Acute Gastric Ulceration in Rats with Obstructive Jaundice with Special Reference to Gastric Mucosal Blood Flow

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SASAKI, I., KONNO, Y., KAMIYAMA, Y, and SATO, T. Acute Gastric Ulceration in Rats with Obstructive Jaundice with Special Reference to Gastric Mucosal Blood Flow. Tohoku J. exp. Med., 1987, 151(3), 351-358 — The mechanism of acute gastric ulceration in rats with obstructive jaundice was investigated in terms of the changes in the gastric mucosal blood flow, and the effect of vagotomy on ulceration was examined. 188 Sprague-Dawley rats weighing about 250 g were prepared and divided into 4 groups as follows; control group (sham operation), jaundiced group (ligation of the bile duct), vagotomized group (vagotomy with pyloroplasty), jaundiced and vagotomized group (simultaneous ligation of the bile duct and vagotomy with pyloroplasty). Two weeks after the operation, water immersion and restraint stress procedures were performed in these 4 groups. The gravity of acute gastric ulcerations was calculated by ulcer index. The gastric mucosal blood flow was measured by hydrogen clearance technique. The following results were obtained: In control group, ulcer index was increased and gastric mucosal blood flow was decreased after the stress procedures. The jaundiced group showed significantly higher ulcer index and early significant decrease of gastric mucosal blood flow after the stress procedures compared to the control group. The vagotomized group showed significantly decreased ulcer index after the stress procedures compared to the control group, however, the gastric mucosal blood flow showed almost the same values as the control group. The vagotomized group showed significantly decreased ulcer index after the stress procedures compared to the control group, however, the gastric mucosal blood flow showed almost the same values as the control group. The jaundiced and vagotomized group showed significant decrease of ulcer index and improvement of decrease of gastric mucosal blood flow compared to the jaundiced group. These results indicated that the gastric mucosal blood flow plays an important role in the occurrence of acute gastric ulceration in rats with obstructive jaundice, and vagotomy might be useful to prevent them by maintaining gastric blood flow in obstructive jaundice. ——— obstructive jaundice; acute gastric ulcer; gastric mucosal blood flow

It is well known that in patients with obstructive jaundice acute gastric ulcerations tend to develop under some kind of stress such as surgical operations. However, little has been known about the mechanism of acute gastric ulcerations in patients with obstructive jaundice. We previously reported that the gastric

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defensive factors may play an important role on acute gastric ulceration in obstructive jaundice in rats (Sakaki et al. 1986). On the other hand, some authors (Hottenrott et al. 1978; Silen et al. 1981) have been pointed out that acute gastric ulcerations closely related to the decreased of gastric mucosal blood flow. However, the effect of obstructive jaundice on the gastric mucosal blood flow has not been reported. In the present study we experimentally investigated the influence of obstructive jaundice on acute gastric ulcerations in rats with special reference to gastric mucosal blood flow. We also studied the prophylactic effect of vagotomy against acute gastric ulcerations in the same way.

**Materials and Methods**

One hundred eighty-eight male Sprague-Dawley rats weighing about 250 g were prepared and divided into four groups: control group (sham operation), jaundiced group (ligation and separation of the bile duct), vagotomized group (bilateral truncal vagotomy with pyloroplasty) and jaundiced and vagotomized group (simultaneously prepared by ligation and separation of the bile duct and bilateral truncal vagotomy with pyloroplasty). Two weeks after the operation, water immersion and restraint stress procedures (Takagi and Okabe 1968) were performed for 10 hr in these 4 groups, and ulcer indexes and gastric mucosal blood flow were measured every two hr. Ulcer indexes were measured by calculating the total sum of the length (mm) of ulcerations on the resected stomach. Gastric mucosal blood flow was measured by hydrogen gas clearance technique described as follows. About one hr before stress procedures, the rats were subjected to laparotomy and a vinyl tube of 2.5 mm in diameter was inserted through the forestomach so that the tip of the tube was in contact with the mucosa of granular stomach (Fig. 1). On measurement, a loop-shaped electrode was inserted so that the tip containing active surface was in contact with gastric mucosa. A reference electrode was placed in the peritoneal cavity. Changes of hydrogen concentration in the gastric mucosa after inhalation of hydrogen gas for 10-20 min was displayed as clearance curve by a regional blood flowmeter (Fig. 2). Gastric mucosal blood flow was calculated from clearance curve obtained by Kety's theoretical expression (Kety 1951).

The values were expressed as mean ± s.e. The significance of the difference of p <0.05

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**Fig. 1.** Schema showing measurement of gastric mucosal blood flow by hydrogen gas clearance technique.

A loop-shaped electrode was inserted to the granular stomach through a gastric fistula of the forestomach. A reference electrode was placed in the peritoneal cavity.
RESULTS

Ulcer indexes and gastric mucosal blood flow

Control group. Ulcer indexes of the control group increased gradually from $0 \pm 0$ before immersion to $28.0 \pm 3.4$ at 10 hr of stress procedures (Fig. 3). Gastric mucosal blood flow of the control group decreased gradually from $160.1 \pm 7.9$ ml/min/100 g before immersion to $58.0 \pm 5.0$ ml/min/100 g at 10 hr of stress procedures (Fig. 3).

Jaundiced group. Ulcer indexes of the jaundiced group increased markedly from $0 \pm 0$ before immersion to $83.1 \pm 10.7$ at 10 hr of stress procedures (Fig. 3). Ulcer indexes of the jaundiced group showed significantly higher values than that of the control group at 6 and 10 hr of stress procedures. Gastric mucosal blood flow of the jaundiced group decreased markedly from $150.2 \pm 11.6$ ml/min/100 g before immersion to $92.1 \pm 8.3$ ml/min/100 g at 10 hr of stress procedures and further decreased to $54.2 \pm 9.0$ ml/min/100 g at 10 hr of stress procedures (Fig. 3). Gastric mucosal blood flow of the jaundiced group showed significantly lower values than that of the control group at 2 and 4 hr of stress procedures.

Vagotomized group. Ulcer indexes of the vagotomized group increased gradually from $0 \pm 0$ before immersion to $13.0 \pm 2.2$ at 10 hr of stress procedures (Fig. 4). Ulcer indexes of the vagotomized group showed significantly lower values than
that of the control group at 2, 4 and 10 hr of stress procedures. Gastric mucosal blood flow of vagotomized group decreased gradually from 167.2 ± 10.5 ml/min/100 g before immersion to 63.9 ± 7.7 ml/min/100 g at 10 hr of stress procedures (Fig. 4). Gastric mucosal blood flow of vagotomized group showed almost the same values as that of the control group.
Jaundiced and vagotomized group. Ulcer indexes of jaundiced and vagotomized group increased gradually from 0 ± 0 before immersion to 28.0 ± 6.6 at 10 hr of stress procedures (Fig. 5). Ulcer indexes of jaundiced and vagotomized group showed significantly lower values than that of the jaundiced group at 4, 6 and 10 hr of stress procedures. Gastric mucosal blood flow of the jaundiced and vagotomized group decreased gradually from 142.2 ± 22.5 ml/min/100 g before immersion to 65.4 ± 11.1 ml/min/100 g at 10 hr of stress procedures (Fig. 5). Gastric mucosal blood flow of the jaundiced and vagotomized group showed significantly higher values than that of the jaundiced group at 2, 4 and 6 hr of stress procedures.

DISCUSSION

Patients with obstructive jaundice tend to develop acute gastric ulcerations under some kind of stress such as surgical operations. Brooks (1966) reported that obstructive jaundice was one of the important back-grounds of acute gastric ulcerations. However, little has been known about the influence of obstructive jaundice on gastric mucosa. On the other hand, it has been reported that a decrease of gastric mucosal blood flow is the most important pathogenesis of acute gastric ulcerations (Hottenrott et al. 1978; Silen et al. 1981). Therefore, we measured the gastric mucosal blood flow of the jaundiced rats at basal and under immersion and restraint stress in the present study.

Hydrogen gas clearance technique was adopted in measurement of gastric mucosal blood flow, because the absolute value of regional mucosal blood flow can
be measured by this method. We devised how to fix the hydrogen electrode to gastric mucosa in unanesthetized rats (Konno et al. 1983). The method of electrode fixation through the gastric fistula (Fig. 1) using Murakami's contact electrode (1982) was convenient in measuring gastric mucosal blood flow in unanesthetized animals. The tip of electrode was gently contacted to the gastric mucosa and not easily slipped by animal movement.

The ulcer indexes of the control group increased gradually in stress procedures, while the gastric mucosal blood flow of the control group decreased in the same manner. These data suggested that the decrease of gastric mucosal blood flow closely related to pathogenesis of acute gastric ulcerations in water immersion and restraint stress procedures, just like as hypovolemic shock (Starlinger et al. 1979), burn (Kitajima et al. 1978) and endotoxin-induced stress ulcer (Richardson et al. 1973).

The ulcer indexes of the jaundiced group showed higher values than that of the control group, while the gastric mucosal blood flow of jaundiced group showed lower values than that of the control group. These data suggested that the extreme decrease of gastric mucosal blood flow was one of exacerbating factors of acute ulceration in rats with obstructive jaundice. It seemed that these decrease of gastric mucosal blood flow participated in the vulnerability of the gastric mucosa in rats with obstructive jaundice shown by decreased energy metabolism (Inui et al. 1984) or lowered electrical potential difference (Sasaki et al. 1986). However, it was not clear why the gastric mucosal blood flow significantly decreased in jaundiced condition.

The ulcer indexes of the vagotomized group showed lower values than that of control group. These data suggested that surgical vagotomy had prophylactic effect against acute gastric ulceration. However, gastric mucosal blood flow of the vagotomized group showed almost the same values as that of the control group. These data are comparable with Delaney's report (1967) or Levine's report (1981) which stated that vagotomy brought no changes in gastric mucosal blood flow in experimental studies. On the other hand, Peter et al. (1963) or Bell and Battersby (1968) reported that vagotomy decreased gastric mucosal blood flow. This discrepancy was explained by the difference of the period after vagotomy. Namely, gastric mucosal blood flow decreased soon after vagotomy as Peter et al. (1963) or Bell and Battersby (1968) reported, but returned to the same level in 2 to 6 weeks after vagotomy as Delaney (1967) or Levine et al. (1981) reported. Our data on gastric mucosal blood flow were measured at 2 weeks after vagotomy, so there was no significant difference between the control group and the vagotomy group. It seemed that the protective effect of vagotomy against acute gastric ulceration was due to reduction of acid output or gastric movement not due to gastric microcirculation.

The ulcer indexes of the jaundiced and vagotomized group showed lower values than that of the jaundiced group, while gastric mucosal blood flow of the
jaundiced and vagotomized group showed higher values than that of the control group. These data suggested that acute gastric ulceration was suppressed by vagotomy in jaundiced condition, and the improvement of gastric microcirculation might participate in suppressive effect of vagotomy on acute gastric ulceration, in addition to reduction of acid output or gastric movement. Now, why vagotomy improved gastric microcirculation in jaundiced condition? Sakaue (1982) reported that vagal tone was accelerated in hepatic injury.

In jaundiced condition, accelerated vagal tone might have reduced gastric mucosal blood flow, and vagotomy might prevent the reduction of gastric blood flow. However, this explanation is only hypothesis. Further investigations were needed to clear the mechanism of acute gastric ulcerations in jaundiced condition.

References


