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Are proton pump inhibitors a double-edged sword in the treatment of *Helicobacter pylori* infection?

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Helicobacter pylori (*H. pylori*) infection is closely associated with peptic ulcers, gastric malignancy and iron deficiency anemia [1]. Triple eradication therapy based on either bismuth compounds or proton pump inhibitors (PPIs) is the routine method used to treat *H. pylori* infection. It is commonly believed that PPIs are safe and effective for patients with peptic ulcer. The adverse effects are extremely rare for PPIs, approximately 1-3% with case reports of interstitial nephritis with omeprazole, hepatitis with omeprazole and lansoprazole and disputed visual disturbances with pantoprazole and omeprazole [2]. PPIs do not cause atrophic gastritis [3], although they may mildly increase serum gastric concentration and induce apoptosis [4,5]. PPIs are supposed not to be associated with gastric or esophageal cancers [6]. However, in one recent case report, a poorly differentiated neuroendocrine carcinoma with enterochromaffin-like (ECL) cell characteristics was supposed to be induced by hypergastrinemia secondary to long-term PPI use [7].

The paper by Bektas et al in this issue of *Annals of Gastroenterology* [8] found that long-term use of PPI and the presence of *H. pylori* infection are risk factors for ECL hyperplasia. They studied 15 patients with dyspeptic symptoms in three groups: group A, *H. pylori*-negative and untreated with PPI previously; group B, *H. pylori*-positive and untreated with PPI previously; and group C, *H. pylori*-negative and treated with PPI consecutively with at least six months. The features of ECL cell in oxyntic glands were examined with electron microscopy on biopsy specimens from corpus and antrum, and they were as follows: normal in group A; moderate hyperplasia and vacuolization in group B; and severe cell hyperplasia and vacuoles with greater amount of granules in enlarged vesicles in group C. Up to now, the long-term use of PPIs has not been convincingly proven to be associated with the increased ECL cell numbers and linear or micronodular hyperplasia [2]. Several reports support the positive association between long-term use of PPIs with ECL hyperplasia in *H. pylori*-positive persons [9-12] although a direct association is not unanimously supported [13-15]. The study by Bektas et al [8] seems to favor the positive association. However, this present study has several limitations. The number of cases enrolled is not large enough and quantitative data on the three study groups are absent, which makes this study not reliable to derive more general conclusions. ECL cell hyperplasia was moderately increased in the *H. pylori*-positive and without PPI treatment group compared with *H. pylori*-negative and without PPI treatment group, and was more pronounced in the *H. pylori*-negative and PPI treatment group. It would be of interest to add a fourth group to check whether there are any cooperative effects between *H. pylori* infections and long-term PPI treatment. In conclusion, the use of PPIs in the treatment of gastric diseases should be comprehensively considered: to utilize its capacity in the inhibition of *H. pylori* growth and to prevent the adverse effects to the host cells.

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