Observational Study

Medicine®

OPEN

Study on the preventive effect of intravenous esomeprazole in the management of nonvarices upper gastrointestinal bleeding

Xing-cheng Sun, BD, Wei-feng Yuan, BD, Wen-jie Ma, MM, Wen-jun Zhang, MD, Shuo-gui Xu, MD*

Abstract

This retrospective study investigated the preventive effect of intravenous esomeprazole (IVEO) in the prevention of nonvarices upper gastrointestinal bleeding (NUGIB).

This study enrolled 130 patients with NUGIB and all of them underwent successful endoscopic hemostasis, of which 65 cases received routine management and IVEO (Group A) and the other 65 cases received routine management alone (Group B). The primary outcome (recurrent bleeding rate within 72-hour, 7-day, and 30-day), and secondary outcomes ((all-cause mortality, bleeding-related mortality, blood transfused, hospital stay (day), and incidence of adverse events)) were compared between 2 groups.

Patients in the group A showed lower recurrent bleeding rate within 72-hour($P < .05$), 7-day ($P < .05$), and 30-day ($P < .05$), than that of patients in the group B. However, no significant differences were identified in all-cause mortality($P = .26$), bleeding-related mortality ($P = .57$), blood transfused ($P = .33$), and hospital stay ($P = .74$) between 2 groups. In addition, both groups had similar safety profile.

This study found that routine management and IVEO was superior to the routine management alone for preventing the recurrent bleeding rate after successful endoscopic hemostasis in patients with NUGIB.

Abbreviations: AEs = adverse events, IVEO = intravenous esomeprazole, NUGIB = nonvarices upper gastrointestinal bleeding.

Keywords: adverse events, effect, esomeprazole, nonvarices upper gastrointestinal bleeding

1. Introduction

Nonvarices upper gastrointestinal bleeding (NUGIB) is one of the most common encountered emergency disorders in daily clinical practice worldwide.[1–5] It is reported that its incidence varies between 50 and 150 cases per 100,000 adults annually.[6–9] Although its therapeutic managements have developed, its morbidity and mortality rate remain substantial.[10–14] It is reported that its 30-day mortality rate ranges from 5% to 10%.[15,16] Thus, the current management of NUGIB aims to stabilize hemodynamic circulation, stop existing bleeding, and prevent its recurrence.[17–22]

Endoscopic hemostatic intervention is reported that it cannot only identify high-risk stigmata on ulcers, but also can help control gastrointestinal bleeding to prevent its rebleeding and to decrease its mortality and morbidity.[23–26] However, there are still some patients who suffer from rebleeding accident. Thus, further medication is needed after successful endoscopic hemostasis. Studies suggested that intravenous esomeprazole (IVEO) can help prevent NUGIB. But there is lacking of evidence to support it for the prevention of recurrent bleeding in Chinese patients with NUGIB.[27,28] This retrospective study evaluated the preventive effect of IVEO for the prevention of recurrent bleeding in patients with NUGIB after successful endoscopic surgery.

2. Methods

2.1. Ethical approval

This retrospective study, based on the clinical data, was approved by the local ethics committee (Medical Ethical Committee of Changhai Hospital Affiliated to Navy Medical University). This study waived the requirement of sign informed consent from patients, because it was not risky for the patients.

2.2. Patients and study design

We performed this study based on the relevant guidelines and regulations. In this retrospective study, 130 eligible patients with

Editor: Jorddy Neves Cruz.

W-JM and W-FY contributed equally to this study.

This study was supported by Clinical Discipline Innovation Project of Changhai Hospital (2019YXK042), Naval Medical University Project (2018-CGPZ-B04), and Shanghai Science and Technology Commission Funds (19441901500).

The authors have no conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Department of Emergency, Changhai Hospital Affiliated to Navy Medical University, Shanghai, China.

* Correspondence: Shuo-gui Xu, Department of Emergency, Changhai Hospital Affiliated to Navy Medical University, No. 168 Changhai Road, Yangpu District, Shanghai 200433, China (e-mail: bonexu@139.com).

How to cite this article: Sun Xc, Yuan Wf, Ma Wj, Zhang Wj, Xu Sg. Study on the preventive effect of intravenous esomeprazole in the management of nonvarices upper gastrointestinal bleeding. Medicine 2021;100:20(e25420).

Received: 5 January 2021 / Received in final form: 20 February 2021 / Accepted: 9 March 2021

http://dx.doi.org/10.1097/MD.0000000000025420

NUGIB treated at Changhai Hospital Affiliated to Navy Medical University in China from June 2016 to May 2018 were included. All those patients achieved successful endoscopic hemostasis and routine management. In addition, among all those patients, 65 cases received IVEO (Group A), while the other 65 cases did not receive it (Group B).

Patients aged between 18 and 75 years old and diagnosed with NUGIB were included in this retrospective study. Moreover, all patients received successful endoscopic hemostasis. Exclusion criteria mainly included the following criteria:

1. bleeding from multiple ulcers or concomitant upper gastrointestinal sources;
2. gastrointestinal cancers;
3. patients had taken IVEO;
4. active GI bleeding;
5. advanced renal and liver diseases;
6. allergy to NUGIB; and
7. incomplete patient case records.

2.3. Intervention schedule

All patients in both groups received successful endoscopic hemostasis and routine management. The routine treatment included monitoring vital signs and circulatory conditions, and replenishing body fluids (established venous channels to replenish blood volume, and applied vasoactive drugs to improve blood perfusion). In addition, patients in the Group A also received IVEO 80 mg (AstraZeneca China, Shanghai, China) as a bolus infusion over 30 minutes. Then, it followed by a continuous intravenous infusion of 8 mg/h over 71.5 hours.

2.4. Outcome measurements

The primary outcome was recurrent bleeding rate within 72-hour, 7-day, and 30-day. The secondary outcomes were all-cause mortality, bleeding-related mortality, blood transfused, hospital stay (day), and adverse events (AEs).

2.5. Statistical analysis

In this study, we utilized SPSS software (SPSS V.19.0, IBM Corp., Armonk, NY) for statistical analysis. The continuous data was calculated as mean and standard deviation, and categorical data was exerted as frequencies and percentages (%). The *t* test or Mann–Whitney *U* test was employed to compare continuous data, and the χ^2 test or Fisher exact test was placed to compare categorical data. For all statistical analysis, a 2-side $P < .05$ was defined statistically significant.

3. Results

3.1. Patient baseline features

A total of 130 eligible patients after successful endoscopic hemostasis were enrolled in this study. Of those, 65 patient cases received routine management and IVEO (Group A), and the other 65 patient cases underwent routine treatment only (Group B). The clinical baseline features of 130 patients in both groups are presented in Table 1. All features were balanced between 2 groups in statistics ($P > .05$, table 1).

Table 1

Comparison of baseline demographics and clinical characteristics.

Characteristics	Group A (n = 65)	Group B (n = 65)	*P* value
Mean age (yr)	54.4 (12.3)	53.9 (11.7)	.81
Gender			
Male	41 (63.1)	45 (69.2)	.46
Female	24 (36.9)	20 (30.8)	–
Race (Asian China)	65 (66.2)	65 (75.4)	–
Body mass index (kg/m^2)	22.9 (3.0)	23.1 (3.2)	.71
Current alcohol consumption	23 (35.4)	20 (30.8)	.58
Current smoking	43 (66.2)	49 (75.4)	.25
Helicobacter pylori status			
Positive	39 (60.0)	42 (64.6)	.59
Negative	19 (29.2)	18 (27.7)	.85
Unclear	7 (10.8)	5 (7.7)	.55
Previous ulcer disease	20 (30.8)	24 (36.9)	.46
History of peptic ulcer			
Duodenal ulcer	15 (23.1)	19 (29.2)	.43
Gastric ulcer	17 (26.2)	13 (20.0)	.41
Both ulcer	3 (4.6)	4 (6.2)	.70
Bleeding ulcer location			
Stomach	14 (21.5)	10 (15.4)	.37
Duodenum	51 (78.5)	55 (84.6)	–

Data are present as mean ± standard deviation or number (%).

3.2. Primary outcome in Group A and Group B

Results of recurrent bleeding rate are listed in Table 2. Patients in the Group A achieved better improvement of overall recurrent bleeding rate within 72-hour ($P < .05$, table 2), 7-day ($P < .05$, table 2) and 30-day ($P < .05$, table 2), than that of patients in Group B. However, there were not significant differences in results of recurrent bleeding rate at different time points when patients were grouped based on the type of age and sex ($P > .05$, table 2).

3.3. Secondary outcomes in Group A and Group B

There were not significant differences in secondary outcomes of all-cause mortality (Group A, 3.1% vs Group B, 7.7%; $P = .26$; Table 3), bleeding-related mortality (Group A, 1.5% vs Group B, 3.1%; $P = .57$; table 3), blood transfused (Group A, 1.57 (2.21)vs

Table 2

Comparison of recurrent bleeding rate between 2 groups.

Outcomes	Groups	72-hour	7-day	30-day
Overall	Group A (n = 65)	2 (3.1)*	3 (4.6)*	3 (4.6)*
	Group B (n = 65)	9 (13.8)	11 (16.9)	12 (18.5)
Age (yr)				
≤65	Group A (n = 65)	1 (1.5)	2 (3.1)	2 (3.1)
	Group B (n = 65)	5 (7.7)	6 (9.2)	8 (12.3)
>65	Group A (n = 65)	1 (1.5)	1 (1.5)	1 (1.5)
	Group B (n = 65)	4 (6.2)	5 (7.7)	4 (6.2)
Gender				
Male	Group A (n = 65)	2 (3.1)	2 (3.1)	2 (3.1)
	Group B (n = 65)	7 (10.8)	8 (12.3)	8 (12.3)
Female	Group A (n = 65)	0 (0)	1 (1.5)	1 (1.5)
	Group B (n = 65)	2 (3.1)	3 (4.6)	4 (6.2)

Data are present as number (%).
* $P < .05$, compared with Group B.

Table 3

Comparison of secondary outcomes within 30 days between 2 groups.

Outcomes	Group A (n = 65)	Group B (n = 65)	*P* value
All-cause mortality	2 (3.1)	5 (7.7)	.26
Bleeding-related mortality	1 (1.5)	2 (3.1)	.57
Blood transfused (unit)	1.57 (2.21)	1.96 (2.38)	.33
Hospital stay (d)	4.6 (5.0)	4.9 (5.3)	.74

Data are present as mean ± standard deviation or number (%).

Group B, 1.96 (2.38); $P = .33$; table 3), and hospital stay (day) (Group A, 4.6 (5.0) vs Group B, 4.9 (5.3); $P = .74$; table 3) between 2 groups.

3.4. AEs in Group A and Group B

There were not significant differences in AEs of serious AEs (Group A, 1.5% vs Group B, 3.1%; $P = .57$; Table 4), duodenal ulcer hemorrhage (Group A, 3.1% vs Group B, 10.8%; $P = .10$; table 4), gastric ulcer hemorrhage (Group A, 1.5% vs Group B, 7.7%; $P = .13$; table 4), vomiting (Group A, 1.5% vs Group B, 4.6%; $P = .33$; table 4), nausea (Group A, 3.1% vs Group B, 6.2%; $P = .41$; table 4), abdominal pain (Group A, 3.1% vs Group B, 7.7%; $P = .26$; table 4), constipation (Group A, 3.1% vs Group B, 9.2%; $P = .16$; table 4), and dyspepsia (Group A, 4.6% vs Group B, 7.7%; $P = .47$; table 4) between 2 groups.

4. Discussion

Previous study investigated the efficacy of IVEO prevents recurrent peptic ulcer bleeding in a multiethnic subject.[29] Its findings suggest that high-dose IVEO after successful endoscopic treatment can benefit participants with high-risk peptic ulcer bleeding decreased recurrent bleeding within 72 hours and even lasts upon to 30 days.[29] Its results partly are consistent with the present study. In this retrospective cohort study, we compared the preventive effect between Chinese NUGIB patients with IVEO combined routine treatment, and routine therapy alone. Our study reported that there were significant differences in preventing recurrent bleeding rate within 72-hour, 7-day, and 30-day between 2 groups. It indicates that IVEO may benefit in preventing recurrent bleeding rate within 30 days after successful endoscopic hemostasis.

On the other hand, we did not detect significant differences in all-cause mortality, bleeding-related mortality, blood transfused, and hospital stay between 2 groups. It suggests that IVEO may not prevent mortality and hospital stay in patients NUGIB. Moreover, no AEs (serious AEs, duodenal ulcer hemorrhage, gastric ulcer hemorrhage, vomiting, nausea, abdominal pain, constipation, and dyspepsia) differed significantly between 2 groups, which showed that treatments in both groups had similar safety profile.

There were several limitations in this retrospective study. The first limitation was its retrospective nature because of the purely observational features when compared with prospective studies. The second limitation was that its very finite sample size made the statistical results that may be inaccurate sufficiently to reach an undisputed conclusion. The third limitation was that a total of 30 days from baseline to the end of observation was quite short. Thus, longer term of preventive effect and safety of IVEO in the prevention of NUGIB should be explored in further studies. To address such limitation, studies should harvest complete data from multiple hospitals to increase its sample size and follow-up period.

Table 4

Comparison of AEs between 2 groups.

AEs	Group A (n = 65)	Group B (n = 65)	*P* value
Serious AEs	1 (1.5)	2 (3.1)	.57
Duodenal ulcer hemorrhage	2 (3.1)	7 (10.8)	.10
Gastric ulcer hemorrhage	1 (1.5)	5 (7.7)	.13
Vomiting	1 (1.5)	3 (4.6)	.33
Nausea	2 (3.1)	4 (6.2)	.41
Abdominal pain	2 (3.1)	5 (7.7)	.26
Constipation	2 (3.1)	6 (9.2)	.16
Dyspepsia	3 (4.6)	5 (7.7)	.47

Data are present as number (%).
AEs = adverse events.

5. Conclusion

The results of this study found that routine management and IVEO can decrease the recurrent bleeding rate after successful endoscopic hemostasis in patients with NUGIB.

Author contributions

Conceptualization: Xing-cheng Sun, Wei-feng Yuan, Wen-jun Zhang, Shuo-gui Xu.
Data curation: Xing-cheng Sun, Wei-feng Yuan, Wen-jie Ma, Shuo-gui Xu.
Formal analysis: Shuo-gui Xu.
Funding acquisition: Shuo-gui Xu.
Investigation: Shuo-gui Xu.
Methodology: Xing-cheng Sun, Wen-jun Zhang.
Project administration: Shuo-gui Xu.
Resources: Xing-cheng Sun, Wei-feng Yuan, Wen-jie Ma, Wen-jun Zhang.
Software: Wen-jie Ma, Wen-jun Zhang.
Supervision: Shuo-gui Xu.
Validation: Xing-cheng Sun, Wen-jie Ma, Shuo-gui Xu.
Visualization: Xing-cheng Sun, Wei-feng Yuan, Wen-jie Ma, Wen-jun Zhang, Shuo-gui Xu.
Writing – original draft: Xing-cheng Sun, Wei-feng Yuan, Wen-jun Zhang, Shuo-gui Xu.
Writing – review & editing: Xing-cheng Sun, Wei-feng Yuan, Wen-jie Ma, Wen-jun Zhang, Shuo-gui Xu.

References

[1] Kim JS, Kim BW, Kim DH, et al. Guidelines for nonvariceal upper gastrointestinal bleeding. Gut Liver 2020;14:560–70.
[2] Barkun AN, Laine L, Leontiadis GI, et al. Management of nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2020;172:573.
[3] Rahman SI, Saeian K. Nonvariceal upper gastrointestinal bleeding. Crit Care Clin 2016;32:223–39.
[4] Park T, Wassef W. Nonvariceal upper gastrointestinal bleeding. Curr Opin Gastroenterol 2014;30:603–8.
[5] Rotondano G. Epidemiology and diagnosis of acute nonvariceal upper gastrointestinal bleeding. Gastroenterol Clin North Am 2014;43:643–63.
[6] Targownik LE, Nabalamba A. Trends in management and outcomes of acute nonvariceal upper gastrointestinal bleeding:1993-2003. Clin Gastroenterol Hepatol 2006;4:1459–66.

[7] van Leerdam ME, Vreeburg EM, Rauws EA, et al. Acute upper GI bleeding: did anything change? Time trend analysis of incidence and outcome of acute upper GI bleeding between 1993/1994 and 2000. Am J Gastroenterol 2003;98:1494–9.
[8] Lassen A, Hallas J, Schaffalitzky de Muckadell OB. Complicated and uncomplicated peptic ulcers in a Danish county 1993-2002: a population-based cohort study. Am J Gastroenterol 2006;101:945–53.
[9] Theocharis GJ, Thomopoulos KC, Sakellaropoulos G, et al. Changing trends in the epidemiology and clinical outcome of acute upper gastrointestinal bleeding in a defined geographical area in Greece. J Clin Gastroenterol 2008;42:128–33.
[10] DiMaio CJ, Stevens PD. Nonvariceal upper gastrointestinal bleeding. Gastrointest Endosc Clin N Am 2007;17:253–72.
[11] Burke SJ, Golzarian J, Weldon D, et al. Nonvariceal upper gastrointestinal bleeding. Eur Radiol 2007;17:1714–26.
[12] Aabakken L. Nonvariceal upper gastrointestinal bleeding. Endoscopy 2005;37:195–200.
[13] Huang CS, Lichtenstein DR. Nonvariceal upper gastrointestinal bleeding. Gastroenterol Clin North Am 2003;32:1053–78.
[14] Rollhauser C, Fleischer DE. Nonvariceal upper gastrointestinal bleeding. Endoscopy 2002;34:111–8.
[15] Barkun A, Sabbah S, Enns R, et al. The Canadian Registry on nonvariceal upper gastrointestinal bleeding and endoscopy (RUGBE): endoscopic hemostasis and proton pump inhibition are associated with improved outcomes in a real-life setting. Am J Gastroenterol 2004;99:1238–46.
[16] Esrailian E, Gralnek IM. Nonvariceal upper gastrointestinal bleeding: epidemiology and diagnosis. Gastroenterol Clin North Am 2005;34:589–605.
[17] Ferguson CB, Mitchell RM. Nonvariceal upper gastrointestinal bleeding: standard and new treatment. Gastroenterol Clin North Am 2005;34:607–21.
[18] Karakonstantis S. Management of nonvariceal upper gastrointestinal bleeding. Ann Intern Med 2020;172:572–3.
[19] Rivkin K, Lyakhovetskiy A. Treatment of nonvariceal upper gastrointestinal bleeding. Am J Health Syst Pharm 2005;62:1159–70.
[20] Park JS, Kim HK, Shin YW, et al. Novel hemostatic adhesive powder for nonvariceal upper gastrointestinal bleeding. Endosc Int Open 2019;7:E1763–7.
[21] Awadalla MS, Desimone M, Wassef W. Updates on management of nonvariceal upper gastrointestinal bleeding. Curr Opin Gastroenterol 2019;35:517–23.
[22] Holzwanger EA, Mahmoud M, Wassef W. Advances in management of nonvariceal upper gastrointestinal bleeding. Curr Opin Gastroenterol 2018;34:436–43.
[23] Hsu E, Law SD. Refractory nonvariceal upper gastrointestinal bleeding requiring surgical intervention. Cureus 2019;11:e4135.
[24] Yip BCH, Sayeed Sajjad H, Wang JX, et al. Endoscopic treatment modalities and outcomes in nonvariceal upper gastrointestinal bleeding. World J Gastrointest Endosc 2020;12:72–82.
[25] Song LM, Levy MJ. Emerging endoscopic therapies for nonvariceal upper gastrointestinal bleeding. Gastroenterol Clin North Am 2014;43:721–37.
[26] Kim KB, Yoon SM, Youn SJ. Endoscopy for nonvariceal upper gastrointestinal bleeding. Clin Endosc 2014;47:315–9.
[27] Bai Y, Chen DF, Wang RQ, et al. Intravenous esomeprazole for prevention of peptic ulcer rebleeding: a randomized trial in Chinese patients. Adv Ther 2015;32:1160–76.
[28] Sung JJ, Mössner J, Barkun A, et al. Intravenous esomeprazole for prevention of peptic ulcer re-bleeding: rationale/design of peptic ulcer bleed study. Aliment Pharmacol Ther 2008;27:666–77.
[29] Sung JJY, Barkun A, Kuipers EJ, et al. Intravenous esomeprazole for prevention of recurrent peptic ulcer bleeding: a randomized trial. Ann Intern Med 2009;150:455–64.