論　文　内　容　要　旨

Serum Gastrin and Pepsinogen Levels after Administration of Acid Secretion Inhibitors for Ulcers due to Endoscopic Submucosal Dissection in Patients with Early Gastric Cancer

（早期胃癌患者における内視鏡的粘膜下層剥離術による潰瘍に対する酸分泌抑制剤投与後の血清ガストリンおよびペプシノーゲン値について）

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主指導教員：大段　秀樹　教授
（医系科学研究科　消化器・移植外科学）
副指導教員：田中　信治　教授
（広島大学病院　内視鏡医学）
副指導教員：伊藤　公訓　教授
（広島大学病院　総合診療医学）

MAIDINA　ABUDUWAILI
（医歯薬保健学研究科　医歯薬学専攻）

【backgrounds】

Gastrin is an important gastrointestinal hormone involved in gastric acid secretion. It is synthesized and secreted by G cells in the gastric pylorus and duodenum, and acts on the wall cells of the gastric body to promote gastric acid secretion. When gastric acid secretion is inhibited by proton pump inhibitors (PPIs), gastrin levels increase due to a negative feedback function.

When the Endoscopic Submucosal Dissection (ESD) is performed for gastric tumors, acid secretion inhibitors such as PPI are used to treat ulcers after treatment. In 2014, a new category of acid secretion inhibitors called potassium ion-competitive acid blocker(P-CAB) became available, expanding treatment options. However, the amount of change in serum gastrin levels before and after use is not clear. On the other hand, PPI and P-CAB have a strong acid secretion inhibitory effect, and there is a concern that they increase serum gastrin levels, which play an important role in the progression of gastrointestinal cancer.

【aim】

The purpose of this study was to investigate the effects of acid secretion inhibitors on serum gastrin , pepsinogens, and gastrin 17 (G17) levels, further examined the associated factors of these alterations.

【Materials and methods】

Between July 2017 and March 2019, we enrolled 167 patients at Hiroshima University Hospital who had blood tests before and after ESD for gastric cancer. Patients were excluded for PPI or P-CAB usage before ESD. To analyze the extent of changes in gastrin, G17, and pepsinogen produced by acid inhibitors, the levels of these blood markers were compared before and after administration. The median amount of change in gastrin and PG levels were used to classify the group as large if it was higher than the median value and small if it was lower. Associated factors with the elevation of serum markers were compared between the two groups.

Additionally, to examine the changes in G17 levels before and after administration, 10 cases from PPI group and 10 cases from P-CAB group were randomly selected for analysis. Fasting serum were collected on the day of the ESD and 4 weeks later and stored at -20 °C until analysis. The levels of serum gastrin (Gastrin RIA Kit II; Dainabot, Tokyo, Japan), G17 (Gastrin-17 Advanced ELISA, Biohit, Finland), and PG (LZ test; Eiken, Tokyo, Japan) and the anti-*H. pylori* antibody titers (E-plate; Eiken, Tokyo, Japan) were evaluated

【Results】

After treatment with the PPI and P-CAB, the gastrin, PGI, and PGII levels increased. Before the administration of acid-secretion inhibitors, the median levels of serum gastrin, PGI, and PGII were 110.5 pg/mL , 36.4 ng/mL, and 8.9 ng/mL, respectively. After administration, the levels significantly increased to 300 (a 167.5-pg/mL increase) pg/mL, 64.7 (a 24.5-ng/mL increase) ng/mL, and 15.8 (a 5.05-ng/mL increase) ng/mL, respectively. The serum G17 level significantly increased (Wilcoxon's signed-rank test $P<0.001$) after administration of the PPI and P-CAB. An examination of between the total gastrin and serum G17 levels revealed a correlation ($r=0.85$, $P<0.001$), and the G17 level was

approximately 20% of the total gastrin fraction.

【Conclusion】

This study was conducted in a group of cases with high potential of carcinogenesis that developed to gastric cancer. In such population, P-CAB resulted in a rapid increase in gastrin compared to PPI. This point should be considered when selecting acid secretion inhibiters like PPI and P-CAB.