

Minireview Article

A Literature Review: Adjunctive Use of Proton Pump Inhibitors to Variceal Band Ligation in Cirrhotic Patients.

Abstract

This review focuses on the effect of Proton pump inhibitors (PPIs), acid-suppressive agents, combined with ligation to manage rebleeding ulcers in cirrhotic patients. Data reviewed during approximately recent 20 years combining different studies showed different results, with most supporting their role in this field.

Keywords :acid suppression ,ligation ulcer ,PPI, varices

Comment [Y1]: Introduction
methods
Result
conclusion

Introduction:

Many recent studies have focused on using Proton pump inhibitors (PPIs), acid-suppressive agents, combined with ligation to manage rebleeding ulcers in cirrhotic patients. Data reviewed during approximately 20 years showed different results, with most supporting their role in this field.

Comment [Y2]: no need of bonding

Body:

Up to 50 % of cirrhotic patients may suffer gastroesophageal varices with a chance of 20% developing a life-threatening acute haemorrhage in advanced cases.[1] Variceal band ligation is an effective, simple and relatively safe technique used to treat oesophageal varices in patients with cirrhosis. It is also a good treatment option for the prevention of variceal rebleeding recurrence, especially for patients who are intolerant, bled or contraindicated to β -blockers treatment prophylaxis.[2]

Comment [Y3]: irrelevant title

Comment [Y4]: should be within pull stop

Comment [Y5]: no need of bolding

Proton pump inhibitors (PPIs) are the most potent pharmacological agents for the inhibition of gastric acid secretion. Their use in peptic ulcer disease and general upper gastrointestinal diseases improves disease conditions due to their faster onset of action, increased healing rates, and greater symptom relief compared with ranitidine and placebo. This is why it is considered the first choice for gastric ulcer treatment.[3]

Comment [Y6]: no need of bolding

In Canada Proton pump inhibitors administered intravenously after endoscopic treatment of peptic ulcers significantly reduce the recurrence of bleeding with a high likelihood of cost-effectiveness (costs of treatment, surgical procedures and hospitalizations). Intravenous proton pump inhibitors are considered standard practice for all upper gastrointestinal bleeding patients.[4]

Comment [Y7]: grammar

Comment [Y8]: these paragraphs are introduction parts

The efficacy of pantoprazole, a proton pump inhibitor as an adjunct to elective oesophageal ligation (EVL) was assessed in a double-blinded, randomized, trial to decrease the risk of variceal haemorrhage. Pantoprazole significantly reduced the size of post-banding ulcers (50%) on follow-up endoscopy compared to subjects who received a placebo. While the total ulcer number and patient symptoms showed no difference.[5]

Comment [Y9]: up to this part it is all about introduction here after the method should be described and followed by discussion

Formatted: Highlight

A meta-analysis was conducted to assess the association between PPI use in cirrhotic patients and spontaneous bacterial peritonitis (SBP) development. The observational studies included ended up with inconsistent results. It concludes that there is a potential association which needs further studies to be clarified and PPIs should be used only when clearly indicated.[6]

Formatted: Highlight

This study was followed by another one evaluating the efficacy of endoscopic variceal ligation (EVL) combined with proton pump inhibitor (PPI) infusion (either omeprazole or pantoprazole) compared to a combination of (EVL) with vasoconstrictor infusion after managing acute variceal bleeding. The conclusion was that the PPI side is similar in terms of initial hemostasis, and rate of very early rebleeding with the benefit of fewer adverse events.[7]

Comment [Y10]: use either abbreviation or full term

Formatted: Highlight

Comment [Y11]: remove the bracket

Another randomized, controlled trial was performed on elective EVL patients assessing the efficacy of rabeprazole, a PPI, on treatment failure defined as either haemorrhage from varices or severe medical complications. It concludes that acid suppression therapy should be considered after EVL since it reduces the risk of treatment failure.[8]

The efficacy and safety of **proton pump inhibitors** (PPIs) in gastroesophageal varices (GEVs) were checked by running a systematic review of 20 studies. Results supported the use of short-course (10 days) of PPI post-EVL since it reduces ulcer size and discouraged prolonged use and high-dose infusion till proven by evidenced data.[9]

Then a study was conducted investigating the general treatment of PPIs in cirrhotic patients related to overall survival. They concluded that PPI use is an independent risk factor for mortality, despite that, a causative role is not found.[10]

After that liver cirrhotic patients who underwent elective EVL for primary prophylaxis of variceal bleeding were enrolled in a study. The occurrence of bleeding post-EVL is the primary

endpoint. The conclusion was that it is important to start PPI therapy as soon as possible after EVL since not starting PPI is the sole risk factor for post-EVL bleeding.[11]

Also, a retrospective cohort study assessing the effect of PPI as part of acid suppression therapy (histamine-2 receptor antagonists were also tried) combined with EVL and vasoconstrictor, in rebleeding cirrhotic patients compared to EVL and vasoconstrictor alone, was carried out evaluating rebleeding and mortality rates. The results said that their role as an adjuvant to normal EVL plus vasoconstrictor therapy may not change the rebleeding and mortality rates.[12]

This recent meta-analysis study reviewed the efficacy and safety of proton pump inhibitors (PPIs) as treatment or prophylaxis on post-band ligation ulcers in cirrhotic patients with gastroesophageal varices (GEVs). Pantoprazole, Rabeprazole, or Omeprazole (the most commonly used) were included. The conclusion is that the risk of bleeding after ligation is reduced by twofold, while the risk of bleeding-related death is reduced by threefold.[13]

Comment [Y12]: research(reference) finding figures (number values should be indicated)

Conclusion:

PPIs use as adjunctive to EVL in cirrhotic patients for either prophylaxis or treatment of bleeding ulcers following ligation show successful results and a good impact on general health and should be tried on those patients to improve their care.

References:

- [1] J. Zhu, X. Qi, H. Yu, C. Su, X. Guo, Acid suppression in patients treated with endoscopic therapy for the management of gastroesophageal varices: a systematic review and meta-analysis, *Expert Rev Gastroenterol Hepatol.* 12 (2018) 617–624. <https://doi.org/10.1080/17474124.2018.1456918>.
- [2] J.C. Garcia-Pagán, J. Bosch, Endoscopic band ligation in the treatment of portal hypertension, *Nat Clin Pract Gastroenterol Hepatol.* (2005). <https://doi.org/10.1038/ncpgasthep0323>.
- [3] B. Gastroenterology, M. Salas, A. Ward, J. Caro, *BMC Gastroenterology* Are proton pump inhibitors the first choice for acute treatment of gastric ulcers? A meta analysis of randomized clinical trials, 2002. <http://www.biomedcentral.com/1471-230X/2/17>.
- [4] R.A. Enns, Y.M. Gagnon, K.P. Rioux, A.R. Levy, Cost-effectiveness in Canada of intravenous proton pump inhibitors for all patients presenting with acute upper gastrointestinal bleeding, *Aliment Pharmacol Ther.* 17 (2003) 225–233. <https://doi.org/10.1046/j.1365-2036.2003.01412.x>.
- [5] N.J. Shaheen, E. Stuart, S.M. Schmitz, K.L. Mitchell, M.W. Fried, S. Zacks, M.W. Russo, J. Galanko, R. Shrestha, Pantoprazole reduces the size of postbanding ulcers after variceal band ligation: A randomized, controlled trial, *Hepatology.* 41 (2005) 588–594. <https://doi.org/10.1002/hep.20593>.

- [6] G. Trikudanathan, J. Israel, J. Cappa, D.M. O'Sullivan, Association between proton pump inhibitors and spontaneous bacterial peritonitis in cirrhotic patients - A systematic review and meta-analysis, *Int J Clin Pract.* 65 (2011) 674–678. <https://doi.org/10.1111/j.1742-1241.2011.02650.x>.
- [7] G.H. Lo, D.S. Perng, C.Y. Chang, C.M. Tai, H.M. Wang, H.C. Lin, Controlled trial of ligation plus vasoconstrictor versus proton pump inhibitor in the control of acute esophageal variceal bleeding, *Journal of Gastroenterology and Hepatology (Australia)*. 28 (2013) 684–689. <https://doi.org/10.1111/jgh.12107>.
- [8] H. Hidaka, T. Nakazawa, G. Wang, S. Kokubu, T. Minamino, J. Takada, Y. Tanaka, Y. Okuwaki, M. Watanabe, S. Tanabe, A. Shibuya, W. Koizumi, Long-term administration of PPI reduces treatment failures after esophageal variceal band ligation: A randomized, controlled trial, *J Gastroenterol.* 47 (2012) 118–126. <https://doi.org/10.1007/s00535-011-0472-0>.
- [9] E.A.G. Lo, K.J. Wilby, M.H.H. Ensom, Use of Proton Pump Inhibitors in the Management of Gastroesophageal Varices: A Systematic Review, *Annals of Pharmacotherapy.* 49 (2015) 207–219. <https://doi.org/10.1177/1060028014559244>.
- [10] G. Dultz, A. Piiper, S. Zeuzem, B. Kronenberger, O. Waidmann, Proton pump inhibitor treatment is associated with the severity of liver disease and increased mortality in patients with cirrhosis, *Aliment Pharmacol Ther.* 41 (2015) 459–466. <https://doi.org/10.1111/apt.13061>.
- [11] S.H. Kang, H.J. Yim, S.Y. Kim, S.J. Suh, J.J. Hyun, S.W. Jung, Y.K. Jung, J.S. Koo, S.W. Lee, Proton pump inhibitor therapy is associated with reduction of early bleeding risk after prophylactic endoscopic variceal band ligation a retrospective cohort study, *Medicine (United States)*. 95 (2016) 1–9. <https://doi.org/10.1097/MD.0000000000002903>.
- [12] C.K. Wu, C.M. Liang, C.N. Hsu, T.H. Hung, L.T. Yuan, S.H. Nguang, J.W. Wang, K.L. Tseng, M.K. Ku, S.C. Yang, W.C. Tai, C.W. Shih, P.I. Hsu, D.C. Wu, S.K. Chuah, The role of adjuvant acid suppression on the outcomes of bleeding esophageal varices after endoscopic variceal ligation, *PLoS One.* 12 (2017) 1–15. <https://doi.org/10.1371/journal.pone.0169884>.
- [13] S.A. Elseidy, A. Sayed, A.K. Awad, D. Mandal, M. Mostafa, A. Adigun, M. Vorla, Z. Zamani, A. Iqbal, PPI efficacy in the reduction of variceal bleeding incidence and mortality , a meta - analysis, *Egypt J Intern Med.* (2022). <https://doi.org/10.1186/s43162-022-00156-2>.

Comment [Y13]: add more references