collected the prescriptions when the patient was subsequently re-examined.

The characteristics of antihypertensive drugs were calculated in terms of the percentage of different drug classes, the percentage of monotherapy and multitherapy, and the percentage of drug change between each follow-up visit. The adherence rate was calculated for each follow-up visit by dividing the number of patients adhering to using antihypertensive drugs by the total number of patients participating in the follow-up examination, within the same period. Patient characteristics and medication factors related to adherence to antihypertensive drugs were analyzed, based on the results after three follow-up visits.

The changes in drug use recorded at follow-up visits were based on the following criteria: 1) No change in antihypertensive drug type or dosage; 2) Change of at least one type of antihypertensive drugs; 3) Increase in dosage and/or added at least one antihypertensive drug; 4) Decrease in dosage and/or discontinuing of at least one antihypertensive drug.

We used an Excel table to encode and input data. The data, after cleaning, were entered into the computer

and processed by Statistical Package for the Social Sciences (SPSS) 26.0 software for descriptive information and statistical analysis. The descriptive statistics method was used to determine the general characteristics of the research sample, which are presented in tabular form. The percentage of some factors related to drug adherence were compared using χ^2 test or Fisher's exact test. Separate Generalized Estimating Equations with Poisson–log linear distribution were used to estimate the overall prevalence ratio (PR) over the three follow-up times, with 95% confidence intervals (CI) for all variables potentially associated with medication adherence for hypertension

Ethics consideration

Before being selected for the study sample, both patients and their families were explained as to the purpose and conduct of the study and were asked for their voluntary agreement to participate. All patient information was encrypted and confidential, and only the researcher could access the information for research purposes only. The study was approved by the Ethics Committee in Biomedical Research of Can Tho University of Medicine and Pharmacy, with number: 181/HDĐD-PCT, on May 28, 2020.

Results

Three hundred and thirty patients were enrolled at the start of the study and were followed up for 7 months. No patient information was lost during the follow-up.

A high percentage of the patients in the sample had the following characteristics: over 60 years of age (75.5%), lived in urban areas (70.6%), had a high school education or higher (57.6%), were retired or a housewife (74.8%), married (97.3%), with BMI of 18.5–22.9 (53.9%), having had a duration of hypertension of 10 years or more (54.8%), had antihypertensive treatment for a duration of 5 years or more (66.4%), and had no family history of hypertension (58.2%). In addition, dyslipidemia (93.3%) and cardiovascular target organ damage (88.5%) accounted for a high proportion of the patients (Table 1).

Table 1 General characteristics of the study sample

General characteristics (N=330)	Frequency (n)	%
Age (years)		
<40	2	0.6
40–60	79	23.9
>60	249	75.5
Gender		
Male	143	43.3
Female	187	56.7
Residence		
Rural area	97	29.4
Urban area	233	70.6
Academic level		
Primary	49	14.8
Secondary	91	27.6
High school or higher	190	57.6
Career		
Retired, housewives	247	74.8
Employee	3	0.9
Sales and services	43	13.0
Public servants	37	11.2
BMI (kg/m^2)		
≤18.5	6	1.8
18.5–22.9	178	53.9
23–24.9	94	28.5
25–29.9	52	15.8
≥30.0	0	0.0
Duration of hypertension		
<1 year	2	0.6
1 to <5 years	48	14.5
5 to <10 years	99	30.0
≥10 years	181	54.8
Duration of treatment		
<1 year	2	0.6
1 to <2 years	30	9.1
2 to <5 years	79	23.9
≥5 years	219	66.4
Marital status		
Single	9	2.7
Married	321	97.3
Family history (with hypertension)		
Yes	192	58.2
No	138	41.8
Comorbidities		
Diabetes	69	20.9
Dyslipidemia	308	93.3
Cardiovascular	292	88.5
Kidney	12	3.6
Brain	9	2.7

BMI=body mass index

In the group beta-blockers were used the most, accounting for 76.1%. Hydrochlorothiazide accounted for the highest rate of 15.2%, when using a diuretic. The combination of two diuretics accounts for 2.4%; wherein, amlodipine was used with the highest rate: 34.9%, in the calcium channel blocker group. Angiotensin-converting enzyme (ACE) inhibitors were used at 18.2% and only used with the active ingredient enalapril. In the Angiotensin II receptor blockers group, losartan was used with the highest rate of 51.5%, telmisartan accounted for 15.8%, while irbesartan accounted for the lowest rate of 7.6%. In the beta-blocker group, bisoprolol was used at the highest rate: 73.9%, with nebivolol usage accounting for the lowest rate: 2.1%. The group of drugs acting on the central sympathetic system using methyldopa accounted for 0.3% (Table 2).

Table 2 Drugs used in the treatment of hypertension

Antihypertensive drug classes	Frequency (n=330)	%
Diuretics	77	23.3
Furosemide	9	2.7
Spironolactone	10	3.0
Hydrochlorothiazide	50	15.2
Furusemide + spironolactone	8	2.4
Calcium Channel Blockers	152	46.1
Amlodipine	115	34.9
Nifedipine	31	9.4
Cilnidipine	4	1.2
Diltiazem	2	0.6
Angiotensin-converting enzyme inhibitors	60	18.2
Enalapril	60	18.2
Angiotensin II receptor blockers	247	74.8
Irbesartan	25	7.6
Losartan	170	51.5
Telmisartan	52	15.7
Beta-Blockers	251	76.1
Bisoprolol	244	73.9
Nebivolol	7	2.1
Centrally-acting alpha-2 adrenergic agonist	1	0.3
Methyldopa	1	0.3

The rate of treatment for hypertension using a combination of two drug groups accounted for the highest rate at 51.8%, the rate of a combination of three drug groups accounted for 32.1%, and the rate of a combination of more than 3 drug groups accounted for the lowest rate at 7.6%; monotherapy accounted for 8.5%. In the monotherapy group for hypertension, angiotensin II AT1 receptor blockers accounted for the highest rate at 4.2%. In combination therapy, there was a high percentage of angiotensin II AT1 receptor blocker + beta-blocker: 27%; angiotensin II AT1 receptor blocker + calcium channel blocker + beta-blocker: 12.1%; diuretic + beta-blocker + calcium channel blocker + angiotensin II AT1 receptor blocker: 6.4% (Table 3).

Table 3 Medications used to treat high blood pressure

Therapeutic options	Frequency (n=330)	%
Monotherapy	28	8.5
CCBs	5	1.5
ACEI	1	0.3
ARBs	14	4.2
BB	8	2.4
2 drug groups	171	51.8
Diuretics + ACEI	2	0.6
Diuretics + ARBs	10	3.0
CCBs + ACEI	4	1.2
CCBs + BB	12	3.6
ACEI + ARBs	2	0.6
ACEI + BB	20	6,1
ARBs + BB	89	27.0
ARBs + CCBs	31	9.4
Diuretics + BB	1	0.3
3 drug groups	106	32.1
Diuretics + CCBs + ACEI	1	0.3
Diuretics + ACEI + BB	5	1.5
ACEI + CCBs + BB	22	6.7
ACEI + ARBs + BB	3	0.9
ARBs + BB + Diuretics	27	8.2
ARBs + CCBs + Diuretics	8	2.4
ARBs + CCBs + BB	40	12.1
>3 drug groups	25	7.6
Diuretics + CB + CCBs + ARBs	21	6.4
Diuretics + ACEI + CCBs + CB	3	0.9
Diuretics + CCBs + ACEI + centrally acting alpha-2 adrenergic agonist	1	0.3
Total	**330**	**100**

ACEI=angiotensin-converting enzyme inhibitor, ARB=angiotensin-receptor blocker, BB=beta-blocker, CCB=calcium-channel blocker

The majority of patients changed their medication through the three follow-up visits; with the rates of drug change being 53.3%, 61.2%, and 63.0%, respectively (Table 4).

The results after three follow-up visits showed that the patient's drug adherence rate gradually decreased over time; from 91.2% at the first assessment to 70% at the last assessment (Table 5).

Factors related to adherence to antihypertensive drugs included: age, residence, education level, occupation, duration of disease, duration of treatment, family history of hypertension, and change of drug use recorded at follow-up visits; with p-value<0.05. On the other hand, gender, BMI, marital status, and comorbidities were not statistically related to adherence to antihypertensive drug use (Table 6).

Table 4 Change of drug use recorded during follow-up visits

Occasion	No change in antihypertensive drug type or dosage (%)	Changed at least one type of antihypertensive drug (%)	Increased dosage and/or added at least one antihypertensive drug (%)	Decreased dosage and/or discontinued at least one antihypertensive drug (%)
1	34.2	53.3	7.6	4.8
2	24.5	61.2	8.8	5.5
3	13.9	63.0	9.7	13.3

Table 5 Percentage of patients with drug adherence; according to the Morisky-8 scale

	Evaluation at re-examination		
	First n (%)	Second n (%)	Third n (%)
Evaluate standard			
1. Sometimes forget to take medicine	301 (91.2)	282 (85.5)	231 (70.0)
2. In the past 2 weeks, there was a day that medicine was not taken	317 (96.1)	314 (95.2)	287 (87.0)
3. Used to reduce, stop taking medicine when feeling worse	316 (95.8)	313 (94.8)	305 (92.4)
4. When leaving home, traveling forget to bring medicine	323 (97.9)	322 (97.6)	315 (95.5)
5. Took medicine yesterday	328 (99.4)	325 (98.5)	324 (98.2)
6. Sometimes stop taking medicine when feel my blood pressure is under control	322 (97.6)	310 (93.9)	286 (86.7)
7. Having trouble with taking medicine every day	323 (97.9)	309 (93.6)	282 (85.5)
8. Finding it difficult to remember a medication schedule	321 (97.3)	312 (94.5)	290 (87.9)
	Get 6-8 points Morisky-8		
Adherence	301 (91.2)	281 (85.2)	231 (70.0)
	Get <6 points Morisky-8		
Poor adherence	29 (8.8)	49 (14.8)	99 (30.0)

Table 6 Factors related to drug adherence

Related factors	Medication adherence (%)			PR (95% CI)	p-value
	After 1 month	After 3 months	After 6 months		
Age (years)					
≤60	76 (93.8)	74 (91.4)	68 (84.0)	1	
>60	225 (90.4)	207 (83.1)	163 (65.5)	0.88 (0.82–0.96)	0.002
Gender					
Male	133 (93.0)	129 (90.2)	102 (71.3)	1.05 (0.97–1.14)	0.248
Female	168 (89.8)	152 (81.3)	129 (69.0)	1	
Residence					
Rural areas	85 (87.6)	71 (73.2)	58 (59.8)	1	
Urban areas	216 (92.7)	210 (90.1)	173 (74.2)	1.15 (1.04–1.28)	0.009
Academic level					
Under high school	113 (80.7)	93 (66.4)	73 (52.1)	1	
Over high school	188 (98.9)	188 (98.9)	158 (83.2)	1.39 (1.26–1.54)	<0.001
Career					
Retired, housewife	222 (89.9)	205 (83.0)	161 (65.2)	1	
Workers, sales, service	44 (95.7)	42 (91.3)	38 (82.6)	1.14 (1.04–1.25)	0.007
Public servants	35 (94.6)	34 (91.9)	32 (86.5)	1.16 (1.04–1.28)	0.006
BMI (kg/m^2)					
<18.5	5 (83.3)	5 (83.3)	2 (33.3)	0.77 (0.5–1.18)	0.226
18.5–22.9	165 (92.7)	152 (85.4)	124 (69.7)	1	
23–24.9	83 (88.3)	81 (86.2)	68 (72.3)	0.99 (0.90–1.09)	0.887
≥25	48 (92.3)	43 (82.7)	37 (71.2)	1.00 (0.89–1.12)	0.995
Duration of hypertension (years)					
<5	47 (94.0)	46 (92.0)	42 (84.0)	1	
5–9	94 (94.9)	91 (91.9)	80 (80.8)	0.99 (0.90–1.09)	0.990
≥10	160 (88.4)	144 (79.6)	109 (60.2)	0.84 (0.76–0.93)	0.001
Duration of treatment (years)					
<5	104 (94.5)	102 (91.9)	90 (81.8)	1	
≥5	197 (89.5)	179 (81.7)	141 (64.1)	0.89 (0.83–0.96)	0.002
Marital status					
Single	8 (88.9)	8 (88.9)	8 (88.9)	1	
Married	293 (91.3)	273 (85.0)	223 (69.5)	0.91 (0.72–1.16)	0.450
Family history (with hypertension)					
No	172 (89.6)	157 (81.8)	126 (65.6)	1	
Yes	129 (93.5)	124 (89.9)	105 (76.1)	1.09 (1.01–1.18)	0.027
Comorbidities					
No	7 (87.5)	7 (87.5)	5 (62.5)	1	
Yes	294 (91.3)	274 (85.1)	226 (70.2)	1.06 (0.78–1.44)	0.730
Change of drug use recorded at follow-up visits					
No change in antihypertensive drug type or dosage	103 (91.2)	70 (86.4)	34 (73.9)	1	
Changed at least one type of antihypertensive drug	159 (90.3)	168 (83.2)	143 (68.8)	0.92 (0.87–0.97)	0.001
Increased dosage and/or added at least one antihypertensive drug	25 (100)	26 (89.7)	24 (75.0)	0.94 (0.88–1.00)	0.060
Decreased dosage and/or discontinued at least one antihypertensive drug	14 (87.5)	17 (94.4)	30 (68.2)	0.91 (0.81–1.01)	0.077

PR=prevalence ratio, CI=confidence interval, BMI=body mass index

Discussion

In our study, the majority of patients being treated for hypertension were aged 60 or older (75.5%), were female (56.7%), lived in urban areas (70.6%), had a high school education or higher (57.6%), were retires or housewives (74.8%), were married (97.3%), and had a sustained treatment period of over five years (66.4%). This result is similar to that of author Nguyen Thu Hang and colleagues (2018), in terms of mean age: 67.1±8.9, females 58.9%, high school education or higher 69.8%, retired or housewives 62.5%, and married people accounting for 100%[16]. However, this study recorded the proportion of patients who were overweight, had the disease for more than ten years, and had a relatively high rate of comorbidities compared with the results of the above authors (corresponding rates were 44.3% vs. 20.6%, 54.8 vs. 31.9%, and 97.6 vs. 73.7%)[16].

These results might be related to social health insurance, which was established in 1992. Social health insurance in Vietnam subsidizes vulnerable populations; such as the underprivileged, the ethnic minority, children under 6, and the elderly above 80. Due to the high expense of treatment, patients with chronic diseases; such as high blood pressure, are covered by social health insurance and are more likely to return for follow-up appointments than those without insurance.

Beta-blockers were the most used group of drugs, accounting for 76.1%; whereas, centrally-acting sympathomimetic drugs accounted for the lowest rate at 0.3%. This is suitable because, while the drug acts on the central sympathetic system lowering blood pressure it also causes dry mouth, drowsiness, and depression, so the rate of use usage is the lowest. Additionally, centrally-acting sympathomimetic drugs are outside the five main groups of antihypertensive drugs according to recommendations on diagnosing and treating hypertension in 2018, by the Vietnam National Heart Association[2]. In another study, by the author Nguyen Ngoc Nha Phuong (2020), the AT1 receptor blockers of the angiotensin II group accounted for the highest rate at 76.1%[17]. Authors Nguyen Thi Ngoc Van and Tran Thi Tuyet Phung (2014), noted that AT1 receptor blockers of the angiotensin II group accounted for the highest rate at 80.6%[18].

Diuretics accounted for 23.3%, of which hydrochlorothiazide accounted for the highest proportion: 15.2%, lower than the authors Bui Tung Hiep and Tran Thi Ngoc Muoi (2018)[19]. Spironolactone accounted for 10%. The combination of two diuretics accounted for 2.4%. In the study sample, there were 88.5% cardiovascular comorbidities. Thiazide and thiazide-like drugs are recommended to be used to treat hypertension, due to their proven effectiveness in preventing cardiovascular complications and mortality in randomized controlled trials (RCTs); particularly in the prevention of heart failure[20].

Amlodipine was used with the highest rate at 34.9%. This is higher than the author Bui Tung Hiep (2019), wherein amlodipine accounted for 28.7%[21]. This is a group of drugs having a lot of evidence in the effectiveness of treating hypertension and reducing cardiovascular complications; especially stroke[20].

ACE inhibitors were used by 18.2%, with the only ingredient being used was enalapril. ACE inhibitors are one of the most commonly used classes of drugs. ACE inhibitors and angiotensin II receptor blockers' effectiveness in reducing blood pressure and cardiovascular morbidity and mortality is similar[20].

The group of AT1 receptor blockers accounted for 74.8%, of which losartan was used with the highest rate at 51.5%, telmisartan accounted for 15.7%, and irbesartan accounted for the lowest rate of 7.6%. Angiotensin II AT1 blockers are among the most commonly used drugs, as they are effective in reducing blood pressure and cardiovascular mortality in addition to being comparable to other major antihypertensive agents in clinical trials.

Bisoprolol was used the highest in the group of beta-blockers; accounting for 74%. This study is quite similar to that of author Pham Thai Tran (2019); wherein, the most

used bisoprolol drug had a rate of 62.4%[22]. Bisoprolol and nebivolol has also improved outcomes in patients with heart failure. This result makes these new beta-blockers to be even more widely used[20].

Centrally-acting sympathomimetic drugs using methyldopa accounted for 0.3%. The results were consistent, because the group used it only in some special situations to treat hypertension; methyldopa is also safe to use in pregnant women[20].

Monotherapy accounted for 8.5%, and the combination of two drug groups accounted for the highest rate at 51.8%. The combination of three drug groups accounted for 32.1%, and the combination of more than three drug groups accounted for the lowest rate: 7.6%. Because the study sample contained 75.5% of patients over 60 years of age, 66.4% had a treatment duration of more than five years, 97.6% had comorbidities, and the ratio of two and three drug groups accounted for a high proportion, which was suitable.

The majority of patients changed their drugs through the three follow-up visits. The rate of drug change was 53.3%, 61.2%, and 63.0%, respectively. However, the rate of drug change is lower than that in the study of Nguyen Thi Phuong Lan and Dam Thi Tuyet, in which the rate of change in the number of drugs was 74.6%[23]. This change may come from objective and subjective reasons for the physician and the patient's condition. The main drug change was the change in the ingredient within the same group, and the most change was in the angiotensin II receptor blocker group (losartan, irbesartan, telmisartan).

Sometimes forgetting to take medication was the most common answer in the interview process at follow-up visits. The question of whether: 'the patient had ever decreased or stopped taking the drug when he felt his condition,' was worse was also chosen more often during the interviews.

Our results show that outpatient adherence to antihypertensive drugs ranges from 70.0 to 91.2%, which is similar to previous studies of 77%[12] and 87.5%[16]. The highlight of our study shows an inverse relationship between the adherence rate and the number of follow-up visits: the higher the number of visits, the lower the adherence rate. This occurred across the entire standard (Table 5), and in individual patient groups, with distinct characteristics (Table 6). This is a matter of greater concern and poses an important challenge for ensuring treatment effectiveness in maintaining and/or enhancing patient adherence. Our results are higher than Tran Quoc Cuong et al. (2018), who reported a medication adherence rate before the intervention of 53.8%.[24]. The cause of this disparity is due to differences in demographics and questionnaires, sample selection criteria, sample size, and samplers.

When surveying the factors related to medication adherence in hypertensive patients, this study found that: the rate of medication adherence is significantly high in patients with an education level of 3 or higher, for those who live in urban areas, those that have jobs related to social interaction (traders and civil servants), and for those that have a family history of relatives with hypertension. To explain this result, it is believed that (1) knowledge, (2) ability/level of social communication, (3) early awareness of the dangers of hypertension, and the importance of treatment are the key factors driving patients' adherence
In contrast, factors; such as advanced age (>60 years old), prolonged disease duration (≥10 years), and prolonged treatment duration, significantly reduced adherence to therapy. Our results are similar to that of author Dang Bao Toan (2017), who reported that with increasing age the ability to adhere to treatment decreases (p-value=0.003)[25]. In addition, author Nguyen Tran Phuong Thao (2018) also reported that patients with a treatment duration of more than three years had a non-adherence rate of 3.98 times higher[12]. This study found that factors; such as age, disease duration, and treatment duration, are interrelated. For example, elderly patients have a memory that gradually declines over time, have comorbidities, undergo long-term

treatment and take many drugs, and have a fear of side effects, leading to a reduced adherence rate[26,27].

In particular, based on Table 6, it was found that changing at least one type of antihypertensive drug significantly reduced the patient's adherence to therapy. This is a factor related to treatment. To overcome this factor suggestions may be to consider a gradual change in treatment, consulting carefully, and checking the ability to recognize medication when the patient receives a new prescription. To accomplish this, pharmaceutical care and patient counseling must be prioritized.

This study has several limitations. Firstly, the study was only conducted in one area, so the overall adherence to generic drug use has not been assessed. Secondly, the patient's blood pressure index was not included at each follow-up visit in the study sample: providing a blood pressure index helps to assess drug adherence more objectively. Finally, the study did not include interviews to monitor the patient's diet and activities. It is necessary 1) to conduct more adherence surveys on diet and living, assessing more comprehensively the adherence to antihypertensive treatment of each patient, carried out on a larger study sample and in different regions; 2) to enhance the pharmacist's role in medication adherence; including prescription management (simplifying therapy, managing adverse drug reactions, and control or modify medication use), providing patient education (about hypertension, lifestyle and diet modifications, and blood pressure self-monitoring), and giving timely reminders to take medication (via phone, text message, email, adherence support device); and 3) to increase appointment scheduling and maintain contact with patients to reduce: "forgot to take medication" as a reason for poor adherence.

The outbreak of the SARS-CoV-2 at the end of 2019 made drug adherence difficult, as most patients were unable or afraid to go to the hospital. Patients may then unintentionally or knowingly fail to adhere to treatment. There are many reasons for the patient not taking the medication as directed; then, the importance of pharmaceutical care comes first. Therefore, it is proposed that the following research direction would be to study the effectiveness of pharmaceutical care and patient counseling on adherence to antihypertensive drug use, in the era of adaptation to SARS-CoV-2. Unlike clinical pharmacy practice, pharmaceutical care focuses only on specific patients; in other words, it focuses on clinical pharmacy practice for each patient. Researching pharmaceutical care in hospitals opens a new path and contributes to helping patients and medical staff improve their collaboration in drug use, medication adherence, and hypertensive prevention.

Conclusion

The percentage of patients who adhered to antihypertensive drugs ranged from 70.0% to 91.2%. Important factors affecting adherence to medication use in hypertensive patients include: (1) a group of factors that increase adherence (high levels of education, high levels of social interaction, and family history), (2) a group of factors that reduce adherence (advanced age, prolonged duration of hypertension and treatment, change of at least one type of antihypertensive drug). Beta-blockers were used the most among the antihypertensive drug classes (76.1%). The rate of drug change through the first, second, and third follow-ups, respectively, accounted for 53.3%, 61.2%, and 63.0%. From a medical perspective, the factors that we can change to improve adherence to medication use are: increasing the patient's awareness of the importance of therapy and limiting changes in drug use. If the physician/pharmacist has to change antihypertensive drugs suddenly, they must advise the patients not only to use, but also to properly use the new drugs in their prescription. It is therefore, recommended that a clinical study be conducted to evaluate the effect of pharmaceutical care and patient counseling on adherence to antihypertensive medication.

Conflict of interest

The authors declare no conflict of interest.

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