

# Appropriate Use of Proton Pump Inhibitor in Inpatients of Central Army Gatot Soebroto Hospital

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## ABSTRACT

**Background:** Evaluation of the use of Proton Pump Inhibitors (PPIs) perceiving the high use of PPIs and likely impacts from inappropriate use of PPPs. The aim of this study was to evaluate the use of PPI on in-patients at Gatot Soebroto Army Center Hospital. **Material and Methods:** the study design was observational analytic descriptive with prospective data collection method base on prescription and medical record. The sample was data of entire adult in-patients with Indonesian National Health Insurance who used PPI at Internal Diseases Department. PPI use was evaluated based on rationality and therapy effectiveness. **Results:** Analysis carried out on 153 PPIs therapy of 91 in-patients. The percentages of PPIs therapies with appropriate indication was 77.78%, appropriate drug selection was 77.78%, appropriate patient condition was 98.69%, appropriate dose was 4.58%, appropriate therapy duration was 66.01% and therapy effectiveness was 86.27%. Only 3.92% PPIs therapies were rational regarding all the appropriate criteria fulfillment. **Conclusion:** Monitoring and

evaluation of PPIs use should be done for attaining properly outcome..

**Key words:** Proton Pump Inhibitor, Appropriateness, In-patient, Indonesian National Health Insurance.

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## INTRODUCTION

Proton pump inhibitors (PPIs) have been among the most widely sold drugs worldwide because of their outstanding efficacy and safety.<sup>1</sup> In 2008, PPIs ranked the third highest-selling drug in the United States.<sup>2</sup> Esomeprazole and pantoprazole were ranked the third and fifth most prescribed drugs in Australia in 2012–2013.<sup>3</sup> Certain clinical studies stated that PPIs are safe and well tolerated if taken correctly.<sup>4</sup>

Recent studies showed some concerns about long-term PPI consumption, including PPI-clopidogrel drug interaction; the possibility of PPIs reducing calcium absorption and vitamin B12, magnesium, and iron levels; long-term acid suppression leading to the development of atrophic gastritis which could be a cancer precursor; PPI being associated with infection risks (pneumonia, *Clostridium difficile*); and PPIs increasing the risk of bone fractures.<sup>2</sup> Because of the negative effect of incorrect usage and overdose of PPIs, it is very important for physicians to only prescribe these drugs when needed.<sup>4</sup> One study in Indonesia showed that there were 55.33% correct diagnoses and treatment effectiveness was 92.38%.<sup>5</sup>

According to Cipolle, Strand, and Morley (1998), the pharmacist has a responsibility in achieving effective treatment. On the basis of pharmaceutical care concepts, pharmacists have responsibilities in identifying, solving, and preventing problems regarding drugs; ensuring the patients get appropriate treatment that is effective and safe and can reach the expected results; and ensuring the purpose of the treatment and optimum outcome is achieved.<sup>6</sup>

Gatot Soebroto Army Center Hospital (GSACH) is a public hospital with 687 beds which is gastrointestinal disorder with the possibility of a high rate of PPI consumption. The purpose of this study was to evaluate the appropriateness and effectiveness of PPI therapy at the GSACH.

## METHOD

This was a descriptive observational study with prospective data collection. Data were prescriptions and medical records of adult inpatients at the Internal Disease Ward of GSACH Only patients who were covered by National Health Insurance from February to April 2016 were assessed. The appropriateness of indication, drug selection, dose, and duration of therapy was assessed according to the literature.<sup>7,8,9,10</sup> The effectiveness of the therapy was assessed according to the patients' complaints.

## RESULTS AND DISCUSSION

We collected 153 PPI usage data of 91 patients. The prevalence of PPI usage in patients was higher among women at 58.24%. The highest PPI consumption was found in the 46–65-year-old age group at 39.56%, while the average age was 48.1 years old. These results were similar to those of the Center for Drug Evaluation and Research at the U.S. Food and Drug Administration (FDA) published in 2010, which showed that PPI was consumed by 57.7%<sup>9</sup> women, while the Muya study showed that 64.3% women consumed PPI.<sup>10</sup> The characteristic of patients which were use PPIs were shown at Table 1.

Only two PPIs were prescribed, namely omeprazole and lansoprazole; the majority used omeprazole (99.35%), which was mostly administered parenterally (67.97%). These results were similar to a study at a hospital in Australia, where omeprazole was prescribed 40.2% of the time, while lansoprazole was only 7%.<sup>11</sup> Other types of PPIs (rabeprazole, pantoprazole, and esomeprazole) did not show up, because only omeprazole and lansoprazole were listed under National Formulary. PPI treatment was given mostly as intravenous preparations, because patients in this study were treated as inpatients; hence, it was more appropriate to be given intravenously. The description of PPI treatment was shown at Table 2.

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**Table 1: Characteristic of patients**

Characteristic	Total (N = 91)	Percentage (%)
<b>Gender</b>		
Woman	53	58,24
Man	38	41,76
<b>Age</b>		
17-25 years old	10	10,99
26-45 years old	28	30,77
46-65 years old	36	39,56
>65 years old	17	18,68
average: 48,1 years old		
<b>Main Diagnosis</b>		
DHF (dengue hemorrhagic fever)	19	20,88
Dyspepsia	10	10,99
GEA (acute gastroenteritis)	8	8,79
DM (diabetes mellitus)	6	6,59
Anemia	5	5,49
Tumor & cancer	5	5,49
Stroke	4	4,40
Gastritis	4	4,40
GERD (gastroesophageal reflux disease)	4	4,40
Ascites	3	3,30
Sepsis	3	3,30
CKD (chronic kidney disease)	3	3,30
Elektrolit imbalance & dehydration	3	3,30
Melena & hematemesis	2	2,20
Thrombocytopenia	2	2,20
Appendicitis	2	2,20
Cephalgia	1	1,10
Angioedema	1	1,10
AIDS	1	1,10
Hypoglycaemia	1	1,10
Cirrhosis	1	1,10
Typhoid fever	1	1,10
Colic abdomen	1	1,10
Hepatomegaly	1	1,10

**Table 2: Description of PPIs treatment**

PPI treatment	Total (N = 153)	Percentage (%)
<b>Types of PPI</b>		
Omeprazole	152	99,35
Lansoprazole	1	0,65
<b>Dosage</b>		
Omeprazole		
20 mg/day	7	4,58
40 mg/day	105	68,63
60 mg/day	1	0,65
80 mg/day	39	25,49
Lansoprazole		
60 mg/day	1	0,65
<b>Dose Regimen</b>		
Omeprazole		
1 x 20 mg	7	4,58
2 x 20 mg	40	26,14
3 x 20 mg	1	0,65
1 x 40 mg	65	42,68
2 x 40 mg	39	25,49
Lansoprazole		
2 x 30 mg	1	0,65
<b>Route of Administration</b>		
Omeprazole		
Intravena	104	67,79
Peroral	48	31,37
Lansoprazole		
60 mg/day	1	0,65
<b>Duration of Administration</b>		
Omeprazole		
1 x 20 mg <2 weeks	7	4,58
1 x 20 mg 2-4 weeks	0	0,00
1 x 20 mg >4 weeks	0	0,00
2 x 20 mg <2 weeks	38	14,84
2 x 20 mg 2-4 weeks	2	1,31
2 x 20 mg >4 weeks	0	0,00
3 x 20 mg <2 weeks	1	0,65
3 x 20 mg 2-4 weeks	0	0,00
3 x 20 mg >4 weeks	0	0,00
1 x 40 mg <2 weeks	60	39,22
1 x 40 mg 2-4 weeks	7	4,58
1 x 40 mg >4 weeks	0	0,00
2 x 40 mg <2 weeks	36	23,53
2 x 40 mg 2-4 weeks	1	0,65
2 x 40 mg >4 weeks	0	0,00
Lansoprazole		
2 x 30 mg <2 weeks	1	0,65
2 x 30 mg 2-4 weeks	0	0,00
2 x 30 mg >4 weeks	0	0,00

The highest prevalence of PPI usage was 68.63% for the dose of 40 mg/day for omeprazole. The highest percentage for PPI duration of administration was 39.22% for 1 x 40 mg omeprazole for more than 2 weeks of administration. In this study, 1 x 40 mg, 2 x 40 mg, and 2 x 20 mg omeprazole, as well as 2 x 30 mg lansoprazole, treatment was given for less than 2 weeks may be caused by the patient's complaint had been diminished or disappeared. Omeprazole 1 x 20 mg and 1 x 40 mg treatment given for 2-4 weeks was approved for dyspepsia treatment, according to DIH and IONI.<sup>12,13</sup>

A study in Canada was comparing the effectivity of lansoprazole and omeprazole in inhibiting acid secretion. This study concluded that lan-

soprazole 30 mg was more effective in increasing pH intra-gastric until more than 40 mg, compared with omeprazole 20 mg.<sup>14</sup> Another study that tested the antisecretion of gastric acid activity showed that lansoprazole did not exhibit any significant difference with omeprazole in potential and action duration terms.<sup>15</sup> Omeprazole was more prescribed than lansoprazole in this study, possibly because the former was cheaper.<sup>16</sup>

The prevalence of PPI usage with the appropriate indication was found in 77.78%. There were 25 cases with main diagnoses suitable for PPI indications, which were recommended by DIH and IONI, including 6 cases of GERD and 19 cases of dyspepsia. A previous study reported that most patients (38.1%) suffering from dyspepsia were patients in the 46–65 age group.<sup>10</sup> Krause (2002) stated that age was associated with dyspepsia, and that in advanced ages, 50% of dyspepsia incidence was caused by *H. pylori* infections and the remaining 50% was caused by the patient's lifestyle and food consumption.<sup>17</sup>

In this study, PPI consumption for DHF as the main diagnosis was 20.88%. This result was dissimilar to another study, in which GERD was found in first place with 73.2% and dyspepsia in sixth place with 2.1%.<sup>18</sup> The prevalence of DHF in this study was affected by high DHF cases during the study period. The clinical manifestations of DHF in the febrile period were nausea, vomiting, and stomachache.<sup>19</sup>

There were 34 cases with inappropriate diagnoses and without complaints that needed PPI treatment based on the information provided from medical records. In another study, 54% of patients were prescribed PPI for reasons other than the indications. According to the researchers, the misindication of PPIs could be caused by the recent guidelines and expert opinions about dyspepsia management and PPI usage, which was too stiff/restricting and not consistent with the patient's wishes and physician's experiences.<sup>20</sup> The use of PPI from the indications may cause denial of the actual indications and relevant duration of administration; hence, it is necessary to communicate appropriate PPI indications to the hospital team.<sup>21</sup> In this study, no patients were pregnant or breastfeeding; these women cannot consume omeprazole, which is a high-risk medicine for pregnant mothers and can be contained in breastmilk.<sup>12</sup>

The prevalence of PPI use with the appropriate patient assessment was found in 98.69%. However, 1.31% of PPI use was inappropriate with the patient's condition. There were two cases where the patients experienced hepatic cirrhosis, but PPIs in this case did not need to be changed or removed from treatment but only adjusted for appropriate dosage.<sup>22,23</sup>

The appropriate dose of PPI was found in 4.58%. In 106 cases with dyspepsia indication, PPI was prescribed in higher doses than the usual PPI dose for dyspepsia, which was 20 mg/day.<sup>12,13</sup> There were four cases of GERD indication, for which higher than the usual PPI dose (40 mg/day) was prescribed.<sup>12,13</sup> The overdose of PPI can lead to hypergastrinemia, since PPI works as a strong inhibitor of acid secretion. Patients who take PPI also have a risk of gastroenteritis caused by pathogenic microorganisms.<sup>4</sup> The higher dose of PPI can be prescribed for the following indications: maintenance dose for severe GERD; chronic cough related to GERD; empirical diagnosis and treatment for laryngopharyngeal reflux; PPI diagnostic test for uncomplicated GERD and non-cardiac chest pain; and the prevention of peptic ulcer rebleeding.<sup>24</sup>

In 34 cases, PPI was prescribed in an inappropriate dose related to unsuitable indications. According to DIH (Drug Information Handbook) and IONI, omeprazole in 40 mg/day dosage form can be given to treat gastric ulcer, duodenal ulcer, and peptic ulcer, while the usual dose of omeprazole to treat dyspepsia according to IONI is 20 mg/day.<sup>12,13</sup>

The prevalence of PPI usage in the appropriate duration of administration was found in 66.01%. The duration of PPI administration consumption for dyspepsia as recommended by DIH and IONI is 2–4 weeks.<sup>12,13</sup> There were two cases of dyspepsia with PPI prescriptions that met the

standard range. There were 93 cases of dyspepsia in which PPI was prescribed for less than 2 weeks. The duration of PPI administration for GERD as recommended by DIH and IONI is 4–8 weeks.<sup>12,13</sup> In all cases of GERD indication, PPI was prescribed for less than 4 weeks. In 34 cases, PPI was prescribed for an inappropriate duration because it was not suitable for the indications.

The effectiveness of PPI therapy was found in 135 cases (88.24%) based on decreasing complaints of nausea, vomiting, bloating, stomach ache, and heartburn. There were five cases of nausea after consuming PPIs, three cases of nausea and heartburn, and one case of nausea and vomiting. In one other case, the patient was still vomiting, and in four cases, patients were still complaining of bloated stomachs after PPI treatment.

## CONCLUSION

Monitoring and evaluating PPI use should be performed for attaining a proper outcome.

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## CONFLICT OF INTEREST

No conflict of interest are declared.

## ABBREVIATIONS USED

**PPI:** Proton Pump Inhibitor; **GSACH:** Gatot Soebroto Army Center Hospital; **FDA:** Food and Drug Administration; **GEA:** Gastro Enteritis Acute; **GERD:** Gastro Esophageal Reflux; **DM:** diabetes Mellitus; **CKG:** Chronic Kidney Disease; **DHF:** Dengue Haemorrhagic Fever.

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