EXPERIMENTAL STUDIES ON GASTRIC ULCER (4)
SEQUENTIAL OBSERVATION AND EVALUATION OF GASTRIC ULCERS BY ENDSCOPE IN THE RAT*

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Abstract—In the present study, a sequential observation of the gastric lesions or ulcers in rats weighing from 100 g was made with an endoscope. It was found that bleeding, edema, hyperemia, fur of ulcer and convergences of the mucosal folds in the stomach could be observed in rats with a SES-1717S ($\phi=1.7$ mm) or SES-2217S ($\phi=2.2$ mm) endoscope. Furthermore, we have devised a method which we named the "sohmen method" for measuring ulcer-sizes with an endoscope. The ulcer-size was compared with 5 mm lengths of sohmen (Japanese vermicelli) which were inserted through the sheath of the endoscope into the stomach. Therefore, the ulcer-size could be accurately measured by this method. By this observation method, it is possible to observe repeatedly over a long term the changes in gastric lesions or ulcers, to measure changes in ulcer-sizes and to evaluate the relapse or recurrence of ulcers in the same rats.

Okabe and Pfeiffer reported that acetic acid-induced ulcers in rats observed after 100 days were re-ulcered lesions and were still apparent even 250 days after ulcer induction (1). However, it is necessary to observe the ulcers and to measure their sizes sequentially in the same animals in determining the relapse or recurrence of ulcers.

Recently, endoscopes capable of observing the stomach or esophagus of experimental animals are coming into use (2-4). Mizushima et al. (5) used an experimental fiberscope of 4.0 mm width to observe stress ulcers and acetic acid ulcers in rats and reported that it was difficult to avoid suffocating rats weighing less than 200 g during examination.

In the present investigation, we attempted to observe gastric lesions and ulcers in smaller rats continuously and repeatedly and to devise a method for measuring sizes of the ulcers with an endoscope.

Materials and Methods

Animals and gastric ulceration: Animals used were Sprague-Dawley strain (Slc-SD) rats weighing from 100 to 220 g (5 to 7 weeks old). The rats were deprived of food but allowed free access to drinking water for 18 hr prior to experiments.

Acetic acid-induced ulcer was prepared according to the method of Takagi et al. (6) as follows: Under pentobarbital anesthesia, a midline, epigastric laparotomy was made; and after exteriorizing the stomach, 0.05 ml of 20% acetic acid was injected into the submucosal layer of the anterior wall of the glandular stomach.

Instruments: Endoscope (SES-1717S and
SES-2217S), cold light source (CLE-F) and endoscope camera (SC16-3R) were purchased from Olympus Optical Co., Ltd. Endoscopes used were the side viewing scope and the straight, hard type without an angle mechanism (needle-scope) and were used together with a sheath. The structure of the tip of the endoscope is shown in Fig. 1. The outside diameters of the sheaths of SES-1717S (ø=1.7 mm) and SES-2217S (ø=2.2 mm) were 2.0 mm and 2.6 mm, respectively.

Observation of ulcers: The animals were deprived of food but allowed free access to drinking water for 18 hr prior to observation. Under ether anesthesia, the endoscope and polyethylene tube (ø=1.0 mm) were inserted into the stomach from the mouth, and about 3~4 ml/100 g body weight of air was inspired into the stomach through the polyethylene tube. After removing the polyethylene tube, the inside of stomach was observed. If it was difficult to observe the ulcer due to food residues, feces or hair in the stomach, the stomach was washed with saline warmed at 37°C introduced through a catheter (ø=2.5 mm). All of these procedures were carried out without binding the rats.

Determination of ulcer-size ("sohmen method"): Dried sohmen sticks (Japanese vermicelli) were cut to exact lengths of 5 mm and inserted into the stomach through a sheath of the endoscope after saline lavage of the stomach. The size of acetic acid ulcer was measured by determining the ratio of the length or width of the ulcer to the 5 mm sohmen stick, and the endoscopical ulcer index [U(e)] was calculated from the product of the measured length and the width of the ulcer [U(e)=length (mm)×width (mm)]. After endoscopical observation, the rats were sacrificed and the stomach removed and opened along the greater curvature. The length and width of the ulcer were measured mechanically, and the macroscopical ulcer index [U(m)] was obtained from: [U(m)=length (mm)×width (mm)].

Results

Animals: Tested rats were 5 to 7 weeks old. Of the rats used, one out of five 5-weeks old rats suffocated during observation. However, the stomachs of the other rats were easy to observe.

Observation of ulcers: Findings such as bleeding, edema, hyperemia, debris or fur on the base of the ulcer and convergences of mucosal folds were ascertained from observing gastric ulcers in rats. Figure 2 shows an acetic acid-induced gastric ulcer on the 3rd day (left) and on the 20th day (right) after ulcer-induction. On the 3rd day, a relatively large and deeply demarcated ulcer is found, and the base of ulcer is covered with necrotic debris. Blood coagulation around the edge of the ulcer is observed. On the 20th day, the ulcer diminished in size and depth. Along with the diminution in the size of the ulcer, slight convergences of the mucosal folds can be seen. The base of the ulcer is covered with white fur.

Determination of ulcer-size: Figure 3 shows a sohmen stick and an acetic acid-induced ulcer on the 175th day after ulcer-induction. The size of the ulcer was determined from
the length of the sohmen stick seen beside the ulcer. As the length of the sohmen stick was 5 mm, the length and width of the left ulcer in the photograph were estimated to be 8.0 mm and 6.5 mm, respectively, and the calculated U1(e) of the ulcer was 52.0. The length and width of the white fur of the right ulcer were estimated to be 2.5 mm and 1.0 mm, respectively, and the U1(e) was 2.5.

Discussion

The endoscope is coming into use for observation of the stomach or esophagus in experimental animals (2-4). Miyazaki et al. (4) reported that the esophagus of 20 weeks old Donryu strain rats could be observed by a fiberscope (ENT US30) whose tip is 4.0 mm in width. However, he stated that it was difficult to insert the fiberscope into the entrance of the esophagus, and sometimes bleeding occurred due to the width of the tip. Mizushima et al. (5) experimented with a fiberscope to observe rat stress ulcers and acetic acid ulcers and reported that it was difficult to use in rats weighing from 150 to 200 g without suffocating the rat during observation since the width of the fiberscope was 4.0 mm. Okada et al. (7) reported success in observing water-immersed stress ulcers with a fiberscope that they designed (φ=3.0 mm) in Wistar strain rats weighing about 300 g, but that it was difficult to observe with the above method in smaller
rats weighing about 100 g because the tip of the fiberscope was too wide.

Tips of many endoscopes in clinical use are fairly flexible and possess an angle mechanism for observing various regions of the stomach. We used a straight, hard type of endoscope without an angle mechanism. The reason for this was that the stomach of a rat is too small to receive the curved tip of an endoscope. Therefore, we attempted to turn and twist the body of the rat instead of turning the tip of the endoscope and could observe most parts of the stomach. It is most important to keep respiration stable under anesthesia in order to handle the rats without difficulty.

In the present study, we were able to observe the gastric ulcers without suffocating the rats weighing about 100 g with a SES-1717S or SES-2217S endoscope. Furthermore, findings such as bleeding, edema, hyperemia, debris or fur on the base of the ulcer and convergences of mucosal folds could be also observed. These findings cannot be observed clearly in sacrificed rats.

On the other hand, it is extremely important to determine the sizes of ulcers for investigating drug effectiveness on ulcers. However, it is difficult to measure the size of an ulcer with an endoscope because the ratio of ulcer-occupied field in the range of the endoscopical view varies with the distance between the tip of the endoscope and the ulcer. Therefore, an attempt to measure exactly the sizes of ulcers with an endoscope was made in rats. The size of an ulcer was measured by comparing the ulcer with 5 mm lengths of sohmen inserted into the stomach through the sheath of the endoscope. According to these procedures, the ulcer-size was accurately measured and the Ul(e) and the Ul(m) showed a high correlation. From these results, it has been recognized that it is possible to evaluate the ulcer-size more exactly by using the “sohmen method”.

We checked many substances such as glass beads, ball sugar, sesame or poppy seeds and pills of several drugs in our search for a standard scale to put into the stomach and to measure ulcer-size. It is suspected that the sohmen stick used caused no irritation and had no pharmacological effects. Furthermore, it did not collapse rapidly in the stomach, and changes in the length of the sohmen were almost never observed, but the width swelled to about 1.5 times in warm water (45°C). We have used a sohmen stick in 5 mm lengths as the standard scale, but it is possible to vary the length of the sohmen stick in accordance with ulcer-size. Therefore, it was expected that the sohmen stick was the most favorable substance for use as the standard scale for measuring ulcer-size.

In application of the method described above, it is possible to observe repeatedly the changes in gastric lesions or gastric ulcers, to measure changes in ulcer-sizes and to evaluate the relapse or recurrence of ulcers in the same rats.

References