Randomized Controlled Trial of High Dose Bolus Versus Continuous Intravenous Infusion Pantoprazole As an Adjunct Therapy to Therapeutic Endoscopy in Massive Bleeding Peptic Ulcer

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Background: *After therapeutic endoscopy is performed in high-risk patients with peptic ulcer bleeding, rebleeding occurs in about 25 to 30%. High dose intravenous proton pump inhibitors (PPI) have been recommended for the use in high-risk patients to prevent rebleeding following successful therapeutic endoscopy.*

Objective: *Compare the efficacy between pantoprazole high dose bolus injections and continuous intravenous infusion to prevent rebleeding in peptic ulcer patients after initial hemostasis is achieved by the therapeutic endoscopy.*

Material and Method: *A clinical block randomized control trial was conducted at Maharaj Nakorn Chiang Mai Hospital in massive peptic ulcer bleeding patients. All patients underwent endoscopic diagnosis and treatment within six hours of admission. Hemostasis was achieved by therapeutic endoscopy in 28 patients who received 80 mg pantoprazole as a loading dose before intervention. They were randomized into two groups. The first group was given a high dose of pantoprazole, 40 mg bolus injections twice daily for seven days (n = 13). The second group was given continuous intravenous infusion of pantoprazole, 8 mg per hour for the first three days, followed with a 40 mg bolus injection twice daily similar to the first group from day 4 until day 7 (n = 15). After the seventh day, both groups were given 20 mg of oral pantoprazole once daily for two months. The data was analyzed by Fisher's exact test to compare the frequency of rebleeding within seven days after therapeutic endoscopy.*

Results: *The frequency of recurrent bleeding between the high dose pantoprazole bolus injection group and the continuous intravenous infusion group was not significantly different, 30.8% and 33.3% respectively (p = 1.0). Three patients in the high dose bolus group and five in the continuous infusion group underwent surgery (p = 0.68). There was no statistically significant difference between the two groups by volume of blood transfusion, length of hospital stay, or mortality.*

Conclusion: *In the present study, both PPI drug administration methods showed an equally effective for massive peptic ulcer bleeding. Further studies with a larger sample size are recommended.*

Keywords: *Massive peptic ulcer bleeding, Proton pump inhibitor (PPI), Pantoprazole, Therapeutic endoscopy*

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Peptic ulcer is the most common cause of upper gastrointestinal hemorrhage (UGIH) among non-variceal disease, and UGIH is an important cause of hospital admission. The term "high-risk ulcers" refers to a variety of endoscopic features (Forrest classification), each carrying a specific risk for an adverse outcome. In the high-risk group, the chance for rebleeding is about 90% for arterial bleeding (Forrest Ia), 50% for oozing (Ib), 18 to 27% for non-bleeding visible vessel (IIa), and 12 to 33% for adherent clot (IIb). In the low risk group, rebleeding is about 5% for clean base ulcer (III)[1].

In addition, the Rockall score is frequently used to predict patient outcomes, and its validity in clinical practice has been studied and supported[2,3]. Although primary hemostasis can be achieved by endoscopic intervention in > 90% of cases, rebleeding during the first 72 hours is still common and associated with a high mortality rate. In about two-thirds of cases, the bleeding sources are acid related lesions[4,5]. For both pharmacological and physiological reasons,

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anti-acid secretion drugs should reduce the rebleeding rate. The aim of prophylactic and acute treatment of UGIH is usually to raise the intragastric pH above 4.0, at which point pepsin is inactivated and fibrinolysis is inhibited[6-8]. Intravenous PPI is a powerful acid-suppression agent that is well known to improve the control of rebleeding of peptic ulcers, especially after therapeutic endoscopic intervention.

Some clinical studies have been performed using repeated bolus injections[9-14] or continuous infusion[15-19] of omeprazole in comparison to a placebo or histamine-2 receptor antagonists as rebleeding prophylaxis. Overall, of the six studies with bolus injections, two showed some clinical benefit and only one showed a significant reduction in rebleeding rates[14]. With continuous infusion, four of five studies showed a statistically significant reduction in surrogate parameters such as rebleeding rates and need for surgery but not in the most relevant parameter, namely, mortality. It should also be noted that the continuous infusion study that failed to demonstrate a significant benefit involved only 10 patients per group, a simple size by far too small to expect any statistical difference to be detectable[19].

Pantoprazole (Controloc®) is a proton pump inhibitor in the same class of compounds as omeprazole. Its unique properties include linear pharmacokinetics[20] and lack of interaction with the cytochrome P450 enzyme system in man[21]. As to acid-suppressing potency, intravenous pantoprazole is equivalent to omeprazole when administered at the same dose[22]. One clinical trial studied outcome in 168 patients with bleeding peptic ulcers after endoscopic therapy (pantoprazole infusion versus ranitidine) and found decreased rebleeding rate in the pantoprazole group but the same mortality rate in both groups[23]. Controversies also exist regarding the best acid- suppressive regimen.

The majority of trials using PPI in the treatment of UGIH have been conducted with Asian patients. There was a less number of parietal cell mass[24] and a higher prevalence of poor metabolizers of cytochrome P4502C19 wild type allele[25] in Chinese than those in a Scottish population. Therefore, the dose of PPI infusion could be decreased while maintaining favorable intragastric pH control. In the Thai population, one study reported the lack of significant differences in CYP2C19 phenotype (representation for PPI drug metabolism and efficacy) among the four populations in Chinese, Thai, Vietnamese, and Japanese. According to the aspect of CYP2C19 polymorphisms related to PPI drug metabolism, high dose PPI therapy efficacy in Thais should be useful as it is the same as in Chinese due to no phenotype difference among Asian populations[26].

The present study aimed to test whether there would be a decrease in the rate of rebleeding using high doses of PPI infusion compared to bolus injections, for patients with peptic ulcer bleeding.

Material and Method

Between August 2005 and October 2007, patients who were admitted to the department of surgery Maharaj Nakorn Chiang Mai Hospital, with non-variceal UGIH. All patients underwent endoscopy within 24 hours of admission for diagnosis and further therapeutic intervention. Endoscopic therapeutic intervention is required in patients who have high endoscopic risk of bleeding peptic ulcer (arterial bleeding, spurting (Forrest Ia), oozing (Ib), non-bleeding visible vessel (IIa), and adherent clot (IIb).

The present study was approved by the Clinical Research Ethical Committee of the Maharaj Nakorn Chiang Mai Hospital, Thailand. Study design was clinical randomized controlled trial. The authors had an estimated sample sized with type I error = 5%, type II error = 10% and Power = 90%. At least 50 patients were essential for each group.

Inclusion criteria: 1) Age 18-80 years, 2) Initial Rockall score of $\geq$ 3, 3) Endoscopic treatment within 24 hours of admission, 4) Patients were accepted for study after the first endoscopic therapeutic intervention was achieved.

Exclusion Criteria: 1) Bleeding form gastric cancer, variceal bleeding, 2) Contraindication for endoscopy or high cardiac risk, bleeding tendency (uncorrectable) and anticoagulant therapy, 3) History of allergies to PPI, 4) Pregnancy or during lactation, 5) Impaired liver function.

Endoscopic therapeutic intervention

Endoscopic hemostasis was performed by an endoscopist and surgeon with experience in endoscopic therapeutic intervention. The high-risk bleeding peptic ulcers were injected with saline-adrenaline and repaired with a metallic hemoclip (Olympus Clip HX-600-090), or injected with saline-adrenaline and adjunct by heater probe (Quick Silver™ bipolar coagulation probe). The saline-adrenaline solution was a mixture of 9 ml 0.9% NSS and 1 ml 1:1,000 adrenaline (dilution 1:10,000). Hemostasis was considered to have been established if bleeding

stopped and formerly bleeding vessels were flattened or cavitated.

Block randomization of acid suppressive therapy

According to successful endoscopic treatment of patients enrolled in the present study, each patient received an 80 mg loading dose of intravenous Controloc® then was randomly assigned to receive Controloc® high dose intravenous infusion or bolus injection. The high dose infusion group received 8 mg of Controloc® continuous infusion per hour for three days, followed by Controloc® 40 mg i.v. q 12 hours for days 4 to 7. The bolus group received 40 mg of Controloc® intravenous q 12 hours for seven days. After seven days both groups received Controloc® 20 mg oral once daily for two months.

Monitoring

Patients were monitored in the surgical ward for signs of further bleeding. Patients' vital signs were checked every hour until they became stable. The hemoglobin and hematocrit were checked at least once daily, and a blood transfusion was given if the hemoglobin decreased below 8 g/dL or if the patients' vital signs deteriorated. If no bleeding was observed, the patient was given a liquid meal and then a solid meal. The patients were discharged and followed up in the outpatient department.

Rebleeding was considered if one of the following occurred:

- Continuous tarry stool passage or vomiting of fresh blood or bloody aspirates after clear lavages through the nasogastric tube.

- Relapse of hemodynamic instability, including a systolic blood pressure < 90 mmHg, postural change of > 20 mmHg and/or pulse rate > 100/min.

- A hemoglobin level drop of more than 3 g/dL within 24 hours was observed.

In such case, emergency endoscopy was performed immediately. Endoscopic therapeutic intervention was repeated. An emergency operation (double set up) was performed if bleeding could not be controlled with endoscopic intervention.

End points

Upon each patient's enrollment in the present study, the following data were recorded: age, sex, endoscopic diagnosis, use of non-steroidal anti-inflammatory drugs (NSAIDs), co morbid illnesses, and type of endoscopic therapeutic intervention. The outcomes measured were volume of transfused blood, hospital stay, rebleeding (re-endoscopic intervention or surgery) and mortality within seven days. These measured outcomes were compared between the two treatment groups.

Statistics

The patients' base-line characteristics and measured outcomes were compared with use of student's t-test for parametric data, the Mann-Whitney U test for nonparametric data, and the Chi-square test for proportions. The Fisher's exact test was used to compare sex, NSAIDs ingestion, number of rebleeding patients, emergency operations, and mortality rates between the two groups. A probability value of less than 0.05 was considered significant. End point data were analyzed according to the intention-to-treat principle**.**

Results

Twenty-eight patients were randomized into the high dose bolus group (n = 13) and the continuous infusion group (n = 15). The demographic characteristics had no significant difference in mean age, sex, administration of NSAIDs, peptic ulcer history, type of coexisting illness, coagulopathy, mean Rockall score, mean hemoglobin at admission, or duration from admission to scope between the two groups (Table 1).

Types of endoscopic features and treatments for bleeding peptic ulcers are shown in Table 2. The endoscopic features were not different between the two groups. Bleeding peptic ulcers were treated with a saline-adrenaline injection in six patients, and saline-adrenaline injection combined with heater probe in seven in the high dose bolus group. In the continuous infusion group nine patients were treated with saline-adrenaline injection, two patients were treated with a metallic clip combined with saline-adrenaline injection, and four patients were treated with saline-adrenaline combined with heater probe. There was no significant difference in the number of patients who underwent the various types of endoscopic treatment between the two groups (Table 2).

Rebleeding, surgery and mortality

The cumulative rebleeding rates during the seven days of pantoprazole intravenous were not significantly different between the high dose bolus and continuous infusion groups (30.8% vs. 33.3%; p = 1.0) and were based on intention-to-treat (Table 3).

Table 1. Demographic characteristics of the study patients

Parameter	High dose bolus (n = 13)	Continuous infusion (n = 15)	p-value
Mean age (years)	56.54 ± 12.3	63.8 ± 14.6	0.11
Age range	25-80	32-80	0.51
Sex (%)			
Male	1 (7.7%)	9 (60%)	0.06
Female	12 (92.3%)	6 (40%)	0.41
NSAID user (%)	5 (38.5%)	3 (20%)	0.71
Previous Peptic ulcer disease (%)	6 (46.2%)	8 (53.3%)	
Association disease			
Hypertension	2 (15.3%)	5 (33.3%)	0.25
Cardiovascular	0	1 (6.7%)	-
CRF	1 (7.7%)	1 (6.7%)	1.00
D M	1 (7.7%)	1 (6.7%)	1.00
Mean Rockall score			
Initial	3.23 ± 1.3	3.87 ± 1.2	0.25
Final	5.85 ± 1.9	6.87 ± 1.2	0.17
Mean Hemoglobin (g/dL)	8.20 ± 3.0	6.31 ± 1.8	0.80
Mean Platelet count (10^3/mm^3)	238.23 ± 108.0	223.8 ± 137.3	0.50
Mean PT (sec)	12.84 ± 2.5	12.85 ± 2.4	0.37
Mean PTT (sec)	25.13 ± 4.5	25.13 ± 4.5	0.28
Time to endoscopy after admission (hr)	11.42 ± 7.1	10.87 ± 7.7	0.74

NSAID = non-steroidal anti-inflammatory drug; CR = chronic renal failure; DM = diabetes insipidus; PT = prothrombin time; PTT = partial thromboplastin time

Table 2. Descriptive data of endoscopic features and treatments

	High dose bolus (n = 13)	Continuous infusion (n = 15)	p-value
Location of bleeding			
Stomach	11 (84.6%)	12 (80%)	0.84
Duodenum	1 (7.7%)	2 (13.3%)	0.56
Both	1 (7.7%)	1 (6.7%)	1.00
Mean ulcer size (cm)	0.87 ± 0.3	1.02 ± 0.3	0.29
Forrest classification			
Spurting (Ia)	7 (53.8%)	6 (40%)	0.10
Oozing (Ib)	1 (7.7%)	2 (13.3%)	0.41
Non-bleeding visible vessel (IIa)	4 (30.8%)	2 (13.3%)	0.56
Adherent clot (IIb)	1 (7.7%)	4 (26.7%)	0.78
Treatment			
Saline-adrenaline	6 (46.2%)	4 (26.7%)	0.53
Saline-adrenaline + metallic hemoclip	-	2 (13.3%)	-
Saline-adrenaline + heater probe	7 (53.8%)	9 (60%)	0.62

In the rebleeding patients in the high dose bolus group, rebleeding occurred within three days (1 patients), seven days (3 patients) after endoscopic therapy. One patient received endoscopic re-treatment and three patients received surgical treatment. These four patients recovered uneventfully. For the continuous infusion group, rebleeding occurred within three days (4 patients), seven days (1 patient). All patients required surgery (Table 4). There were fewer surgical treatments in the high dose group (23.1% vs. 33.3%) but the difference was not significant (p = 0.68). All patients in the present study were safe, with no mortality. There were no serious adverse effects from intravenous pantoprazole.

Table 3. Result of treatments

	High dose bolus (n = 13)	Continuous infusion (n = 15)	p-value
No. of rebleeding	4 (30.8%)	5 (33.3%)	1.00
3 days	1	4	
7 days	3	1	
Endoscopic re-treatment	1 (7.7%)	0	0.51
Requiring surgery	3 (23.1%)	5 (33.3%)	0.68
Mean blood transfusion (units)	6.31 $\pm$ 3.8	6.07 $\pm$ 3.8	0.67
Hospital stay (days)	10.15 $\pm$ 3.2	9.93 $\pm$ 4.3	0.57
Mortality	0	0	-

Table 4. Descriptive data of the patients with rebleeding after success first therapeutic endoscopy

Patient	Group	Lesion	Forrest class.	Treatment	Rebleeding day	Endoscopy re-treat.	Surgery
Case 1	Bolus	GU	Ib	A + H	1	Yes**	No
Case 2	Bolus	GU	Ib	Adrenaline injection	4	No	Yes
Case 3	Bolus	GU	IIb	A + H	4	No	Yes
Case 4	Bolus	DU	IIb	A + H	6	No	Yes
Case 5	Continuous	DU	Ia	A + H	2	No	Yes
Case 6	Continuous	GU	Ia	Adrenaline injection	1	No	Yes
Case 7	Continuous	GU	Ia	A + MC	2	No	Yes
Case 8	Continuous	GU	Ib	Adrenaline injection	2	No	Yes
Case 9	Continuous	GU	IIa	A + H	6	No	Yes

** Successful stop bleeding by endoscopy re-treatment
A + H = adrenaline injection with heater probe; A + MC = adrenaline injection with metallic hemoclip

Hospital stay and transfusion requirement

There was no significant difference in hospital stay between the two groups. The mean stay for the 13 patients in the high dose bolus group was 10.15 days (range, 5 to 15), compared to a mean stay of 9.93 days (range, 5 to 20) for the 15 patients in the continuous infusion group (p = 0.57). The mean ($\pm$ SD) number of units of blood transfusion was not significant between the two groups (p = 0.67) (Table 3).

Discussion

A bleeding peptic ulcer remains a serious medical problem with significant morbidity and mortality. Endoscopic therapy significantly reduces further bleeding, the need for surgery, and mortality in patients with bleeding peptic ulcers and is now recommended as the first hemostatic modality for these patients.

After obtaining initial hemostatis, rebleeding is another important factor to the patient's prognosis. An ideal therapy includes a successful endoscopic therapy plus a low rebleeding rate. Rebleeding episodes occur within three days in most instances. In addition, an intragastric pH higher than 6.0 is a prerequisite for preventing rebleeding in patients with bleeding peptic ulcers. Therefore, a drug that rapidly increases intragastric pH and lasts for three to four days is necessary to prevent rebleeding.

During the last decade, the treatment strategies for acid related disease were anti-secretory agents. However, many agents failed to demonstrate the potential benefits in the treatment of non-variceal gastrointestinal hemorrhage, such as H2 receptor antagonists[27]. Udd et al[28] compared a continuous infusion of high dose omeprazole (80 mg bolus dose followed by 8 mg/hr for 72 hours) (n = 69) to i.v. omeprazole 20 mg once daily for 72 hours (n = 73). Patients with Forrest Ia, Ib, IIa, IIb, and IIc ulcers who underwent endoscopic treatment were enrolled in this trial. The regular dose group included 42 patients with high-risk lesion, compared with 40 patients in the high dose group. The primary endpoint examined was the

frequency of rebleeding episodes. No statistically significant differences of rebleeding were found between the regular and high dose groups (8.2% vs. 11.6%, respectively). While the present study enrolled a high percentage of patients with low risk lesions, there were no significant differences in the rebleeding rates in patients with high-risk lesions in the regular and high dose groups (7.1% vs. 12.5%, respectively). No significant difference in mortality, transfusion requirement, need for surgery and length of stay were found.

Schonekas et al[29] randomized control trial patients with Forrest Ia-IIa ulcers received either 40 mg of intravenous pantoprazole once daily for three days (n = 74) or a 40 mg bolus dose of pantoprazole followed by a continuous infusion 8 mg/hr for three days. All patients underwent endoscopic treatment. The rebleeding rates at 72 hours were 12% in the 40 mg group and 13% in the continuous infusion group. The authors stated that no statistically significant difference was found, but p-values were not provided. Mortality rates and the need for transfusion did not differ between the two groups (again, no p-values were provided). Recent guidelines have recommended the use of high dose intravenous PPI in the post-endoscopic treatment setting[30].

The present study shows that high dose bolus or continuous infusion of pantoprazole after successful endoscopic treatments were not significantly different for prevention of recurrent bleeding and number of operation. The authors controlled factors that could affect rebleeding rate, such as endoscopic treatment being performed within 24 hours, full resuscitation, and well stabilized patients before being randomized into the two groups. Total recurrent bleeding occurred in 32% of all patients within the first seven days, and it was successfully stopped with endoscopic re-treatment in one of nine patients (high bolus group), and with surgery in eight or nine (3 in high bolus, 5 in continuous group). When the authors analyzed the rate of recurrent bleeding, it was found that only one patient in the high dose bolus PPI administration group with rebleeding in the first three days was successfully stopped by re-endoscopic therapy. Four patients in the continuous group rebleed within the first three days, had profuse bleeding, and underwent immediate surgery rather than endoscopic therapy. However, the rate of recurrent bleeding within seven days and number of surgical requirement of the two groups were similar (p = 1.0, 0.68 respectively). Patients with ulcers located at the posterior wall of duodenal bulb (n = 3, 1 in high bolus and 2 in continuous group) had a higher rebleeding rate than patients with ulcers in other locations. In addition, the volume of blood transfusion, hospital stay and mortality rates of the two groups were not statistically different.

Conclusion

The present pilot study demonstrated that high dose bolus or continuous intravenous infusions of PPI are equally effective for adjunct therapies after endoscopic treatment in massive bleeding peptic ulcers. A study with a larger population is recommended.

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Potential conflicts of interest

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การศึกษาไปข้างหน้าเปรียบเทียบระหว่างการบริหารยาแพนโทพราโซลแบบฉีดเข้าหลอดเลือดดำขนาดสูงและการให้แบบหยดเข้าหลอดเลือดดำ เพื่อรักษาเสริมหลังการรักษาด้วยการส่องกล้องในผู้ป่วยแผลเปปติกที่มีเลือดออกรุนแรง

สิริกาญจน์ ยามาดะ, พัลลภา วงษ์วนากุล

วัตถุประสงค์: *หลังการรักษาด้วยการส่องกล้องในผู้ป่วยแผลเปปติกเลือดออกที่มีความเสี่ยงสูงต่อการมีเลือดออกซ้ำ พบว่าอัตราการมีเลือดออกซ้ำเกิดขึ้นประมาณร้อยละ 25-30 การให้ยาลดกรดกลุ่ม Proton Pump Inhibitor (PPI) ทางหลอดเลือดดำขนาดสูงแนะนำให้ใช้ในผู้ป่วยที่มีความเสี่ยงสูง เพื่อช่วยป้องกันภาวะเลือดออกซ้ำหลังการรักษาหยุดเลือดออกผ่านกล้องสำเร็จ การศึกษานี้มีจุดมุ่งหมายเพื่อศึกษาเปรียบเทียบประสิทธิภาพระหว่างการบริหารยาแพนโทพราโซลแบบฉีดเข้าหลอดเลือดดำขนาดสูงและการให้แบบหยดเข้าหลอดเลือดดำเพื่อป้องกันภาวะเลือดออกซ้ำในผู้ป่วยแผลกระเพาะอาหารหลังการรักษาหยุดเลือดออกครั้งแรกได้สำเร็จ โดยการรักษาผ่านกล้องส่องทางเดินอาหาร*

วัสดุและวิธีการ: *ทำการศึกษาเป็นแบบสุ่มไปข้างหน้าในโรงพยาบาลมหาราชนครเชียงใหม่ ในผู้ป่วยที่มีเลือดออกทางเดินอาหารส่วนต้นรุนแรงที่เกิดจากแผลเปปติก ผู้ป่วยทุกคนจะได้รับการส่องกล้องทางเดินอาหารภายใน 6 ชั่วโมงหลังเข้ารับการรักษาในโรงพยาบาล สามารถทำการหยุดเลือดออกได้สำเร็จในผู้ป่วย 28 คน หลังจากได้รับการส่องกล้องและฉีดยาแพนโทพราโซลขนาด 80 มิลลิกรัม ทางหลอดเลือดดำก่อนการรักษาด้วยกล้องส่องทางเดินอาหาร โดยผู้ป่วยจะถูกสุ่มเลือกหลังการรักษาด้วยกล้องสำเร็จในการบริหารยาแพนโทพราโซลออกเป็น 2 กลุ่ม โดยในผู้ป่วยกลุ่มแรกมีจำนวน 13 คน ได้รับยาแบบฉีดเข้าหลอดเลือดดำขนาดสูงขนาด 40 มิลลิกรัม ทุก 12 ชั่วโมง เป็นเวลา 7 วัน และกลุ่มที่ 2 มีจำนวน 15 คน ได้รับยาแบบหยดเข้าหลอดเลือดดำ ขนาด 8 มิลลิกรัมต่อชั่วโมง เป็นเวลา 3 วัน และให้ต่อในขนาด 40 มิลลิกรัม ทุก 12 ชั่วโมงจนครบ 7 วัน หลังจากนั้นผู้ป่วยจะได้รับยาแพโทพราโซลขนาด 20 มิลลิกรัม รับประทานวันละ 1 ครั้งเป็นเวลา 2 เดือน ประเมินผลและประสิทธิภาพการรักษาโดยการศึกษาอัตราการเกิดเลือดออกซ้ำภายใน 7 วัน หลังการหยุดเลือดออกด้วยกล้องส่องทางเดินอาหารและทำการวิเคราะห์ข้อมูลด้วยวิธีการทางสถิติ (Fisher's exact test) เพื่อเปรียบเทียบอัตราการมีเลือดออกซ้ำภายใน 7 วัน หลังการส่องกล้องเพื่อหยุดเลือดออก*

ผลการศึกษา: *พบว่าไม่มีความแตกต่างของอัตราการเกิดเลือดออกซ้ำอย่างมีนัยสำคัญทางสถิติสำหรับระหว่างการบริหารยาทั้ง 2 กลุ่ม โดยอัตราการเกิดเลือดออกซ้ำ ในกลุ่มที่ 1 เท่ากับร้อยละ 30.8 และกลุ่มที่ 2 เท่ากับร้อยละ 33.3 เปอร์เซนต์ ตามลำดับ (p = 1.0) พบว่ามีจำนวนผู้ป่วยที่ต้องการการผ่าตัดในกลุ่มที่ 1 จำนวน 3 คน และกลุ่มที่ 2 จำนวน 5 คน (p = 0.68) รวมทั้งไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติของจำนวนเลือดที่ใช้ อัตราการนอนโรงพยาบาล และอัตราการตาย*

สรุป: *จากการศึกษานี้พบว่าวิธีการบริหารยา ยาลดกรดกลุ่ม Proton Pump Inhibitor (PPI) 2 วิธี มีประสิทธิภาพใกล้เคียงกัน ในผู้ป่วยแผลเปปติกที่มีเลือดออกรุนแรง การศึกษาในกลุ่มประชากรที่มากขึ้นอาจช่วยให้การศึกษามีความชัดเจนมากขึ้น*