ISSN: 2474 - 9206

Short Review Article

Journal of Anesthesia & Pain Medicine

Potential Carcinogenicity with Prolonged Use of Proton Pump Inhibitors as Gastric Acid Suppressants

[1]Amit Sharma, [2]Vikram Vohra

[1]Consultant, Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, India

[2]Senior Consultant, Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, India

***Corresponding author**
Amit Sharma, Consultant, Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, India

Submitted: 30 Dec 2021; **Accepted:** 06 Jan 2022; **Published:** 31 Jan 2022

Citation: *Amit Sharma, Vikram Vohra. (2022). Potential Carcinogenicity with Prolonged Use of Proton Pump Inhibitors as Gastric Acid Suppressants. J Anesth Pain Med 7(1): 24 -25.*

Introduction

The mainstay of the treatment of Peptic Ulcer Disease (PUD), Gastro-esophageal reflux Disease (GERD) and other forms of gastritis including ulcers caused by non-Steroidal anti-inflammatory drugs (NSAID), is the group of Drugs known as Proton Pump Inhibitors (PPI). PPI include Omeprazole, Pantoprazole, Rabeprazole, Esomeprazole etc. The action is exerted by suppression of acid production in the stomach by blocking the gastric H+K+-ATPase. They are effective also in the prevention of PUD and form an integral part in the eradication of Helicobacter Pylori along with antibiotics from the gastric-duodenal part of the alimentary Canal [1].

However, there is some evidence to suggest that regular use of PPI for more than 2 years may be associated with increased risk of Gastric Cancer which may be as high as 40% as suggested in a meta-analysis of 94558 patients collectively in 11 observational trials [2]. Gastric acid production is a normal physiologic process of the human body and its prolonged suppression is bound lead to some adverse outcomes. There is evidence to show that PPI use may disturb the gastric microbiome and this disruption may be even more than the disturbances caused by the use of Antibiotics [3].

Carcinoma of the stomach is a very common cancer in the world accounting for almost one-fifth of Cancer cases and for almost one-third of Cancer-related deaths [4]. There is greatly increased risk of Carcinoma for stomach (around 80 to 90%) in chronic infection of H. Pylori [5].

PPI with their strong suppression of gastric acid may cause significant alterations in the physiological environment of the gastric mucosa which may include hyperplasia of the enterochromaffin cells and increased levels of gastrin (hypergastrinemia). Moreover, as already mentioned above, because of its acid-suppressing action, PPIs can disturb the gastric microbiota and worsen atrophy of gastric mucosa. All these factors acting separately and/or in unison may contribute to an enhanced risk of Carcinoma of the stomach [6-8].

Hypergastrinemia's association with an enhanced risk of Gastric Carcinoma has been clearly documented in a study of Finnish smokers (all male) with follow-up of above 24 years numbering 29133 [9].

Helicobacter pylori infection is strongly associated with risk of Gastric Cancer but even after successful eradication of H. Pylori, there is evidence to suggest that there still exists an increased risk of Gastric Carcinoma in long term PPI users [10].

The major other group of acid suppressant drugs namely the H2-Receptor Antagonists (H2-RA) decrease gastric acid secretion by binding reversibly to histamine receptors (H2) on parietal gastric cells thereby blocking binding to Histamine and functioning as competitive antagonists for H2 Receptors. There is some evidence to suggest that long term use of H2-RA may not be associated with increased risk of Gastric Cancer [11].

A meta-analysis which combined studies consisting of pre-medication with PPI (omeprazole, pantoprazole etc.) was less effective than Ranitidine (H2-RA) in reducing the gastric secretion volume and raising gastric pH mostly in the context of preventing Acid Aspiration Syndrome (AAS) in patients administered General Anaesthesia [12, 13].

Conclusion

To conclude, though the efficacy of PPI for treatment of GERD, PUD and healing and maintenance erosive forms of gastric diseases, remains supreme, but continuous use especially more than 2 years carries a risk of gastric carcinoma which the treating physician should be aware of. In view of the comparative safety of the H2-RA for long term use, these may be given to the patient when there is adequate relief of symptoms and a longer maintenance treatment duration is required.

References

1. Ahmed A, Clarke JO (2021) Proton Pump Inhibitors (PPI). StatPearls Publishing 2021. https://www.ncbi.nlm.nih.gov/books/NBK557385.

2. Ahn JS, Eom CS, Jeon CY, Sang Min Park (2013) Acid suppressive drugs and gastric cancer: a meta-analysis of observational studies. World J Gastroenterol 19: 2560-2568.
3. Imhann F, Bonder MJ, Vich Vila A, Jingyuan Fu, Zlatan Mujagic, et al. (2016) Proton pump inhibitors affect the gut microbiome. Gut 65: 740-748.
4. Fitzmaurice C, Christine Allen, Ryan M Barber, Lars Barregard, Zulfiqar A Bhutta, et al. (2017) Global, Regional, and National Cancer Incidence, Mortality, Years of Life Lost, Years Lived with Disability, and Disability-Adjusted Life-years for 32 Cancer Groups, 1990 to 2015: A Systematic Analysis for the Global Burden of Disease Study. JAMA Oncol 3: 524-548.
5. Helicobacter and Cancer Collaborative Group (2001) Gastric cancer and Helicobacter pylori: a combined analysis of 12 case control studies nested within prospective cohorts. Gut 49: 347-353.
6. International Agency for Research on Cancer (2014) Helicobacter pylori eradication as a strategy for preventing gastric cancer. IARC Working Group Reports 8: 1-181.
7. Lundell L, Vieth M, Gibson F, Nagy P, Kahrilas PJ (2015) Systematic review: the effects of long-term proton pump inhibitor use on serum gastrin levels and gastric histology. Aliment Pharmacol Ther 42: 649-663.
8. Sanduleanu S, Jonkers D, De Bruine A, Hameeteman W, Stockbrügger RW (2001) Non-Helicobacter pylori bacterial flora during acid-suppressive therapy: differential findings in gastric juice and gastric mucosa. Aliment Pharmacol Ther 15: 379-388.
9. Cheung KS, Leung WK (2018) Risk of gastric cancer development after eradication of Helicobacter pylori. World J Gastrointest Oncol 10: 115-123.
10. Murphy G, Abnet CC, Choo Wosoba H, Vogtmann E, Weinstein SJ, et al. (2017) Serum gastrin and cholecystokinin are associated with subsequent development of gastric cancer in a prospective cohort of Finnish smokers. Int J Epidemiol 46: 914-923.
11. Cheung KS, Leung WK (2019) Long-term use of proton-pump inhibitors and risk of gastric cancer: a review of the current evidence. Therap Adv Gastroenterol 12:1756284819834511.
12. Johnson AG, Jick SS, Perera DR, Jick H (1996) Histamine-2 receptor antagonists and gastric cancer. Epidemiology 7: 434-436.
13. Clark K, Lam LT, Gibson S, Currow D (2009) The effect of ranitidine versus proton pump inhibitors on gastric secretions: a meta-analysis of randomised control trials. Anaesthesia 64: 652-657.