Description of Urea and Creatinine Levels in Dyspepsia Patients Taking Proton Pump Inhibitor Drugs at the Indonesian Christian University Hospital in 2018

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ABSTRACT

Dyspepsia is a health problem often encountered by doctors in daily practice. Many people complain of symptoms of dyspepsia but do not seek help for treatment. Proton pump inhibitors are the drugs for the treatment of dyspepsia, such as omeprazol, lansoprazol, esomeprazol, rabeprazol, and pantoprazol. Some studies have explained that proton pump inhibitor drugs can interfere with kidney function due to acute interstitial nephritis due to the consumption of proton pump inhibitors, and this condition can end with chronic kidney disease that occurs due to undiagnosed acute interstitial nephritis. This study aimed to see how urea and creatinine levels in dyspepsia patients at Universitas Kristen Indonesia Hospital were taking proton pump inhibitors. This research is a descriptive research content analysis, hospital-based. Based on medical records at Universitas Kristen Indonesia Hospital in 2018, 80.3% high ureum levels and 19.7% normal ureum levels were found. In creatinine levels, it was found that men had more normal creatinine levels of 57.7% and high ureum levels of 42.3%, and women found more normal creatinine levels of 62.5% and high creatinine levels of 37.5%.

Keywords: Dyspepsia, Proton Pump Inhibitor, Creatinine, Ureum

INTRODUCTION

Dyspepsia is a health problem most often encountered by doctors in daily practice. It is estimated that 60% of cases in gastroenterology practice are dyspepsia, and around 30% are encountered in general practice. In Western countries, the prevalence rate is around 7 - 41%, but only 10 - 20% seek help. The prevalence of dyspepsia worldwide is estimated at 11 – 29% of the total population in the world. [1] According to research by Jones et al. using endoscopy and barium enema in one-fifth of 9936 subjects, the prevalence of functional dyspepsia was around 23.8%; previous research by Jones and Lydeard in 20% of 2066 adults estimated that 11.5% experienced functional dyspepsia. [2] In the prospective Domestic International Gastro Enterology Surveillance Study (DIGEST), a survey of more than 5500 people showed that around one in three people interviewed had symptoms of dyspepsia, including acute dyspepsia in 6.5% and chronic dyspepsia in 22.5% of cases. [3]

In Iceland, in a population study over ten years from 1996 to 2006, there was an increase from 13.9% to 16.7%. In Norway, 14% of 2027 adults experienced dyspepsia after being

screened, while in Japan, there was a 17% prevalence of functional dyspepsia in a gastric cancer screening program. Asia itself shows that the prevalence of dyspepsia is quite high, namely in Hong Kong, where as much as 43% of 1,353 patients, Malaysia 62% of 210 patients, China 69% of 782 patients, and Korea 70% of 476 patients were examined. [4] In 2004, dyspepsia was ranked 15th on the list of 50 diseases with the most hospitalized patients in Indonesia, with a proportion of 1.3%. According to the 2007 Indonesian Health Profile data, dyspepsia was ranked 10th in the disease category, with the most inpatients in hospitals in 2006, with 34,029 patients or around 1.59%. 4.5 In 2010, the prevalence of dyspepsia patients at Cipto Hospital Mangunkusumo was 4.7%. [5]

Dyspepsia is used when the patient feels symptoms in the epigastrium and surrounding areas. Dyspepsia can be divided into two: organic and functional dyspepsia. Functional dyspepsia is used when the patient has had several examinations, including endoscopy, but there are no other abnormalities. Causes of organic dyspepsia include peptic ulcers, gastroesophageal reflux disease, stomach cancer, pancreatic disorders, drug and food intolerance, and infection. Symptoms of dyspepsia include feeling full, uncomfortable, feeling full quickly, heartburn, nausea and vomiting. [6; 7] If the symptoms are mild and rare, dyspepsia can be treated by changing lifestyle by reducing the consumption of fatty, spicy foods, caffeine, alcohol, and chocolate. Sleeping at least seven hours every night can also overcome dyspepsia. The doctor will prescribe antacids, H-2 receptor antagonists, and proton pump inhibitors in severe and persistent cases. Proton pump inhibitors are very effective for some people with gastroesophageal reflux disease (GERD). Proton pump inhibitors reduce stomach acid production and are stronger than the -H-2 receptor antagonist group. [8]

PPIs are drugs that are often used for diseases related to stomach acid because PPIs can reduce stomach acid production by blocking H+/K+ATPase. [9] PPIs are stronger stomach acid inhibitors than H2 antagonists. There are many types of PPI drugs, such as Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, and Rabeprazole. [10] According to research, the proportion of PPI use is 79%, but the indications are incorrect as much as 45%. [11] PPIs are among the most frequently used medications in the United States, and between 25% and 75% of PPI prescriptions do not correspond to the indication for treatment. Since the introduction of PPI drugs on the United States market in 1990, several studies have shown that PPIs can cause several health problems such as hip fractures, Clostridium difficile infection, acute interstitial nephritis (AIN), acute kidney injury (AKI). PPIs are a risk factor for chronic kidney disease (CKD) due to recurrent acute kidney disease or hypomagnesium. [12] The combination of PPIs and antiplatelets can even increase the risk of cardiovascular disease. In a prospective cohort study consisting of 10,000 adults, it was found that PPI use was associated with a 20-50% higher risk of chronic kidney failure, and PPI was a risk factor for acute kidney injury (AKI) and chronic kidney disease (CKD). [13] Several studies also state that there is an increased risk of acute kidney injury (AKI), chronic kidney disease (CKD), and end-stage renal disease (ESRD) in PPI users. [14]

Therefore, researchers wanted to know the description of urea and creatinine in dyspepsia patients who took proton pump inhibitor drugs at the Indonesian Christian University Hospital. By paying attention to the background of the problem above, the research problem can be formulated in the form of a research question, namely: description of urea and creatinine levels in dyspepsia patients who took proton pump inhibitors at the Indonesian Christian University Hospital in 2018. The

research aims to determine the description of urea and creatinine levels in dyspepsia patients who took proton pump inhibitors at the Indonesian Christian University Hospital in 2018.

LITERATURE REVIEW

Dyspepsia comes from the Greek words meaning "duis" (difficult) and "peptin" (to digest). Dyspepsia, usually called indigestion, is a condition with discomfort in the upper stomach. Dyspepsia usually refers to symptoms such as bloating, discomfort, nausea, and belching. Dyspepsia is similar to indigestion and is not a disease; dyspepsia is a collection of symptoms that cause discomfort in the stomach. [15] Dyspepsia is a common complaint a person can experience at certain times. Dyspepsia complaints are a clinical condition that is often encountered in daily practice. [16]

Dyspepsia can be divided into [17]: a) Organic dyspepsia, caused by erosive esophagitis, gastric erosion, acute or chronic gastritis, gastric ulcer, duodenal ulcer, duodenitis, malignancy (carcinoma, lipoma). Organic dyspepsia can be proven by upper gastrointestinal endoscopy. It can be suspected if several symptoms occur, such as anemia, bleeding, loss of appetite, or several symptoms at night. Functional or non-ulcer dyspepsia is a patient who experiences excessive anxiety due to an illness such as cancer. There were no organic lesions on examination; b) Dyspepsia due to drugs, such as aspirin, nonsteroidal anti-inflammatory drugs, antibiotics, bisphosphonates, estrogens, steroids, digoxin, chloroquine, iron, etc.; and c) Dyspepsia due to diseases outside the digestive tract such as diabetes mellitus, hypothyroidism, hyperthyroidism, Addison's disease.

An individual's lifestyle and food usually cause dyspepsia. Usually, it can also be related to infection or other digestive disorders. Some causes of dyspepsia are usually eating too much or too fast, consuming fatty and spicy foods, drinking too much alcohol and caffeine, consuming too much chocolate and soda, gastritis, obesity, nervousness, peptic ulcers, smoking, consuming drugs such as antibiotics and NSAIDs, cancer stomach.

Acid secretion is important in identifying the cause of dyspepsia, such as duodenal ulcers and gastroesophageal reflux disease (GERD). Impaired digestive motility is also associated with the pathogenesis of dyspepsia, but its role is still doubtful. In patients with dyspepsia who do not change after therapy, there is strong evidence of a relationship between stress, dysfunctional gastrointestinal tract, mucosal lesions, and other symptoms. Helicobacter pylori infection can also play a role in the occurrence of dyspepsia. [18]

Although functional dyspepsia does not affect a person's length of life, it does affect their quality of life. Functional dyspepsia is a heterogeneous disorder, and a variety of mechanisms cause its symptoms. [19] Factors such as impaired gastric motility, Helicobacter pylori infection, stomach acid, visceral hypersensitivity, and psychological factors can cause functional dyspepsia. Other factors that can play a role are lifestyle, environment, diet, and history of previous digestive infections.

Symptoms that usually appear in dyspepsia include nausea, pain, bloating, and feeling full in the stomach. In some instances, digestive tract disorders can point to a diagnosis of gastric cancer. A person should go to the doctor when there is loss of appetite, vomiting, breathing pain, shortness of breath, and pain radiating to the neck. Heartburn and dyspepsia must be differentiated even though they sometimes occur simultaneously. Heartburn is a symptom of acid reflux, usually felt as heat in the chest after eating. [20] Dyspeptic symptoms can increase with increasing stress. Symptoms of dyspepsia are divided into reflux-type (retrosternal burning, regurgitation), ulcer-type (epigastric pain on empty stomach relief with bland food, antacids or acid-suppressing drugs), dysmotility-type

(postprandial fullness, distension, early satiety, nausea).

The Asia-Pacific Consensus (2012) followed the Rome III concept diagnosis with additional symptoms such as upper abdominal bloating, usually found in functional dyspepsia. Based on the Rome III criteria, dyspepsia is a disease with one or more accompanying symptoms with gastroduodenal disorders [21]: a) Epigastric pain; b) Burning sensation in the epigastrium; c) The stomach feels full and uncomfortable after eating; and d) Feel full quickly.

These symptoms must be present at least in the last three months, with onset six months before the diagnosis. Rome III divided functional dyspepsia into two subgroups, namely epigastric pain syndrome and postprandial distress syndrome. Evaluation of alarm signs must also be carried out in patients with complaints of dyspepsia. Alarm signs for dyspepsia include weight loss, progressive dysphagia, repeated vomiting, digestive tract bleeding, anemia, fever, mass in the upper abdomen, family history of stomach cancer, and dyspepsia with new onset in patients aged 45 years and over. Patients with the above symptoms should be investigated with endoscopy. [21]

When lesions are found on the mucosa and have been investigated by endoscopy, therapy is given based on the abnormalities found. Abnormalities include gastritis, duodenitis, gastric ulcers, bleeding, or malignant processes. In peptic ulcers, the therapy that can be used is a combination of PPI, rabeprazole 2 x 20 mg or lansoprazole 2 x 30 mg, and mucosal protection, such as rebamipide 3 x 100 mg. [21]

When no lesions are found on the mucosa after investigation, treatment can be given in the presence of functional dyspepsia. Prokinetics such as metoclopramide, domperidone, cisapride, itopride, and others can improve the symptoms of functional dyspepsia. This drug can be associated with slow gastric emptying, one of theophysiologies of functional dyspepsia. Special caution should always be exercised when using cisapride, as cardiovascular complications may occur. Data regarding the use of antidepressants or anti-anxiolytics in patients is still too little. [21]

The proton pump inhibitor class is a drug that inhibits acid secretion most effectively. PPI drugs are stomach acid-blocking drugs that are stronger than H2 antagonists. Some of the proton pump inhibitors available for clinical use are omeprazole, esomeprazole, lansoprazole, rabeprazole, and pantoprazole. Omeprazole is the most frequently used drug because it is cheap. [22] The difference between these five drugs is the substitution in the pyridine or benzimidazole ring. PPI drugs work by inhibiting enzymes that work to carry out the process of releasing stomach acid. Treatment of excessive gastric acid secretion by PPIs has been shown to mask Helicobacter pylori infection, which is the main cause of chronic gastritis and peptic ulcer disease.

Proton pump inhibitors are prodrugs that require acid to become the active form. After passing through the stomach and entering the alkaline intestinal lumen, the enteric coating will dissolve and be absorbed into the systemic circulation. This prodrug will diffuse into the gastric parietal cells and accumulate in the canaliculi. Then, the drug precursor will be converted into a thiophilic sulfonamide cation, which will react with $H+/K+ATPase$ and inactivate it irreversibly. [23]

Proton Pump Inhibitors are given preferably one hour before meals so that peak levels can be reached during the maximum proton pump activity. Tablets that break in the stomach undergo activation and then bind to various sulphihydryl groups of mucus and food so that their bioavailability decreases by up to 50%. PPIs should be administered in enteric-coated form to prevent degradation of the active substance in an acidic environment. [24] Administration of proton pump inhibitors when given with other acid-blocking drugs can

reduce their effectiveness. Proton pump inhibitors have a short half-life, but the duration of their inhibition against acid can last up to 24 hours due to irreversible pump inactivation. To form a new proton pump, synthesis takes around 18 hours; therefore, this drug is enough to be given once a day. Not all pumps are deactivated at the first dose of therapy, so administration of this drug takes approximately 3-5 days to achieve maximum acid resistance. Proton pump inhibitors are rapidly absorbed, have high protein binding, and are metabolized by the enzymes CYP2C19 and CYP3A4. [25]

Indications for administering proton pump inhibitor drugs include GERD, peptic ulcers, non-ulcer dyspepsia, prevention of stress-related mucosal bleeding, gastritis, and other hypersecretory conditions. [26] The Food and Drug Association (FDA) approves IV administration only for GERD complicated by severe erosive esophagitis (oral intolerance) and Zollinger-Ellison syndrome. Another condition for IV administration is the prevention of recurrent peptic ulcer bleeding after endoscopy, massive bleeding that requires immediate endoscopic action. JSS College of Pharmacy added another indication, namely patients with an indication for proton pump inhibitors but who cannot receive oral treatment. According to the American Society of Health-System Pharmacists guidelines, prevention of stress-related mucosal bleeding can be administered IV if the criteria for one absolute indication or two or more relative indications are met. The absolute indications are coagulopathy (total platelets <50,000 mm3/International Normalization Ratio (INR) >1.5/ Partial Thromboplastin (PT) > 2x control) and the use of a mechanical ventilator. Relative indications are sepsis, invisible bleeding, use of high doses of corticosteroids, use of NSAIDs for more than three months, enteral nutrition, use of anticoagulants, kidney failure, and liver failure.

The side effects that most often occur due to the consumption of PPIs include headaches, diarrhea, constipation, abdominal pain, flatulence, fever, vomiting, flushing, and nausea. Diarrhea, headache, and abdominal pain have been reported in 1-5% of patients. Deficiency of certain nutrients such as vitamin B12, iron, zinc, and calcium can occur with long-term use because acid plays an important role in releasing these substances from food so that they are easily absorbed. [27]

Several studies have shown that long-term use of PPIs can develop gastric atrophy, where changes occur in the structure of the gastric mucosa. The use of PPIs in patients infected with Helicobacter pylori is more susceptible to changes in the gastric mucosa and can increase gastric cell proliferation. [28]

Long-term use of PPIs is also associated with widespread complications such as small intestinal bacterial overgrowth (SIBO), enterochromaffin-like cell hyperplasia, and gastrin-cell tumors. However, atrophic gastritis is a risk factor for gastric cancer, where PPIs can cause atrophic gastritis. PPI use is also associated with a higher risk of hypo magnesium, Clostridium difficile infection, hip and back fractures, and the development of dementia. [29]

PPIs were first recognized as a cause of acute interstitial nephritis (AIN) in 1992. In research, it was found that PPI drugs can increase the risk of AIN in older people (>60 years). In research comparing PPI drugs and H2 antagonists, it was found that PPI drug users had a greater risk of increasing creatinine levels. There is a relationship between long-term use of PPI drugs and CKD. The increased risk of CKD is usually due to undiagnosed and resulting AIN arising from PPI use. AIN can be caused by the use of PPIs, which can cause tubulointerstitial inflammation and progress to chronic interstitial fibrosis.

The ureum is the final product of catabolism from proteins and amino acids produced by the liver and distributed through intracellular and

extracellular fluids in the blood. The ureum will then be filtrated by the glomerulus, where urea examination can help confirm the diagnosis of acute renal failure. Serum urea can be used to see or evaluate kidney function hydration status, assess nitrogen balance, assess the progression of kidney disease, and assess hemodialysis results. [28]

Several methods have been developed to measure serum urea levels, and the most frequently used is the enzymatic method. The enzymatic method measures ammonium ions, where these ions are the result of urea hydrolysis by the urease enzyme. Increased urea in the blood is called azotemia. Meanwhile, the condition of kidney failure, which is characterized by high plasma urea levels, is called uremia.

Creatinine results from the breakdown of muscle creatinine phosphate, produced by the body constantly depending on muscle mass. Creatinine levels are related to muscle mass, describing changes in creatinine and kidney function. Diet does not affect creatinine levels, so these levels are relatively stable. The National Kidney Disease Education Program recommends using serum creatinine to measure glomerular filtration ability, which can serve to monitor the course of kidney disease. [30]

RESEARCH METHOD

This research is a descriptive content analysis, hospital-based research. This research was conducted at the Indonesian Christian University Hospital on Jalan Mayor Jendral Sutoyo No. 3, Kramatjati, Cawang, East Jakarta. This research was carried out for five months, from August 2018 to October 2019, by taking medical record data from January 2018 to December 2018. The population of this study was all patients diagnosed with dyspepsia and taking proton pump inhibitors at RSU UKI in 2018. This study's sample is all populations included in the inclusion and exclusion criteria. The sampling technique in

this study used total sampling by taking all medical record data that met the inclusion criteria and were not included in the exclusion criteria. The instrument in this study was medical record data from patients diagnosed with dyspepsia who were given PPI and had urea, and creatinine checked at RSU UKI for the period January 2018 – December 2018 and Statistical Product and Service Solutions software version 2. Data analysis in this study used univariate descriptive analysis to find out the description of urea and creatinine in dyspepsia patients taking proton pump inhibitors using Statistical Product and Service Solutions (SPSS) software version 2.4 by presenting numerically (in table form) the number of cases of dyspepsia patients at RSU UKI.

RESULT AND DISCUSSION

Table 1. Distribution of Dyspepsia Patients Taking Proton Pump Inhibitors Based on Gender

Gender	N	%
Male	26	39,4
Female	40	60,6
Total	66	100,0

Based on Table IV.1, in 2018, the patients who experienced more dyspepsia were 40 female patients (60.6%) and 26 male patients (39.4%).

Table 2. Distribution of Dyspepsia Patients Taking Proton Pump Inhibitors Based on Age

Age	N	%
16 – 30	8	12,1
31 – 45	13	19,7
46 – 60	23	34,8
61 – 75	21	31,8
76 – 90	1	1,5
Total	66	100,0

Based on Table IV.2, the age group that experienced the most dyspepsia was 46 – 60, with as many as 23 patients (34.8%). Then, in patients with a range of 61 – 75 years, there were 21 patients (31.8%); in patients with a range of 31 – 45 years, there were 13 patients (19.7%); in patients with a range of 16 – 30 years there were eight people (12.1%), and the

smallest were patients in the range 76 – 90 years as many as one patient (1.5%).

Table 3. Distribution of Dyspepsia Patients Taking Proton Pump Inhibitors Based on Creatinine Levels

Creatinine Levels	N	%
Male		
Low (<0,7 mg/dL)	0	0,0
Normal (0,7 – 1,3 mg/dL)	15	57,7
High (>1,3 mg/dL)	11	42,3
Total	26	100
Female		
Low (<0,6 mg/dL)	0	0,0
Normal (0,6 – 1,1 mg/dL)	25	62,5
High (>1,1 mg/dL)	15	37,5
Total	40	100

Based on Table IV.3, creatinine levels are differentiated based on male and female groups because of the differences in the normal range of creatinine levels in men and women. In men, creatinine levels were highest, with normal creatinine levels in 15 patients (57.7%), then high creatinine levels in 11 patients (42.3%), and no male patients had low creatinine levels (0%). In women, creatinine levels were highest, with normal creatinine levels in 25 patients (62.5%), then high creatinine levels in 15 patients (37.5%), and no female patients had low creatinine levels (0%).

Table 4. Distribution of Dyspepsia Patients Taking Proton Pump Inhibitors Based on Urea Levels

Urea Levels	N	%
Low (<7 mg/dL)	0	0,0
Normal (7 – 20 mg/dL)	13	19,7
High (>7 mg/dL)	53	80,3
Total	66	100,0

Based on Table IV.4, urea levels in dyspepsia patients were the highest, with 53 patients (80.3%) having high urea levels, 13 patients (19.7%) having normal urea levels, and no patients having low urea levels (0%).

Table 5. Distribution of Dyspepsia Patients Taking Proton Pump Inhibitors Based on the Type of Proton Pump Inhibitor Drug Consumed

Proton Pump Inhibitor	N	%
Lansoprazole	13	19,7
Omeprazole	53	80,3
Total	66	100,0

Based on Table 3, the proton pump inhibitor class of drugs consumed by dyspepsia patients was omeprazole, namely 53 patients (80.3%), and lansoprazole, 13 patients (19.7%).

This study looked at the picture of urea and creatinine in dyspepsia patients who took proton pump inhibitors at the Indonesian Christian University Hospital in 2018. At the Indonesian Christian University Hospital, it was found that the number of dyspepsia patients who took proton pump inhibitors was 66 people.

From this research, data on the gender of the patients who experienced dyspepsia were mostly 40 women (60.6%) compared to 26 men (39.4%). It is following research conducted by Hannisa (2016) at RSUD. Dr. Moewardi said that dyspepsia sufferers often occur in 40 women (55.56%) and 32 male patients (39.3%). It also follows research conducted by Grazyna Piotrowicz et al. (2013), where the results were 140 women (60.9%) and 90 men (39.1%). The high number of dyspepsia patients in women is due to the influence of depression and stress experienced. Stress will cause anxiety related to lifestyle, which can result in physiological changes in the body. Depression can cause acetylcholine to increase, resulting in a hypersympathotonic gastrointestinal system, which triggers increased gastric acid secretion. The diet that women usually follow can also cause irregular eating patterns, resulting in dyspepsia. [31]

The age most commonly found in dyspepsia patients taking proton pump inhibitors at the Indonesian Christian University Hospital in 2018 was in the range of 46 – 60 years with 23 patients (34.8%). It is following research conducted by Grazyna Piotrowich et al. (2013), where it was found that patients aged 46 - 60 years experienced the most dyspepsia, while patients aged 76 - 90 years were the age range where the fewest patients experienced dyspepsia and following The results obtained at the Indonesian Christian University Hospital showed that patients with an age range of 76 - 90 years were the age range that experienced

the least dyspepsia. It can be caused by increasing age, which increases the risk of experiencing dyspepsia.

In dyspepsia patients at the Indonesian Christian University Hospital who took proton pump inhibitors, it was found that most patients had normal creatinine levels, 15 people (57.7%) in men and 25 people in women (62.5%). It is not following research conducted by Xie et al., where the study compared users of proton pump inhibitor drugs with H2 blockers. The results of the research found that users of proton pump inhibitor drugs were at higher risk of having twice the amount of creatinine. In proton pump inhibitor users, the risk of experiencing kidney damage increases significantly with long-term use of proton pump inhibitor drugs.

The urea levels of dyspepsia patients at the Indonesian Christian University Hospital who took proton pump inhibitors in 2018 had the highest urea levels, 53 people (80.3%). It is following research conducted by Xie et al. that the use of proton pump inhibitor drugs can increase the risk of kidney problems. It is also following research conducted by Dennis et al. that there is a relationship between the use of proton pump inhibitors and the incidence of chronic kidney failure. The incidence of chronic renal failure increases in patients with acute interstitial nephritis and acute renal failure who take proton pump inhibitor drugs. This study argues that the increase in chronic renal failure is due to undiagnosed and untreated acute interstitial nephritis, which causes inflammation in the tubulointerstitial area and progressively results in chronic interstitial fibrosis.

The Indonesian Christian University Hospital results showed that the most frequently used proton pump inhibitor drug was omeprazole, namely 53 people (80.3%). It is following research conducted by Hannisa (2016) at RSUD. Dr. Moerwadi stated that the most frequently used proton pump inhibitor drug class was omeprazole by 65 people (27.90%).

It is also by research conducted by Rinza (2016), which states that the most frequently used proton pump inhibitor drug is omeprazole. Omeprazole can block the action of the H+K+ATPase enzyme, which breaks down H+K+ATPase to produce energy, which is used to remove HCl from parietal cells to the gastric lumen cells. [32] Proton pump inhibitor drugs are most widely used in patients with gastritis and dyspepsia because this class of drugs is indicated for long-term therapy for GERD and short-term therapy for patients experiencing gastrointestinal symptoms. Apart from that, proton pump inhibitor drugs are also used as prophylaxis (prevention) in patients suffering from other diseases. Proton pump inhibitor drugs are the first line of therapy for patients diagnosed with gastrointestinal disorders.

CONCLUSION

Based on the results of research and discussion regarding the description of urea and creatinine in dyspepsia patients at the Indonesian Christian University Hospital in 2018 with 66 populations and samples, conclusions can be drawn: a) Dyspepsia patients who consumed PPIs based on gender at the Indonesian Christian University Hospital in 2018 more in women as many as 40 people (60.6%) and men as many as 26 people (39.4%); b) Dyspepsia patients who consumed PPIs at the Indonesian Christian University Hospital in 2018 based on age, namely in the age range 46 – 60 years, were 23 people (34.8%) followed by those in the age range 61 – 75 years, 21 people (31.8%), the age range 31 – 45 years was 13 people (19.7%), the age range 16 – 30 years was eight people (12.1%) and the smallest was in the age range 76 – 90 years as many as one people (1.5%). Dyspepsia patients who took PPIs at the Indonesian Christian University Hospital in 2018 were more men who had normal creatinine levels, 15 people (57.7%) followed by high creatinine levels, 11 people (42.3%). In women, creatinine levels were

higher than normal in 25 people (62.5%), followed by high creatinine levels in 15 people (37.5%). In 2018, the highest urea levels in dyspepsia patients who took PPIs at the Indonesian Christian University Hospital were high in 53 people (80.3%), followed by normal urea levels in 13 people (19.7%). PPI drugs used in dyspepsia patients at the Indonesian Christian University Hospital mostly used omeprazole for as many as 53 people (80.3%), followed by lansoprazole for as many as 13 people (19.7%). Thus: a) Further research is needed to be related to the use of PPI drugs and dyspepsia; b) So that the Christian University Hospital complete existing medical record data so that it can be facilitated by researchers and reduce existing bias; c) The Indonesian Christian University Hospital has data on a computer to make it easier to research large amounts of data, and d) Indonesian Christian University Hospital provides more time to check data in the medical records room.

REFERENCES

1. Black CJ, Houghton LA, Ford AC. Insights into the evaluation and management of dyspepsia: recent developments and new guidelines. Therapeutic advances in gastroenterology. 2018 Oct; 11:1756284818805597.
2. Sari A, Anggaraini RS, Prasetyo RB. Upaya Pencegahan Dispepsia Menggunakan Bahan Alami sebagai Obat Herbal serta Kegiatan Penanaman Toga (Tanaman Obat Keluarga) Kota Batam 2022. PUNDIMAS: Publikasi Kegiatan Abdimas. 2022 Jan 22;1(1):29-36.
3. Vanheel H, Tack J. Therapeutic options for functional dyspepsia. Digestive Diseases. 2014 Apr 1;32(3):230-4.
4. Sari A, Anggaraini RS, Prasetyo RB. Upaya Pencegahan Dispepsia Menggunakan Bahan Alami sebagai Obat Herbal serta Kegiatan Penanaman Toga (Tanaman Obat Keluarga) Kota Batam 2022. PUNDIMAS: Publikasi Kegiatan Abdimas. 2022 Jan 22;1(1):29-36.
5. Sulistiyo MD, Dayawati RN, Pahirawan PM. Iridology-based dyspepsia early detection using linear discriminant analysis and Cascade Correlation Neural Network. In2014 2nd International Conference on Information and Communication Technology (ICoICT) 2014 May 28 (pp. 139-144). IEEE.
6. Ford AC, Mahadeva S, Carbone MF, Lacy BE, Talley NJ. Functional dyspepsia. The Lancet. 2020 Nov 21;396(10263):1689-702.
7. Wee EW. Evidence-based approach to dyspepsia: from Helicobacter pylori to functional disease. Postgraduate Medicine. 2013 Jul 1;125(4):169-80.
8. Azzam RS. Are the persistent symptoms to proton pump inhibitor therapy due to refractory gastroesophageal reflux disease or to other disorders? Arquivos de gastroenterologia. 2018 Oct 4;55:85-91.
9. Kakar MU, Saeed M, Luo K, Suheryani I, Shuang W, Deng Y, Dai R. Phytochemistry and medicinal values of Mahonia bealei: A review. Tropical Journal of Pharmaceutical Research. 2019;18(10):2219-27.
10. Abed MN, Alassaf FA, Jasim MH, Alfahad M, Qazzaz ME. Comparison of antioxidant effects of the proton pump-inhibiting drugs omeprazole, esomeprazole, lansoprazole, pantoprazole, and rabeprazole. Pharmacology. 2020 Nov 17;105(11-12):645-51.
11. Savarino V, Marabotto E, Zentilin P, Furnari M, Bodini G, De Maria C, Pellegatta G, Coppo C, Savarino E. Proton pump inhibitors: use and misuse in the clinical setting. Expert review of clinical pharmacology. 2018 Nov 2;11(11):1123-34.
12. Fusaro M, Giannini S, Gallieni M. Adverse effects of proton pump inhibitors in chronic kidney disease. JAMA internal medicine. 2016 Jun 1;176(6):866-.
13. Khan SU, Lone AN, Asad ZU, Rahman H, Khan MS, Saleem MA, Arshad A, Nawaz N, Sattur S, Kaluski E. Meta-analysis of efficacy and safety of proton pump inhibitors with dual antiplatelet therapy for coronary artery disease. Cardiovascular Revascularization Medicine. 2019 Dec 1;20(12):1125-33.
14. Hart E, Dunn TE, Feuerstein S, Jacobs DM. Proton pump inhibitors and risk of acute and chronic kidney disease: a retrospective cohort study. Pharmacotherapy: The Journal of Human

Pharmacology and Drug Therapy. 2019 Apr;39(4):443-53.

15. Mishra A, Kesherwani R, Tiwari AK, Patel DK. Dyspepsia-A Gastrointestinal Problem: A Review.

16. Siregar GA, Halim S. Correlation between Severity of Dyspepsia and Helicobacter pylori Infection. The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy. 2014 Apr 30;15(1):3-8.

17. Overland MK. Dyspepsia. Medical Clinics. 2014 May 1;98(3):549-64.

18. Enck P, Azpiroz F, Boeckxstaens G, Elsenbruch S, Feinle-Bisset C, Holtmann G, Lackner JM, Ronkainen J, Schemann M, Stengel A, Tack J. Functional dyspepsia. Nature Reviews Disease Primers. 2017 Nov 3;3(1):1-20.

19. Vanheel H, Farré R. Changes in gastrointestinal tract function and structure in functional dyspepsia. Nature reviews Gastroenterology & hepatology. 2013 Mar;10(3):142-9.

20. Vandenplas Y, Kindt S. Gastroesophageal reflux. Textbook of Pediatric Gastroenterology, Hepatology and Nutrition: A Comprehensive Guide to Practice. 2022:125-55.

21. Syam AF, Simadibrata M, Makmun D, Abdullah M, Fauzi A, Renaldi K, Maulahela H, Utari AP. National consensus on management of dyspepsia and Helicobacter pylori infection. Acta Medica Indonesiana. 2017 Nov 2;49(3):279.

22. Aguilera-Castro L, Martín-de-Argila-dePrados C, Albillos-Martínez A. Practical considerations in the management of proton-pump inhibitors. Rev Esp Enferm Dig. 2016 Mar 1;108(3):145-53.

23. Srebro J, Brniak W, Mendyk A. Formulation of dosage forms with proton pump inhibitors: state of the art, challenges and future perspectives. Pharmaceutics. 2022 Sep 25;14(10):2043.

24. Srebro J, Brniak W, Mendyk A. Formulation of dosage forms with proton pump inhibitors: state of the art, challenges and future perspectives. Pharmaceutics. 2022 Sep 25;14(10):2043.

25. El Rouby N, Lima JJ, Johnson JA. Proton pump inhibitors: from CYP2C19 pharmacogenetics to precision medicine. Expert opinion on drug metabolism & toxicology. 2018 Apr 3;14(4):447-60.

26. Savarino V, Tosetti C, Benedetto E, Compare D, Nardone G. Appropriateness in prescribing PPIs: a position paper of the Italian Society of Gastroenterology (SIGE)—study section "digestive diseases in primary care". Digestive and Liver Disease. 2018 Sep 1;50(9):894-902.

27. Awuchi CG, Igwe VS, Amagwula IO. Nutritional diseases and nutrient toxicities: A systematic review of the diets and nutrition for prevention and treatment. International Journal of Advanced Academic Research. 2020;6(1):1-46.

28. Smolka AJ, Schubert ML. Helicobacter pylori-induced changes in gastric acid secretion and upper gastrointestinal disease. Molecular pathogenesis and signal transduction by helicobacter pylori. 2017:227-52.

29. Savarino E, Marabotto E, Zentilin P, Furnari M, Bodini G, Pellegatta G, Lorenzon G, Della Coletta M, Ghisa M, Coppo C, Marinelli C. A safety review of proton pump inhibitors to treat acid-related digestive diseases. Expert Opinion on Drug Safety. 2018 Aug 3;17(8):785-94.

30. Qaseem A, Hopkins Jr RH, Sweet DE, Starkey M, Shekelle P. Screening, monitoring, and treatment of stage 1 to 3 chronic kidney disease: a clinical practice guideline from the American College of Physicians. Annals of internal medicine. 2013 Dec 17;159(12):835-47.

31. Amerikanou C, Kleftaki SA, Valsamidou E, Chroni E, Biagki T, Sigala D, Koutoulogenis K, Anapliotis P, Gioxari A, Kaliora AC. Food, Dietary Patterns, or Is Eating Behavior to Blame? Analyzing the Nutritional Aspects of Functional Dyspepsia. Nutrients. 2023 Mar 22;15(6):1544.

32. Prasetyaningtias D. Tingkat pengetahuan istilah-istilah dan informasi dalam kemasan obat yang digunakan untuk Swamedikasi Penyakit Maag terhadap mahasiswa Universitas Islam Negeri Maulana Malik Ibrahim Malang (Doctoral dissertation, Universitas Islam Negeri Maulana Malik Ibrahim).

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