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

1Amit Sharma, 2Vikram Vohra

1Consultant, Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, India
2Senior Consultant, Tuberculosis and Respiratory Diseases, National Institute of Tuberculosis and Respiratory Diseases (NITRD), New Delhi, India

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 to 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

Copyright: ©2022 Amit Sharma. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.