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Research Article

A Study of Potential Drug-Drug Interactions in Peptic Ulcer Patients in Dr. M. Djamil Hospital Padang in 2019

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ABSTRACT

A peptic ulcer is a gastrointestinal tract disorder caused by excessive secretion of acid and pepsin by the gastric mucosa. The combined use of drugs in peptic ulcer management may potentially cause drug-to-drug interactions. Drug interactions are caused when two or more drugs interact and may affect the effectiveness of the other drugs. This study aims to analyze the potential drug reactions in peptic ulcer patients in the internal medicine ward of Dr. M. Djamil General Hospital Padang in 2019. This study was a descriptive, non-experimental study with retrospective data, while data analysis used Drugs.com and Medscape applications. The study results revealed that 29 patients fit the inclusion criteria and 5 (16.6%) potential drug pharmacokinetic interactions. The severity of drug interactions shows 4 cases (80%) with moderate severity potential and 1 case (20%) with minor severity potential. The study concluded that there were potential drug interactions in peptic ulcer patients in the internal medicine ward of Dr. M. Djamil General Hospital Padang in 2019.

INTRODUCTION

Peptic ulcers are acid-induced gastrointestinal tract lesions commonly located in the stomach or proximal duodenum and are characterized by a denuded mucosa with defects extending to the submucosa or muscularis propria. (Narayan et al., 2018). Every year, 4 million people suffer from peptic ulcers worldwide; about 10%–20% of complications occur, and 2%–14% have perforated peptic ulcers. Peptic ulcer perforation is relatively small but can be life-threatening, with a mortality rate ranging from 10% to 40% (Saverio et al., 2014). Based on the Indonesian Health Profile in 2011, peptic ulcers are one of the 10 most common diseases in hospitalized patients in Indonesia, with a total of 30,154 cases (4.9%). (RI, 2013). Data retrieved from the West Sumatra Provincial Health Office show that peptic ulcers ranked 3rd out of the 10 most common diseases in West Sumatra in 2014, which amounted to 86,874 cases (10.94%). (Sumbar, 2016)

Traditionally, mucosal disruption in patients with acid peptic disease is considered a result of a hypersecretory acidic environment, together with dietary factors or stress. Risk factors for developing peptic ulcers include H. pylori infection, alcohol and tobacco consumption, non-steroidal anti-inflammatory drug (NSAID) use, and Zollinger-Ellison syndrome (Søreide et al., 2015). The main risk factors for gastric and duodenal ulcers are H. pylori infection and NSAID use (Zhang et al., 2014). However, only a small proportion of people with H. pylori or using NSAIDs develop peptic ulcer disease, meaning that individual susceptibility is important at the beginning of mucosal damage. Functional polymorphisms in different cytokine genes are associated with peptic ulcers. For example, polymorphisms of interleukin 1 beta (IL1B) affect mucosal interleukin 1β production, causing H. pylori-associated gastroduodenal diseases (Datta-De, 2015).

Pectic ulcer drugs are often used in combination since there are some factors that cause gastric ulcers, the use of single therapy does not provide a satisfactory therapeutic effect, or there is a need for other therapies to treat the disease suffered by the patient other than peptic ulcer disease. The problem of drug interactions in hospitalized patients should get serious attention since it can increase toxicity or reduce the effectiveness of the drug. Astiti (2017) found that 58.3% of hospitalized patients had adverse side effects caused by drug interactions (Saula, 2019). Information about drug interactions will help health workers identify and prevent unwanted reactions from drug use and improve patient safety.

Moreover, Sari (2012) found nine cases of drug interactions out of a total of 47 peptic ulcer inpatients at Dr. Soebandi General Hospital in January. The interactions found were between antacids and lansoprazole in 6 patients and between sucralfate and lansoprazole in 3 patients. Meanwhile, Prakoso (2015) found data in a hospital in Surakarta regarding drug interactions in pharmacokinetic mechanisms with an incidence of 32 cases, or 48.5%, while the drug interactions in pharmacodynamic mechanisms were 34 cases, or 51.5%. With these previous studies in mind, this study aims to analyze the potential for drug interactions in peptic ulcer patients in the internal medicine ward of Dr. M. Djamil General Hospital Padang in 2019.

METHODS

Manuscripts Type and Design of the Study

This is a non-experimental descriptive study where data was collected retrospectively and samples were gathered using the total sampling method. The data used was patient medical records diagnosed with peptic ulcers at Dr. M. Djamil General Hospital Padang in 2019. This study received ethical clearance from the medical research ethics committee at Dr. M. Djamil General Hospital Padang, Number 224/KEPK/2020, and approval from the President and Director of Dr. M. Djamil General Hospital Padang.

Materials and Instruments of the Study

The materials used in the study were inpatient medical records diagnosed with peptic ulcers in the internal medicine ward of Dr. M. Djamil Padang General Hospital in 2019. Data collection used tables containing patient demographics, length of stay, and the drug therapies they received.

Population and Sample of the Study

The population in this study was all patients diagnosed with peptic ulcers and inpatients in the internal medicine ward of Dr. M. Djamil General Hospital Padang in 2019. The samples in the study were members of the population that fulfilled the inclusion criteria, including patients aged 18 and above, diagnosed with a peptic ulcer with or without comorbidities, receiving a minimum of two items of medication, and inpatients in the internal medicine ward of Dr. M. Djamil General Hospital Padang in 2019.

Data Analysis

The data was analyzed by observing the potential for drug interactions using the applications Drugs.com and Medscape.com. Data for potential drug interactions were analyzed descriptively and grouped based on the drug interaction that occurred as well as the level of severity.

RESULTS AND DISCUSSION

This study was conducted to discover the potential for drug interactions in peptic ulcer patients in the internal medicine ward of Dr. M. Djamil General Hospital, Padang. The study was conducted from March 16th, 2020, to February 9th, 2021. The study population was peptic ulcer patients, namely 29 patients fulfilling the inclusion criteria. Criteria for inclusion included qualified medical record data, meaning that the patient's medical record was thoroughly written. All patients diagnosed with a peptic ulcer with or without comorbidities were aged 18 years and older. The data collected were presented in Table 1.

Table 1 shows most of the peptic ulcer patients were aged between 51 and 70 years old, namely 25 patients (86.21%). Older people are more likely to suffer from peptic ulcers because the gastric mucosa tends to grow thinner as patients grow older, making it more susceptible to infections (Lombeng, 2013). In the older age group, peptic ulcers are assumed to be a result of long-term NSAID (non-steroid anti-inflammatory drug) use as a single drug or a combined regimen to manage various degenerative diseases. However, this was not the only cause identified. The presence of comorbidities (such as coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease, kidney failure, hypertension, and congestive heart failure) and the administration of combined therapies for the diseases may also cause peptic ulcers.

Table 1. General Patient Characteristics

Characteristic	Patients: n (%)
Sex	
Male	17 (58.6)
Female	12(41.8)
Age	
18-30 years old	1 (3.45)
31-50 years old	3 (10.34)
51-70 years old	25 (86.21)
Number of drugs per patient	
2-5	14 (48.27)
6-10	10 (34.48)
>10	5 (17.24)
Number of comorbidities	
Without comorbid	2 (6.89)
With comorbid	27 (93.10)
Length of stay	
1-5 days	8 (27.58)
6-10 days	5 (17.24)
> 10 days	16 (55.17)
Total	29 (100)

Diabetic gastroparesis is the most common symptom associated with vegetative neuropathy in the gastrointestinal tract in diabetic patients. It is a disease that results in delayed gastric emptying in the absence of any identifiable factor that blocks the passage of food into the duodenum. An additional element that controls the activity of the digestive tract is the endocrine system (i.e., gastrin and secretin). A state of hyperglycemia will inhibit gastric emptying, hypoglycemia will have the opposite effect, food from the stomach will eventually be absorbed, and glycemia will increase (Kuźnik et al., 2020).

In addition, other factors like the reduced function of the gastric mucosa and duodenum's protective layer from aging processes caused by reduced blood flow to the mucosa, the secretion of gastric protective layers, bicarbonate secretion, or mucosal cell proliferation are significant risk factors (Gokakin, 2016).

In terms of the patient's sex, peptic ulcers are more commonly found in males. Lee & Tung (2016) stated the identified peptic ulcer patient distribution showed higher numbers in males, i.e., 75%, compared to only 24.1% in females. Likely, this study shows the same result, where 17 patients (58.6%) were males compared to 12 female patients (41.8%). One theory that may explain why male patients more commonly suffer from a peptic ulcer is due to several behaviors and lifestyles, such as smoking and alcohol consumption, that cause peptic ulcers. Smoking may cause gastroduodenal reflux and inhibit bicarbonate secretion from the pancreas, causing mucosal damage in the stomach. Meanwhile, alcohol may damage the gastric mucosa by changing the permeability of the epithelial barrier, allowing reverse diffusion, especially in the bloodstream (Strate, 2016).

Table 2 shows the most commonly administered peptic ulcer drug was sucralfate, administered to 23 patients (4.81%). Sucralfate works by releasing the aluminum hydroxide pole that binds with the positive pole of protein molecules, creating a physicochemical layer on the base of the ulcer and protecting the ulcer from the effects of acid and pepsin. Furthermore, its effects include helping prostaglandin synthesis, increasing bicarbonate and mucosal secretion, and improving mucosal defense and repair capabilities (Setiawati, 2015).

Drug interaction mechanisms include pharmaceutic interactions, pharmacokinetic interactions, and pharmacodynamic interactions (Table 3). Pharmaceutical interactions or incompatibilities happen outside of the body before the drug is administered, and they happen between drugs that cannot be mixed (incompatible). The mixing of these drugs is because of direct physical or chemical interaction, with results that may be visible as sedimentations, color changes, or visually invisible results. This interaction usually inactivates the drugs (Stockley, 2008).

Pharmacokinetic interactions affect drug processes that are absorbed, distributed, metabolized, and excreted, commonly known as the ADME (absorption, distribution, metabolism, and excretion) process. The absorption process involves the gastrointestinal tract; distribution involves the shifting of plasma protein bonds; metabolism includes interactions in the form of metabolic inhibitions, metabolism induction, and hepatic blood flow; and excretion is a drug interaction mechanism that happens during the excretion process through the gall bladder and in the enterohepatic circulation, the kidney's tubular secretions, and the urine pH (Palleria et al., 2013).

Pharmacodynamic interactions are interactions where the effects of one drug are altered by another drug at its site of action. Sometimes, the drugs directly compete with certain receptors, but the reactions often happen indirectly and involve physiological mechanisms. This interaction can also be described as an interaction between drugs that work in the same receptor system, site of action, or physiologic system, resulting in an additive,

synergistic, or antagonistic effect without a change in drug levels in the plasma (Palleria et al., 2013).

The study results show there was one patient with potential drug interaction in pharmacokinetics in the absorption stage. This potential drug interaction happened between sucralfate suspension and lansoprazole (patient no. 9). In the study, the patient was administered both drugs at the same time, at 7 in the morning, both given orally. Administration of sucralfate with lansoprazole may reduce the effects of lansoprazole. Simultaneous administration of lansoprazole with sucralfate may delay absorption and reduce the bioavailability of lansoprazole by as much as 30% (Drugs.com). Lansoprazole should be administered before meals and at least one hour before or after the administration of sucralfate (Drugs.com; Sulochana et al., 2016).

Table 2. Number based on the patient's peptic ulcer medication

No	Peptic ulcer medication is used.	Number of patients	Percentage (%)
1	Lansoprazole inj	20	36.36
2	Lansoprazole	2	3.63
3	Omeprazole inj	6	10.90
4	Sucralfate susp	23	41.81
5	Ranitidine inj	4	7.3
	Total	55	100

Table 3. Number of drug interactions based on pharmacokinetics and pharmacodynamics

No	Drug Interaction	Type of Interaction	Severity	Number of Cases
1.	Lansoprazole and Sucralfate	Pharmacokinetics: Sucralfate can decrease the absorption and effect of the drug lansoprazole. Lansoprazole should be given at least 1 hour before or after sucralfate (drugs.com).	Moderate	1
2.	Sucralfate and Bicnate	Pharmacokinetics: Taking sucralfate together with bicnate may decrease the effect of sucralfate. Sucralfate and bicnate doses should be separated by at least half an hour. (drugs.com)	Moderate	2
3.	Sucralfate and bisoprolol	Sucralfate can decrease the absorption and therapeutic effect of bisoprolol. Concomitant administration of sucralfate may decrease the oral bioavailability of bisoprolol (drugs.com).	Minor	1
4.	Sucralfate and ciprofloxacin	Ciprofloxacin and sucralfate should not be taken together. Products containing magnesium, aluminum, calcium, iron, other minerals can interfere with the absorption of ciprofloxacin into the blood and reduce its effectiveness (drugs.com).	Moderate	1

Table 4. Number of Peptic Ulcer Patients Based on Severity of Drug Interactions

Level of Severity	Number of Potential Cases with Severity	Percentage (%)
Moderate	4	80
Minor	1	20
Total	5	100

In addition, another patient experienced potential drug interaction in pharmacokinetics in the absorption stage (patient no. 14). In the study, the patient was administered sucralfate suspension along with ciprofloxacin at the same time, at 7 in the morning, with both drugs given orally and on the same day. Ciprofloxacin and sucralfate cannot be administered simultaneously. Products that contain magnesium, aluminum, calcium, iron, and other minerals may disturb and reduce the absorption of the antibiotic ciprofloxacin through the digestive tract. Absorption may also be reduced with the use of sucralfate, which contains aluminum and polyvalent cations, forming complexes that are hard to absorb in the gastrointestinal tract. The bioavailability of ciprofloxacin is reduced by up to 90% when administered with drugs containing aluminum or magnesium hydroxide (Drugs.com; Sulochana et al., 2016).

Potential for drug interaction also happened in patient no. 14. The patient was administered sucralfate suspension along with bisoprolol at the same time at 7 in the morning, both orally and on the same date. Sucralfate may reduce the absorption and therapeutic effects of bisoprolol. Simultaneous administration of both drugs may also reduce the oral bioavailability of bisoprolol (Drugs.com; Sulochana et al., 2016).

Two patients experienced potential drug interactions in pharmacokinetics with the administration of sucralfate suspension and bicnate, namely patients no. 18 and 22. In patient no. 18, sucralfate and bicnate were both administered at the same time, at 2 in the afternoon and 10 at night, both orally and on the same date. While in patient no. 22, they were administered at the same time: 7 in the morning, 2 in the afternoon, and 10 at night, both orally and on the same date. Simultaneous administration of sucralfate and bicnate may cause the binding of the mucus-rich bicnate ion and provide buffer effects in the mucosal areas (Nadia et al., 2018). Therefore, the use of sucralfate and bicnate together may reduce the effects of sucralfate. Administration of sucralfate and bicnate should be separated at least half an hour apart (Drugs.com; Sulochana et al., 2016).

Based on severity, drug interactions are grouped into minor, moderate, and major severity. Minor severities are when the effects are normally light; the consequences may bother or are not too apparent and do not affect therapeutic results significantly. Additional medications are usually not necessary. Moderate severities are when the occurring effects may cause worsening in the patient's clinical status. Additional medications, inpatient care, or a longer stay in the hospital may be necessary. Major severities are when there is a high probability, it is life-threatening, or it may cause permanent damage (Serefko et al., 2020).

There is one potential drug interaction with minor severity in the interaction between bisoprolol and sucralfate, which makes up 20%. As a preventive measure, the use of beta-blockers (bisoprolol) with drugs that contain magnesium or aluminum should be done a minimum of 2 hours apart (Drugs.com; Medscape.com).

Table 4 shows four moderate potential drug interactions. One case was between lansoprazole and sucralfate, making up 20%. Lansoprazole should be administered at least an hour before or after the administration of sucralfate (Drugs.com). There were two potential drug interactions between bicnate and sucralfate, making up 40%. Sucralfate and bicnate dosages should be separated at least half an hour apart (Drugs.com; Medscape.com).

Aside from the aforementioned cases, there was also one case of potential drug interaction between sucralfate and ciprofloxacin (20%). Ciprofloxacin dosages should be administered 2 to 4 hours before or 4 to 6 hours after the administration of sucralfate to minimize the potential for interaction (Drugs.com; Medscape.com).

CONCLUSIONS

In conclusion, this study found potential for drug interactions in peptic ulcer patients in the internal medicine ward of Dr. M. Djamil General Hospital Padang in 2019. Five cases for potential drug interaction in pharmacokinetics were found (16.6%). Four cases had moderate

severity (80%), and one case had minor severity (20%).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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