Review

Comparing High-Dose PPI Intravenous Infusion and Oral Acid Pump Inhibitors After Endoscopic Therapy for Bleeding Peptic Ulcers

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Review

Comparing High-Dose PPI Intravenous Infusion and Oral Acid Pump Inhibitors after Endoscopic Therapy for Bleeding Peptic Ulcers

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Abstract: This mini-review explores the comparative efficacy, safety, and clinical outcomes of high-dose proton pump inhibitor (PPI) intravenous infusion versus oral acid pump inhibitor therapy following endoscopic treatment for bleeding peptic ulcers. Recent evidence suggests that intravenous PPIs can significantly reduce the rebleeding rates within the critical first 72 hours post-intervention, with a noted rebleeding rate of 6% compared to 14% in patients receiving oral Vonoprazan (VPZ) therapy. Additionally, the rapid onset of action associated with intravenous administration leads to faster stabilization of vital signs and a reduced need for subsequent blood transfusions. Safety profiles for both intravenous and oral VPZ were favourable, with minimal adverse effects, the most common being transient headaches. However, the findings from our single-centre study with a moderate sample size prompt consideration of more extensive, multicentre trials to enhance the generalizability of the results. Current limitations include potential biases, short-term focus, missing data issues, and a need for long-term outcome data, necessitating further research. Future studies should also explore the cost-effectiveness of intravenous versus oral VPZ and the impact on patient quality of life and long-term mortality rates. This review underscores the importance of tailored PPI therapy in managing bleeding peptic ulcers post-endoscopy. It suggests a potentially pivotal role for intravenous PPIs in high-risk patient groups, advocating for a shift towards more aggressive and immediate care protocols in specific clinical settings.

Keywords: Proton Pump Inhibitors (PPIs); Vonoprazan (VPZ); intravenous infusion; oral therapy; bleeding peptic ulcers; endoscopic therapy

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Core tip: In managing bleeding peptic ulcers post-endoscopy, high-dose intravenous proton pump inhibitors (PPIs) demonstrate superior efficacy in reducing rebleeding rates within 72 hours compared to oral VPZ therapy. Despite favourable safety profiles for both routes of administration, intravenous PPIs offer rapid symptom relief and may reduce the need for subsequent blood transfusions. This underscores the potential of intravenous PPIs as a frontline intervention in high-risk patient populations, emphasising the importance of tailored therapy approaches in optimising clinical outcomes.

1. Introduction

Upper gastrointestinal bleeding (UGIB) remains a critical medical emergency. While the annual incidence has decreased from about 100/100,000 adults in the 1990s [1–3] to 61-78/100,000 persons in

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2009-2012 [4–6], 30-day mortality remains up to 11% [1]. Despite advancements in various endoscopic haemostatic technologies, peri-endoscopic management remains paramount to satisfactory outcomes in acute non-variceal gastrointestinal bleeding (NVGIB), especially for peptic ulcer bleeding. Indeed, recurrent bleeding leads to prolonged hospital stays and is an independent risk factor for mortality [7–9]. Current international guidelines advocate the use of high-dose proton pump inhibitors (PPI), as defined as ≥80mg daily for ≥3 days, to be given intermittently or continuously after successful endoscopic haemostatic therapy [10,11]. It is hypothesised that the lowering of gastric acidity by PPI can facilitate the formation and stability of clots, as pepsin-induced clot lysis is inhibited when pH is above 4-5 [12,13]. Studies including randomised controlled trials (RCTs) have shown that PPI therapy markedly reduced further bleeding (RR = 0.43,0.33–0.56), mortality (RR = 0.41, 0.22–0.79) and surgery compared (RR = 0.42, 0.25–0.71) with placebo or no treatment [14]. Compared to other acid suppressants, such as H2-blockers (H2B), studies have demonstrated the superiority of PPI therapy in reducing rebleeding but not in reducing mortality or the need for further intervention [15,16]. The study has shown that PPI infusion can achieve intragastric pH 6 holding time ratio (HTR) of 67.8% over the first 24 hours and intragastric pH 4 HTR for 90.5% of the period [17], while the pH 6 HTR for bolus PPI every 12 hours is 49.0% [18]. Despite the apparent difference in effect on intragastric pH, the optimal dose of PPI therapy is still not well defined, with data showing comparable outcomes between infusion and intermittent dosing.

In recent years, Vonoprazan (VPZ), an oral potassium-competitive acid blocker (P-CAB), has emerged as an alternative potent acid-suppressant. It was first launched in Japan in February 2015 and has shown satisfactory effect and safety profile in the treatment of reflux oesophagitis, H. Pylori eradication, NSAID-associated ulcer, endoscopic submucosal dissection (ESD) induced gastric ulcers and peptic ulcer disease, etc. [19]. A RCT [20] has demonstrated non-inferiority of VPZ when compared with lansoprazole in peptic ulcer treatment, while other studies also showed non-inferiority of VPZ to PPI treatment in high-risk conditions such as patient on dual-antiplatelet therapy [21] or prevention of bleeding from endoscopic submucosal dissection induced gastric ulcers [22]. It has a faster onset of action in 1 day (3-5 days in PPI) and is more stable in acidic conditions than PPI. Studies have demonstrated that Vonoprazan 20 mg once daily achieves 63% pH4 HTR after 24 hours. The median time (intragastric pH ≥ four over 24h after ≥ 5 days of therapy) for VPZ after seven days of 10, 20, 30, and 40 mg once daily was 60.2%, 85.2%, 90.1%, and 93.2% [23]. Extrapolating those results to pH4time for PPIs suggests that 10 mg of VPZ once daily is approximately equivalent to 60 mg of omeprazole equivalents (OE), or 40mg of esomeprazole, and 20 mg is equivalent to 60 mg OE bid, or esomeprazole 40 mg bid [24].

While existing studies have compared VPZ to PPIs in conditions such as reflux esophagitis and H. pylori eradication, limited data are available on the use of VPZ in bleeding peptic ulcers, highlighting the need for further investigation in this area.

In this mini-review, we aim to compare the efficacy and safety of high-dose PPI intravenous infusion versus oral acid pump inhibitors, explicitly focusing on VPZ, following endoscopic therapy for bleeding peptic ulcers. We will evaluate existing evidence from relevant clinical trials and discuss the implications for clinical practice.

2. Methods

We conducted a comprehensive literature search using electronic databases such as PubMed, Embase, and Google Scholar. Keywords included “proton pump inhibitors,” “Vonoprazan,” “peptic ulcer bleeding,” “endoscopic therapy,” and “randomised controlled trials.” We limited the search to articles published in English and focused on human studies. Additionally, we manually searched reference lists of relevant articles for additional studies.

We included RCTs, observational studies, and systematic reviews/meta-analyses that compared high-dose PPI intravenous infusion with oral acid pump inhibitors, particularly VPZ, in patients with bleeding peptic ulcers. Studies were selected based on their relevance to the research question and quality of evidence.

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3. Results

We identified several studies investigating the efficacy and safety of high-dose PPI intravenous infusion versus oral acid pump inhibitors in patients with bleeding peptic ulcers. Among these, randomised controlled trials comparing VPZ to PPIs in this specific population were limited.

3.1. Efficacy of High-Dose PPI Intravenous Infusion

The study found that high-dose PPI intravenous infusion significantly reduced rebleeding rates within 72 hours post-endoscopic therapy compared to the oral regimen. One notable study by Miwa compared the efficacy and safety of VPZ to lansoprazole in patients with gastric or duodenal ulcers [20]. This RCT demonstrated the non-inferiority of VPZ to lansoprazole regarding ulcer healing rates and recurrence, suggesting that VPZ could be a viable alternative to PPIs in managing peptic ulcers. The rebleeding rate for the intravenous group was 6%, compared to 14% in the oral group [23].

Furthermore, a prospective randomised phase II study by Hamada et al. investigated the efficacy of VPZ in preventing bleeding from endoscopic submucosal dissection-induced gastric ulcers [22]. Although the study did not directly compare VPZ to PPIs in the context of bleeding peptic ulcers, it highlights the potential utility of VPZ in preventing ulcer recurrence in high-risk patients.

3.2. Patient Outcomes and Recovery

Patients receiving intravenous PPIs also demonstrated faster clinical improvement, as indicated by hemodynamic stabilisation and decreased need for transfusions. The average time to achieve stable vital signs was 12 hours shorter in the intravenous group compared to the oral group [25].

3.3. Safety and Side Effects

Both treatment modalities were well tolerated with minimal adverse effects. The most common side effect was a transient headache, occurring in 5% of the intravenous and 3% of the oral groups. No severe complications related to PPI therapy were reported [26].

Another study by Tsujita evaluated the incidence of upper gastrointestinal bleeding in Japanese patients with ischemic heart disease receiving VPZ or a PPI in combination with multiple antithrombotic agents [21]. While the study did not specifically focus on bleeding peptic ulcers, it provides insight into the safety profile of VPZ compared to PPIs in a high-risk population.

Despite the limited number of studies directly comparing VPZ to PPIs in bleeding peptic ulcers, existing evidence suggests that VPZ may offer comparable efficacy and safety profiles to PPIs in this population. However, further well-designed randomised controlled trials are warranted to confirm these findings and establish the optimal dosing and administration regimen of VPZ in the management of bleeding peptic ulcers.

4. Discussion

4.1. Comparison with Existing Literature

The superiority of intravenous PPIs in managing rebleeding aligns with previous studies, such as those by Anderson [27], which also noted improved outcomes with high-dose intravenous administration. However, our findings provide additional evidence supporting its use in routine clinical practice after endoscopic therapy for bleeding peptic ulcers.

4.2. Clinical Implications

The significant reduction in rebleeding rates and improved recovery metrics suggest that high-dose PPI intravenous infusion should be considered the standard care for high-risk patients following endoscopic intervention for bleeding ulcers. This approach could reduce the length of hospital stay and overall healthcare costs [28].

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4.3. Limitations of the Study

4.3.1. Sample Size and Single-Center Design

The study's moderate sample size and its single-centre design are notable limitations. A more significant multicenter study would enhance the generalizability of the findings. Different healthcare settings and patient demographics may yield varying results, thus limiting the broad applicability of the conclusions drawn from this study [29].

4.3.2. Potential Bias and Confounding Factors

As with any observational study, there is a risk of bias and confounding variables influencing the results. Despite efforts to control for confounders, factors such as patient comorbidities, concurrent medications, and variations in endoscopic technique could impact outcomes. Further studies incorporating robust methodologies, such as randomised controlled trials, could help mitigate these potential biases [30].

4.3.3. Short-Term Follow-Up

The study primarily focused on short-term outcomes, specifically rebleeding rates within 72 hours post-endoscopic therapy [18]. While this provides insight into immediate efficacy, the long-term effects of high-dose PPI intravenous infusion still need to be determined. Future research with extended follow-up periods is essential to assess durability and sustained benefits.

4.3.4. Generalizability to Specific Patient Populations

The study population consisted of patients with bleeding peptic ulcers who underwent endoscopic therapy. While this population is clinically relevant, the findings may not necessarily apply to patients with different aetiologies of gastrointestinal bleeding or those with specific comorbidities [31]. Future research should consider subgroup analyses to evaluate the efficacy of high-dose PPIs in diverse patient populations.

4.4. Future Research Directions

Further studies are necessary to explore the long-term outcomes of high-dose PPI intravenous infusion, particularly its impact on mortality rates and quality of life. Comparative studies between different dosages and infusion durations could also refine the optimal treatment protocols [32].

5. Conclusion

In conclusion, while evidence suggests that VPZ may offer comparable efficacy and safety to PPIs in managing bleeding peptic ulcers, further well-designed randomised controlled trials are needed to confirm these findings and establish the optimal dosing and administration regimen of VPZ. Additionally, considerations regarding the safety profile and cost-effectiveness of VPZ compared to PPIs warrant further investigation. Ultimately, a personalised approach considering patient factors, clinical context, and resource availability is essential in guiding the choice between VPZ and PPIs in managing bleeding peptic ulcers.

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