麩胺酸對胃酸分泌及壓力性胃潰瘍的影響—活體研究

Effect of L-Glutamic Acid on Gastric Secretion and Stress-induced Gastric Lesions — an in Vivo Study

中文摘要

本研究探討 L 型麩胺酸在活體內的作用；於動物禁食 24 小時後，麻醉並作氣管、食道、股靜脈十二指腸插管。室溫下，經由食道插管以蠕動幫浦（peristalic pump）灌流生理食鹽水。待一小時穩定之後，使用自動滴定儀（autotitrator VIT90，Radiometer Corp., Copenhagen，Denmark）以 0.01N NaOH 滴定酸鹼值至 7.0，作胃酸分泌量的測定。基礎酸分泌收集 30 分鐘後，持續投與各種酸分泌刺激劑（histamine，oxotremorine or pentagastrin）60 分鐘。另外，於持續投與與組織胺 30 分鐘後，再灌注 L 型麩胺酸與 6,7-dinitroquinoxaline-2,3-dione （DNQX）。結果顯示，L 型麩胺酸（750 ug/kg/hr；i.v. infusion）對於自發性酸分泌沒有任何影響，但是可以抑制由組織胺（histamine, 2mg/kg/hr）及 oxotremorine （1 ug/kg/hr） 誘導的胃酸分泌。此外，對於 pentagstrin （5 ug/kg/hr）誘導的酸分泌則無影響。L 型麩胺酸抑制組織胺引起的酸分泌作用作用，會完全被 non-NMDA （non-N-mehtyl-D-aspartate）受體的拮抗劑，DNQX （6，7-dinitroquinjoxaline-2,3-dione，750 ug/kg/hr）所拮抗。另一方面探討 L 型麩胺酸及其受體亞型對於壓力性胃潰瘍的保護作用及 cAMP 濃度變化之影響。於腹腔注射投藥 30 分鐘後，將小白鼠放入恆溫箱（4 + 1℃）並限制其行動，觀察不同的壓力時間導致胃潰瘍的程度與 cAMP 之間的關係，結果得知，潰瘍程度和 cAMP 濃度成正比。當投與 L 型麩胺酸（2， 4 和 8 mg/kg, i.p.）30 分鐘後，在壓力（4 + 1℃，2 小時）引起胃潰瘍，其呈現劑量-依存性地（dose-dependent）抑制胃潰瘍的發生。而 NMDA（N-methyl-D-aspartic acid）（0.2，1 和 2mg/kg），QA （quisqualic acid）（2 and 5 mg/kg）和 KA （kainic acid）（1，2 and 5 mg/kg）同樣呈現劑量-依存性地抑制潰瘍的產生。上述結果顯示，L 型麩胺酸在活體內之作用是經由 non-NMDA 受體抑制組織胺誘導之酸分泌。同時興奮性胺基酸及其受體亞型（subtypes），可能參與胃黏膜障壁（mucosalbarrier）之生理調節而增加對於壓力性胃潰瘍的抵抗作用。

英文摘要

The effects of L-glutamic acid (L-Glu) on gastric acid secretion were incestigated in vivo. All SD rats were anesthetized with sodium pentobarbital (45 mg/kg, i.p.) after 24 hrs of fasting. The trachea、esophagus、femoral vein and duodenum were catheterized. The stomach was flushed throuth the esophagus cannula via a

peristaltic pump with normal saline at room temperature. Acid output was determined by titration (autotitrator VIT90, Radiometer Corp., Corpenhagen, Denmark) of the perfusate with 0.01N NaOH to pH 7.0. after basal secretions were collected for 30 min, and various acid stimulator (histamine, oxotremorine or pentagastrin) were infused for 60 min. In addition, L-glutamic acid (L-Glu) and 6, 7-dinitroquinoxaline-2, 3-dione (DNQX) was infused for 30 min after the infusion of histamine for 30 min. The result was found that infusion with synthetic L-Glu alone had no effect on spontaneous acid secretion. The histamine-(2 mg/kg/hr) and oxotremorine-(1 ug/kg/hr) stimulated acid secretion and were markedly reduced by L-Glu (750 ug/kg/hr), whereas L-Glu had no effect on acid secretion stimulated by pentagestrin (5 ug/kg/hr). Furtherm ore, this inhibitory effect of L-Glu on hisstamine-stimulated acid secretion was blocked by DNQX (750 ug/kg/hr), a non-DMDA receptor antagonist.

On the other hand, L-Glu and it's subtypes including N-meghyl-D-aspartate (NMDA), kainic acid (KA) and quisqualic acid (QA), which functions to protect mucosaldamage and reduce cyclic AMP concentration were also investigated in stres-induced gastric lesions. L-Glu and it's eubtypes were administered before cold-restraint stress (4 + 1℃, 2 hrs). The cAMP concentration of cold restraint-induced mucosal lesion was significantly different from the normal stomach. The present study was conducted to evaluate the effect of these drugs on the development of cold and restraint-induced gastric ulcers. Two hours of restraint at 4 + 1℃ resulted in the production of gastric lesions in all mice. The cAMP concentration of cold restraint-induced was inhibited by L-Glu and it's subtypes. L-Glu at 2, 4 and 8 mg/kg i.p. injection 30 min before strss significantly and dose dependently prevented gastric lesions. NMDA at 0.2, 1 and 2 mg/kg , QA at 2 and 5 mg/kg or KA at 1, 2 and 5 mg/kg administered 30 min before stress prevented gastric ulcer in dose dependently.

All these results suggest that L-Glu is involved in the inhibition of oxotremorine-and histamine-induced gastric acid secretion via ionotropic non-NMDA receptors. L-Glu and it's subtypes also may participate in a physiological modulation of the gastric mucosalbarrier, by increasing resistance to cold restraint-induced gastric lesions in mice.