上皮生長因子對老鼠十二指腸潰瘍癒合機制之探討

The Possible Mechanism of Epidermal Growth Factor on Duodenal Ulcer Healing in Rats

中文摘要

本研究主要是探討口服上皮生長因子（epidermal growth factor; EGF）對醋酸誘發的十二指腸潰瘍老鼠之腸道黏膜修復所扮演的角色，並研究口服 EGF 是否藉由影響胃壁酸鹼值，及胃腸道黏膜 EGF 含量，而調節潰瘍癒合。本實驗將雄性 Sprague-Dawley 老鼠（約 200-250 公克重），隨機分成 15 組，（每組各十隻，包括病理切片與拍照各一隻）：無潰瘍無口服 EGF 1 天、5 天、10 天、15 天組，無潰瘍口服 EGF 5 天、10 天、15 天組，潰瘍無口服 EGF 1 天、5 天、10 天、15 天組，及潰瘍口服 EGF 5 天、10 天、15 天組，另外有十隻不接受任何手術之正常老鼠，作爲控制組。所有之無潰瘍老鼠皆接受假手術（sham operation），潰瘍老鼠則以 30% 醋酸誘發。口服 EGF 之老鼠於手術後隔天（第 1 天），以每天每公斤體重 60 (g 劑量之人類重組 EGF，加於 35 mL 之飲用水中，持續投予至 5、10 或 15 天。

結果顯示：在巨觀的生長情形上，口服 EGF 並不會改變潰瘍老鼠攝食量，亦不會增加老鼠體重。在微觀的病理檢查上，對於潰瘍老鼠，口服 EGF 組在第 5 天時，其潰瘍處黏膜修復情形較潰瘍無口服 EGF 組爲佳。口服 EGF 對於十二指腸潰瘍的影響是在第 15 天時，潰瘍口服 EGF 組之十二指腸黏膜 DNA 含量高於潰瘍無口服 EGF 組。而口服 EGF 亦會促進胃黏膜細胞生長：在第 5 天時，無論有無潰瘍，口服 EGF 組之胃黏膜 RNA 含量高於無口服 EGF 組，在第 10 天時潰瘍口服 EGF 組高於其他各組；在第 15 天時，無論有無潰瘍，口服 EGF 組的胃黏膜 DNA 含量均高於無口服 EGF 組。口服 EGF 並不影響十二指腸黏膜之 EGF 含量，僅在第 5 天時潰瘍口服 EGF 組高於無口服 EGF 組；但口服 EGF 會影響胃黏膜 EGF 含量，在第 5 天時，潰瘍口服 EGF 組其胃黏膜中 EGF 含量高於其他各組，並在第 10 天時高於潰瘍無口服 EGF 組。由以上結果可知，外生性口服 EGF 可經由促進十二指腸潰瘍老鼠之胃與十二指腸黏膜生長，與增加胃黏膜 EGF 含量，而加速十二指腸潰瘍之癒合，但並不會透過調節胃壁酸鹼值來促進修復。

關鍵詞：上皮生長因子、十二指腸潰瘍、黏膜修復、胃壁酸鹼值、老鼠

英文摘要

This study was to investigate the role of orally administered EGF on the healing of intestinal mucosa in the rats with acetic acid-induced duodenal ulcer, and to study if the healing effect of oral EGF was via affecting gastric pH value and EGF content in the gastrointestinal tract. Male Sprague-Dawley rats (200-250 g) were randomly divided into fifteen groups (10 rats per group, including one for pathological

assessment and for photography, respectively): no ulcer without oral EGF on day 1, 5, 10, and 15, no ulcer with oral EGF on day 5, 10, and 15, ulcer without oral EGF on day 1, 5, 10, and 15, and ulcer with oral EGF on day 5, 10, and 15 groups. The additional 10 rats without any operation were as the control group. The rats without ulcer were done by sham operation, and those with duodenal ulcer were induced by 30% acetic acid. The rats with EGF treatment were orally administered at a dose of 60 (g recombinant human EGF/kg body weight in 35 mL drinking water daily next day of operation (day1), and continuously oral intake of EGF to day 5, 10 or 15.
The results showed that oral EGF had no effect on food intake and body weight in the ulcer rats from the aspect of macroscopic growth. From the pathological aspect of microscopic assessment, the ulcer rats with oral EGF had better healing in the ulcer mucosa on day 5 compared to those without oral EGF. The effect of oral EGF on duodenal mucosa indicated that the ulcer rats with oral EGF had higher DNA content in the duodenal mucosa than those without oral EGF on day 15. Oral EGF also increased the growth of the gastric mucosa. Oral EGF groups had higher RNA content in the gastric mucosa than without oral EGF groups in both ulcer and sham-operated rats on day 5. On day 10, the ulcer rats with oral EGF had the highest RNA content in the gastric mucosa compared to others. On day 15, oral EGF groups had higher DNA content in the gastric mucosa than without oral EGF groups in both ulcer and sham-operated rats. Oral EGF did not affect EGF content in the duodenal mucosa. The ulcer rats with oral EGF had higher EGF content in the duodenal mucosa than without oral EGF groups only on day 5. However, oral EGF affected EGF content in the gastric mucosa. On day 5, the ulcer rats with oral EGF had the highest EGF content in the gastric mucosa compared to others. On day 10, the ulcer rats with oral EGF had higher EGF content in the gastric mucosa than those without oral EGF. Therefore, exogenously oral EGF treatment accelerated the healing of duodenal ulcer in the rats by stimulating the growth of gastric and duodenal mucosa, and by increasing EGF content in the gastric mucosa rather than by regulating gastric pH value.
Key words: epidermal growth factor, duodenal ulcer, mucosal healing, gastric pH, rats