Gastric pH Comparison between Mild and Severe Cirrhotic Portal Hypertensive Gastropathy

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ABSTRACT

Background: *One of the causes of upper gastrointestinal bleeding in patients with liver cirrhosis is the presence of portal hypertensive gastropathy (PHG). The prevalence of PHG in patients with liver cirrhosis is quite high but there is still inconsistency regarding the studies about gastric pH in cirrhosis patient. The aim of this study is to compare the gastric pH in mild and severe PHG due to liver cirrhosis.*

Method: *Cross sectional method with consecutive sampling was done to all liver cirrhotic patients who came to Clinic of Gastroenterology and Hepatology in Cipto Mangunkusumo hospital from March to May 2014. Sixty two patients with portal hypertensive gastropathy underwent endoscopy to measure the degree of gastropathy based on McCormack classification and the mean basal gastric pH using pH-metric.*

Results: *There are 50 (80.6%) male patients and 12 (19.4%) female patients participated in this study. Portal hypertensive gastropathy is mostly caused by hepatitis C (56.5%), hepatitis B (32.3%), non-hepatitis (8.1%) and alcohol (3.2%). The mean of gastric pH in all liver cirrhosis patients with portal hypertensive gastropathy was 2.13. The mean gastric pH in liver cirrhosis patient with mild portal hypertensive gastropathy (2.00 mEq/L) was lower than the gastric pH in severe portal hypertensive gastropathy (2.25 mEq/L) with significant differences ($p < 0.05$).*

Conclusion: *The gastric pH in liver cirrhosis patient between mild and severe portal hypertensive gastropathy are significantly different.*

Keywords: *gastric pH, liver cirrhosis, portal hypertensive gastropathy, pH-metric*

ABSTRAK

Latar belakang: *Salah satu penyebab perdarahan saluran cerna pada pasien dengan sirosis adalah adanya gastropati hipertensi portal. Prevalensi gastropati hipertensi portal pada pasien sirosis cukup tinggi tetapi masih terdapat inkonsistensi dalam studi mengenai pH lambung pada pasien sirosis. Tujuan penelitian ini adalah untuk membandingkan pH lambung pada gastropati hipertensi portal ringan dan berat akibat sirosis hati.*

Metode: *Penelitian ini menggunakan metode potong lintang dengan pengambilan sampel secara konsekutif terhadap semua pasien sirosis di poliklinik gastroenterologi dan hepatologi di Rumah Sakit Cipto Mangunkusumo pada Maret hingga Mei 2014. Enam puluh dua pasien dengan gastropati hipertensi portal menjalani endoskopi untuk mengukur derajat gastropati berdasarkan klasifikasi McCormack dan rerata pH lambung basal menggunakan pH meter.*

Hasil: *Terdapat 50 (80,6%) pasien laki-laki dan 12 (19,4%) pasien perempuan yang berpartisipasi dalam penelitian ini. Gastropati hipertensi portal sebagian besar disebabkan oleh hepatitis C (56,5%), hepatitis B (32,35), non-hepatitis (8,15), dan alkohol (3,2%). Rerata pH lambung pada pasien sirosis dengan gastropati hipertensi portal ringan (2,00 mEq/L) lebih rendah dibandingkan gastropati hipertensi portal berat (2,25 mEq/L) dengan perbedaan signifikan ($p<0,05$)*

***Simpulan*:** *Terdapat perbedaan yang bermakna antara pH lambung gastropati hipertensi portal ringan dan berat pada pasien sirosis.*

Kata kunci: *pH lambung, sirosis hati, gastropati hipertensi portal, pH meter*

INTRODUCTION

Upper gastrointestinal bleeding in patients with liver cirrhosis is caused by several factors such as peptic ulcer, esophageal varices, and the presence of portal hypertensive gastropathy (PHG).[1-3] Portal hypertensive gastropathy is a term used to describe endoscopic gastric mucosa characterized by mosaic-like pattern with or without red spots, which is most likely found in patients with cirrhotic or non-cirrhotic portal hypertension. The prevalence rate of PHG, was reported around 51-98%, with the prevalence of the severe PHG is about 9-46% and mild PHG is approximately 29-57%.[4] The incidence of acute bleeding due to PHG is extremely low and generally occurs in severe PHG, while the prevalence of chronic bleeding due to PHG is reported approximately 38%-62% (severe PHG), and 3.5-31% (mild PHG). Chen et al reported an increased prevalence of gastric ulcers in patients with portal hypertension in liver cirrhosis compared to the normal population, with the prevalence of 3.7-20%, similar to studies conducted in Japan and West countries.[1]

Recently, the use of proton pump inhibitor (PPI) is greatly increased. These drugs are a class of drugs that are highly effective in inhibiting gastric acid secretion, and their usage is increasing in diseases associated with gastric acid. This class of drugs also widely used in patients with cirrhosis of the liver, with the main objective to prevent complications of the peptic ulcer in patients with esophageal varices or in PHG patients treated with multiple drugs.[5] The report on the efficacy supporting the use of a proton pump inhibitor in patients with liver cirrhosis is scarce. Some studies reported that gastric acid secretion in patients with liver cirrhosis is decreased, while five other studies reported normal gastric acid secretion. Whereas in experiments using dogs reported an increased production of acid production in cholestasis, hepatocellular injury and collateral portal-systemic circulation.[6,7] These studies take measurements of gastric acid in the basal state or by stimulation of acid secretion.[5,6,7] Savarino et al conducted a study to evaluate the gastric acid in patients with liver cirrhosis for 24 hours and concluded that there is a significant reduction of gastric acidity in patients with liver cirrhosis than in control.[8] Acidity in the antrum was significantly lower than in the corpus at night, with no difference at any other time. Gastric acidity in patients with liver cirrhosis with PHG is not significantly different with patients without PHG.[8]

Due to inconsistency in studies related with gastric pH in patients with liver cirrhosis, while the use of proton pump inhibitors become routine in liver cirrhosis patients with or without PHG, it is necessary to conduct a study on gastric pH in patients with liver cirrhosis in relation with the degree of PHG. The aim of this study is to find the average gastric pH and the mean differences in patient with mild and severe PHG caused by liver cirrhosis. The hypothesis of this study is that the gastric pH in patient with mild PHG is lower than the gastric pH in patient with severe PHG.

METHOD

This is a cross-sectional study conducted in Cipto Mangunkusumo Hospital from March to May 2014. The general population in this study is all patient with PHG caused by liver cirrhosis. Expected population is all patient that visit Cipto Mangunkusumo Hospital as an outpatient or inward patients. The study participant was obtained from expected population consecutively.

Inclusion criteria for this study are liver cirrhosis patient age 18-75 years old, whose consent was taken for this study and through endoscopy. Exclusion criteria are patients with hepatic coma, malignancy, PHG caused by liver cirrhosis who consumes PPI less than a week or H2 receptor antagonist less than three days and/or antacid, comorbidities such as diabetes mellitus with uncontrolled blood sugar, severe infection, sepsis, kidney failure, consumption of histamine drug and uncooperative patient. Patients whose consent were taken, underwent endoscopy to assess the degree of PHG, and were measured with pH-metric. The acquired data were analyzed with SPSS 22.0. This study was already given ethical clearance from Ethical Committee from Faculty of Medicine, University of Indonesia.

RESULTS

Table 1. General characteristics of patients

Variable	n (%)
Age (mean)	53.39 ± 9.850
Sex	
Male	50 (80.6)
Female	12 (19.4)
Ethnic	
Javanese	21 (33.9)
Sundanesse	8 (12.9)
Betawi	16 (25.8)
Outside Javanese	17 (27.4)
Degree of PHG	
Severe	38 (61.3)
Mild	24 (38.7)
Caused of liver cirrhosis	
Hepatitis B	20 (32.3)
Hepatitis C	35 (56.5)
Non hepatitis	5 (8.1)
Alcohol	2 (3.2)
Child Pugh	
A	33 (53.2)
B	9 (14.5)
C	20 (32.3)

PHG: portal hypertensive gastropathy

There were 67 cirrhosis patients in the study period, with 3 patients were excluded due to hepatoma and ovarium tumor metastases and 2 patients refused in having gastric pH measurement due to unbearable feeling at insertion of the equipment through nose. The patients of this study is 62 (80.6%) with mostly male and age around 26-74 (mean = 53.39 ± 9.85).

Before being analyzed, the data was assessed their normality with Kolmogorov-Smirnov method. The data was normally distributed and therefore was analyzed with T-test independent to measure mean differences of gastric pH between mild PHG and severe PHG. The difference is shown as p = 0.035 as stated in Table 2.

Table 2. Mean differences of gastric pH between mild and severe PHG

Variable	PHG		p
	Severe	Mild	
pH	2.25 (mean = 0.55)	2.00 (mean = 0.37)	0.035

PHG: portal hypertensive gastropathy

DISCUSSION

The subject of this study was predominantly male (80.6%) with ratio between male and female is 4 :1. This ratio is higher than the general ratio in liver cirrhosis that is 1.3-4:1.[9,10] This difference is due to the subject of this study which is PHG patient caused by liver cirrhosis. Primary cause of liver cirrhosis in this study is hepatitis C (56.5%) and hepatitis B (32.3%). This result is concordance with primary cause of liver cirrhosis in Indonesia which dominated by hepatitis B and hepatitis C.[11]The same result also shown in United States that most cirrhosis caused by hepatitis C and non alcoholic steatohepatitis (NASH). In East countries and South East Asia, hepatitis B is endemic disease as well as in North Africa, Egypt, and Middle East Country. In Egypt, Sudan, South Africa and Sub Sahara, Caribbean and South America, schistosomiasis is also an important caused of liver cirrhosis.[11]

Most study assumed the degree of gastropathy is mostly correlated with the degree of Child Pugh score.[12] In this study, there is no significant differences in degree of PHG caused by cirrhosis based on the degree of Child Pugh (p = 0.114). This is caused by the amount of subject in this study that was inadequate to assess this differences. In addition, most subjects who had Child Pugh A also has severe PHG. Most subjects were consuming propranolol which can amend the degree of PHG. Corresponding with the randomized controlled study by Hosking et al in 24 patient with PHG with clinically esophageal varices and PHG who were diagnosed at least 6 weeks before the study, were given propranolol 160 mg once daily or placebo 6 weeks continuously, then crossover in 6 weeks to assess the reduction of bleeding, increasing hemoglobin and the changing in mucosal lesion after endoscopy compared to placebo, even when statistically not significant.[13]

Some scientific evidence also support the use of propranolol to prevent re-bleeding in patients with cirrhosis of the liver due to severe PHG. Random controlled studies in patients with acute and chronic bleeding due to PHG given propranolol (26 patients) and were not given any treatment is only given iron supplements if necessary (28 patients).The ultimate goal of the mentioned study was to assess the presence of re-bleeding of PHG due to cirrhosis, defined as: 1) the presence of acute upper gastrointestinal bleeding known from a decrease in hematocrit and a picture of the red spots on the gastric as the source of bleeding in emergency endoscopic examination performed in the first 12 hours; 2) the presence of chronic upper gastrointestinal bleeding defined by occult bleeding which need three or more packed red cell transfusion in three months or need ferron supplementation continuously. The study conclude that patient who administered propranolol was free from re-bleeding more than patient who given the placebo, whether acute bleeding (85% vs. 20%) or chronic bleeding (63%

vs. 40%) within 3 months, even though statistically insignificant.[14]

The mean gastric pH in normal population is less than 2 mEq/L. In this study, the mean gastric pH in all subjects is 2.13 mEq/L. Meanwhile, the mean gastric pH in mild PHG subjects is 2.00 ± 0.37 and mean gastric pH in severe PHG is 2.25 ± 0.55. These differences are statistically significant ($p = 0.035$). These results is accordance with report from Savarino et al who measured mean gastric pH within 24 hours and obtained gastric pH in liver cirrhosis patient with PHG 2.5 ± 1.1. This study proves that there is no statistically significant among patients with PHG and without PHG caused by liver cirrhosis.[8]

The mean gastric pH differences in mild and severe PHG subject in this study is statistically significant. This supporting evidence from Scobie et al obtained a decrease secretion in gastric acid among cirrhosis patient whether basal acid output or maximum acid output. This condition is correlated with increasing ulcer incident among liver cirrhosis and the role of acid-pepsin reflux in the mechanism of bleeding in esophageal varices.[15] By using spectrophotometry, a study described an insignificant decreased gastric mucosal perfusion in antrum among severe PHG patient compared to control and mild PHG patient, while there is significant decreased gastric mucosal perfusion in corpus in patient with severe PHG compared to mild and control.[16]

Another study described that straight arterial and dilatation found mainly in precapiller, capiller, and veins in submucosa and subserous in patients with liver cirrhosis. This morphology decrease arteriovenous gastric resistance among liver cirrhosis patient.[14] Aside from the mucosal damage and disturbance of microcirculation, Sarfeh et al also obtained significant reduction in gastric mucosal oxygenation in tested animal with portal hypertension. Gastric mucosal oxygenation is more reduced with aspirin and more susceptible to gastric damage. This proves that mucosal damage in portal hypertension was a consequence of oxygenation damage in gastric mucosa.[17]

Agnihotri et al concluded that there was significant reduction in the amount of parietal in mice with portal hypertension than in control. Elevation of gastric pH in liver cirrhosis with PHG shown that mucosal damage was not caused by aggressive factor, but it decreased the defensive gastric mucous due to disturbance of microcirculation gastric mucous, reducing oxygenation and blood stream to gastric mucous.[18]

Reduction of defensive factor which causes the gastric mucosa became very vulnerable to the damage is caused by aggressive factors such as bile acid, aspirin and alcohol. Some studies showed PHG is a risk factor for the occurrence of peptic ulcer. Until now there has been no clear pathogenesis of peptic ulcers in cirrhosis patients.[5]

This study shows that there are mean differences in gastric pH between mild to severe PHG patients that showed the damage to the gastric mucosa due to PHG is a major factor pH changes in patients with liver cirrhosis. Changes in gastric pH is very likely an attempt to protect from gastric mucosal damage due to various changes in the area of the gastric mucosa, so that the heavier PHG, gastric pH will increase, but this assumption must be proven by further study to assess the effectiveness of the increase in gastric pH in an effort to protect the gastric mucous.

This study used homogeneous sample of subjects with PHG due to liver cirrhosis that were categorized into mild and severe according to the McCormack criteria. In an effort to minimize the factors that may affect the results of measurements, the whole subject has been freed from PPI medications and drugs that are likely to affect the pH of the stomach. Meanwhile, to minimize bias against the degrees of PHG, the endoscopic procedure performed had to be confirmed by a consultant in charge in Digestive Endoscopy Center, Cipto Mangunkusumo Hospital. The study that distinguish the degree of PHG in liver cirrhosis have never been performed and the pathogenesis of gastric pH changes in patients with cirrhosis due PHG is still uncertain. Therefore, by assessing the mean gastric pH differences between mild and severe PHG due to cirrhosis, an insight of the pathogenesis of gastric pH changes in patients PHG due to liver cirrhosis would be uncovered. This study did not asses gastrin levels, which are the main role in the mechanism of gastric acid secretion due to the constraints on time and cost factors of this study.

CONCLUSION

The mean gastric pH in mild PHG patients due to liver cirrhosis is lower than the mean gastric pH in severe PHG patients due to liver cirrhosis. It is necessary to conduct further study on the effectiveness of the use of PPIs in liver cirrhosis patient with PHG in preventing peptic ulcer and upper gastrointestinal bleeding.

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