Advances in Health Sciences Research, volume 33
Proceedings of the 4th International Conference on Sustainable Innovation 2020–Health Science and Nursing (ICoSIHSN 2020)

Evaluation of Potential Drug-Drug Interactions in Hypercholesterolemia Patients at Teaching Hospital Surabaya

Ana Khusnul Faizah[1,*] Nani Wijayanti Dyah Nurrahman[2]

[1] *Program Study of Pharmacy, Faculty of Medicine, University of Hang Tuah*
[2] *Program Study of Pharmacy, Faculty of Medicine, University of Hang Tuah*
[*]*Corresponding author. Email:* ana.faizah@hangtuah.ac.id

ABSTRACT
Drug-drug interactions increase the effectiveness of therapy but can also have undesirable effects on toxicity. A pharmacist has the responsibility to prevent the undesirable effect of drug-drug interactions. The purpose of this study was to evaluate the potential drug-drug interactions in hypercholesterolemia patients at Teaching Hospital Surabaya. This study was conducted with a prospective method for a month. We obtained 54 patients and identified 45 patients that have potential drug-drug interactions. The total potential drug-drug interactions were 101. The severity of potential drug-drug interactions is serious (24,7%) and moderate (75,3%). Based on the mechanism action of drug interactions are pharmacodynamics (59,4%), pharmacokinetics (32,7%), and unknown (7,9%). The role of the pharmacist in providing safe, effective and rational drug therapy can be done by either identifying drug interactions, prevent and minimize the negative effect of drug interactions.

Keywords: *Drug interactions, pDDIs, Pharmacokinetic, Pharmacodynamics, Hypercholesterolemia*

1. INTRODUCTION

Dyslipidemia is a lipid metabolism disorder characterized by a decrease and an increase in the levels of lipid fractions in the blood. Dyslipidemic patients generally have comorbidities that require drugs to be taken together with anti dyslipidemia.

Drug is one of the important factors that can affect drug response. Drug interactions occur when one kind of drug receive effects of other drugs, food, beverages, and chemicals [1]. Drug-drug interaction (DDI) is defined as a modification of the effect of one drug with previous use or concomitant use of another drug. Drug-drug interactions which are one of the drug-related problems, are rarely noticed by pharmacists in the service at pharmacies and in hospitals.

The incidence of drug interactions based on the FDA is 3-5% of all drug problems in the hospital and is the cause of patients entering the emergency room. In Indonesia, the exact number of drug interactions has not been obtained because the assessment of prescriptions by pharmacists has not been carried out thoroughly, including aspects of drug interactions. Apart from these reasons, doctors' knowledge about drug interactions is still limited, and documentation of drug interactions has not been optimal.

Drug interactions can increase the effectiveness of drugs but can cause side effects or toxicity [2]. One of the drug interactions that provides benefits is antihypertensive (captopril) and diuretic (furosemide) which can reduce and maintain the patient's blood pressure within the desired limit. The increased effect of the drug can improve or even cure the patient's illness. The combination of isoniazid with vitamins and carbidopa with levodopa is an example of a drug interaction that minimizes drug side effects [3]. The disadvantages of drug interactions include reduced effects and toxicity, which can cause death. The decrease in effect can be caused by tetracyclines with antacids, forming complex compounds that are difficult to absorb. An example of a drug interaction that can increase toxicity is that the combination of furosemide and gentamicin has a higher ototoxic potential than when used alone [4]. Based on 1 systematic review, 3 research articles and 17 case reports, it is stated that the interaction of methotrexate and sulfamethoxazole-trimethoprim could be life-threatening [5]. If the pharmacist does not identify the disadvantages of drug interactions it will affect the patient's recovery and can affect patient compliance. To prevent such a thing from happening, it is necessary to identify, prevent, and provide solutions if there is a drug interaction and counseling the patient about the drug interactions that are obtained.

This study aimed to identify potential drug-drug interactions of serious and significant severity. We hope that the data from this study will be useful in considering modifications in prescribing patterns and optimizing drug therapy in patients.

2. METHOD

The study was conducted using a prospective cohort method. Patients included in the study were pneumonia patients who were hospitalized at the Surabaya Teaching Hospital, who meet the inclusion criteria. The inclusion criteria were patients diagnosed with pneumonia who were outpatient at the Teaching Hospital and received at least 2 drugs. This research has been declared ethical by the ethical committee of the Surabaya teaching hospital (RSPAL) with a number B/ND-83/IV/2019.

The tool used was a data collection form. Data collected was based on patient medical records, including patient

identity, diagnosis, medical history, clinical data, laboratory data, therapy, dose, frequency, assessment with patients, discussions with doctors and nurses. Drug interactions were identified using Stockley's Drug Interaction and Medscape Drug Interaction Checker.

Data analysis was carried out descriptively and presented in table.

3. RESULTS AND DISCUSSION

There were 54 dyslipidemia outpatient prescriptions in the study. Consisting of 67% male patients, and the last was female. Patient ages ranged from 26 to more than 65 years old, and the highest was 46-65 years (63%). The three most common comorbidity in this study were Hypertensive Heart Disease (HHD) (31%), Congestive Heart Disease (CHD) (19%), and Hypertension (14%). The demography was shown in Table 1.

The analysis showed that more than three-quarters of the outpatient prescriptions for dyslipidemia had potential drug interactions (78%). The highest number of potential drug interactions on an outpatient prescription for dyslipidemia is 2 interactions (18), followed by 1 interaction (12), 3 interactions (8), 4 interactions (3), and finally 6 interactions (2), which are listed in the Table. 2. This indicates that one patient can experience more than one potential drug interaction. Therefore, a pharmacist's role is needed to monitor patients so as to prevent or minimize adverse effects and drug interactions.

Table 1. Patient demography

	n (%)
Gender - Man - Woman	 67% 33%
Age - 26-35 years - 36-45 years - 46-65 years - >65 years	 4% 19% 63% 14%
Comorbid - HHD - CHD - Hypertension	 31% 19% 14%
Medicine - Bisoprolol - ASA - Amlodipine - Candesartan	 18% 16% 13% 8%

The severity of drug interactions assessed in this study was only drug interactions that had clinical effects (moderate, major, and contraindicated). In this study, no drug interactions were found with the severity of contraindications. The severity of potential drug interactions found was moderate 73 (74%) and followed by serious 25 (26%). The results of this study were supported by research carried out by 100 patients with moderate potential drug interactions (69.75%) [4].

Table 2. Number of Interactions

Number of DDI in every patients	N (%)
None	22
1	22
2	33
3	15
4	5
6	3

In addition, drug interaction studies conducted in Saudi Arabia hospital also showed drug interactions with moderate severity predominate with their respective incidence 55% [5]. In contrast to the results of research on 96 Acute Lymphoblastic Leukemia (ALL) patients, it showed that severe drug interactions occupy the first position (60%) [6].

The drug interaction mechanisms found in this study were Pharmacodynamics (57), Pharmacokinetics (34%), and unknown mechanisms (9%). The pharmacokinetic interaction mechanism is divided into absorption, distribution, metabolism, and excretion phase.

Table 3. Serious Potential Drug-Drug Interactions

Drugs	Mechanism DDIs	Effects
Amlodipin Simvastatin	PK	Potential for risk of rhabdomyolysis.Limit simvastatin dose to no more than 20 mg/day.
Nifedipin Simvastatin	PK	Increase level of simvastatin
Aspirin ACEI	PD	ASA reduces synthesis of vasodilating renal prostaglandin
Diltiazem Simvastatin	PK	Increase the level of simvastatin. Limit dose of simvastatin (no more than 20 mg/day) and diltiazem (No more than 240 mg/day)
Diltiazem Bisoprolol	PD	Increase risk of bradycardia

Drug interactions with serious severity need regular monitoring. Substitution of drugs to other drugs can also be done to prevent the adverse effects of drug interactions. In the absence of other alternative drugs, patients need to be counseled regarding signs of adverse effects from drug interactions. Thus, there are no unexpected effects that can worsen the patient's condition.

Potential drug-drug interactions can be caused by 2 things. First, as the prescribing writer, the doctor does not understand whether there is an interaction between the prescribed drugs. Second, pharmacists have not carried out their responsibility in screening drug interactions for each prescription, which is a clinical pharmacy service by Minister of Health regulations No. 35 of 2014. Pharmacists are responsible for administering the right, effective, and safe drugs for patients. If pharmacists perform tasks in clinical pharmacy services, the pharmacist can find drug-related problems (DRP), prevent and solve them. Therefore, pharmacists should do clinical pharmacy services in their practice.

This study has several limitations; for example, the data collection of this study was carried out in a short time. Therefore, the number of samples is limited. Further research needs to be cobducted regarding the pharmacokinetic relationship with the unwanted effects of drugs from drug interactions

4. CONCLUSION

Based on the results of this study, drug interactions that occurred in prescribing dyslipidemia outpatients obtained drug interactions (78%) with the moderate (74%) and the serious (26%). Therefore, the role of pharmacists in providing clinical pharmacy services is necessary to prevent the adverse effects of potential drug interactions.

AUTHORS CONTRIBUTIONS

All authors have made substantial contributions to the conception, design, collecting, analysis, and interpretation data. The first author has been involved in drafting and revising the manuscript.

ACKNOWLEDGMENTS

Our gratitude goes to the Pharmacy Study Program, Faculty of Medicine and Research Institute of Hang Tuah University, for the support provided in this research.

REFERENCES

[1] Baxter I.A., Davis M., Driver S.,& Garner R. 2010. Stockley's Drug Interactions. 9th ed. Pharmaceutical Press, London.

[2] Cipolle, R., Strand, L., & Peter, M., 1998, *Pharmaceutical Care* (Edisi Kedua ed.), Pharmaceutical Care, New York.

[3] Ritter, Lionel Lewis, Timothy Mant, Albert Ferro. Edition 5th Edition. First Published 2008. eBook Published 25 April 2008. Pub. location London.

[4] Widyaningrum, R., & Mutmainah, N., 2016, Identifikasi Potensi Interaksi Obat Pada Pasien Rawat Inap Penyakit Dalam di RSUD dr. Moewardi, Universitas Muhammadiyah, Surakarta.

[5] Murtaza, G., Yasie, M., Khan, G., & Azhar, S, 2016, March, Assessment of potential drug-drug interactions and its associated factors in the hospitalized cardiac patients, *Saudi Pharmaceutrical Journal, 24*, 220- 5.

[6] Fitriani, S. W., Mutiara, R., Malik, A., & Andriastuti, M., 2016, Agustus 2, Angka Kejadian Dan Faktor Yang Memengaruhi Potensi Interaksi Obat Dengan Obat Pada Pasien Leukemia Akut Anak Yang Menjalani Rawat Inap, *Sari Pediatri*, 129-36.