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Protective effect of omeprazole on gastric mucosal of cirrhotic portal hypertension rats

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ABSTRACT

Objective: To observe the protective effect of omeprazole on gastric mucosal of cirrhotic portal hypertension rats. **Methods:** All rats were randomly divided into normal control group, cirrhosis and treatment group. Thioacetamide was used to establish rat model of cirrhotic portal hypertension. The necrotic tissue of gastric mucosa ulcer focus, degree of neutrophils infiltration at the ulcer margin, portal pressure, portal venous flow, abdominal aortic pressure, abdominal aortic blood flow at front end, gastric mucosal blood flow (GMBF), glycoprotein (GP) of gastric mucosa,basal acid secretion, H^+ back -diffusion, gastric mucosal damage index, NO, prostaglandin E_2 (PGE_2) and tumor necrosis factor- α (TNF- α) were determined respectively, and the pathological changes of gastric mucosa were also observed by microscope. **Results:** Compared with cirrhosis group and the control group, the ulcer bottom necrotic material, gastric neutrophil infiltration and UI of the treatment group were all decreased significantly (P<0.01), GMBF value, GP values, serum NO, PGE_2, TNF- α were all significantly increased. **Conclusions:** Omeprazole has an important protective effect on gastric mucosal and it can increase gastric mucosal blood flow and related to many factors.

1. Introduction

Portal hypertension gastropathy (PHG) of cirrhotic has become a main clinical manifestations of the decompensated cirrhosis in clinical. It threatens life because of the high incidence of gastric mucosal bleeding. Omeprazole is one of the most common drugs to treat gastric mucosal lesion. Its significant inhibition effect on the gastric acid secretion has been very clear, but the protective effect on gastric mucosal is still unclear. This study is to explore the protective effect of omeprazole on gastric mucosal of cirrhotic portal hypertension rats, and the possible mechanisms.

2. Materials and methods

2.1. Animals and grouping

A total of 30 6-week-old male SD rats were selected, weighting 200-220 g, which were purchased from Experimental Animal Department, XX University. The animals were randomly divided into three groups, including the normal control group (n=10), cirrhosis group (n=10), treatment group (n=10). If rats died or abandoned during the study, they were supplemented again. All rats were fed by standards pellet then kept under constant humidity and temperature

2.2. Reagents and instruments

0.03% thioacetamide (TAA), omeprazole capsules 20 mg

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were purchased from Haikou Qili Pharmaceutical Co., Ltd. Rat prostaglandin E_2 (PGE_2), tumor necrosis factor-α (TNF-α) ELISA kit were purchased from Wuhan Boster Reagent Company. Optical microscopy, laser doppler flowmeter, digital millivoltmeter, electronic scales, micro adding sample appliance, *etc*. were provided by the laboratory.

2.3. Model establishement

Rats in the normal control group received 25 mg/kg ketamine under intraperitoneal anesthesia, draped in a sterile manner. They were opened layers by layers and the left suprarenal vein was isolated without special intervention. After adequate hemostasis, they were sutured layers by layers. Animals received water after operation. Rats in the cirrhosis group and treatment group underwent double ligation after left suprarenal vein fully exposed. If there was a branch of small blood vessels, the vessels were also ligated together, then were sutured after hemostasis. The rats received concentration of 0.03% TAA solution as drinking water. Body weight was monitored, and was maintained between 200-260 g. If the margin of body weight increase was more than 20 g or decrease more than 10 g in one week, then concentration of TAA was increased or decreased by 50%. All rats were continuously fed for 14 weeks, then the treatment was stopped for two weeks. After three days of molding, the treatment group were fed by omeprazole 15 mg/kg • d one time everyday. The sampling was performed after 2 weeks.

2.4. Indexes observation

2.4.1. Hemodynamic index detection

Using laser doppler flowmeter, free portal pressure (FPP), portal venous flow (PVF), abdominal aortic pressure (AAP) and abdominal aorta blood flow (AAF) at the beginning point was measured. Greater and lesser curvatures of gastric body, greater and lesser curvatures of gastric antrum on the surface of gastric mucosa were also measured. The average value were obtained as gastric mucosal blood flow (GMBF).

2.4.2. Glycoprotein (GP) of gastric

Mucus were scraped on the surface of mucosa in gastric gland area and weighed. Glycoprotein content was measured by Coomassie brillient blue method.

2.4.3. Basal acid secretion (BAS)

Gastral cavity was washed with normal saline. The beginning part of the duodenum was intubated and the duodenum was ligated. One mL/min saline was added with uniform injection pump, the remote casing was open once every 10 mins for 6 times. H^+ concentration was measured by 0. 2 mol/L NaOH microtitration and the average value were obtained.

2.4.4. H^+ back diffusion (H^+ BD)

Gastral cavity was washed with sarfeh solution (100 mmol/L HCl and 50 mmol/L NaCl). The duodenum was ligated. Sarfeh solution was injected at 3 mL/times, 20 min/times for 3 times. H^+ concentration was also measured by microtitration. The value was obtained by minusing Sarfeh fluid H+ concentration.

2.4.5. Index of gastric mucosal lesion

Stomach tissue was removed, cut and flatted.The score was calculated by Guth standard. Spot-like erosions was 1, erosion <1 mm was 2, erosion between 1 -2 mm was 3, erosion between 2-4 mm was 4, erosion> 4 mm was 5.

2.4.6. Histological observation

The gastric tissues were fixed, paraffin routinely embedded, sectioned, and HE stained. Necrotic status and neutrophil infiltration was observed under light microscope, Judgement standard was as follows: No necrotic material or neutrophil infiltration was 0; A few necrotic material and neutrophil infiltration at the bottom edge of the ulcer was 1; Thick layer of necrotic at the ulcer floor and obvious neutrophil infiltration at the marginal tissue of ulcer was 3; Between them was 2.

2.4.7. Serum NO, PGE_2, TNF-α measurment

Venous blood samples were collected before the rats were sacrificed. After centrifugation, the serum NO content was measured. The serum PGE_2, TNF-α levels were measured by radioimmunoassay.

2.5. Statistical analysis

The data was analyzed with SPSS 13.0 software. Data were expressed as mean±SD. Homogeneity of variance was carried out for the measurement material, and multiple comparison was used if there is significant differences. P <0.05 was considered as statistical significance.

3. Results

3.1. Mucosa observation

The gross specimen of gastric in normal control rats showed smooth and complete surface. Microscope showed glands arranged regularly. Gross specimen of cirrhotic rats gastric showed obvious hyperemia and edema, one or more strip-shaped erosion and hemorrhagic focus, necrotic