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Experimental Model of Gastritis Induced by Sodium Taurocholate in Rats

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ABSTRACT

Experimental gastritis was produced in rats by administration of sodium taurocholate (5 mM) for 3 months. The gastritis was associated with mucosal surface injury (erosion), inflammatory cell infiltration and proliferation of interstitial fibrosis in the gastric mucosa. The number of parietal cells per unit area and the mucosal thickness, however, were not different from those in the normal mucosa, indicating that this kind of gastritis was not atrophic but erosive gastritis. The model of erosive gastritis is most useful in studies on gastroprotection and various drugs.

It has been considered for many years that a number of factors such as mechanical, chemical, radiation, and immunological factors play a role in the development of gastritis in man[12,15,17,18]. These factors, however, may not be causative because gastritis cannot be reproduced in animals by such factors except for gastritis induced by immunological and radiation methods in dogs and rats. It has been accepted in man that duodenal contents, bile acids and lysolecithin, in particular, can cause gastritis which is most marked in the distal part of the stomach[6,21,27]. In the present study, the authors attempted to produce experimental gastritis in rats by administering sodium taurocholate, a component of bile acids which is one of the chemical factors of gastritis.

MATERIALS AND METHODS

Male Wistar rats, weighing around 180 g, were fed with usual standard meal and water containing 5 mM sodium taurocholate (TCA, Difco) for 3 months. At the end of 3 months, the rats were sacrificed by decapitation and the abdomen was opened. The stomach was then excised, opened along the greater curvature, laid flat without any artificial damage, and examined carefully for any evidence of gross macroscopic damage. The flattened stomach was divided into five parts with each excised and rolled in a Swiss manner (Fig. 1). The Swiss rolled tissue specimens were fixed in Bouin's solution for 12 hr at 4°C and then paraffin wax tissues of the embedded blocks were prepared by the usual method.

Hematoxylin and eosin-stained sections were used for histopathological evaluation and azan-stained sections for interstitial fibrosis.

The criteria employed in the present study for experimental gastritis were as follows: (1) mucosal surface injury (erosion), (2) reduction of parietal cells per unit area, (3) inflammatory cell infiltration, (4) shortened mucosal thickness and (5) proliferation of interstitial fibrosis.

Using an ocular eye grid provided with an objective lense, the length of surface mucosal injury was measured on the entire length of each tissue section from the asterick to the asterick as shown in Fig. 1 under a visual field of 100 power-magnification. The surface mucosal lesions (mm) were expressed as the sum total of 5 parts per stomach. The number of parietal cells was

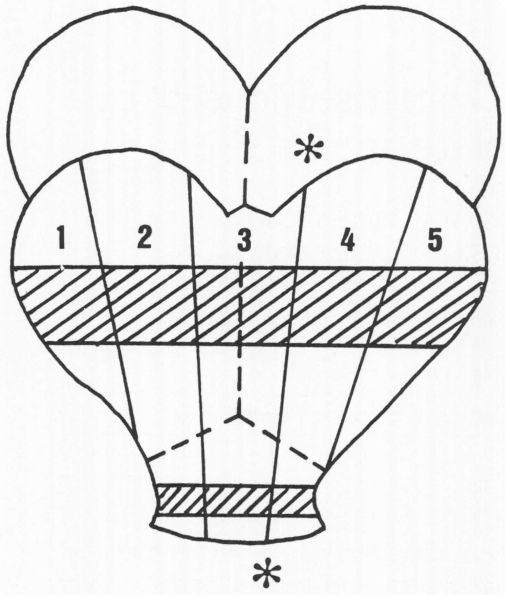

Fig. 1. Each part of the stomach (No 1-5). Samples were taken from the asterisk to asterisk.

counted per unit area (2.5 mm square) under a visual field of 400 power-magnification and the mucosal thickness (mm) was measured under a visual field of 100 power-magnification both using an ocular eye grid. The number of parietal cells and the mucosal thickness were evaluated in all vertical sections of 5 parts as shown in Fig. 1. The degree of inflammatory cell infiltration and the extent of fibrosis were evaluated in grades (0), (+, 1), (++, 2) and (+++, 3) in the entire mucosa of each part under a visual field of 100 power-magnification.

Male Wistar rats, weighing around 180 grams, were used as controls. They were fed in a routine manner without TCA for 3 months and sacrificed at the end of three months.

Measurements of the length of mucosal injury, number of parietal cells per unit area, and mucosal thickness were averaged to obtain a single value for each group.

The length of mucosal surface injury, the number of parietal cells and the mucosal thickness are presented as mean ± SEM. The difference between the experimental group and control group was evaluated statistically by Student's T-test for the length of surface mucosal injury, the number of parietal cells and the mucosal thickness and by x^2-test for the degree of inflammatory cell infiltration and the extent of fibrosis.

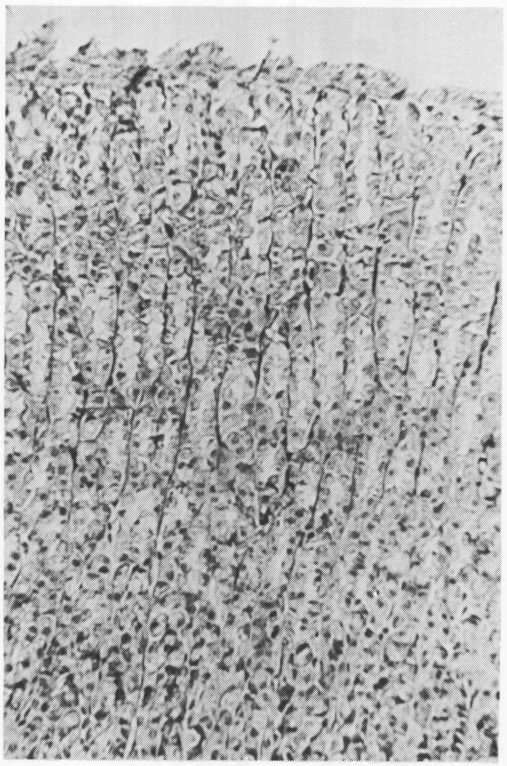

Fig. 2. The mucosal surface exfoliation and/or destruction are present in the stomach of the control group (HE stain, ×100).

RESULTS

Macroscopic evidence of mucosal injury could hardly be noted in any of both the experimental and control stomach specimens. By microscopic examination, no injury could be detected in any part of the control tissues. However, surface exfoliation and/or destruction were observed because the mucous layer and surface epithelial cells were occasionally absent (Fig. 2). The length of these regions was 1.97 ± 0.30 mm (Table 1). Extensive lesions of the gastric mucosal surface were noted in the experimental group with virtually the entire length of the epithelium showing evidence of injury. The length of such mucosal surface injury was 619.4 ± 66.4 mm (Fig. 3, Table 1).

The structure of the glands and glandular cells was somewhat loose and irregular in the body and antral mucosa of the experimental group. However, in general, no marked difference in the mucosal structure was noted between the experimental and control group. The number of parietal cells per unit area was 100.5 ± 28.7

Table 1. Summary of the data

Group	Experimental	Control	
Erosion (mm)	619.4 ± 66.4	1.9 ± 0.3	($p<0.001$)
P-cells/UA	100.5 ± 28.7	98.4 ± 14.8	(NS)
Mucosal thickness			
Body	0.59 ± 0.06	0.58 ± 0.08	(NS)
Antrum	0.27 ± 0.04	0.26 ± 0.02	(NS)
Cell Infiltration			
Body	1 to 2	0 to 1	(NS)
Antrum	1 to 2	0 to 1	(NS)
Fibrosis			
Body	1 to 2	0 to 1	$(p<0.05)^1$
Antrum	1 to 2	0 to 1	$(p<0.05)^2$

1: $X^2 = 8.182$
2: $X^2 = 7.543$

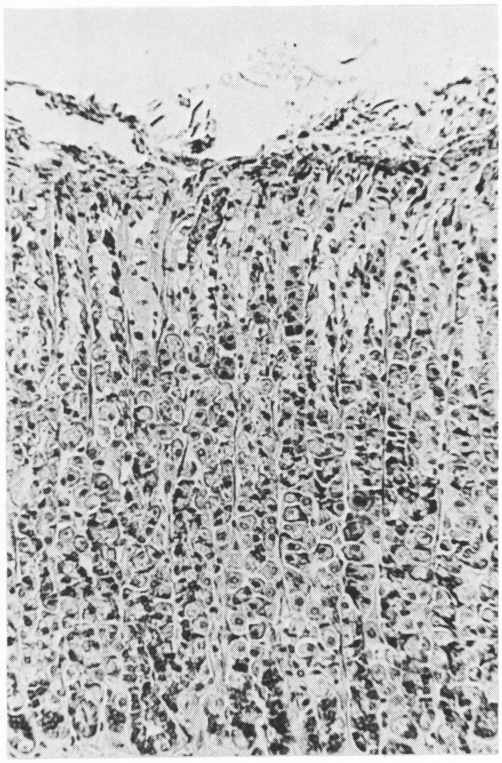

Fig. 3. The mucosal surface injury (erosion) is noted in the stomach of the experimental group (HE stain, ×100).

cells in the experimental group and 98.4 ± 14.8 cells in the control group with the difference not being statistically significant (Table 1).

The mucosal thickness of the gastric body and antrum was 0.59 ± 0.06 mm and 0.27 ± 0.04 mm, respectively, in the experimental group, while it was 0.58 ± 0.08 mm and 0.26 ± 0.02 mm, respectively, in the control group, the difference between the two being statistically insignificant (Table 1).

Inflammatory cell infiltration was marked (1 to 2) in the antrum but scarce (0 to 1) in the body of the experimental group. The difference was statistically not significant in the antrum between the experimental and control group (Table 1).

Interstitial fibrotic proliferation was noted both in the body and antrum of the experimental group (1 to 2), while fibrotic proliferation was rare in the control group (0 to 1) (Fig. 4 A and B). The difference was statistically significant between the experimental and control group (Table 1).

DISCUSSION

Although a number of factors have been considered for many years to play a role in the development of atrophic gastritis, attention has been directed in particular to the possible role of duodenal contents which affect the human stomach[7,24]. Duodenal contents, bile acids and lysolecithin in particular considered to be a mucosal barrier breaker can cause atrophic gastritis which is most marked in the distal part of the stomach[6,21,28]. Bile reflux gastritis or bile gastritis is frequently observed after gastric surgery and its extent and severity increase with time following surgery[1,10,14]. Recently, such a bile reflux gastritis has been noted not only after gastric surgery but also after cholecystectomy[3,9,29]. These reports suggest that the bile plays a major and causative role in the de-

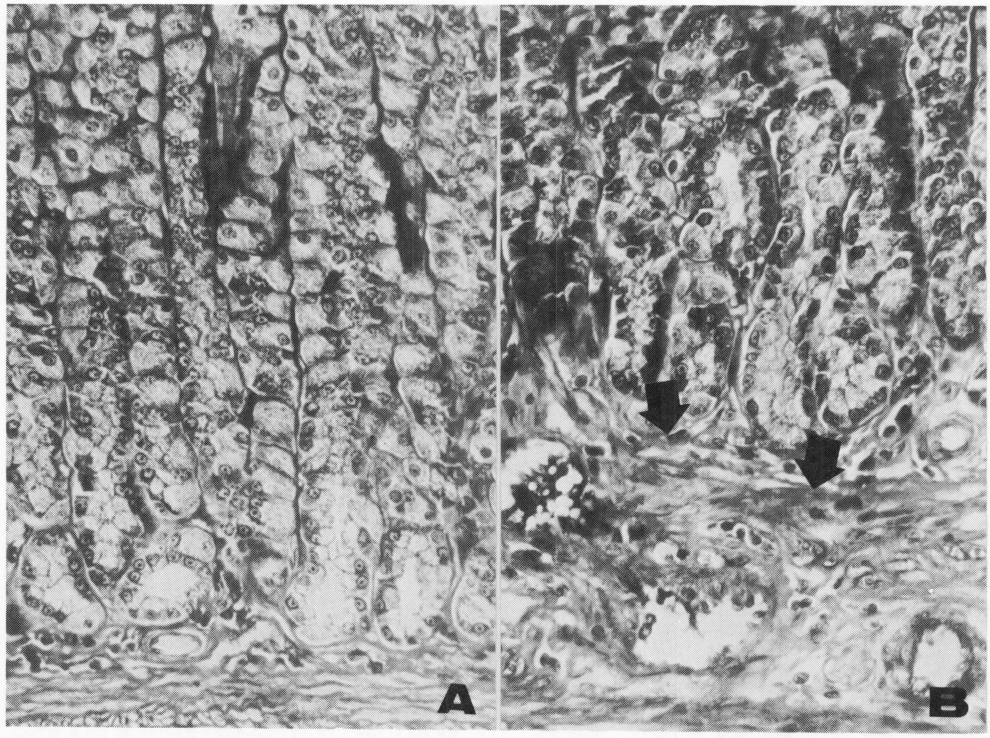

Fig. 4. Interstitial fibrotic proliferation is present in the antrum of the experimental group (B), while this is rare in the stomach of the control group (A) (Azan stain, ×100).

velopment of gastritis not only in man but also in animals. If it is applicable in animals, gastritis may be induced in animals by exogenous and/or endogenous administration of bile.

Experimental studies with animals have demonstrated that endogenous bile causes gastritis after different operations of bile reflux into the dog stomach[20,21]. The authors have observed that taurocholic acid, a component of bile acids, can cause atrophic gastritis in rats[15,16]. In the present study, the authors attempted to produce gastritis by administration of TCA in rats for such a short period as these months. The results showed that mucosal surface injury (erosion) and inflammatory cell infiltration as well as interstitial fibrosis developed. These are considered to be findings of erosive gastritis. Therefore, the authors consider that a short period as 3 months of administration of TCA can induce erosive gastritis in rats. The number of parietal cells per unit area and the mucosal thickness in the experimental rats were similar to those in the control rats. This implys that atrophic gastritis cannot develop during such a short period of administration of TCA because the reduction of parietal cells and the shortened thickness of the gastric mucosa are typical of atrophic gastritis[17,18].

Bile acids can damage the gastric mucosa[23]. A mechanism has been proposed that the mucosal barrier to ionic movement of sodium and hydrogen ions is broken by bile salts, resulting in loss of hydrogen ions and back diffusion of hydrogen ions into the mucosa from the lumen, bringing rise to mucosal damage[5,11,26,26]. In the mucosa exposed to taurocholic acid in acidic solution, DNA efflux paralleled gastric surface cell injury and physiologic alterations in cation fluxes and potential difference[13], indicating clearly that gastric pH with bile may contribute to gastric mucosal surface injury (erosion and ulcer) which occurs in animals and man[2,4,8,27]. Gastric mucosal pH in the experimental rats of this study was between 1 and 2. It is, therefore, considered that TCA in acidic environment in the stomach may have caused mucosal surface injury (erosion). A mechanism of inflammatory cell infiltration and proliferation of fibrosis is still

under consideration. However, one possibility might be repititive irritation of the gastric mucosa by bile acid (TCA). The model of erosive gastritis in rats is most useful in studies on gastroprotection and on the action of various drugs.

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