

Current Status of Pharmacotherapy for Functional Dyspepsia Based on Its Pathophysiology

Hiroshi Kaneko¹, Toshihiro Konagaya², Akihito Iida³

(1: Dept. of Neurology, Div. of Psychosom. Med., Fujita Health Univ.

Bannbuntane-Hotokukai Hsp, 2: Dept. of Gastroenterology, Nagoya Univ. Sch. of Med. & Marine Clinic, 3: Dept. of Gastroenterology, Aichi Med. Univ. Sch. of Med.)

Functional dyspepsia (FD) is defined as the presence of symptoms thought to originate in the gastroduodenal region, in the absence of any organic (e.g. peptic ulcer, gastric cancer), systematic, or metabolic disease that is likely to explain the symptoms such as epigastric pain and fullness. FD seems identical to so-called nervous gastritis and unidentified upper abdominal symptoms. Proposed pathogeneses of FD include gut dysfunctions such as gastro-intestinal motor dysfunction, hypersensitivity against distension and/or gastric acid, and impaired adaptive relaxation reflex to reserve ingested food temporally (dysaccommodation). Approved drugs for FD from the clinical trials in Japan consist of acid secretion inhibitors (proton pump inhibitors: PPI, H₂-receptor antagonists), prokinetics (5-HT₄- receptor agonist, D₂-receptor antagonists), and anti-depressants. FD has new diagnostic categories of (1) meal-induced dyspeptic symptoms (e.g. fullness and satiation) (PDS), and (2) epigastric pain (EPS). The investigation on the pathophysiology for respective group and the drug selection algorithm based on its pathogenesis have been intensively explored. It was reported that a bloating perceived threshold is correlated with the gastric adaptive relaxation volume and that hypersensitivity against gastric distension occurs during duodenal acid infusion. We have demonstrated the possibility that a 5-HT₄- receptor agonist increases the accommodation and the phenomenon that PPI increases the perception threshold to gastric distension via an inhibition of acid secretion, suggesting that respective agent might be effective PDS and EPS. In addition, a certain anxiolytic belonging to the azapirones (5-HT_{1A}- receptor agonist), Kampos (herbal medicines), and selective serotonin re-uptake inhibitors have been reported to be effective to FD. Novel agents targeting to the brain-gut interactions in FD seem worthy of search.