

Comparison of High Dose and Standard Dose Proton Pump Inhibitor before Endoscopy in Patients with Non-Portal Hypertension Bleeding

Attapon Rattanasupar MD*,
Siriwan Sengmanee MD**

* Division of Gastroenterology, Department of Internal Medicine, Hatyai Hospital, Songkhla, Thailand

** Department of Internal Medicine, Hatyai Hospital, Songkhla, Thailand

Background: Gastrointestinal bleeding with non-portal hypertension bleeding (non-PHT) is the most common cause of gastrointestinal emergencies with high mortality rate. The majority of non-PHT patient stem from acid related disease. The practice guideline recommends using pre-endoscopic proton pump inhibitors (PPIs). However, the dose and route of PPIs administration were still unclear according to the Association for Gastroenterology.

Objective: To compare the efficiency of PPIs between high dose and standard dose before endoscopy in patients suffering with gastrointestinal bleeding due to non-PHT.

Material and Method: The present study was designed as a prospective, randomized controlled trial. The patients were randomly categorized into two groups, the first group received intravenous pantoprazole 80 mg bolus then continuously drip 8 mg per hour (high dose group) and the other group received intravenous pantoprazole 40 mg twice daily before endoscopy (standard dose group). Baseline characteristics, Blatchford score, endoscopic findings, morbidity, and other complications were recorded.

Results: One hundred thirteen patients were recruited. Fifty-eight patients were in the high dose group and 55 patients in the standard dose group. Blatchford scores in the high dose group were slightly higher than the standard dose group but there was no statistically significant difference (12.49±3.29 and 12.38±4.06, respectively, $p = 0.876$). Twenty-two patients were high-risk for peptic ulcer bleeding from endoscopy. There were significantly less numbers of patient who were high-risk of peptic ulcer bleeding in the high dose group compared to the standard dose group (10 patients [17.24%] and 12 patients [21.82%], respectively, $p = 0.025$). There was no difference between the two groups in average time of hospital stay (3.03 and 2.89 days, respectively, $p > 0.05$), mean unit of blood transfusion (1.79 and 1.63 units, respectively, $p > 0.05$), and the complications after endoscopy such as recurrent bleeding (0 and 1 patient, respectively, $p > 0.05$), recurrent bleeding and death (0 and 1 patient, respectively, $p > 0.05$). The Blatchford score greater than 10, 11, and 12 showed high sensitivity of 100%, 95%, and 95% respectively with negative predictive values (NPV) of 100%, 97%, and 97% respectively, in predicting high-risk peptic ulcer bleeding.

Conclusion: The high dose of PPIs administration before endoscopy reduced the chance of high-risk peptic ulcer bleeding compared to the standard dose. Both high dose and standard dose of PPIs did not affect the time of hospital stay, unit of blood transfusion, the complications after endoscopy, and mortality rate. Standard dose PPIs can be considered using in patients with Blatchford scores lower than 10. High dose PPIs would be beneficial in patients who have Blatchford scores between 10 and 12. For patients who have Blatchford scores greater than 12, high dose PPIs are recommended.

Keywords: Peptic ulcer bleeding, Proton pump inhibitors before endoscopy, Blatchford score

J Med Assoc Thai 2016; 99 (9): 988-95

Full text. e-Journal: <http://www.jmatonline.com>

Gastrointestinal bleeding with non-portal hypertension (non-PHT) is the most common cause of gastrointestinal emergencies^(1,2). The mortality rate varies between 3.5 and 10⁽³⁻⁷⁾ from different studies. The majority of non-PHT bleeding stems from acid related disease and eventually the bleeding stops

spontaneously⁽⁸⁾. Approximately 25% of the patients may encounter recurrent gastric bleeding due to acidic condition.

An acidic condition will affect the coagulation of blood clotting and later leads to re-bleeding specifically due to thrombolysis, which induced by the enzyme pepsin^(9,10). As a consequence, the gastric mucosal barrier could be lost. Generally, pepsin is reduced significantly as gastric pH level is higher than 4.0 while the platelets aggregation is decreased when pH level is lower than 6.0⁽⁶⁾. Therefore, the reduction

Correspondence to:

Rattanasupar A, Division of Gastroenterology, Department of Medicine, Hat Yai Hospital, Songkhla 90110, Thailand.

Phone: +66-74-273261, Fax: +66-74-273264

E-mail: james_med22@yahoo.com

of acid level inside gastric environment results in neutral pH which probably disturbs blood clotting⁽⁹⁾. The previous studies found that the use of high dose pantoprazole, the intravenous 80 mg/hour bolus, then continuously intravenous drip 8 mg per hour can possibly increase the gastric acidity to be greater than 4.0 and 6.0 respectively when compared with the bolus injection in every 8 to 12 hours⁽¹¹⁾. Apart from the use of different proton pump inhibitors (PPIs) doses, placebo can also be introduced in the treatment. It was found that the stigmata of recent hemorrhage (SRH) at high-risk could also be reduced. The symptoms of SRH at high-risk can be detected as spurting or non-bleeding visible vessel (NBVV) or adherent clotting. The endoscopy and low rate of hemostasis during endoscopy have no effect on the risk of re-bleeding, surgery and death.

Practice guideline for using PPIs in patients with gastrointestinal bleeding with non-PHT is remained unclear. Some studies recommended using the high dose of PPIs with intravenous pantoprazole 80 mg bolus then continuously drip 8 mg per hour before the endoscopy in patients with suspected gastrointestinal bleeding with non-PHT in all cases⁽¹²⁾. However, in 2011 the guideline of the Asia-Pacific Working Group had consensus on the use of high dose PPIs before endoscopy only in non-variceal upper gastrointestinal bleeding patients. The guideline did not recommend using the high dose of PPIs before the endoscopy in all patients with suspected non-PHT bleeding⁽¹³⁾ because of high cost and limitation of supportive data.

Review of literatures revealed some studies had found that there was no significant difference between the use of the high dose PPIs and the standard dose PPIs after the endoscopy⁽¹⁴⁻¹⁶⁾. Unfortunately, there was insufficient study comparing high and standard dose of PPIs before the endoscopy. Some of the previous studies of the pre-endoscopic PPIs were mostly compared between the high dose of PPIs and placebo.

The present study focused on the efficacy of applying the high and standard doses of PPIs before the endoscopy. The patients with gastrointestinal bleeding due to non-PHT were received high dose PPIs with intravenous Pantoprazole 80 mg bolus then continuously drip at 8 mg per hour, compared to the standard dose of PPIs with intravenous Pantoprazole 40 mg every 12 hours. The outcomes of the present study could be beneficial for the future updated treatment guideline for patients with gastrointestinal bleeding with non-PHT.

Material and Method

The present study was a prospective, randomized, controlled trial, which based on all patients over 18 years of age with gastrointestinal bleeding with non-PHT in whom the endoscopy was performed within 72 hours of upper gastrointestinal bleeding. The patients were admitted into an emergency room and treated at the Department of Medicine, Hatyai Hospital between October 2012 and March 2014. The endoscopic procedures were performed by a single gastroenterologist (the author). The patients were excluded from this study if there was one or more of the following features: patient aged younger than 18 years old, pregnancy, allergic to PPIs, patient with PHT bleeding which confirmed by endoscopy, patient with upper gastrointestinal bleeding caused by gastrointestinal malignancy, bleeding from pancreas or biliary system and vascular abnormalities and any history of prior gastric surgery. The present study protocol was approved by the Ethics Committee of the Department of Medicine, Hatyai Hospital.

The study participants were randomly recruited to join the program with box of four methods when they were in the emergency ward. The participants had committed to take advice about information and signed inform consent before entering this study. The population were divided into two groups, the high dose of PPIs with intravenous pantoprazole 80 mg bolus then continuously drip at 8 mg per hour and the standard dose of PPIs with intravenous Pantoprazole 40 mg every 12 hours before endoscopy.

All data were collected by reviewing the in-patient charts for clinical history including age, gender, chief complaint (hematemesis or coffee ground or hematochezia or melena or syncope), underlying disease (ischemic heart disease or congestive heart failure or renal failure or CVA or malignancy). Physical sign at the time of the index upper gastrointestinal bleeding including vital signs (systolic blood pressure; SBP <100 mmHg, pulse pressure; Pulse >100 bpm), nasogastric lavage showed fresh blood, as well as laboratory data of an initial hemoglobin (Hb) <10 g/dL, blood urea nitrogen (BUN) 6.5-7.5 or 8.0-9.9 or 10.0-24.9 or >25 mmol/L. Blatchford score and time of the endoscopy were also recorded.

Statistical analysis

Computer software was used to analyze the data. The population data were shown in terms of percentage, average, and standard deviation. They were compared in their differences and relationships by

using statistical odds ratio, Chi-square test, 95% confidential interval (95% CI), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) to indicate the statistical significance.

Results

One hundred thirteen patients were recruited in the present study. The participants were categorized into two groups of high and standard doses of PPIs. There were 58 patients in high dose of PPIs group and 55 patients in standard dose of PPIs group. The mean age of the patients was 59 and 62 years old in the high and standard dose PPIs group, respectively. The

majority of the recruited participants were males 56.4% and 65.5%, in high dose and standard dose group respectively. Although the Blatchford scores were slightly more in the high dose PPIs group compared to the standard dose PPIs group, there were no statistically significant differences between both groups (12.49+3.29 and 12.38+4.06, respectively, $p = 0.876$). The average time of the endoscopy was early performed within 24 hours in both groups (23.92+1.87 hours and 21.69+1.70 hours, respectively, $p = 0.876$) (Table 1).

There were 22 patients found to be high-risk for peptic ulcer bleeding from endoscopy. There were significantly less patients who had high-risk of peptic

Table 1. Characteristics of the 113 patients with gastrointestinal bleeding due to non-PHT both groups (the high dose of PPIs vs. standard dose of PPIs)

Characteristics	High dose of PPIs (n = 58)	Standard dose of PPIs (n = 55)	p-value
Gender			
Male	38 (65.52%)	31 (56.36%)	0.323
Age	59.62±19.69	61.50±19.55	
>60 years	35 (60.34%)	29 (52.73%)	0.419
Chief complaint			
Hematemesis	19 (32.76%)	19 (34.55%)	0.842
Coffee ground	19 (32.76%)	16 (29.09%)	0.677
Hematochezia	3 (5.17%)	-	0.089
Melena	39 (67.24%)	37 (67.27%)	0.997
Syncope	24 (41.38%)	24 (43.64%)	0.810
Underlying diseases			
Ischemic heart disease	7 (12.07%)	3 (5.45%)	0.220
Congestive heart failure	3 (5.17%)	-	0.089
Renal failure	10 (17.24%)	5 (9.09%)	0.205
Cerebro vascular accident	6 (10.34%)	2 (3.64%)	0.168
Malignancy	-	1 (1.82%)	0.307
Initial physical examination (at Emergency Room)			
Systolic blood pressure (SBP)			
- <90 mmHg	4 (6.90%)	3 (5.45%)	0.674
Pulse rate			
- ≥100 bpm	14 (24.14%)	15 (27.27%)	0.444
Nasogastric lavage			
Fresh blood	8 (13.79%)	6 (10.91%)	0.681
Initial investigations			
Hemoglobin (Hb)			
- <10 g/dL	33 (56.90%)	34 (61.82%)	0.831
Blood urea nitrogen (BUN)			
- 6.5-7.5 mmol/L	-	1 (1.82%)	0.307
- 8.0-9.9 mmol/L	-	1 (1.82%)	0.307
- 10.0-24.9 mmol/L	19 (32.76%)	18 (32.73%)	0.231
- ≥25 mmol/L	39 (67.24%)	35 (63.64%)	0.437
Blatchford score*	12.49+3.29	12.38+4.06	0.876
Time EGD (hours)	23.92+1.873	21.69+1.697	0.381

non-PHT = non-portal hypertension bleeding; PPI = proton pump inhibitors, EGD = esophagogastroduodenoscopy

* Blatchford score is including of chief complaint (melena, syncope), underlying disease (liver failure, cardiac failure), initial physical examination at ER (SBP, Pulse), and initial investigation (Hb, BUN)

ulcer bleeding in high dose group compared to standard dose group (10 patients [17.24%] and 12 patients [21.82%], respectively, $p = 0.025$). There was no difference between high dose and standard dose groups in terms of average time of hospital stay (3.03 and 2.89 days, respectively, $p > 0.05$), mean amount of blood transfused (1.79 and 1.63 units, respectively, $p > 0.05$) (Table 2).

One patient of each group had recurrent bleeding and underwent repeated endoscopy. In the high dose group, there was no patient who had recurrent bleeding or died, in comparison, there was one patient died after recurrent bleeding in the standard dose group. However, there was no statistically significant difference in terms of recurrent bleeding and mortality between the two groups ($p > 0.05$). There were small number of patients from both groups died from other causes not associate with upper gastrointestinal bleeding condition (such as pneumonia, septicemia). There was no statistically significant difference between high dose and standard dose groups in terms of average time of hospital stay (3.03 and 2.89 days, respectively, $p > 0.05$), mean amount of blood transfused (1.79 and 1.63 units, respectively, $p > 0.05$) and the complications after endoscopy such as recurrent bleeding (0 and 1 patient, respectively, $p > 0.05$), recurrent bleeding who died (0 and 1 patient, respectively, $p > 0.05$) as shown in Table 2.

Patients with high-risk of peptic ulcer bleeding from endoscopic findings had slightly higher Blatchford score compared to the non-high-risk patients, without statistically significant difference

(15 and 11, respectively, $p = 0.45$). Analysis using relative statistics revealed that Blatchford scores of greater than or equal to 10, 11, and 12 had high-risk of peptic ulcer from endoscopic findings with high sensitivity of 100%, 95%, and 95%, respectively and high NPV of 100%, 97%, and 97%, respectively for predicting high-risk peptic ulcer bleeding. Nevertheless, prediction of high-risk peptic ulcer bleeding using Blatchford scores of greater than or equal to 10, 11, and 12 had low specificity of 35%, 37%, and 41%, respectively (Table 3).

Discussion

The present study showed that the high dose of PPIs administration before endoscopy reduced the chance of high-risk peptic ulcer bleeding compared to the standard dose of PPIs. Both high dose and standard dose of PPIs administration before endoscopic procedure did not affect the time of hospital stay, unit of blood transfusion, the complications after endoscopy (recurrent bleeding who underwent repeat endoscopy or emergency surgery), and mortality. These outcomes were similar to the previous studies that the high dose of PPIs reduced rate of high-risk of SRH during endoscopy when compared to the placebo. However, the high dose of PPIs did not improve the clinical outcomes such as further bleeding, surgery, and death⁽¹⁸⁻²⁰⁾.

The present study also revealed that patients with non-PHT bleeding had low-risk of peptic ulcer from endoscopic findings. Over 80% of the participants in this study did not need further endoscopic therapy which was similar to the earlier studies that total amount

Table 2. Endoscopic finding in the 113 patients with non-PHT bleeding (primary outcomes)

Characteristics	High dose of PPI (n = 58)	Standard dose of PPI (n = 55)	p-value
Endoscopic finding*			0.892
High-risk	10 (17.24%)	12 (21.82%)	0.025*
Low-risk	33 (56.90%)	25 (45.45%)	0.400
Gastritis	7 (12.07%)	9 (16.36%)	0.289
Esophagitis	2 (3.45%)	5 (9.09%)	0.532
Negative study	6 (10.34%)	4 (7.27%)	0.002*
Duration of stay at the hospital	3.03±1.6	2.89±1.8	0.568
Received red blood corpuscle during hospital stay (units)	1.79±2.3	1.63±2.4	0.649
Major complications occurred after endoscopy			0.662
Recurrent bleeding who underwent repeat endoscopy	1 (1.72%)	1 (1.82%)	
Recurrent bleeding who underwent emergency surgery	-	1 (1.82%)	
Recurrent bleeding who died	-	1 (1.82%)	
Death from other causes	2 (3.45%)	1 (1.82%)	

* Endoscopic finding is divided with the Forrest classification of peptic ulcer bleeding the following to

- High-risk: arterial spurting, non-bleeding visible vessel, adherent clot

- Low-risk: clean base, flat pigmented spot

Table 3. Sensitivity, specificity, PPV, and NPV of Blatchford score for predicting high-risk peptic ulcer at the time of endoscopy

Blatchford score	High-risk peptic ulcer 22 patients (%)	Non-high-risk peptic ulcer 91 patients (%)	Sensitivity	Specificity	Positive predictive value (PPV)	Negative predictive value (NPV)
≥10	22 (100)	59 (64.83)	100	35	27	100
≥11	21 (95.45)	57 (62.63)	95	37	27	97
≥12	21 (95.45)	53 (58.24)	95	41	28	97
≥13	19 (86.36)	45 (49.45)	86	50.5	29.6	93.8
≥14	18 (81.81)	39 (42.85)	81.8	57	31.5	92.8
≥15	12 (54.54)	26 (28.57)	54.5	71	31.5	86.6
≥16	9 (40.90)	19 (20.87)	40.9	79	32	84.7
≥17	4 (18.18)	8 (8.79)	18	91	28.5	82
≥18	0 (0)	2 (2.19)	0	97.8	0	80

of 75 to 85% patients with upper gastrointestinal bleeding due to non-PHT can eventually stop bleeding spontaneously⁽⁸⁾.

Even though some meta-analysis of randomized controlled trials suggested that the use of high dose of PPIs and standard dose of PPIs had no difference⁽¹⁴⁻¹⁶⁾, those studies compared the efficiency of two different regimens of PPIs administered after endoscopy. Similar results were found in terms of major complications such as recurrent bleeding who underwent repeated endoscopy, recurrent bleeding who underwent emergency surgery, recurrent bleeding who died, these outcomes did not improve significantly in both groups, because these major complications depended on the finding of endoscopy and effective therapeutic procedure more than the PPIs regimen.

The use of high dose PPIs reduces the severity of SRH during endoscopy because it reduces acid level of gastric environment to neutral pH, which leads to blood clotting stability⁽⁹⁾. Thus, administration of high dose PPIs results in increasing efficiency to stabilize clot over bleeding ulcer.

According to the update practice guideline, the use of PPIs before endoscopy recommend the administration of high dose PPIs in patients who have non-PHT bleeding was still unclear. Nevertheless, the guideline of the gastroenterologist of the Asia-Pacific Working Group consensus⁽¹³⁾ and USA⁽²⁰⁾ suggest that consideration of using high dose of PPIs before the endoscopy can be optional. This is due to non-PHT bleeding can be resumed spontaneously in 80% of the patients. Therefore, the use of high dose of PPIs in all patients with ulcer bleeding resulted in high cost and low benefits⁽¹³⁾.

The present study found that the patients with Blatchford scores more than or equal to 10, 11, and 12 had high sensitivity of 100%, 95%, and 95%, respectively for predicting high-risk of peptic ulcer bleeding with low specificity of 35%, 37%, and 41%, respectively, they also had high NPV of 100%, 97%, and 97%, respectively for predicting the high-risk of peptic ulcer bleeding. Thus, the Blatchford scores of less than 10 rarely had the chance of high-risk of peptic ulcer bleeding (<5%). As the consequence, the administration of high dose of PPIs in these patients may not be beneficial.

The present study also demonstrated that patients with Blatchford scores more than or equal to 13, 14, 15, and 16 had sensitivity of 86%, 81.8%, 54.5%, and 40.9%, respectively and specificity of 50.5%, 57%, 71%, and 79%, respectively for predicting high-risk of peptic ulcer bleeding. The use of high dose PPIs before endoscopy can be considered in the patients who have Blatchford scores of more than or equal to 13 in order to reduce the number of patients with higher risk stigmata recent hemorrhage and also decrease the repeated endoscopic intervention.

The Blatchford score is a favorable measuring scheme and suitable for evaluating the degree of non-variceal upper gastrointestinal bleeding⁽¹³⁾. Correspondingly, the Blatchford score is used to tailor the dose of PPIs according to the patient. It helps managing the patient with upper gastrointestinal bleeding due to non-PHT bleeding and also decrease the cost of treatment. It is in agreement that the Blatchford score of less than 10 can be considered using standard dose PPIs before endoscopy. Patients with Blatchford score between 10 and 12 will be

beneficial in using high dose PPIs. Finally, the patients with Blatchford score of more than 12 should be considered using high dose PPIs. Nevertheless, the present study did not focus on the relation between the Blatchford score and endoscopic findings. Both groups were performed with PPIs which may be decreased the severity of higher risk of SRH while endoscopic therapy.

Prior data of the Blatchford score were used to evaluate the severity of non-PHT bleeding that needed to be hospitalized or other therapy⁽¹⁷⁾. There were no data to consider adjustable dose and route of PPIs.

In the future, there may be more data about the association between the Blatchford score and PPIs in patients with non-PHT bleeding. This might prove that the use of pre-endoscopic PPIs in the present study population with the accuracy and effectiveness. Moreover, the research outcomes might be recommended the use of the pre-endoscopic PPIs in the practice guideline.

Conclusion

The use of the high dose PPIs before the endoscopy in the patients can be able to reduce the chance of high-risk peptic ulcer bleeding compared with the standard dose of PPIs. The use of high dose and standard dose PPIs did not effect on time of hospital stay, unit of blood transfusion and the complications after endoscopy, such as recurrent bleeding and mortality rate. The Blatchford can be used for tailoring the use of PPIs therapy in the patients with non-PHT bleeding. Standard dose PPIs can be considered using in patients with Blatchford scores less than 10. High dose PPIs would be beneficial in patients who have Blatchford scores between 10 and 12. For patients who have Blatchford scores greater than 12, high dose PPIs are recommended.

What is already know on this topic?

The use of high dose PPIs reduces the severity of SRH during endoscopy. However, the high dose of PPIs did not improve the clinical outcomes such as further bleeding, surgery, and death. All the clinical practice guideline, the dose of PPIs before endoscopy in patients with non-portal hypertension bleeding were still not clear.

What this study adds?

The Blatchford can be used for tailoring the use of PPIs therapy in the patients with non-PHT

bleeding. Standard dose PPIs can be considered using in patients with Blatchford scores less than 10. High dose PPIs would be beneficial in patients who have Blatchford scores between 10 and 12. For patients who have Blatchford scores greater than 12, high dose PPIs are recommended.

Potential conflicts of interest

None.

References

1. Leontiadis GI, Howden CW. The role of proton pump inhibitors in the management of upper gastrointestinal bleeding. *Gastroenterol Clin North Am* 2009; 38: 199-213.
2. Holster IL, Kuipers EJ. Management of acute nonvariceal upper gastrointestinal bleeding: current policies and future perspectives. *World J Gastroenterol* 2012; 18: 1202-7.
3. Targownik LE, Nabalamba A. Trends in management and outcomes of acute nonvariceal upper gastrointestinal bleeding: 1993-2003. *Clin Gastroenterol Hepatol* 2006; 4: 1459-66.
4. Yavorski RT, Wong RK, Maydonovitch C, Battin LS, Furnia A, Amundson DE. Analysis of 3,294 cases of upper gastrointestinal bleeding in military medical facilities. *Am J Gastroenterol* 1995; 90: 568-73.
5. Longstreth GF. Epidemiology of hospitalization for acute upper gastrointestinal hemorrhage: a population-based study. *Am J Gastroenterol* 1995; 90: 206-10.
6. Rockall TA, Logan RF, Devlin HB, Northfield TC. Risk assessment after acute upper gastrointestinal haemorrhage. *Gut* 1996; 38: 316-21.
7. Charatcharoenwitthaya P, Pausawasdi N, Laosanguaneak N, Bubthamala J, Tanwadee T, Leelakusolvong S. Characteristics and outcomes of acute upper gastrointestinal bleeding after therapeutic endoscopy in the elderly. *World J Gastroenterol* 2011; 17: 3724-32.
8. Berstad A. Antacids, pepsin inhibitors, and gastric cooling in the management of massive upper gastrointestinal haemorrhage. *Scand J Gastroenterol Suppl* 1987; 137: 33-8.
9. Green FW, Jr., Kaplan MM, Curtis LE, Levine PH. Effect of acid and pepsin on blood coagulation and platelet aggregation. A possible contributor prolonged gastroduodenal mucosal hemorrhage. *Gastroenterology* 1978; 74: 38-43.
10. Brunner G, Luna P, Hartmann M, Wurst W.

- Optimizing the intragastric pH as a supportive therapy in upper GI bleeding. *Yale J Biol Med* 1996; 69: 225-31.
11. Dorward S, Sreedharan A, Leontiadis GI, Howden CW, Moayyedi P, Forman D. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. *Cochrane Database Syst Rev* 2006; (4): CD005415.
 12. Gralnek IM, Barkun AN, Bardou M. Management of acute bleeding from a peptic ulcer. *N Engl J Med* 2008; 359: 928-37.
 13. Sung JJ, Chan FK, Chen M, Ching JY, Ho KY, Kachintorn U, et al. Asia-Pacific Working Group consensus on non-variceal upper gastrointestinal bleeding. *Gut* 2011; 60: 1170-7.
 14. Andriulli A, Loperfido S, Focareta R, Leo P, Fornari F, Garripoli A, et al. High- versus low-dose proton pump inhibitors after endoscopic hemostasis in patients with peptic ulcer bleeding: a multicentre, randomized study. *Am J Gastroenterol* 2008; 103: 3011-8.
 15. Wang CH, Ma MH, Chou HC, Yen ZS, Yang CW, Fang CC, et al. High-dose vs non-high-dose proton pump inhibitors after endoscopic treatment in patients with bleeding peptic ulcer: a systematic review and meta-analysis of randomized controlled trials. *Arch Intern Med* 2010; 170: 751-8.
 16. Sachar H, Vaidya K, Laine L. Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: a systematic review and meta-analysis. *JAMA Intern Med* 2014; 174: 1755-62.
 17. Worapratya P, Wuthisuthimethawee P, Vasinanukorn P, Geater AF. Blatchford score to predict necessary endoscopic treatment in upper gastrointestinal bleeding patients in the Emergency Department at Songklanagarind Hospital. *Sonkla Med J* 2013; 31: 11-9.
 18. Lau JY, Leung WK, Wu JC, Chan FK, Wong VW, Chiu PW, et al. Omeprazole before endoscopy in patients with gastrointestinal bleeding. *N Engl J Med* 2007; 356: 1631-40.
 19. Leontiadis GI, Sreedharan A, Dorward S, Barton P, Delaney B, Howden CW, et al. Systematic reviews of the clinical effectiveness and cost-effectiveness of proton pump inhibitors in acute upper gastrointestinal bleeding. *Health Technol Assess* 2007; 11: iii-iv, 1-164.
 20. Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol* 2012; 107: 345-60.

เปรียบเทียบประสิทธิภาพของให้ยาขับยั้งการขับโปรตอนขนาดสูงและขนาดปกติ ก่อนการส่องกล้องในผู้ป่วยที่มีเลือดออก
ในทางเดินอาหารจากภาวะ *non-portal hypertension*

อรรพด รัตนสุภา, สิริวรรณ เข้มมณี

ภูมิหลัง: ภาวะเลือดออกในทางเดินอาหารจากภาวะ *non-portal hypertension* เป็นภาวะฉุกเฉินที่พบบ่อยและมีอัตราการเสียชีวิตสูง สาเหตุส่วนใหญ่เกิดจากภาวะที่มีกรดสูง แนวทางการรักษาหลักก่อนการส่องกล้องจึงเป็นการให้ยาขับยั้งการขับโปรตอน แต่ขนาดและวิธีการให้ยาขับยั้งการขับโปรตอนในสมาคมแพทย์โรกระบบทางเดินอาหารต่าง ๆ ยังไม่มีข้อสรุปที่ชัดเจนว่าควรจะเป็นอย่างไร

วัตถุประสงค์: เพื่อศึกษาเปรียบเทียบประสิทธิภาพของยาขับยั้งการขับโปรตอนขนาดสูงและขนาดปกติก่อนการส่องกล้องในผู้ป่วยที่มีเลือดออกในทางเดินอาหารจากภาวะ *non-portal hypertension* ว่ามีความแตกต่างกันหรือไม่ และแนวทางการให้ยาขับยั้งการขับโปรตอนก่อนการส่องกล้องควรจะเป็นอย่างไร

วัสดุและวิธีการ: เป็นการศึกษาแบบสุ่มไปข้างหน้าโดยแบ่งประชากรที่ศึกษาแบบสุ่มแบบการจัดเรียงกลองกระดาดสองกลุ่มออกมาเป็นกอง ๆ กองละ 4 กลอง โดยกลุ่มหนึ่งจะได้รับยา *pantoprazole* ขนาดสูง 80 มิลลิกรัม ฉีดแล้วตามด้วยหยดเข้าหลอดเลือดดำในอัตราเร็ว 8 มิลลิกรัมต่อชั่วโมง และอีกกลุ่มจะได้รับยาขนาดปกติ 40 มิลลิกรัม ฉีดเข้าเข้าหลอดเลือดดำทุก 12 ชั่วโมง แต่ให้การรักษารักษาอื่น ๆ ตามมาตรฐานปกติเหมือนกัน แล้วเก็บข้อมูลทั่วไป *Blatchford score* ผลการส่องกล้อง ผลการรักษา และภาวะแทรกซ้อนอื่น ๆ แล้วนำข้อมูลมาวิเคราะห์ทางสถิติ

ผลการศึกษา: มีผู้ป่วยในการศึกษาทั้งหมด 113 ราย แบ่งเป็นกลุ่มที่ได้รับยาขับยั้งการขับโปรตอนขนาดสูงจำนวน 58 ราย และขนาดปกติจำนวน 55 ราย ค่า *Blatchford score* ในกลุ่มที่ได้รับยาขับยั้งการขับโปรตอนขนาดสูงมีค่ามากกว่ากลุ่มที่ได้รับยาขนาดปกติเล็กน้อยแต่ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติคือ $12.49+3.29$ และ $12.38+4.06$ ตามลำดับ ($p = 0.876$) ผลการส่องกล้องพบแผลเป็ปดิกชนิดมีความเสี่ยงสูงจำนวนทั้งหมด 22 ราย โดยจะพบว่าในผู้ป่วยกลุ่มที่ได้รับยาขับยั้งการขับโปรตอนขนาดสูงจะมีผลการส่องกล้องพบแผลเป็ปดิกชนิดมีความเสี่ยงสูงน้อยกว่าผู้ป่วยกลุ่มที่ได้รับยาขับยั้งการขับโปรตอนขนาดปกติอย่างมีนัยสำคัญทางสถิติคือ 10 ราย (ร้อยละ 17.24) และ 12 ราย (ร้อยละ 21.82) ตามลำดับ ($p = 0.025$) ระยะเวลาในการนอนโรงพยาบาล (3.03 และ 2.89 วัน) อัตราการให้เลือดแดง (1.79 และ 1.63 ยูนิต) ภาวะเลือดออกซ้ำจันต้องผ่าตัด (0 และ 1 ราย) และภาวะเลือดออกซ้ำจันเสียชีวิต (0 และ 1 ราย) ไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติในกลุ่มที่ได้รับยาขับยั้งการขับโปรตอนขนาดสูงและขนาดปกติตามลำดับ ($p>0.05$) ค่า *Blatchford score* มากกว่า 10, 11 และ 12 คะแนนมีความไวสูงถึงร้อยละ 100, 95 และ 95 และมีค่า *negative predictive value (NPV)* ที่สูงถึงร้อยละ 100, 97 และ 97 ตามลำดับ ในการทำนายผลการส่องกล้องพบแผลเป็ปดิกชนิดมีความเสี่ยงสูง

สรุป: การให้ยาขับยั้งการขับโปรตอนในขนาดสูงก่อนการส่องกล้องในผู้ป่วยที่มีเลือดออกในทางเดินอาหารจากภาวะ *non-portal hypertension* สามารถลดโอกาสการเกิดแผลเป็ปดิกชนิดเสี่ยงสูงได้เมื่อเทียบกับการให้ยาขับยั้งการขับโปรตอนในขนาดปกติ แต่ไม่มีผลต่อระยะเวลาในการนอนโรงพยาบาลจำนวนเม็ดเลือดแดงที่ได้รับภาวะแทรกซ้อนหลังการส่องกล้องและอัตราการเสียชีวิต หากค่า *Blatchford score* น้อยกว่า 10 ก็อาจจะให้ยาขับยั้งการขับโปรตอนขนาดปกติได้ หากค่า *Blatchford score* มีค่าระหว่าง 10-12 ก็อาจจะให้ยาขับยั้งการขับโปรตอนขนาดสูง แต่หากมีค่า *Blatchford score* มากกว่า 12 ก็ควรจะให้ยาขับยั้งการขับโปรตอนขนาดสูง