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【 EDITORIAL 】

Proton Pump Inhibitor-associated Mucosal Change

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Recently, proton pump inhibitors (PPIs) have been widely used as the first-line treatment for acid-related diseases such as gastroesophageal reflux disease (GERD), gastric ulcers and duodenal ulcers. The number of PPI users has been increasing throughout the world. The suppression of gastric acid by the long-term use of PPIs is suggested to be associated with a number of disorders, including community-acquired pneumonia, clostridium enteritis and osteoporosis. Pathological changes, including parietal cell protrusion and oxyntic gland dilatation have appeared in PPI users (1). Furthermore, the development and enlargement of fundic gland polyps has been detected by endoscopy (2). Endoscopists have a great interest in the relationship between PPI use and changes to the gastric mucosa, including black spots and white-and-flat elevated lesions (3, 4).

Takahari et al. described a new type of PPI-associated mucosal change in an article entitled, "Proton pump inhibitor induction of gastric cobblestone--like lesions in the stomach" (5). Gastric cobblestone-like lesions (GCLs) were defined as lesions with a cobblestone-like appearance that were detected in the gastric corpus. GCLs were detected in 60 of 171 (35.1%) patients who underwent upper gastrointestinal endoscopy after more than 6 months of PPI use. Pathological examinations revealed cystic dilation of the fundic gland, parietal cell hyperplasia and cytoplasmic vacuolation in the GCLs. These findings suggest that the trophic effect of PPIs on parietal cells induces endoscopic changes of the gastric mucosa.

We pointed out same lesions as cracked- and cobblestone-like changes of the gastric mucosa (6). The cracked mucosa (CM) on endoscopy appears as multiple depressed lines in the corpus under white light. In a single-center observational study of successive 538 PPI users (whose use was not limited to >6 months) showed that the CM and GCL were detected in 10.0% and 3.3% of patients, respectively. The frequency at which the CM and GCL are observed in than PPI users is significantly higher than that in non-users. The characteristics of subjects with GCL included a non-atrophic mucosa and *H. pylori* negativity. The prevalence of CM and GCL was not affected by the duration of PPI use.

The present study clarified that GCL is a PPI-associated mucosal change. However, the clinical importance of GCL remains uncertain. Due to the limitations of these two studies, further investigations are required.

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References

1. Kumar KR, Iqbal R, Coss E, Park C, Cryer B, Genta RM. Helicobacter gastritis induces changes in the oxyntic mucosa indistinguishable from the effects of proton pump inhibitors. Hum Pathol **44**: 2706-2710, 2013.
2. Martin FC, Chenevix-Trench G, Yeomans ND. Systematic review with meta-analysis: fundic gland polyps and proton pump inhibitors. Aliment Pharmacol Ther **44**: 915-925, 2016.
3. Hatano Y, Haruma K, Ayaki M, et al. Black spot, a novel gastric finding potentially induced by proton pump inhibitors. Intern Med **55**: 3079-3084, 2016.
4. Kato M. Endoscopic findings of *H. pylori* infection. In: Helicobacter. Suzuki H, Warren R, Marshall B, Eds. Springer Japan, Tokyo, 2016: 157-167.
5. Takahari K, Haruma K, Ohtani H, et al. Proton pump inhibitor induction of gastric cobblestone-like lesions in the stomach. Intern Med **56**: 2699-2703, 2017.
6. Miyamoto S, Kato M, Tsuda M, et al. Gastric mucosal cracked and cobblestone-like changes by the use of proton pump inhibitors. Dig Endosc **29**: 307-313, 2017.

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