

Potential Drug-Drug Interactions and Associated Factors on Ambulatory Patients with Hypertension of a Secondary Care Hospital in Bandar Lampung

Noni Zahwa Salsabila, Citra Yuliyanda Pardilawati*, Dwi Aulia Ramdini and Oktafany
Department of Pharmacy, Faculty of Medicine, University of Lampung, Indonesia

Keywords: Hypertension, Drug Interaction, Associated Factor.

Abstract: Hypertensive patients are often given combination therapy according to the patient's condition, the drugs used have a high risk of potential drug interactions. The aim of this research is to determine potential drug-drug interactions and associated factors on ambulatory patients with hypertension of a secondary care hospital in Bandar Lampung. This research is a cross-sectional study. Data were collected from patient's medical records. Evaluation of potential drug-drug interactions refers to Drugs.com. The associated factors are analyzed by Chi-Square test. Of the 135 prescriptions, there are 90 (66,67%) prescriptions that have the potential for drug-drug interactions. Potential drug-drug interactions based on severity levels are major (6,88%), moderate (72,10%) and minor (21,01%). Bivariate statistical analysis showed that there was an influence of age and number of medications on potential drug-drug interactions.

1 INTRODUCTION

Hypertension is a disease condition that occurs due to an increase in systolic blood pressure exceeding 140 mmHg and diastolic blood pressure exceeding 90 mmHg (Hastuti, 2020). Hypertension is a health problem in the world because it is a major risk factor for cardiovascular disease. An estimated 1.28 billion adults aged 30-79 years worldwide suffer from hypertension¹⁵. Various drugs used to reduce blood pressure such as diuretics, beta-blockers, ACE inhibitors, angiotensin II receptor blockers (ARBs), calcium antagonists, and vasodilators (PERHI, 2021). This can cause the drugs and antihypertensive therapy used by hypertension sufferers to vary and there is a risk of drug interactions (Chalik, 2021).

Drug interactions can cause effects in the form of increasing or decreasing activity or producing new effects that were not present before. The occurrence of drug interactions can also affect the body's response, thereby affecting the desired therapeutic outcome (Mahamudu, 2017). Treatment therapy needs to be carried out optimally by selecting the best treatment so that it can provide benefits to patients by improving quality of life (Whittlesea, 2019). One way

that can be done to achieve this goal is to identify, reduce and prevent potential drug interactions that can occur, thus having an impact on the success of therapy (Parulian, 2019).

Therefore, this research was conducted to determine the potential for drug interactions and the factors that influence the potential for drug interactions in hypertensive patients. This research aims to ensure that potential drug interactions are more carefully considered and prevented, so the incidence of drug interactions can be minimized.

2 METHOD

This research is a descriptive-analytic study with a cross-sectional approach, carried out retrospectively on the medical records of ambulatory patients with hypertension of a secondary care hospital in Bandar Lampung. The data used medical record for the period January – June 2023. The sample size was determined using the purposive sampling method.

Determination of the minimum sample size in this study was determined based on the proportion estimation formula.

$$n = \frac{Z^2 p (1 - P) N}{d^2 (N-1) + Z^2 p (1 - p)}$$

Explanation:

n: Number of samples

N: Number of populations

Z: Degree of trust

p: The proportion of cases to the population

d: The degree of deviation from the desired population

$$n = \frac{95\% ^2 \cdot 50\% (1 - 50\%) 205}{5\% ^2 (205 - 1) + 95\% ^2 \cdot 50\% (1 - 50\%)}$$

$$n = \frac{196,8}{1,47}$$

$$n = \pm 133,8 \quad (\text{Rounded up to } 135)$$

The population of ambulatory patients with hypertension of a secondary care hospital in Bandar Lampung on 2023 is 205 patients. The minimum sample size for this research is 135 samples. In this study, the inclusion criteria applied were patients aged ≥ 18 years and having medical records with complete information. The exclusion criteria applied were patient who get <2 types of drugs.

The main guidelines that will be used as a guide in assessing drug interactions are Drugs.com. In bivariate analysis using the Chi-Square analysis method with a categorical measurement scale (Dahlan, 2014).

3 RESULTS AND DISCUSSION

The sociodemographic characteristic on Ambulatory Patients with Hypertension of a Secondary Care Hospital in Bandar Lampung on January – June 2023 was showed in table 1. Hypertensive patients at a secondary care hospital in Bandar Lampung tends to be more common in women, namely 78 (57.78%) patients compared to male patients, namely 57 (42.22%) patients. In the age category, the highest number of hypertension cases was in individuals aged ≥ 59 years with 58 (42.96%) patients followed by the >45 -59 years age category with 54 (40%) patients while the lowest number of cases was recorded in the age 19-45 years with 23 (17.04%.) patients. There were 79 (58.52%) prescriptions that used 2-4 drugs and there were 56 (41.48%) prescriptions that used ≥ 5 drugs. Patients involved in this study had comorbidities, with 108 (80%) patients.

Table 1. Sociodemographic characteristics on Ambulatory Patients with Hypertension of a Secondary Care Hospital in Bandar Lampung on January – June 2023

Variable	Frequency	Percentage
Gender		
Male	57	42.22%
Female	78	57.78%
Age		
19 – 45 years	23	17.04%
> 45 - 59 years	54	40.00%
> 59 years	58	42.96%
Number of Medications		
2 – 4 drugs	79	58.52%
> 4 drugs	56	41.48%
Comorbid condition		
Present	108	80%
Absent	27	20%
Potential Drug-drug Interaction		
Present	90	66.67%
Absent	45	33.33%

Based on table 1, it is explained that the drug-drug interactions from 135 samples contained 90 (66.67%) cases with potential drug interactions and 45 (33.33%) cases without potential drug interactions. Patients suffering from hypertension have a high risk of experiencing drug interactions due to long-term treatment and are often given combination therapy.

Table 2: Severity Levels of Potential Drug-drug Interactions on Ambulatory Patients with Hypertension of a Secondary Care Hospital in Bandar Lampung on January – June 2023

Level of Interaction	Number of Potential Interactions	Percentage (%)
Major	19	6,89%
Moderate	199	72,10%
Minor	58	21,01%
Total	276	100 %

Table 2 shows the results of the evaluation of potential drug-drug interactions of moderate severity. It was found that these interactions were the most common. At major severity levels, the potential drugs found are combinations that all involve antihypertensive drugs. The most potential drug-drug interactions that occur in the combination of amlodipine and simvastatin are 15 potential interactions. For major interactions between amlodipine and simvastatin it can cause a potential increase in the risk of myopathy (Baxter, 2010). Amlodipine may significantly increase plasma concentrations of simvastatin and its active metabolite and increase the risk of statin-induced myopathy (Baxter, 2010).

Then the most moderate interactions occur when using amlodipine together with bisoprolol. The use of amlodipine and bisoprolol together has a potential interaction mechanism. Amlodipine can inhibit the oxidative metabolism of beta blockers and additive pharmacological effects by reducing blood pressure and heart rate (Pikir, 2015). This is in accordance with research at RSUP Haji Adam Malik Medan which states that the highest interaction based on severity level is moderate at 69.8% (Dasopang, 2015).

There are 58 (21,01%) potential minor interactions. An example of a minor interaction between amlodipine and lisinopril may have additive hypotensive effects. Although these drugs are often safe to use together, careful monitoring of systemic blood pressure is recommended during coadministration, especially during the first one to three weeks of therapy (Triyanto, 2014).

Awareness and understanding of potential drug interactions needs to be the main focus for doctors and pharmacists. Regular monitoring by assessing the patient's clinical signs and, if possible, checking for drugs in the blood. This action is very important to reduce the risk of possible drug interactions that may arise.

Based on the bivariate analysis test between age of patient and potential drug-drug interactions carried out using chi-square test, p-value of 0.008 was obtained. The same thing was shown in research by Khairiyah et al. (2022) who stated that interactions commonly occur in geriatric patients, especially pharmacodynamic interactions caused by additive or synergistic interactions. Therefore, it can be concluded that there is a relationship between age of patient and potential drug-drug interactions in hypertensive patients at a secondary care hospital in Bandar Lampung on 2023.

Table 3. Associated Factors of Potential Drug-drug Interactions on Ambulatory Patients with Hypertension of a Secondary Care Hospital in Bandar Lampung on January – June 2023

Factor	Potential Drug-drug Interaction		P-value
	Yes	No	
Age			
19 – 45 years	9 (6.67%)	14 (10.37%)	0,008
> 45 - 59 years	38 (28.15%)	16 (11.85%)	
> 59 years	43 (31.85%)	15 (11.11%)	
Number of medications			
2 – 4 drugs	44 (32.59%)	34 (25.19%)	0,003
> 4 drugs	46 (34.07%)	11 (8.15%)	
Comorbid condition			
Present	75 (55.55%)	33 (24.44%)	0,171
Absent	15 (11.11%)	12 (8.88%)	

The results of the analysis of the relationship between the number of medications and the potential drug-drug interactions carried out using chi-square test showed p-value of 0.003, so it can be concluded that there is a significant relationship between the number of medication and the potential drug-drug interactions. In research conducted by Parulian et al. (2019), the number of medications that had a relationship with the number of interactions obtained a positive correlation (very strong correlation), namely the greater the number of drugs, the more interactions that occurred.

Then the results of the analysis of the relationship between comorbid condition and potential drug-drug interactions using the chi-square test obtained p-value of 0.171, so it can be concluded that there is no significant relationship between comorbid condition and potential drug interactions. In contrast to previous research at RSU X in Makassar City, it showed a significant influence on potential drug-drug interactions. These results indicate that the number of medications prescribed is the factor that has the greatest influence on the potential for drug interactions.

4 CONCLUSION

The results of the evaluation of potential drug interactions on 135 prescriptions assessed using tools, namely drugs.com, showed that in patients receiving antihypertensive drugs, there were 90 prescriptions that experienced potential drug interactions, which were divided into three based on the level of severity, namely 19 potential major level interactions (6.88%) interaction potential, moderate level interaction potential is 199 (72.10%) interaction potential, minor level interaction potential is 58 (21.01%) interaction potential.

There is a relationship between the number of medications and age of patient on potential drug-drug interactions in hypertensive patients, but there is no relationship between comorbid condition and potential drug-drug interactions in hypertensive patients. The variable most related to potential drug-drug interactions on ambulatory patients with hypertension of a secondary care hospital in Bandar Lampung on January – June 2023 is the number of medications with p-value of 0.003.

REFERENCES

- Baxter, K., & Stockley, I. (2010). Stockley 's Drug Interactions Ninth edition. In Pharmaceutical Press (Ninth Edit). Pharmaceutical Press.
- Chalik, R., Karim, D., Dewi, S. T. R., & Hidayati, H. (2021). Analisis Faktor Yang Berpengaruh Terhadap Kejadian Interaksi Obat Pada Pasien Hipertensi Di Rumah Sakit Umum X Kota Makassar. *Media Farmasi*, 17(1), 55.
- Dahlan, S. (2014). Statistik untuk Kedokteran dan Kesehatan Seri 1 Edisi 6 (Ed.6). Jakarta: Salemba Medika.
- Dasopang, E., Harahap, U., & Lindarto, D. (2015). Polipharmacy and Drug Interactions in Elderly Patients with Metabolic Diseases. *Indonesian Journal of Clinical Pharmacy*, 4(4), 235–241.
- Hastuti, A. P. (2020). Hipertensi. Jateng: Lakeisha.
- Khairiyah, U., Yuswar, M. A., & Purwanti, N. U. (2022). Pola Penggunaan Obat Antihipertensi Pada Pasien Hipertensi Di Instalasi Rawat Jalan Rumah Sakit. *Jurnal Syifa Sciences And Clinical Reasearch (JSSCR)*, 4, 609–617.
- Mahamudu, Y. S., Citraningtyas, G., & Rotinsulu, H. (2017). Kajian Potensi Interaksi Obat Antihipertensi Pada Pasien Hipertensi Primer Di Instalasi Rawat Jalan Rsud Luwuk Periode January – Maret 2016. *Jurnal Ilmiah Farmasi*, 6(3), 1–9.
- Parulian, L. (2019). Indonesian Journal of Pharmacy and Natural Product. *Indonesian Journal of Pharmacy and Natural Product*, 02(July), 4–7.
- PERHI, K. (2021). Konsensus Penatalaksanaan Hipertensi: Update Konsensus PERHI 2019. I-Hefcard.Com, 118.
- Pikir, B. S., Aminuddin, M., Subagjo, A., Darmadati, B. B., Suryawan, I. G. R., & P, J. N. E. (2015). Hipertensi Menejemen Komprehensif. Surabaya: Airlangga University Press.
- Setyoningsih, H., & Zaini, F. (2022). Hubungan Interaksi Obat Terhadap Efektivitas Obat Antihipertensi Di Rsud Dr. R. Soetrasno Rembang. *Cendekia Journal Of Pharmacy*, 6(1), 76–88.
- Triyanto, E. (2014). Pelayanan Keperawatan bagi Penderita Hipertensi secara terpadu. Yogyakarta: Graha Ilmu.
- Well, B. G., Dipiro, J., Schwinghammer, T. L., & DiPiro, C. V. (2015). *Pharmacotherapy Handbook* (Ninth Edit). MC Graw Hill Education.
- Whittlesea, C., & Hodson, K. (2019). *Clinical Pharmacy and Therapeutic* (Sixth Edit). Elsevier.