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Drug-Related Problems and Pharmacists' Interventions in Hypertensive Outpatients: A Multicenter Prospective Study in 3 Vietnamese Hospitals

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Abstract

Background: Clinical pharmacists' interventions (PIs) on drug-related problems (DRPs) in Vietnamese hypertensive outpatients are limited. **Objectives:** The objective was to investigate the prevalence and nature of DRPs, and factors which are likely to have DRPs, types of PIs, and their acceptance rate in 3 Vietnamese hospitals. **Method:** A prospective interventional study was conducted over a period of 3 months in 3 hospitals (from October 2021 to March 2022). Clinical pharmacists conducted medication reviews after collecting patient information from prescriptions and patient interviewing, and then identified the DRPs and suggested PIs according to the Vi-Med tool. These DRPs and PIs were reviewed by other superior clinical pharmacists and a consensus meeting with 3 cardiologists. **Results:** Of 381 patients included, 344 (90.23%) experienced 1 or more DRPs. A total of 820 DRPs were identified with an average of 2.15 DRPs per patient and 415 (50.61%) were hypertension-related issues. The most common DRPs identified were "administration mode" (46.34%), "missing indication" (18.05%), "non-conformity indication" (17.80%), and "dosage" (11.95%). Comorbidity (adjusted odds ratio [AOR] = 3.985, 95% CI: 1.597-9.942, $P = 0.003$) was the predictor of DRPs. Clinical pharmacists provided 739 PIs and 94.45% were accepted by physicians. **Conclusion:** The results of this study showed that DRPs were very common in hypertensive outpatients and highlighted the role of clinical pharmacists to identify and resolve DRPs through prompt interventions.

Keywords

clinical pharmacist, drug-related problems, pharmacist's intervention, hypertension, Vietnam

Impacts on Practice

- Drug-related problems (DRPs) are very common in hypertensive outpatients and frequently include inappropriate administration drugs, missing indication, nonconformity indication, the use of an inappropriate dose, major drug-drug interactions, unnecessary indication, and drug side effects.
- Clinical pharmacists should focus especially on performing medication reviews for detecting DRPs that could have a negative impact on the patient's health and providing recommendations to solve the DRPs in hypertensive outpatients.

Introduction

Hypertension (HTN) is 1 of the biggest global public health concerns. Hypertension is a major cause of heart complications,

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stroke, kidney failure, and even death and disabilities. According to the estimation of the World Health Organization, worldwide prevalence of high blood pressure (BP) was 22% and BP could be monitored in less than 20% of hypertensive patients in 2015.[1] In Vietnam, the overall prevalence of HTN was rapidly increasing, from 25.1% in 2008 to 47.3% in 2015.[2,3] In particular, only 31.0% of hypertensive patients controlled their BP.[3]

A drug-related problem (DRP) is an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.[4] Hypertensive patients are at high risk of having DRPs. The majority of patients will require combination therapy to achieve a BP. Furthermore, hypertensive patients with advanced age, high prevalence of comorbidities, and severity of the disease often received multiple medications.[5] Polypharmacy has been strongly associated with DRPs.[6] Globally, DRPs among hypertensive patients were reported in studies as an average of 1.26-6.3 DRPs per hypertensive patient.[7-12] Several studies in some Southeast Asian countries such as Malaysia and Indonesia about DRPs in hypertensive patients reported more than 56% of the patients had at least 1 DRP.[11,13,14]

DRPs may lead to elevating morbidity, mortality, treatment costs, poor adherence, and longer hospitalization.[11,15] To prevent or minimize the DRP, an effective intervention strategy is required. Clinical pharmacists are well situated in the health care system to identify and resolve DRPs, and develop the therapeutic plans.[15,16]

The role of clinical pharmacists in Vietnam is spreading. Clinical pharmacy was first developed in Vietnam in the 1990s.[17] The most recent development in this area was Vietnam's Ministry of Health's release of a *Guideline on clinical pharmacy practice for pharmacists in the number of noncommunicable diseases* in 2019.[18] This is considered a national and professional guide with scientific and practical value that will help implement and evaluate clinical pharmacy activities at hospitals. Of those, there is a detailed guideline of clinical pharmacy practice for the management of HTN. However, there have been no studies that evaluate clinical pharmacists' interventions (PIs) on DRPs in Vietnamese hypertensive outpatients.

Aim of the Study

The aim of this study was to investigate the prevalence and nature of DRPs, and factors which are likely to have DRPs, types of PIs, and their acceptance rate in 3 Vietnamese hospitals.

Methods

Study Design and Clinical Setting

A prospective multicenter interventional study was conducted over a period of 3 months in 3 hospitals, namely Nguyen Tri Phuong Hospital (from October to December 2022) and Gia Dinh People's Hospital (from December 2022 to February 2023) located in the south, and Hoa Vang District Medical Center (from January to March 2023) located in the middle of the country. The average number of outpatients per day for 3 hospitals is about 2000, 3000, and 250 patients, respectively.

The pharmacy departments of the 3 hospitals have started staffing clinical pharmacists in "the pharmacist-led clinic" as a pilot practice model of the multidisciplinary team since 2021. These pharmacists performed clinical functions including (1) medication review for identifying, preventing, and addressing DRPs and making PIs to physicians to improve patient outcomes and (2) patient education about HTN, goals of treatment, lifestyle changes, the importance of medication adherence, and home BP measurement. These activities were comprehensively documented. The results of patient education are presented in another article. This article only reported the results of medication review activities.

Study Participants

Eligibility criteria were as follows: adult patients older than 18 years diagnosed with primary HTN, taking antihypertensive drugs for at least the past 1 month, came to the outpatient department for a refill, and voluntarily participated in this study. Patients who were pregnant, could not respond to or receive counseling by clinical pharmacists (Alzheimer's disease, depression, bipolar disorder, etc), and were not accompanied by a family member were excluded.

Sample Size

Single proportion formula was used to calculate the minimum sample size needed.[19] We set α at 0.05 ($Z_{\alpha/2} = 1.96$). A previous study showed that the prevalence of DRPs in hypertensive outpatients was 0.81,[20] 95% confidence interval, 5% margin of error, the minimum sample size was calculated to be 236 participants.

Identification of DRPs, Suggestion of PIs, and Their Acceptance

Medication orders are generated by physicians, either electronically or manually, and then forwarded to the pharmacy for dispensing. Hypertensive outpatients were invited into a pharmacist-led clinic for a history medication review, and collecting information including patient general information, diagnosis, medical history, allergy status, adverse drug reactions (ADRs), lifestyle, drugs, laboratory data, and BP monitoring. Patients' clinical

characteristics and medication data were obtained from the prescriptions and direct interviews using a data collection form (see the Online Appendix A).

The 3 hospitals employed 2, 2, and 1 clinical pharmacist, respectively, to conduct medication reviews for detecting DRPs. These clinical pharmacists were trained for 8 hours 3 days, including (1) the purpose and process of the study; (2) skills to perform medication review; (3) knowledge of HTN and treatment; and (4) knowledge of antihypertensive drugs (indication, contraindication, dose, drug interaction, ADRs, principles of antihypertensive drug treatment, selection of antihypertensive drug in specific clinical condition). If any DRP was found, the pharmacist wrote a complete report that included all relevant patient information, the type and details of the DRP, and PIs for its management.

Identification of DRPs was based on guidelines of Vietnam's Ministry of Health,[18,21-23] the European Society of Cardiology/European Society of Hypertension (ESC/ESH) Guidelines for the management of arterial HTN,[24] and medication information leaflets. Vi-Med was used to categorize DRPs and PIs.[25] Vi-Med was validated as a tool to support the analysis of DRPs and PIs in Vietnamese hospitals. This form contains essential information on PIs that needs to be recorded, such as patient information, short descriptions and classifications of DRPs and PIs, methods by which a pharmacist and a physician communicate with respect to PI-related recommendations, and a physician's acceptance of PIs. Vi-Med classified DRPs into 8 categories, including (1) unnecessary indication, (2) nonconformity indication, (3) missing indication, (4) dosage, (5) administration mode, (6) adverse drug effect, (7) drug interaction, and (8) drug monitoring. Vi-Med form and criteria for DRP identification are presented in Online Appendix B and Appendix C, respectively.

For content validation of DRPs and PIs, 3 superior clinical pharmacists reviewed them and followed by a consensus meeting with 3 cardiologists (1 from each hospital) 1 month later. If all cardiologists agree with the PI, this intervention is defined as "acceptance." If 1 or more experts do not agree with the PI, this intervention is defined as "non-acceptance."

Data Analysis

SPSS software version 20.0 was used to analyze the gathered data. Univariate binary logistic regression analysis was used to find association between patient's characteristics and the presence of DRPs. To obtain the final variables associated with the presence of DRPs, all variables with a value of $P < 0.2$ in univariate analysis were entered in the multivariate logistic regression. A value of $P < 0.05$ was considered statistically significant.

An overview of the study procedure and main results are shown in Figure 1.

Ethics Approval

This study protocol was approved by ethics committees at 3 hospitals in Vietnam (institutional review board [IRB] number: 01/TTYTHHV-HDK HKT; 1049/ NTP-CDT; 1050/ NTP-CDT; 24/NDGD-HDDD) and by the IRB, Thailand (IRB number: 78.0319/EC.583). All patients provided written informed consent to participate in the study.

Results

Demographic Details of Patients With HTN

Of 381 patients, the mean age was 62.6 ± 8.6 years and 52.0% were female. About two-fifths of patients were retired and only 9.4% had a bachelor's degree or more. The most common comorbidities were dyslipidemia (66.1%), diabetes (34.9%), and ischemic heart disease (18.9%). Regarding their lifestyle, current drinkers, current smokers, and individuals who exercise were 26.8%, 18.1%, and 58.8%, respectively. Duration of HTN and treatment was 8.2 ± 6.1 and 8.1 ± 6.1 years, respectively. The mean systolic and diastolic BP values were 139.4 ± 16.7 and 81.8 ± 10.5, respectively. About two-thirds of patients monitored their BP at home. Details of the patient's baseline characteristics are summarized in Table 1.

Drug-Related Problems

Prescribing pattern in antihypertensive medications. The mean number of drugs prescribed per patient was 5.0 ± 2.5, while the average of antihypertensive drugs per patient was 2.3 ± 0.8. About 40% of antihypertensive drugs were in the fixed-dose combination form. Regarding antihypertensive drug regimens, 2 combined drugs were most common, accounting for 53.6%, out of which angiotensin-converting enzyme inhibitors (ACEis) + thiazide diuretic (TD) (21.3%) were the most common pattern, followed by angiotensin II receptor blocker (ARB) + calcium channel blocker (CCB) (13.6%) and ARB + beta-blocker (BB) (12.9%). The fixed-dose combination of antihypertensive drugs was quite common, as 39.1% of patients had dual fixed-dose combination and only 1.0% of patients had the triple fixed-dose combination. The prescribing patterns in hypertensive patients are listed in Online Appendix D.

Types of DRPs. Among 381 patients, 344 (90.3%) experienced 1 or more DRPs. A total of 820 DRPs were identified with a mean (±SD) number of DRPs per patient of 2.2 ± 1.4. Overall, 50.6% of DRPs were due to HTN medications with a mean number of 1.1 ± 1.0 DRPs per patient. The most common DRPs were administration mode (46.3%). The reasons for these DRPs were inappropriate timing of administration, incomplete information on the drug regimen, inappropriate frequency of administration, and inappropriate

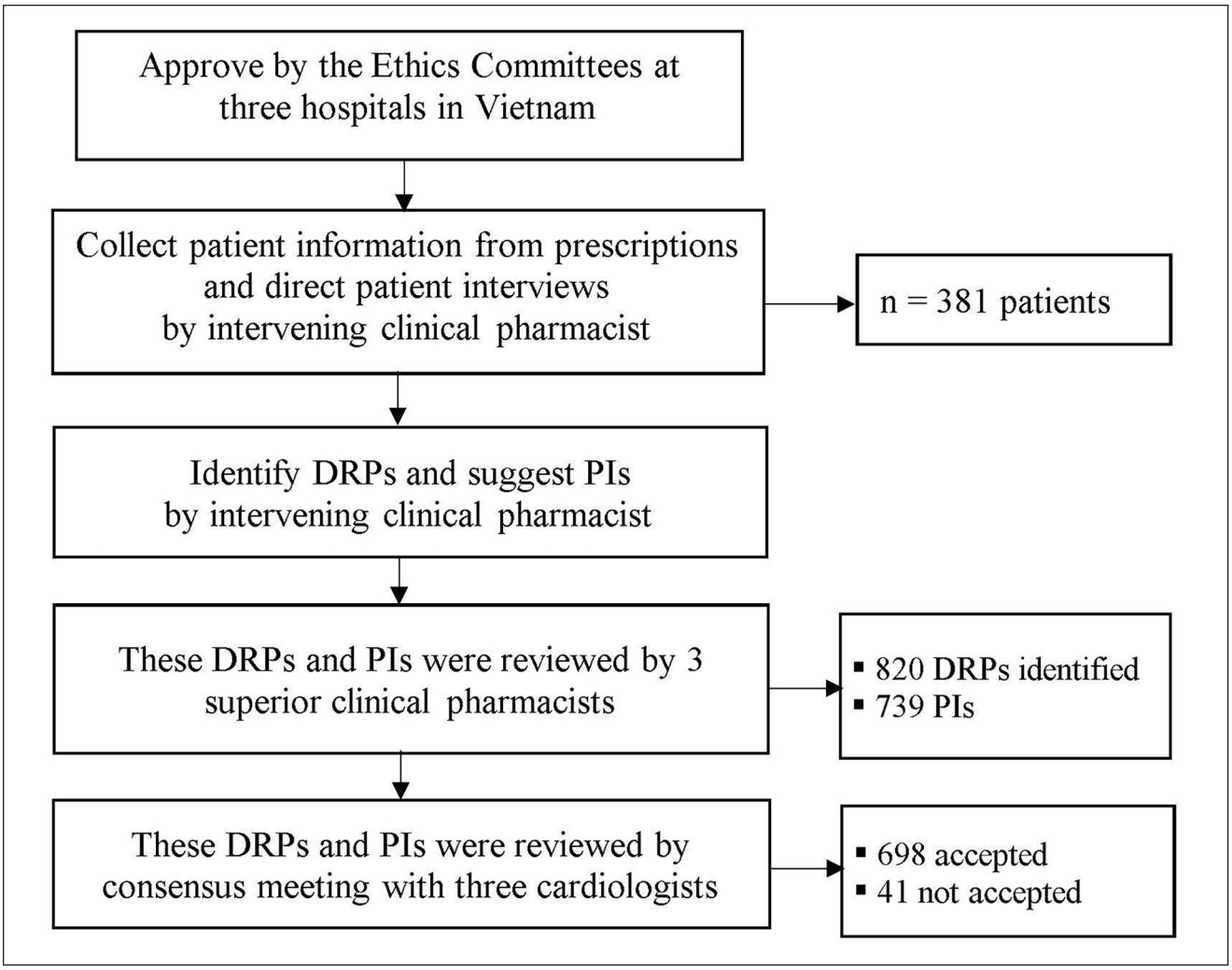

Figure 1. Overview of the study procedure and main results.
Abbreviations: DRPs, drug-related problems; PIs, pharmacists' interventions.

selection of drug form. The other frequently identified DRPs were missing indication (18.0%), nonconformity indication (17.8), dosage (12.0%), major drug-drug interactions (2.6%), and ADRs (1.1%) of the total DRPs. Details of types of DRPs are shown in Table 2.

Common drugs involved in DRPs. Regarding drugs commonly implicated in DRPs, BBs were the most frequently involved inappropriate drug choice and subtherapeutic dosage. There were 29 (7.6%) of the patients having HTN with specific conditions, for example, heart failure, angina, post-myocardial infarction, and atrial fibrillation which were in need of additional BBs. Meanwhile, 86 (22.6%) patients were prescribed BBs without having any specific conditions, and 53 (13.9%) of the patients were in need of increasing BB dose. Hypoglycemic medications were most commonly associated with inappropriate timing of administration (129 patients with 33.9%). Sodium-glucose transporter 2 (SGLT2) inhibitors were commonly not prescribed while patients had a valid indication. Common drugs involved in DRPs are presented in Table 3, while details of drugs implicated in DRPs are listed in Online Appendices E-K.

Factors associated with DRPs. The multivariate logistic regression results revealed that comorbidity was the final factor having a statistically significant correlation with the presence of DRPs. This implies that the hypertensive patients with comorbidity were about 4 times more likely to have DRPs than hypertensive patients without comorbidity (adjusted odds ratio [AOR] = 3.985, 95% CI:1.597-9.942, $P = 0.003$). DRP determinants in prescribing are presented in Table 4.

Pharmacists' Interventions to Solve the DRPs

A total of 739 PIs were suggested, an average of 1.9 PIs per patient. The most common PIs were administration mode

Table 1. Demographic Details of Patients With Hypertension.

Characteristics	Number (%)
Age (mean ± SD, year)	62.6 ± 8.6
<65 years	217 (57.0)
≥65 years	164 (43.0)
Gender, female	198 (52.0)
Occupation	
Retirement	152 (39.9)
Housewife	94 (24.7)
Private servant	47 (12.3)
Farmer	44 (11.5)
Other (teacher, worker, businessman, security guard, jobless, trader, civil servant)	44 (11.5)
Educational level	
Primary school or not graduated from primary school	61 (16.0)
Junior high school	132 (34.6)
Senior high school	152 (39.9)
Bachelor's degree or more	36 (9.4)
Comorbidities (mean ± SD)	2.1 ± 1.5
Yes	338 (88.7)
No	43 (11.3)
Dyslipidemia	252 (66.1)
Diabetes	133 (34.9)
Ischemic heart disease	74 (19.4)
Stomach disorder (GERD, stomach ulcer, gastritis)	54 (14.2)
Angina	33 (8.7)
Varicose vein	24 (6.3)
Gout	16 (4.2)
Heart failure	8 (2.1)
Lifestyle	
Alcohol status, currently	102 (26.8)
Smoking status, currently	69 (18.1)
Doing exercise	224 (58.8)
BMI (mean ± SD)	24.5 ± 3.2
Blood pressure	
Duration of HTN (mean ± SD, year)	8.2 ± 6.1
Duration of treatment for HTN (mean ± SD, year)	8.1 ± 6.1
Systolic BP (mean ± SD, mm Hg)	139.4 ± 16.7
Diastolic BP (mean ± SD, mm Hg)	81.8 ± 10.5
Monitoring BP at home	265 (69.6)

Abbreviations: BMI, body mass index; BP, blood pressure; GERD, gastroesophageal reflux disease; HTN, hypertension.

optimization (50.7%), out of which change in timing of administration (29.8%) for the drugs recommended to be used before meals, during meals, or after meals was the most common. The second common intervention was the addition of drugs (20.4%) which were most commonly associated with the addition of antihypertensive drugs for better control of BP and the addition of SGLT2 inhibitors for preventing cardiovascular events in patients with type 2 diabetes mellitus and high cardiovascular disease. The third common intervention was drug switch (17.1%), followed by dose increasing (5.8%). Detailed information on PIs is indicated in Table 5. A total of 698 (94.5%) interventions were accepted.

Discussion

This is the first prospective study conducted in Vietnam to implement medication reviews by clinical pharmacists to detect DRPs and to identify factors associated with the occurrence of DRPs in 3 tertiary care hospitals in Vietnam.

Prescribing Pattern in Antihypertensive Medications

In our study, the number of antihypertensive drugs per patient was 2.3 ± 0.8. This finding was higher than the outcome of a study done in Northern Ethiopia which was 1.41 ± 0.53 antihypertensive drugs per patient.[26] Previous studies showed that fixed-dose combination provided better BP control than either free combination or monotherapy.[24,27] In this study, 39.1% of patients had the dual fixed-dose combination and 1.0% of patients had the triple fixed-dose combination. The use of 2-drug combinations was the most common pattern of pharmacotherapy (53.6%) which was consistent with current guidelines; preferred 2-drug combinations are an RAS blocker with a CCB or a diuretic.[21,24]

Identified DRPs

The study found that DRPs were extremely common among hypertensive patients, as 90.23% of hypertensive patients experienced 1 or more DRPs. The average number of DRPs per patient was 2.2 ± 1.4. This result is slightly higher than the finding done in Malaysia[6] and in Ethiopia[10] which were 1.9 ± 1.5 and 1.86 ± 0.53, respectively. On the contrary, it is lower than the finding done in Jordan (6.3 ± 2.6).[7] There are several explanations for these differences: variability in DRP classification, study participants, prescriber's qualifications, how and when DRPs were identified, and references to identify DRPs.

In this study, inappropriate administration was the most common DRP, accounted for 46.3% of total DRPs. The primary reason for this DRP was the inappropriate timing of administration (27.1%), which was mostly related to hypoglycemic agents and proton pump inhibitor drugs. The second reason was incomplete information on the drug regimen (9.0%), which was common with nifedipine retard, felodipine modified release, and trimetazidine modified release. These special dosage forms should be swallowed whole, not chewed or crushed, but there were no instructions provided. The third reason was the inappropriate frequency of

Table 2. Type of DRPs.

DRPs	Number (%), n = 820	Example
Unnecessary indication	18 (2.2)	
Drug use without indications	15 (1.8)	Patient was not diagnosed with dyslipidemia, risk of MI, risk of angina, or risk of stroke and was prescribed atorvastatin
Duplicate prescription	3 (0.4)	Patient taking 2 medications from the telmisartan in different medication brands
Nonconformity indication	146 (17.8)	
Inappropriate drug choice compared with guidelines	120 (14.6)	There is no specific indication for using bisoprolol, eg, HF, angina, post-MI, AF, or younger women with or planning pregnancy
Inappropriate drug combination	11 (1.4)	Combination of an ACEi and ARB to treat hypertension
Contraindication	15 (1.8)	Hydrochlorothiazide is contraindicated in hypertensive patient with gout
Missing indication	148 (18.0)	
Valid indication without drug prescribed	96 (11.7)	Hypertensive patient with heart failure without SGLT2 inhibitor prescribed
Missing drug combination	52 (6.3)	Mono-antihypertensive drug therapy could not control BP
Dosage	98 (12.0)	
Low dose	97 (11.8)	Bisoprolol 2.5 mg daily to treat hypertension Losartan 25 mg daily to treat hypertension
Missing dose	1 (0.2)	Missing dose of Novomix 30 Flexpen
Administration mode	380 (46.3)	
Inappropriate drug form	18 (2.2)	Amlodipine 5 mg was prescribed, 2 tablets once daily
Inappropriate timing of administration	222 (27.1)	Metformin, ivabradine, etc are recommended to be used with meals, but the prescription is insufficiently instructed
Incomplete information on the drug regimen	74 (9.0)	Nifedipine retard should be taken whole, do not chew or crush it, but the prescription is insufficiently instructed
Inappropriate frequency of administration	66 (8.0)	Lisinopril 10 mg was prescribed twice daily Losartan 50 mg was prescribed twice daily
Drug side effect	9 (1.1)	Dry cough (enalapril) Peripheral edema (amlodipine)
Major drug-drug interactions	21 (2.6)	Spironolactone—lisinopril Enalapril—losartan

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BP, blood pressure; DRPs, drug-related problems; HF, heart failure; MI, myocardial infarction; SGLT2, sodium-glucose transporter 2.

administration (8.0%); it was observed frequently among users of ARBs, BBs, or CCBs. These drugs can be taken once daily but were prescribed 2 times daily.

Missing indication (18.0%) was the second most common DRP in this study. The first reason for this DRP was a valid indication without drug prescribed (11.7%), lower than the finding reported by Kusumawardani et al[13] (25.6%) and by Weldegebreal et al[26] (17.1%). The second reason for this DRP was the missing drug combination (6.3%).

The third most common DRP was nonconformity indication (17.8%). The first explanation for this DRP was inappropriate drug choice compared with guidelines (14.6%) which was lower than the finding reported by Ukoha-Kalu et al[28] (18.9%), but higher than the finding presented by Zaman Huri et al[6] (8.8%). The second explanation was contraindication (1.8%) which was lower than the figure published by Zaman Huri et al[6] (7.5%), but higher than the figure published by Kefale et al[10] (0.8%). The third explanation was inappropriate drug combination (1.4%).

Inappropriate dose selection was quite common in our study (12.0%), including low dose (11.8%) and missing dose (0.2%). This finding was in line with the previous study.[10] Low doses may reduce the effectiveness of treatment, while missing dose might cause problems in taking drugs by patients.

Major drug interactions accounted for 2.6% of the total DRPs identified in our study, which was lower than the finding reported by Zaman Huri et al[6] (16.3%). The difference might be due to our study only using major interactions for DRPs and using different interaction checkers.

Unnecessary indications were found in a small proportion (2.2%). These DRPs occurred when patients were prescribed by medications which were not indicated, such as ivabradine, atorvastatin, or therapeutic duplication. The studies about DRPs done in Malaysia and Indonesia also showed that unnecessary indications accounted for a small proportion of the total DRPs identified, 0.3% and 13.5%, respectively.[6,13]

Table 3. Common Drugs Involved in 820 DRPs.

Drugs/Drug classes	Number
Antihypertensive drugs	
Beta-blockers	
Bisoprolol	139
Carvedilol	12
Metoprolol	6
Nebivolol	4
Angiotensin-converting enzyme inhibitors (ACEis)	
Enalapril	12
Lisinopril	9
Perindopril	4
Angiotensin II receptor blockers (ARBs)	
Losartan	32
Telmisartan	11
Candesartan	8
Valsartan	6
Irbesartan	2
Calcium channel blockers (CCBs)	
Amlodipine	25
Nifedipine	25
Lercanidipine	13
Felodipine	13
Diuretic	
Hydrochlorothiazide	9
Spironolactone	9
Indapamide	3
Other cardiovascular disease drugs	
Trimetazidine	27
Ivabradine	18
Atorvastatin	21
Aspirin	11
Fenofibrate	3
Rosuvastatin	2
Hypoglycemic drugs	
Metformin	95
Gliclazide	45
Insulin	9
Proton pump inhibitors (PPIs)	
Esomeprazole	12
Omeprazole	8
Pantoprazole	7
Others	
Tramadol	17

Abbreviation: DRPs, drug-related problems.

During the conduct of our study, we found that ADRs were uncommon, and represented only 1.1% of the total DRPs identified. When interviewing patients, we recorded 8 patients with dry cough due to enalapril or lisinopril and 1 patient with peripheral edema due to amlodipine. These ADRs were only detected when clinical pharmacists interviewed patients. In previous studies, cough is 1 of the common adverse effects in patients taking ACEis, approximately 1.5%-11% of patients treated with ACEis.[29]

Factors Associated With DRPs

Participants with comorbidity were about 4 times more likely to develop DRPs than participants without comorbidity. Our outcome was consistent with the studies conducted by Kefale et al[10] and Weldegebreal et al.[26] In our study, 88.7% of hypertensive patients had at least 1 comorbidity. Hence, more attention should be paid to current treatment guidelines to limit unnecessary prescribing.

Pharmacists' Interventions to Solve the DRPs

The study reported a very high rate of physician's acceptance (94.5%) which is higher than 52.4% in India as well as 71.6% in Ghana.[15,30] The main reason is the research team has developed a comprehensive clinical pharmacy practice procedure for hypertensive outpatients. All clinical pharmacists who conducted clinical pharmacy activities received a significant amount of training and were supervised by hospital pharmacotherapy specialists, and comprehensive patient information was collected by direct interview.

Strengths and Limitations

The study has several strengths. First, the study was conducted in 3 large hospitals in Vietnam. As a result, the findings were relatively robust and other hospitals can use our study as a reference to replicate pharmacy services in the care of hypertensive patients. Second, medication review was conducted based on fully completed patient's clinical characteristics, and medication data were obtained from the prescriptions and direct patient interviews. Third, PIs were evaluated by experts including 3 cardiologists with a high acceptance rate which may reflect the high quality of PIs.

However, some limitations include PIs being evaluated retrospectively by a consensus group of 3 cardiologists without transferring to treated physicians for patients and lack of evaluation of PI's impact. Further research work, most preferably, a randomized controlled trial, should be performed to confirm the benefit of the service.

Conclusion

This study showed that the addition of a clinical pharmacist in the pharmacist-led clinic was effective to detect DRPs and suggests PIs to optimize drug use for hypertensive outpatients. It is needed that training and daily teamwork procedures based on these results should be implemented. These activities should be maintained and developed in

Table 4. Univariate and Multivariate Binary Logistic Regression Analysis of Predictors of DRPs.

Variables	Category	DRPs		COR (95% CI)	*P* value	AOR (95% CI)	*P* value
		Yes (n = 344)	No (n = 37)				
Gender	Male	167 (48.5%)	16 (43.2%)	1			
	Female	177 (51.5%)	21 (56.8%)	0.808 (0.408-1.600)	0.540		
Age, years	<65	195 (56.7%)	22 (59.5%)	1			
	≥65	149 (43.3%)	15 (40.5%)	1.121 (0.562-2.234)	0.746		
Occupation	Farmer	37 (10.8%)	7 (18.9%)	1		1	
	Retirement	134 (39.0%)	18 (48.6%)	1.408 (1.408-3.627)	0.478	0.670 (0.232-1.935)	0.459
	Housewife	88 (25.6%)	6 (16.2%)	2.775 (0.873-8.817)	**0.084**	1.305 (0.377-4.514)	0.674
	Private servant	45 (13.1%)	2 (5.4%)	4.257 (0.834-21.738)	**0.082**	1.581 (0.282-8.880)	0.603
	Other	40 (11.6%)	4 (10.8%)	1.892 (0.512-6.993)	0.339	0.992 (0.246-4.000)	0.991
Education	Primary school or not graduated	53 (15.4%)	8 (21.6%)	1			
	Junior high school	119 (34.6%)	13 (35.1%)	1.382 (0.541-3.531)	0.499		
	Senior high school	140 (40.7%)	12 (32.4%)	1.761 (0.682-4.548)	0.242		
	Bachelor degree or more	32 (9.3%)	4 (10.8%)	1.208 (0.336-4.334)	0.772		
Comorbidities	Yes	314 (91.3%)	24 (64.9%)	5.669 (2.620-12.268)	**<0.001**	3.985 (1.597-9.942)	**0.003**
	No	30 (8.7%)	13 (35.1%)	1		1	
Smoking	Yes	65 (18.9%)	4 (10.8%)	1			
	No	279 (81.1%)	33 (89.2%)	0.520 (0.178-1.520)	0.232		
Drink	Yes	93 (27.0%)	9 (24.3%)	1			
	No	251 (73.0%)	28 (75.7%)	0.868 (0.395-1.907)	0.724		
Exercising	Yes	197 (57.3%)	27 (73.0%)	1		1	
	No	147 (42.7%)	10 (27.0%)	2.015 (0.946-4.292)	**0.069**	2.035 (0.901-4.594)	0.087
HTN duration in years	<5	113 (32.8%)	21 (56.8%)	1		1	
	≥5	231 (67.2%)	16 (43.2%)	2.683 (1.348-5.340)	**0.005**	1.986 (0.904-4.360)	0.087
Polypharmacy	Yes	169 (49.1%)	26 (70.3%)	2.448 (1.172-5.109)	**0.017**	1.367 (0.590-3.166)	0.466
	No	175 (50.9%)	11 (29.7%)	1		1	
Number of antihypertensive medication	1	46 (13.4%)	3 (8.1%)	1	0.369		
	≥2	298 (86.6%)	34 (91.9%)	0.572 (0.169-1.937)			

Abbreviations: AOR, adjusted odds ratio; COR, crude odds ratio; DRPs, drug-related problems; HTN, hypertension. *P*-values set in boldface indicate statistical significance ($p<0.05$).

Table 5. Suggestions Provided by Intervening Pharmacists.

Suggestions provided	Number (%), n = 739	Example
Drug addition	151 (20.4)	Addition of dapagliflozin in hypertensive patients with heart failure
Drug switch	126 (17.1)	Switch from bisoprolol to enalapril in patients with no specific indication for using beta-blocker, eg, heart failure, angina, post-myocardial infarction, atrial fibrillation
Dose increasing	43 (5.8)	Increase of atorvastatin dose from 5 to 10 mg for better reduction of low-density lipoprotein cholesterol
Drug discontinuation	27 (3.7)	Discontinuation of ivabradine where there were unclear indications of ivabradine
Drug monitoring optimization	17 (2.3)	Suggestions to monitor serum potassium in patients receiving spironolactone and lisinopril (major drug-drug interaction)
Administration mode optimization	375 (50.7%)	
Change in timing of administration	220 (29.8%)	Suggestions to take gliclazide 30 minutes before meal time
Add instructions to the prescription for special dosage forms (long-acting, modified release, etc)	74 (10.0%)	Suggestions or instructions to take drugs in patients receiving trimetazidine MR, nifedipine retard, alendronate, etc
Change in frequency of administration	63 (8.5%)	Switch from taking losartan twice daily to taking it once daily
Change in the selection of drug form	18 (2.4%)	Switch from amlodipine 5 mg to amlodipine 10 mg in patients who are taking 2 tablets of amlodipine 5 mg once daily
Total	739 (100)	

these 3 hospitals as well as replicated in other hospitals for hypertensive outpatients.

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Supplemental Material

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