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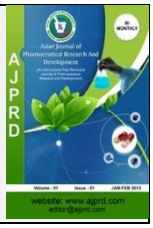

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Research Article

Potential Interactions of Hypertension Drug in Medan City Pharmacy

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A B S T R A C T

Background: Hypertension is a disease that can cause complications without the patient realizing it. Therapeutic management needed to control the patient's blood pressure is complex enough to potentially lead to drug interactions. The purpose of this study was to analyze the interaction of hypertension drugs that occurred in a pharmacy in the city of Medan.

Method: The study was conducted retrospectively involving 101 patient data in February-May 2022. Patient data was processed descriptively and potential drug interactions were analyzed using the Medscape Drug Interactions Checker, Stockley's Drug Interaction, and the drugs.com database

Result: Based on the study results, it was found that from 101 patients, 57 patients had no drug interactions (56.4%), but 45 cases of drug interactions were found in 44 patients (43.6%). Drug interactions found in 27 cases occurred pharmacokinetically (60%) and 18 cases occurred pharmacodynamically (40%). The most frequent drug interactions are Amlodipine and Simvastatin.

Conclusion: Based on this study, it can be concluded that most patients who have drug interactions occur through pharmacokinetic mechanisms.

Keywords: Hypertension, polypharmacy, drug interactions.

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INTRODUCTION

Hypertension is an increase in systolic blood pressure greater than 140 mmHg and diastolic blood pressure greater than 90 mmHg.[1] The prevalence of hypertension has increased in Indonesia from 2013 to 2018. In 2013, the prevalence of hypertension in Indonesia was only 25.8%.[2] Meanwhile, in 2018, the prevalence of hypertension had increased to 34.1%.[3]

Hypertension is known as a silent killer because it can cause complications without any previous symptoms. [4] Complications of hypertension can cause patients to experience heart problems (heart failure and myocardial infarction), kidney problems, stroke (ischemic and hemorrhagic), senility, cognitive decline, dementia and can even cause sudden death. Complications that occur in patients can increase the risk of drug interactions in hypertensive patients. [5,6]

Drug interactions are one part of Drug related problems (DRPs). Based on the Pharmaceutical Care Network Europe (PCNE) Drug Related Problems are events or events related to drug therapy, either real or potential that can affect the desired therapeutic outcome for patients.[7]

Drug interactions that occur in patients, can affect clinical outcomes or interfere with the desired therapeutic results. Unwanted events as a result of these DRPs can be in the form of symptoms or medical complaints.[6] Therefore, in this study, an analysis of the potential for drug interactions was carried out in one of the pharmacy in Medan City.

METHODS AND PARTICIPANS:

This research was conducted using a retrospective method with a descriptive non-experimental research design. The research was conducted in one of the pharmacy in the city of Medan in February-May 2022.

The population in this study was data on prescriptions who received antihypertensive drugs. The number of patient data included in this study was 101 patients. Patient data were then analyzed descriptively. Potential drug interactions that occur were analyzed using the Medscape Drug Interactions Checker, Stockley's Drug Interaction, and the drugs.com database.

The data inclusion criteria for this patient are 1). Patients who have been diagnosed with hypertension by a doctor 2). Patients who are prescribed hypertension medication 3). Patients get experienced complications. The exclusion criteria for this patient data were that the patient only received one drug in the prescription.

RESULTS AND DISCUSSIONS

In this study, the number of prescriptions recorded in the period February-May 2022 amounted to 101 samples. The prescriptions used in this study were taken from one of the pharmacy in the city of Medan. The results of the descriptive analysis related to the number of drug interactions are presented in table 1.

Table 1: Percentage of drug interactions

Interaction events	Number of Patients (n= 101)	Percentage %)
Interaction occurs	44	43,6
No interaction occurs	57	56,4

Based on the table above, out of 101 patients, 44 people experienced drug interactions (43.6%) and 57 people did not experience drug interactions (56.4%). The number of patients experiencing drug interactions is quite high. Almost half of the total patients experience drug interactions.

A drug interaction is an event or event related to drug therapy, either real or potential that can affect the desired therapeutic outcome for the patient.[7] If the patient experiences drug interactions, then this has the potential to not achieve the desired therapeutic target. According to Parulian et al (2019), one of the factors that determine the occurrence of drug interactions is the number of drugs received by the patient. [8]

Based on the mechanism of drug interactions, the following table 2 presents data related to drug interactions that occur pharmacokinetically and pharmacodynamically.

Table 2: Mechanism of Drug Interaction

Mechanism of Drug Interaction	Number of cases (n=45)	Percentage (%)
Pharmacokinetic Interaction	27	60
Pharmacodynamic Interaction	18	40

Based on the table above, pharmacokinetic drug interaction occurred 27 cases (60%). Meanwhile, pharmacodynamic drug interactions occurred in 18 cases (40%). The incidence of pharmacokinetic drug interactions is higher than that of pharmacodynamic drug interactions. Research conducted by Parulian et al in 2019 at the Ario Wirawan Hospital also showed that in hypertensive patients who experienced drug interactions, the most common mechanism pattern also occurred pharmacokinetic, as many as 53.97%.[8]

Based on the literature, pharmacokinetic interactions are interactions that occur if the absorption, distribution, metabolism, and excretion profile of a drug changes due to the influence of other drugs. Changes in the absorption, distribution, metabolism, and excretion of a drug will cause changes in the amount of drug in the blood plasma which affects the effectiveness of the drug.[9]

Pharmacodynamic interactions are interactions that occur at the receptor level that result in changes in the effect of a drug. If the effect is synergistic, then the effect will be even stronger. Meanwhile, if the drug is an antagonist, then this will reduce the desired effect of the drug.[9]

In this study, the recorded drug interactions were those that occurred at major and moderate levels. While minor drug interactions are not summarized or ignored because only interactions with major and moderate levels need to be monitored for and must receive attention. Table 3 presents the interactions of antihypertensive drugs with other antihypertensives/drugs along with their severity.

Table 3. Interaction of antihypertensive drugs with other antihypertensives/another drug

Mechanism of Drug Interaction	Drug A	Drug B	Number of cases (45)	Percentage (%)	Severity
Pharmacokinetic Interaction	Amlodipine	Simvastatin	20	44.4	Major
	Valsartan	Simvastatin	2	4.4	Moderate
	Candesartan	Bisoprolol	2	4.4	Moderate
	Telmisartan	Atorvastatin	2	4.4	Moderate
	Valsartan	Furosemide	1	2.2	Moderate
Pharmacodynamic Interaction	Amlodipine	Metformin	12	27	Moderate
	Candesartan	Aspirin	2	4.4	Moderate

	Captopril	Insulin	2	4.4	Moderate
	Telmisartan	Insulin	1	2.2	Moderate
	Amlodipine	Bisoprolol	1	2.2	Moderate

Based on the table above, it is known that the most common drug interactions were between amlodipine and Simvastatin, which occurred in 20 cases (44.4%). Concomitant use of amlodipine and simvastatin can significantly increase the plasma concentrations of simvastatin and its active metabolite simvastatin acid. This will result in an increased risk of developing statin-induced myopathy.[10]

The interaction of amlodipine and simvastatin is pharmacokinetically. The mechanism is that amlodipine inhibits simvastatin metabolism through the intestine and liver. Amlodipine inhibits the CYP450 3A4 enzyme which functions to metabolize Simvastatin. Administration of a single dose of simvastatin 80 mg and amlodipine at a dose of 10 mg once daily, increased the peak plasma concentration of simvastatin (Cmax) and systemic exposure (AUC) on day 10 by an average of 1.5 and 1.8 times. While the Cmax and AUC of simvastatin acid increased by an average of 1.6 times.[10]

Increased peak plasma concentrations of simvastatin and simvastatin acid result in an increased risk of musculoskeletal toxicity. This can lead to myopathy which manifests as muscle pain. This toxicity can also cause Rhabdomyolysis although it is rare. Not only that, this interaction can cause acute renal failure secondary to myoglobinuria and can lead to death.[9,10]

The use of amlodipine and simvastatin should be avoided. If forced to use, then the dose of simvastatin should not exceed 20 mg daily. We recommend that if using amlodipine, simvastatin can be replaced with the use of Fluvastatin, pravastatin, and rosuvastatin because they are not metabolized by CYP450 3A4 so their use is safer. It is hoped that patients receiving statin therapy should report muscle pain immediately, especially if it is accompanied by fever, malaise, and/or dark urine. Therapy should be discontinued if creatine kinase is markedly elevated without strenuous exercise or if myopathy is suspected or diagnosed.[10,11]

The second most common drug interaction was amlodipine with metformin in 12 cases (27%). The literature suggests amlodipine reduces the effects of metformin by pharmacodynamic antagonism. The interaction of amlodipine with metformin does not affect blood pressure, but inhibits the action of metformin to lower blood sugar that occurs pharmacodynamically.[11]

Another pharmacokinetic drug interaction that was found was Valsartan with Simvastatin in 2 cases (4.4%), Candesartan with bisoprolol in 2 cases (4.4%), telmisartan with atorvastatin in 2 cases (4.4) and Valsartan with furosemide in as many as 1 cases (2.2%). The severity of all these interactions was moderate.

Based on the literature, it is known that the interaction of Valsartan with Simvastatin can increase the pharmacokinetic effect of valsartan. Its use must be closely monitored. The use of Candesartan with bisoprolol can be dangerous because both drugs increase serum potassium. Concurrent use of telmisartan and atorvastatin can increase the effect of atorvastatin, so its toxicity should also be considered. Another interaction that occurs in pharmacokinetics is the use of valsartan with furosemide, both of which also increase serum potassium.[11]

Other drug interactions that occurred pharmacodynamically were candesartan with aspirin in 2 cases (4.4%), Captopril with insulin in 2 cases (4.4%), telmisartan with insulin in 1 case (2.2%) and amlodipine with bisoprolol. as many as 1 case (2.2%). The severity of all these interactions was moderate.[10,11]

Based on the literature, it is known that the interaction of candesartan with aspirin can reduce the antihypertensive effect of candesartan. Aspirin is a non-steroidal anti-inflammatory drug (NSAID) that can attenuate the antihypertensive effect of angiotensin II receptor antagonists. The mechanism is that aspirin inhibits the synthesis of prostaglandins in the kidneys which can cause hypertension. In addition, aspirin which is classified as an NSAID can cause fluid retention which can also increase blood pressure Amlodipine drug interactions with bisoprolol can cause heart failure and angina. The use of amlodipine with bisoprolol should be monitored and monitored.[10]

Captopril drug interactions with insulin and telmisartan with insulin do not affect blood pressure but can increase the hypoglycemic effect. This happens because the hypoglycemic effect of insulin can be strengthened by certain drugs such as ACE inhibitors and angiotensin receptor blockers (ARBs).[10]

Drug interactions that occur in patients should be of concern to medical personnel. If the patient is hospitalized, monitoring of drug use can be done directly during a patient visit. If the patient is outpatient, information must be obtained regarding the symptoms and complaints felt by the patient when he returns to visit. The goal is to achieve the maximum therapeutic target. If undesirable symptoms occur, then the drug that causes the interaction must be replaced with a safer drug.

CONCLUSION

In this study, it was found that from 101 patients, 57 patients had no drug interactions (56.4%), but 45 cases of drug interactions were found in 44 patients (43.6%). Drug interactions found in 27 cases occurred pharmacokinetically (60%) and 18 cases occurred pharmacodynamically (40%). The most frequent drug interactions are Amlodipine and Simvastatin. Based on this

study, it can be concluded that most patients who experience drug interactions occur through pharmacokinetic mechanisms.

CONFLICT OF INTEREST

All author have no conflict of interest to declare.

REFERENCE

1. Williams B, Mancia G, & Spiering. The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. *Journal of Hypertension*. 2018; 36:1953-1963.
2. Kementerian Kesehatan Republik Indonesia . *Riset kesehatan dasar Republik Indonesia*. Jakarta: Kementerian Kesehatan Republik Indonesia. 2013.
3. Kementerian Kesehatan Republik Indonesia *Riset kesehatan dasar Republik Indonesia* Jakarta: Kementerian Kesehatan Republik Indonesia. 2013.
4. Leung A.A, Daskalopoulou S.S, & Dasgupta K. Hypertension Canada's guidelines for diagnosis, risk assessment, prevention, and treatment of hypertension in adults. *Can J Cardiol*. 2017;33:557–576.
5. Kusumawardani L.A, Andrajati R, & Nusaibah A. Drug-related problems in hypertensive patients: A cross-sectional study from Indonesia. *J Res Pharm Pract.* 2020; 9:140-5.
6. Samaila, Aliyu, Biambo, Aminu, Usman, & Nuruddeen. Drug related problems and implications for pharmaceutical care interventions in hypertensive outpatients in a Nigerian hospital. *Journal of Science and Practice of Pharmacy*. 2019; 17. 69-78.
7. Van Mil J.W.F, Horvat N, & Zuidlaren T.W. Classification for Drug Related Problems V9.0. *Pharmaceutical Care Network Europe Foundation (PCNE).* 2019.
8. Parulian L, Listyanti E, Hati A.K, & Sunnah I. Analisis Hubungan Polifarmasi dan Interaksi Obat Pada Pasien Rawat Jalan Yang Mendapat Obat Hipertensi Di Rsp. Dr. Ario Wirawan Periode Januari-Maret 2019. *Indonesian Journal of Pharmacy and Natural Product.* 2019; Volume 2. No 2.
9. Stockley I.H. Stockley's Drug Interaction. 8th Edition. *Pharmaceutical Press.* 2008. Great Britain.
10. Drug.com Database. 2022. (online), https://www.drugs.com/interaction/, accessed on 2 August 2022.
11. Medscape. Drug Interaction Checker. 2011 (online), (http://www.reference.medscape.com/drug interactionchecker), accessed on 1 August 2022.