Japan Aims toward Appropriate Concomitant Use of Antiplatelets and Antisecretory Agents?

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Percutaneous coronary intervention by using drug-eluting stents (DESs) has become increasingly popular as standard therapy for patients with acute coronary syndrome. At this point in time, 12 months of dual antiplatelet therapy (DAT), aspirin and clopidogrel, is recommended for all patients who receive a DES unless there is a high risk of bleeding (1). Concerning bleeding risks, because these antiplatelet agents have recognizable gastroduodenal injury (2, 3), concomitant use of proton pump inhibitors (PPIs) is recommended for all patients with DAT as a guideline (4). In terms of less acid suppressive agents, H₂-receptor antagonists (H₂RAs), there is little data on their use in conjunction with DAT and it is still believed that PPIs are superior to H₂RAs in preventing ulcer occurrence and overall symptom control in patients with DAT, although a randomized control trial from UK revealed the effectiveness of H₂RA for the prevention of gastroduodenal ulcers in patients taking low-dose aspirin (5). Recent evidence, however, revealed that PPI may reduce the antiplatelet effects of clopidogrel (6), because these medications share common metabolic pathways mediated by cytochrome p450 isoenzymes (ie, CYP2C19) in the liver (7). Prospects of the controversial issue are gloomy for the combinational use owing to clinical studies with worse outcomes for the patients with clopidogrel and PPI (8, 9).

It is well known that the prevalence of *Helicobacter pylori* (*H. pylori*) infection is high in Japan. A large epidemiologic study revealed that the frequency of *H. pylori* infection for persons born after 1950 has increased at approximately 1% per year and that for those born before 1950 it was 70%-80% and relatively constant (10). *H. pylori* infection is considered to lead to atrophic gastritis and intestinal metaplasia, which is strongly associated with low gastric acidity (11). Based on the regional differences in prevalence of *H. pylori* infection, the data for gastroduodenal bleeding obtained from individuals in Western countries and Japan should be carefully interpreted considering different gastric acidity.

As far as I know, the study conducted by Yasuda H et al is the first study which shows clinical data concerning DAT and PPI in the Japanese population (12). Their study revealed that no patient with anti-secretory agent had gastroduodenal bleeding and even half of the standard dose of H₂RAs seemed to show a preventative effect on the occurrence in their case series. Furthermore, patients with PPI had significantly more stenotic lesions of the coronary artery than those without anti-secretory agent at the follow-up coronary angiography after DES implantation, whereas no significant difference in the proportion of patients with stenotic lesions was observed between patients with H₂RAs and those without anti-secretory agent. These findings imply that concomitant use of DAT and H₂RA is the best choice for populations with a low gastric acidity such as Japanese. Although the biggest and crucial drawback of their study is the small sample size with retrospective settings in a single institution, the study encourages us to conduct well-designed prospective large-scale studies, such as nationwide studies related to this issue. One of the possibilities is a tailor-made medication of anti-secretory agents according to gastric acidity in patients with DAT. By combining the novel findings by Yasuda H et al and serum pepsinogens levels (13), we may arrange the doses of H₂RA, e.g., from half the standard doses to double the standard dose, owing to the predicted extent of gastric atrophy. Also the positioning of PPI for the preventative effect on gastroduodenal bleeding should be reconsidered even for patients without *H. pylori* infection or gastric atrophy.

When considering the fact that the proportion of Japanese with *H. pylori* infection has markedly decreased in the last few decades, the situation may become similar to that in...
Western countries in the near future. Considering that there are fewer Japanese with *H. pylori* infection, now is the time to be undertaking studies to obtain original scientific evidence from Japan. It will be important for us to make a big wave from Japan, using the very small toehold made by Japanese investigators.

References


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