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RESEARCH ARTICLE

Drug-related problems (DRPs) in hypertensive patients at Karsa Husada Batu Hospital, East Java, Indonesia: Evaluation based on drug selection

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Abstract

Background: Hypertension significantly contributes to premature deaths globally. Drug selection has a vital role in the success of hypertension treatment, but incorrect selection could promote Drug-related problems (DRPs). **Objective**: This study evaluates DRPs based on the drug selection of inpatient hypertensive patients at Karsa Husada Batu Hospital, which is located in East Java, Indonesia. **Method**: This study was an observational study with a retrospective research design. The cases of DRPs were classified using the Pharmaceutical Care Network Europe (PCNE) DRP classification tool V9.1. This was total sampling research with the population of medical records of patients with hypertension without complications who were hospitalised at Karsa Husada Batu Hospital in 2018-2021. **Result**: This study involved 66 patients' medical records. The DRPs of the drug selection occurred in 47 patients (71.21%), including 15 cases of drug use that did not comply with guidelines, 34 cases without indication for the drug used, 51 cases of improper combination of drugs, nine cases of inexact duplication of the therapeutic group, and 31 cases of no adequate drug for existing indication. **Conclusion**: Inappropriate drug combinations are the primary cause of DRPs based on drug selection, and there are no cases in which too many drugs are prescribed for an indication.

Introduction

Hypertension contributes to 12.8% of premature deaths globally (World Health Organisation, 2022). Hypertension is diagnosed when the systolic is ≥140 mmHg and/ or diastolic is ≥90 mmHg (Unger *et al*., 2020). Hypertension can be treated by pharmacological therapy, but some risks can occur to the patients, called drug-related problems.

Drug-related problems (DRPs) are unexpected events related to drug therapy that disrupt the patient's medication. Pharmaceutical Care Network Europe (PCNE) (2020) classifies the causes of DRPs into several domains, including drug selection.

Research conducted by Blessing, Maxwell, and Chinwe in 2020 shows that the leading cause of DRPs was drug selection (50.1%) (Blessing *et al*., 2020). Moreover, the DRPs study in hypertensive patients in Indonesia evidenced that DRPs were found in 57% of hypertensive outpatients, and the leading cause of DRPs was drug selection (97.14%) (Kusumawardani *et al*., 2020).

A rational selection of drugs is needed to achieve the desired therapy. Irrational drug usage leads to poor therapeutic results and treatment failure (Maxwell, 2016). The DRPs related to drug selection impact the potential risk of high hospitalisation rates and increased medication side effects, especially in the elderly (Krustev *et al*., 2022).

This research was conducted at Karsa Husada Batu Hospital in East Java, Indonesia. This hospital is an advanced referral health facility that receives referrals

from clinics and other primary health facilities in Batu City and surrounding areas. This study evaluates DRPs based on drug selection in inpatient hypertensive patients at Karsa Husada Batu Hospital.

Methods

This observational study was held in October 2022 in the medical records room of Karsa Husada Batu Hospital in East Java, Indonesia, with the ethics number 072/2739/102.13/2022. This total sampling research involved a population that was the medical records of inpatients with hypertension without complications at Karsa Husada Batu Hospital in 2018-2021. The DRPs domains to be studied were the drug selection, adapted from Pharmaceutical Care Network Europe (PCNE) DRP classification tool V9.1. The medication review was based on JNC VIII and Drug Information Handbook 23rd edition. Univariate descriptive analysis was performed to assign patient characteristics and DRPs frequency distribution.

Results

Demographic characteristics of patients

This study involved as many as 66 patients' medical records. The characteristics of the samples are stated in Table I. Most of the patients were female, with patients aged ≥60 being the most common age group, with a percentage of 42.42%.

Table I: Demographic characteristics sample of inpatients with hypertension without complications at Karsa Husada Batu Hospital in 2018-2021

Characteristics		Frequency (n)	Percentage (%)
Gender	Male	21	31.82
	Female	45	68.18
Age	18-44 years	13	19.70
	45-59 years	25	37.88
	≥60 years	28	42.42
Total		**66**	**100**

Evaluation of drug-related problems based on drug selection

The causes of DRPs related to drug selection were identified in as many as 140 cases in 47 patients (71.21%). The cases were classified into several subdomains, including 15 cases of inappropriate drug according to guidelines, 34 cases of no indication for the drug, 51 cases of inappropriate combination of drugs, nine cases of inappropriate duplication of the therapeutic group, and 31 cases of no or incomplete drug treatment for existing indication, as shown in Figure 1.

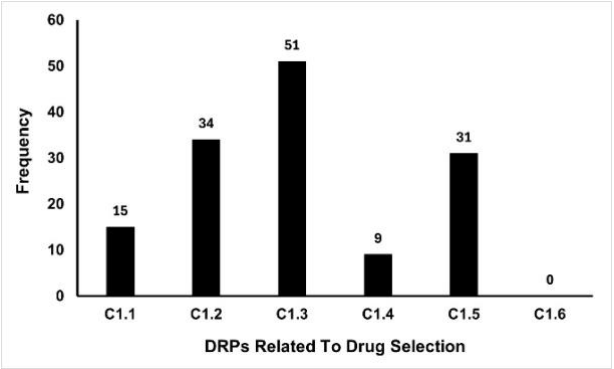

Figure 1: DRPs based on drug selection in inpatients with hypertension without complications at Karsa Husada Batu Hospital in 2018-2021

The leading cause of DRPs related to drug selection in this study is the improper combination of drugs, drugs + herbal medications, or drugs + dietary supplements (36.43%). DRPs related to drug selection are classified into several subdomains, as stated in Table II.

C1.1 Subdomain of inappropriate drug according to guidelines

This study has 15 cases of drug use that did not comply with guidelines, and 11 of those are the improper use of ondansetron. The next four inappropriateness in this subdomain is the use of hydrochlorothiazide in hypokalaemia patients.

C1.2 Subdomain of no indication for drugs

As many as 34 cases of the usage of the drugs did not have any clear indications. The highest proportion in this case is the usage of omeprazole and ranitidine. It counted 61.76% of the total cases in this domain.

C1.3 Subdomain of the inappropriate combination of drugs, drugs + herbal medications, or drugs + dietary supplements

This study found as many as 51 cases in this domain. Over 80% of patients received an improper combination of drugs, which is the concomitant use of analgesics and antihypertension drugs, such as ibuprofen and amlodipine, in six patients.

Table II: The subdomains of DRPs based on drug selection in inpatients with hypertension without complications at Karsa Husada Batu Hospital in 2018-2021

Code V9.1	Causes	Frequency
C1.1	**Inappropriate drug according to guidelines**	**15**
	Ondansetron	11
	Hydrochlorothiazide	4
C1.2	**No indication for drugs**	**34**
	Aspirin	1
	Combivent (ipratropium bromide and salbutamol)	1
	Cetirizine	1
	Citicoline	1
	Clopidogrel	1
	Diphenhydramine	1
	Methylprednisolone	1
	Metoclopramide	3
	Ondansetron	2
	Ranitidine	7
	Pantoprazole	1
	Omeprazole	14
C1.3	**Inappropriate combination of drugs, drugs + herbal medications, or drugs + dietary supplements**	**51**
	Mefenamic acid + Captopril	1
	Mefenamic acid + Furosemide	1
	Mefenamic acid + Nifedipine	1
	Aspirin + Amlodipine	1
	Aspirin + Captopril	1
	Aspirin + Nicardipine	1
	Ibuprofen + Amlodipine	6
	Ibuprofen + Bisoprolol	2
	Ibuprofen + Candesartan	4
	Ibuprofen + Hydrochlorothiazide	2
	Ibuprofen + Telmisartan	2
	Ketorolac + Amlodipine	3
	Ketorolac + Candesartan	1
	Ketorolac + Captopril	1
	Ketorolac + Ciprofloxacin	1
	Metamizole + Amlodipine	5
	Metamizole + Candesartan	5
	Metamizole + Captopril	5
	Metamizole + Ceftriaxone	2
	Metamizole + Nicardipine	1
	Metamizole + Nifedipine	1
	Metamizole + Hydrochlorotiazide	2
	Omeprazole + Diazepam	1
	Omeprazole + Hydrochlorotiazide	1
C1.4	**Improper duplication of the drugs or active ingredients in the same therapeutic group**	**9**
	Analsik (metamizole and diazepam) + Antalgin (metamizole)	1
	Amlodipine + Nicardipine	3
	Candesartan + Valsartan	1
	Cetirizin + Diphenhydramine	1
	Ibuprofen + Paracetamol	3
C1.5	**No or incomplete drug treatment for the existing indication**	**31**
	Cough	1
	Fever	1
	Diarrhea	2
	Nausea and vomiting	2
	Hypertension	5
	Hypertension stage 2	2
	Hypertension stage 3	8
	Hypokalemia	10
C1.6	**Too many drugs or active ingredients prescribed for an indication**	**0**

C1.4 Subdomain of improper duplication of the drugs or active ingredient in the same therapeutic group

This research found four cases of duplication of antihypertensive drugs. Three patients received amlodipine and nicardipine, both calcium channel blockers (CCB). Duplication of CCB was also the most common case in the study conducted by Moriarty, Bennett, and Fahey (2019). Other antihypertensive drugs classified as duplication in this study were candesartan and valsartan, which are angiotensin receptor blockers (ARB).

C1.5 No or incomplete drug treatment for existing indication

As many as 15.15% of patients did not receive therapy for hypokalemia. Moreover, 15 patients diagnosed with hypertension did not receive adequate drugs. This finding is similar to the research conducted by Appleton *et al*. (2013), in which more than 40% of hypertension cases were untreated.

C1.6 Too many drugs or active ingredients prescribed for an indication

This study describes no cases of too many different active drug ingredients for indications.

Discussions

In this study, the women's hypertension cases are more than men's, with patients over 60 years old being the dominant age class. In that age, there is a cardiovascular ageing process. Thickening and elasticity loss in the walls of the large arteries, especially the aorta, will reduce the buffer function of the arterial channel near the heart and increase the speed of the pulse wave. Thus, there will be an increase in systolic pressure and pulse rate (Sun, 2015). Furthermore, Iorga *et al*. (2017) reported that geriatric women are less protected from hypertension because oestrogen levels decrease at menopause. In the cardiovascular system, oestrogen has a role in homeostasis and vasodilatation of endothelial through upregulation of the nitric oxide pathway and inhibition of the sympathetic activity and the renin-angiotensin systems. Thus, oestrogen can influence the blood pressure.

The evaluation of DRPs in this study is based on the selection of the drugs. The improper combination of drugs, herbal medications, and dietary supplements is the main cause of the DRPs. Using herbal drugs and dietary supplements could promote polypharmacy, in which this combination can interact with prescribed drugs and is associated with diverse unwanted side effects. Also, it can potentially reduce the efficacy or bioavailability of the prescription drug.

The inappropriate drug domain has been defined as events in drug usage that are unsuitable for the patient's clinical condition (Rochon, 2022). In this study, 73.33% of inappropriate drug use is related to the use of ondansetron. Indications of ondansetron are nausea and vomiting due to chemotherapy, radiation therapy, and surgery (Drug Information Handbook, 2014). This drug is unsuitable as an antiemetic drug for patients unrelated to those conditions. Therefore, nausea and vomiting patients in this research should be given dopamine antagonists, not ondansetron. The mechanism of action of dopamine antagonists is to block the Dopamine-2 receptor that stimulates vomiting (Denholm & Gallagher, 2018). Besides ondansetron, there is other inappropriate use of the drugs. Four cases of hydrochlorothiazide use in hypokalaemia patients can be classified as improper use because this drug has a potassium-wasting effect on the kidneys. This loss of potassium ions can potentially cause hypokalaemia (Reilly & Jackson, 2012). It will aggravate the hypokalaemia status.

No indication for the drug has been defined as there is no legitimate medical indication for the drug therapy, and the drug must be discontinued (Cipolle *et al*., 2015). In this research, there are cases of usage of omeprazole and ranitidine without any proper indication, 14 and seven cases, respectively. The use of drugs without indications can escalate the incidence of side effects. Other impacts are the addition of burden charges on patients and the decreased availability of drugs at health centres (Garg *et al*., 2014).

Kumar and colleagues (2022) define the inappropriate combination of drugs subdomain as interactions between drugs, drugs with herbs, and drugs with supplements. Identifying and managing drug interactions is essential to preventing the associated risk (Rodrigues *et al*., 2017). In this study, the subdomain C1.3 dominates the cause of DRPs in drug selection. This result is similar to Hussein *et al*.'s (2014) research. More than 60% of hypertensive patients experience DRP through drug interactions.

In this research, the interaction between Non-steroidal Anti-Inflammatory Drugs (NSAIDs) and antihypertensives was the predominant cause of drug interaction. Simultaneously, using NSAIDs and antihypertensives can reduce antihypertensive efficacy as NSAIDs decrease prostaglandin synthesis in the kidneys and increase fluid retention. In addition, using both groups of drugs can intensify the risk of acute kidney injury (Vostinaru, 2017).

Improper duplication of the drugs or active ingredients in the same therapeutic group can be classified as a

concomitant prescription of drugs from the same class of medications (Rahmanzade *et al*., 2020). The duplication found in this study is the use of antihypertensive drugs together. Duplication of drugs from the same antihypertensive drugs must be avoided because it can promote the risk of adverse effects (Lee *et al*., 2019). group is ineffective and potentially dangerous (Whelton *et al*., 2018). Possible side effects of duplicating CCB are hypotension, headaches, and angina. Moreover, duplication of the ARB can cause hypotension (Zhao *et al*., 2019).

No or incomplete drug treatment for existing indications involves cases where the patient has not been prescribed medication even though the medical condition requires initiating or additional drug therapy to achieve synergistic or additive effects. Hypokalaemic patients who did not receive drug therapy were the most common cases in this subdomain.

Some patients did not receive therapy for hypokalaemia and hypertension. Low potassium leads to sodium retention, stimulated renin activity, and worsening endothelial function (Gonçalves & Abreu, 2020). Hypokalaemia can be treated by giving potassium supplements to maintain the adequate body's potassium level (Krogager *et al*., 2021). In addition, hypertension is a primary risk factor for morbidities or mortalities related to cardiovascular, cerebrovascular, and renal diseases. Thus, hypertension treatment should be comprehensive.

The last domain refers to prescribing more drugs than is clinically necessary. In this study period, there are no cases of too many diverse active drugs for indications in this hospital. This report shows that the number of drugs used to treat hypertensive patients at Karsa Husada Batu Hospital in East Java, Indonesia, was based on the patient's clinical necessity.

Conclusion

An inappropriate combination of drugs remains the leading cause of the DRPs based on drug selection in this study. Furthermore, this research cannot find too many drugs prescribed for an indication. The impropriety in drug selection domains could make DRPs and Pharmacists' monitoring is needed to improve drug therapy selection to minimise the DRPs. Further research is needed to improve the quality of drug selection, including research related to evaluating drug combinations.

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