Borneo Journal of Pharmacy
Vol 6 Issue 1 February 2023
Pages 87 – 92

https://journal.umpr.ac.id/index.php/bjop/article/view/3664
DOI: https://doi.org/10.33084/bjop.v6i1.3664
e-ISSN: 2621-4814

Research Article

Association between Drug-Related Problems and Blood Pressure of Hypertensive Patients Admitted to Universitas Sumatera Utara Hospital

Mutiara Siahaan [1]
Azizah Nasution [1*]
Wiryanto [1]
Iksen [2]

[1] Department of Pharmacology, Universitas Sumatera Utara, Medan, North Sumatera, Indonesia

[2] Department of Pharmacy, Sekolah Tinggi Ilmu Kesehatan Senior Medan, Medan, North Sumatera, Indonesia

*email: nasution.azizah4@gmail.com

Keywords:
Blood pressure
DRP
Hypertension

Abstract

Patients with hypertension usually experience chronic comorbidities and complications that require complex treatment (polypharmacy), which can further cause drug-related problems (DRPs) and interfere with the required clinical outcomes. This study, by using a case-control prospective cross-sectional, aimed to analyze the association between DRPs and blood pressures (BPs) of hypertensive patients admitted to Universitas Sumatera Utara (USU) hospital from July to September 2021. The incidence of DRPs was analyzed and classified according to the Cipolle classification system and reliable literature. Blood pressures of the patients were classified into controlled and uncontrolled BPs. The association between DRPs and BP was analyzed using the Chi-Square test. Most of the patients (57.5%) were female. Their mean age was 59±9.94 (years). The mean incidence of DRPs experienced by the patients was 1.78±0.79. The most frequently occurred DRPs were drug interactions. There was a significant association between the number of DRPs experienced by the patients and their BPs (p=0.02). DRPs are the contributing factor to the uncontrolled BPs of hypertensive patients.

Received: June 24th, 2022
1st Revised: November 3rd, 2022
Accepted: January 14th, 2023
Published: February 28th, 2023

INTRODUCTION

Hypertension is a chronic disease that affects 600 million people worldwide, with an annual mortality of 12.8%[1]. In 2025, hypertension cases are estimated to increase to around 80%. Increased cases of hypertension also occur in Indonesia. Fact indicated that hypertension cases increased from 25.8% in 2013 to 34.1% in 2018[2].

Hypertension must be controlled to avoid further complications such as heart disease, stroke, kidney failure, eye disorders, and even pose a risk of premature death. Therefore, appropriate pharmacological therapy is crucial to obtain the desired outcomes[3]. Hypertensive patients require complex medical therapy because they generally have chronic comorbidities[4]. This condition can eventually lead to drug-related problems (DRPs)[5]. Drug-related problems in hypertensive patients can result in ineffective treatment, further interfering with the desired clinical outcome[6]. Uncontrolled blood pressure (BP) can increase the risk of complications such as heart failure, kidney failure, and cerebrovascular disease[7].

These DRPs could also decrease the patient's quality of life (QoL). The low QoL of hypertensive patients is influenced by uncontrolled systolic and diastolic BPs, obesity, complications in target organs, the number of antihypertensive drugs used, and side effects[8]. Several studies on the incidence of DRPs in hypertensive patients have been conducted. A study on the incidence of DRPs in managing hypertensive patients (n=107) admitted to four primary health centers in Medan, Indonesia, was conducted. This study identified 66 DRPs experienced by nearly half (45.8%) of the patients[9]. Additionally, a study on DRPs conducted in a tertiary hospital in Malaysia found 387 DRPs in 200 patients with hypertension with type 2 diabetes mellitus[10]. Identification and analysis of DRPs are essential to improve the management and outcomes of hypertensive

How to cite: Siahaan M, Nasution A, Wiryanto, Iksen. Association between Drug-Related Problems and Blood Pressure of Hypertensive Patients Admitted to Universitas Sumatera Utara Hospital. Borneo J Pharm. 2023;6(1):87-92. doi:10.33084/bjop.v6i1.3664

patients[4,6]. Based on those problems, this study was conducted to analyze the incidence of DRPs and their association with BPs of hypertensive patients admitted to Universitas Sumatera Utara hospital.

MATERIALS AND METHODS

Materials

This prospective cross-sectional analytical study was conducted to analyze the association between DRPs and clinical outcomes of hypertensive patients admitted to Universitas Sumatera Utara Hospital, period July to September 2021. This study involved 120 hypertensive patients who met the inclusion criteria: patients diagnosed with hypertension for more than three months; aged 18 years or older with or without comorbidities and complications; and willing to participate in this study with evidence of their willingness to sign an informed consent. Exclusion criteria were pregnant and breastfeeding patients, patients with Human Immunodeficiency Virus/acquired immunodeficiency syndrome (HIV/AIDS), and tuberculosis (TBC). This research was approved by the Health Research Ethics Committee, Faculty of Medicine, Universitas Sumatera Utara, Medan.

Methods

Study design

The identification and classification of DRPs were carried out using the Cipolle DRPs classification system, and reliable[11,12]. Some points need to be mentioned with Cipolle DRPs in specific classifications, such as intervention acceptance and status of DRPs that can't be stated. The patients' BPs were assessed from their medical records and stratified into controlled and uncontrolled groups based on JNC 8 guidelines for hypertension algorithm[13]. The patients were also stratified according to the number of DRPs that they encountered.

Statistical analysis

The association between DRPs and the patients' BPs was statistically analyzed using the Chi-Square test in the SPSS program version 22.0 ($p < 0.05$ was considered significant).

RESULTS AND DISCUSSION

Patient characteristics

Characteristics of the patients with hypertension are listed in **Table I**. Most of the patients (57.5%) were females. The mean age of the patients was 59±9.937 (years). Of the 120 patients, 48 (40%) were 61-70 years old. Nearly half of them (45%) graduated from high school, and as many as 112 patients (93.4%) had comorbidities.

Table I. Characteristics of the patients with hypertension

Characteristics of patient		Number (120)	Percentage (%)
Gender	Male	51	42.5
	Female	69	57.5
Age	<40	4	3.3
	41-50	11	9.2
	51-60	44	36.7
	61-70	48	40
	≥ 71	13	10.9
Education	University	35	29.2
	Senior high school	54	45
	Junior high school	14	11.7
	Primary school	17	14.2
Duration of hypertension (year)	<1	13	10.8
	1-5	78	65
	>5	29	24.2
Patient	With comorbidities	112	93.4
	Without comorbidities	8	6.6

DRPs incident and relationship with clinical outcome

The incidence of DRPs in managing hypertensive patients was classified into controlled and uncontrolled groups, as listed in **Table II**. As much as 58.3% of the hypertensive patients (70 patients) had controlled BP; only 41.7% had uncontrolled BP (50 patients). The four most frequently occurring DRPs were drug interactions, ineffective drugs, unnecessary therapy, and insufficient drug dose. The overall incidence of DRPs experienced by patients with hypertension was 213.

Table II. Number of events of DRPs in management of hypertensive patients (n=120)

Category of DRPs	Number of events		Total events in both groups	%
	Controlled BP (n=70)	Uncontrolled BP (n=50)		
Unnecessary drug therapy	3	2	5	2.3
Needs additional drug therapy	1	0	1	0.5
Ineffective drug therapy	16	1	17	7.9
Dose too low	0	5	5	2.3
Dose too high	2	0	2	0.9
Drug interactions	123	60	183	86.1
Total			**213**	**100**

According to **Table III**, the first identified DRPs in this group of patients were the category of unnecessary therapy. Only 4.3% of the patients experienced unnecessary therapy in the controlled group, and 4% experienced unnecessary drug therapy in the uncontrolled group. These patients were prescribed drugs not indicated, including gabapentin, simvastatin, cetirizine, diclofenac sodium, allopurinol, and omeprazole. The second detected DRP category was an additional drug needed by the patients. In the controlled BP group, only one patient (1.4%) required additional drugs, and the patient experienced vertigo, but no medication was provided to treat the symptoms. The patient experience obtained from previous prescription treatment or medical records is categorized as inpatients; therefore, the status of DRPs can't be described with the use of the Cipolle method. None of the patients in the uncontrolled group experienced this DRPs category.

This study found that 22.8% of the patients experienced ineffective therapy in the controlled group. Only one patient (2%) experienced DRPs in the uncontrolled BP group. Few patients received antihypertensive combinations when their BP reached the therapeutic target (<140/90 mmHg). According to the JNC 8 hypertension guideline algorithm[13], the main goal of hypertension treatment is to achieve and maintain BP targets. If the target BP is not achieved within one month of treatment, the initial dose may be increased, or a second drug from other classes may be added (thiazide diuretic, CCB, ACEI, or ARB)[14]. A similar study[15] conducted on 90 hypertensive patients at the Yogyakarta Health Center found a significant association between DRPs and BP targets for hypertensive patients ($p < 0.05$). In this case, the presence of DRPs failed to achieve the BP target.

With regard to the under-dose problem, none of the patients in the control group experienced this problem. However, five patients (10%) experienced under-dose problems in the uncontrolled group. They were prescribed amlodipine with the lowest dosage strength (5 mg). According to the JNC 8 hypertension guideline algorithm[13], the dose of antihypertensive drugs can be increased if the patient's BP does not show a significant decrease within one month of therapy. Many factors can affect the successfulness in the management of hypertensive patients, such as the accuracy of drug selection based on the patient's condition, the dose of the drug given, psychological factors such as the presence of white coat hypertension characterized by the patient's fear while in the hospital dealing with doctors or nurses causing higher BP compared to those measured in the patient's typical environment[16-18]. In addition to pharmacological therapy, the patients must be educated to practice non-pharmacological approaches[19].

The following identified DRP was a drug overdose. Two patients (2.8%) in the control group experienced drug overdose. These patients were given a combination of amlodipine and telmisartan. During the treatment period, the patients' BPs were below standard. None of the patients experienced drug overdose in the uncontrolled BP group. Even though these combinations are recommended due to their excellent efficacy in reducing BPs, the patients' BPs were below the normal value due to the interaction between these antihypertensive drugs[20]. Thus, close monitoring of these patients is crucial.

The last DRP identified was drug interactions. Drug interactions were the most frequently identified incidence, reaching 183 events (86.1%). In the controlled BP group, 41 patients (58.6%) experienced 123 drug interactions. In the uncontrolled BP group, 36 patients (72%) experienced 60 drug interactions. This finding is in line with a study conducted by Hussein *et al.*[21] at Adama Hospital Medical College, East Ethiopia, in which the most frequently occurring DRPs were drug interaction categories that reached 58.7%.

The results showed that hypertensive patients were susceptible to DRPs due to various factors such as polypharmacy that they received, comorbidities that they experienced, and also their ages. This study found that, on average, each patient was prescribed eight different drugs. The high number of drugs provided to the patients has the possibility for DRPs to occur, which can interfere with the clinical outcomes[22,23].

Table III. Incidence of DRPs in management of hypertensive patients (n=120)

DRPs category	Patient clinical outcome			
	Controlled BP (n=70)	%	Uncontrolled BP (n=50)	%
Unnecessary drug therapy				
+ DRPs	3	4.3	2	4
- DRPs	67	95.7	48	96
Needs additional drug therapy				
+ DRPs	1	1.4	0	0
- DRPs	69	98.6	50	100
Ineffective drug therapy				
+ DRPs	16	22.8	1	2
- DRPs	54	77.2	49	98
Dose too low				
+ DRPs	0	0	5	10
- DRPs	70	100	45	90
Dose too high				
+ DRPs	2	2.8	0	0
- DRPs	68	97.8	50	100
Drug interactions				
+ DRPs	41	58.6	36	72
- DRPs	29	41.4	14	28

Note: + DRPs: Presence of DRPs; - DRPs: Absence of DRP

The grouping of DRPs based on the number of incidences experienced by 92 hypertensive patients is listed in **Table IV**. The number of DRPs experienced by hypertensive patients varies from 1 to 8. The three highest incidences by number were 1, 2, and 3 DRPs experienced by 42, 20, and 12 hypertensive patients, respectively. There was a significant association between the number of DRPs and the mean BP of the hypertensive patients (p=0.02). The higher the number of DRPs experienced by hypertensive patients, the higher the patients' BPs[24]. This study proved a significant association between the number of DRPs and the mean BP of hypertensive patients. Other similar studies have been conducted elsewhere, including a retrospective cross-sectional study at the Gondar University Hospital in Ethiopia. They found that variation in DRPs occurrence was significantly associated with controlled and uncontrolled BPs in hypertensive patients[25]. Drug-related problems are a significant challenge for healthcare providers in managing hypertensive patients. The incidence of DRPs can interfere with the required patients' clinical outcomes, directly affecting the patient's QoL. Thus, rationality in prescribing drugs to patients with hypertension is critical in improving their clinical outcomes and QoL[6,24].

Table IV. Association between total incidence cases in each prescribed treatment DRPs experienced by 92 hypertensive patients and their BPs

Number of prescribed DRPs incidence	Number of patients	Mean of BP (mmHg)	P value
1	42	148±20.90	0.02
2	20	152±21.30	
3	12	157±19.74	
4	5	162±28.58	
5	9	161±13.86	
6	0	-	
7	2	148±1.41	
8	2	155±11.31	

CONCLUSION

The incidence of DRPs in managing hypertensive patients admitted to the Universitas Sumatera Utara Hospital was still high. The highest DRP incidence experienced by hypertensive patients was drug interaction. Drug-related problems contributed significantly to the failure to achieve the BP target. Efforts should always be made to minimize these problems and optimize the patient's clinical outcomes.

ACKNOWLEDGMENT

We thank the Director of Universitas Sumatera Utara Hospital, Medan, Indonesia, for the support and facilities provided to conduct this study. We would also like to thank all the nurses for the assistance provided.

AUTHORS' CONTRIBUTION

All authors have an equal contribution in carrying out this study.

DATA AVAILABILITY

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16(4):223-37. doi:10.1038/s41581-019-0244-2

2. Ridwanah AA, Megatsari H, Laksono AD. Hypertension in Indonesia in 2018: An Ecological Analysis. Indian J Med Forensic Med Toxicol. 2021;15(2):2073-9. doi:10.37506/ijfmt.v15i2.14669

3. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Himmelfarb CD, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Hypertension. 2018;71(6):1269–324. doi:10.1161/hyp.0000000000000066

4. Farha RA, Saleh A, Aburuz S. The impact of drug related problems on health-related quality of life among hypertensive patients in Jordan. Pharm Pract. 2017;15(3):995. doi:10.18549/pharmpract.2017.03.995

5. van Mil JWF, Horvat N, Westerlund T, Zuidlaren IR. Classification for Drug related problems Ann Pharmacother. 2004;38(5):859-67. doi:10.1345/aph.1d182

6. Kusumawardani LA, Andrajati R, Nusaibah A. Drug-related Problems in Hypertensive Patients: A Cross-sectional Study from Indonesia. J Res Pharm Pract. 2020;9(3):140-5. doi:10.4103/jrpp.jrpp_20_16

7. Zhou D, Xi B, Zhao M, Wang L, Veeranki SP. Uncontrolled hypertension increases risk of all-cause and cardiovascular disease mortality in US adults: the NHANES III Linked Mortality Study. Sci Rep. 2018;8(1):9418. doi:10.1038/s41598-018-27377-2

8. Patil M, Hedaoo RP, Shah RP, Tauseef SM, Marzo RR, Ching SM, et al. Assessment of Health-Related Quality of Life Among Male Patients With Controlled and Uncontrolled Hypertension in Semi Urban India. Inquiry. 2023;60:469580231167010. doi:10.1177/00469580231167010

9. Nasution A, Khairunnisa K, Tanjung HR. Drug Therapy Problems in Management of Hypertensive Outpatients Admitted to Four Indonesia Primary Health Centers. Asian J Pharm Clin Res. 2016;9(1):87-90.

10. Huri HZ, Wee HF. Drug related problems in type 2 diabetes patients with hypertension: a cross-sectional retrospective study. BMC Endocr Disord. 2013;13:2. doi:10.1186/1472-6823-13-2

11. Cipolle RJ, Strand LM, Morley PC. Pharmaceutical Care Practice: The Clinician's Guide, Second Edition. New York: McGraw-Hill; 2004.

12. Quest DW. Stockley's drug interactions. 8th edition; Stockley's drug interactions 2008 pocket companion. Can Fam Physician. 2008;54(7):1025.

13. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA. 2014;311(5):507-20. doi:10.1001/jama.2013.284427

14. Mahajan R. Joint National Committee 8 report: How it differ from JNC 7. Int J Appl Basic Med Res. 2014;4(2):61-2. doi:10.4103/2229-516x.136773

15. Prihapsari AN, Rahmawati F, Andayani TM. Hubungan antara Drug Related Problems (DRPs) dan Capaian Target Terapi Hipertensi di Puskesmas Kota Yogyakarta [Thesis]. Yogyakarta: Universitas Gadjah Mada; 2016.

16. Carey RM, Calhoun DA, Bakris GL, Brook RD, Daugherty SL, Dennison-Himmelfarb CR, et al. Resistant Hypertension: Detection, Evaluation, and Management: A Scientific Statement From the American Heart Association. Hypertension.2018;72(5):e53-90. doi:10.1161/hyp.0000000000000084

17. Cobos B, Haskard-Zolnierek K, Howard K. White coat hypertension: improving the patient-health care practitioner relationship. Psychol Res Behav Manag. 2015;8:133–41. doi:10.2147/prbm.s61192

18. Handler J. Managing white-coat effect. J Clin Hypertens. 2008;10(8):649-54. doi:10.1111/j.1751-7176.2008.08064.x

19. Verma N, Rastogi S, Chia YC, Siddique S, Turana Y, Cheng HM, et al. Non-pharmacological management of hypertension. J Clin Hypertens. 2021;23(7):1275-83. doi:10.1111/jch.14236

20. Littlejohn 3rd TW, Majul CR, Olvera R, Seeber M, Kobe M, Guthrie R, et al. Results of treatment with telmisartan-amlodipine in hypertensive patients. J Clin Hypertens. 2009;11(4):207-13. doi:10.1111/j.1751-7176.2009.00098.x

21. Hussein M, Lenjisa JL, Woldu MA, Tegegne GT, Umeta GT, Dins H, et al. Assessment of Drug Related Problems Among Hypertensive Patients on Follow up in Adama Hospital Medical College, East Ethiopia. Clin Pharmacol Biopharm. 2014;3:122. doi:10.4172.2167-065X.1000122

22. Tharanon V, Putthipokin K, Sakthong P. Drug-related problems identified during pharmaceutical care interventions in an intensive care unit at a tertiary university hospital. SAGE Open Med. 2022;10:20503121221090881. doi:10.1177/20503121221090881

23. Bhatty E, Meraj A, Malik M, Imtiaz M, Nasir A, Saleem N, et al. Drug Related Problems Associated with Polypharmacy: A Literature Review. Pak J Pharm. 2017;30(1):10–6.

24. Farha RA, Basheti I, Al Ruz HA, Alsaleh A, AbuRuz S. Assessment of drug-related problems and their impact on blood pressure control in patients with hypertension. Eur J Hosp Pharm. 2016;23(3):126-30. doi:10.1136/ejhpharm-2015-000712

25. Abegaz TM, Tefera YG, Abebe TB. Antihypertensive drug prescription patterns and their impact on outcome of blood pressure in Ethiopia: a hospital-based cross-sectional study. Integr Pharm Res Pract. 2017;6:29–35. doi:10.2147/iprp.s124047