The Influence of Truncal Vagotomy on Acute Gastric Mucosal Lesion in Obstructive Jaundice

Osamu KODAMA, Hitoshi TAKEUCHI, Nobuaki ITO, Tsuneo TANAKA, Rokuro SEIKOH, Yasuyuki ICHIBA and Kiyohiko DOHI

The Second Department of Surgery, Hiroshima University School of Medicine, 1-2-3, Kasumi, Minami-ku, Hiroshima 734, Japan

(Received June 21, 1985)

Key words: Obstructive jaundice, AGML, Truncal vagotomy, Amine

ABSTRACT

With a view to examining the influence of truncal vagotomy on acute gastric mucosal lesion (AGML) in obstructive jaundice, the authors prepared the non-vagotomized group and the vagotomized group of rats with obstructive jaundice. Further, cold restraint stress was loaded on the two groups for 30 min, and the following results were obtained:

1) The incidence of AGML in the vagotomized group before stress was inhibited to 17% in both the 3-week group and 4-week group, as compared to 33-38% in the non-vagotomized group. The incidence of AGML in the vagotomized group after stress was inhibited to 17% in the 3-week group and 33% in the 4-week group, as compared to 78% in the non-vagotomized group.

2) Gastric mucosal histamine (HA) contents in the vagotomized group before stress in both the 3-week group and the 4-week group were significantly increased (p < 0.05) as compared with the levels in the non-vagotomized group. As concerns gastric mucosal serotonin (5-HT) contents, however, no significant difference was noted between both groups. The contents of both amines in the gastric mucosa in the non-vagotomized group, a significant decrease (p < 0.05) was observed in both the 3-week group and 4-week group after stress, while in the vagotomized group no significant changes were found.

Once acute gastric mucosal lesion (AGML) in obstructive jaundice occurs, the treatment is extremely difficult, and the prognosis is very poor. It is considered therefore that we should take preventive measures against it beforehand¹⁰. In the present study, therefore, the authors examined the influence of vagotomy on gastric mucosal amine contents and on the incidence of AGML in order to pursuit the usefulness of vagotomy as a prophylactic measure for AGML.

MATERIALS AND METHODS

1) Animal procedures

Wistar-strain male rats (200-250g) were used for the study. Under Nembutal anesthesia, their

common bile ducts were ligated and cut, and simultaneously bilateral subdiaphragmatic truncal vagotomy and pyloroplasty (Heineke-Mikulicz) were performed on the animals. After breeding them for 3 weeks and 4 weeks, the 3-week vagotomized group and the 4-week vagotomized group were prepared. For the control, the non-vagotomized 3-week group and the 4-week group on which ligation and cutting of common bile duct alone was given were prepared. Subsequently cold restraint stress⁷⁾ was loaded on each group for 30 min. The animals in each group were fasted for 24 hr before using them for the study.

2) Observation of AGML

After the animals were sacrified by decapitation, the stomachs were extracted and incised on the side of the greater curvature, the occurrence of AGML was observed macroscopically.

3) Determination of gastric mucosal amine contents

After extracting the amines from tissue with the method of Wada et al¹¹, fluorescent quantitation of histamine (HA) was performed by the method of Shore et al⁸ and serotonin (5-HT) by the method of Maickel-Miller⁵.

RESULTS

1) The incidence of AGML

The incidence of AGML in the vagotomized 3-week group and 4-week group before stress was decreased by 17% for each, as compared with 33% and 38% in the non-vagotomized group. On the other hand, the incidence of AGML in the vagotomized group after stress was decreased by 17% in the 3-week group and 33% in the 4-week group, as compared with 78% in the non-vagotomized group (Table).

2) Changes in the HA contents

The HA contents in the vagotomized group before stress was $70.4 \pm 20.1 \,\mu\text{g/g}$ in the 3-week group, and $68.2 \pm 15.2 \,\mu\text{g/g}$ in the 4-week group, both showing significantly higher levels as compared with the levels in the non-vagotomized group (p<0.05, Fig. 1). The HA contents in the non-vagotomized group in both the 3-week and 4-week groups showed significantly lower levels (p<0.05) after stress, whereas in the vagotomized group no significant changes were noted (Fig. 1).

3) Changes in the 5-HT contents

The 5-HT contents in the vagotomized group before stress were $11.0 \pm 3.3 \, \mu g/g$ in the 3-week group, and $15.3 \pm 6.9 \, \mu g/g$ in the 4-week group, showing no significant changes as compared with the levels in the non-vagotomized group (Fig. 2). The 5-HT contents in the non-vagotomized group in both the 3-week and 4-week groups after stress showed significantly lower levels (p<0.05), while in the vagotomized group no significant changes were noted (Fig. 2).

DISCUSSION

By loading a mild stress of cold restraint for 30 min on the non-vagotomized group, the incidence of AGML was markedly increased, and this result suggested that the gastric mucosa in obstructive jaundice was in the preliminary stages of ulcerogenesis⁴. Contrary to this finding, when truncal vagotomy and pyloroplasty was given prophylactically to rats with obstructive jaundice, the incidence of AGML was markedly inhibited. This finding may suggest the prophylactic effect of vagotomy against the onset of AGML.

So far, the authors have often reported that the gastric mucosal amines were closely associated with the mechanism of onset of AGML in obstructive jaundice^{4,9}. However, while in the non-vagotomized group, the incidence of AGML was markedly increased after stress but gastric mucosal HA and 5-HT contents were decreased significantly, whereas in the vagotomized group in which the incidence of AGML was inhibited, no significant decrease in both amines was noted after stress. These findings may be consi-

Table	Incidence	of	AGML	(A:	pre-stress.	B:	post-stress)	,
-------	-----------	----	------	-----	-------------	----	--------------	---

duration of obstruc	group	non-vagotomized	vagotomized
3 weeks	A	3/8 (38%)	1/6 (17%)
	В	7/9 (78%)	1/6 (17%)
4 weeks	A	3/9 (33%)	1/6 (17%)
	В	7/9 (78%)	2/6 (33%)

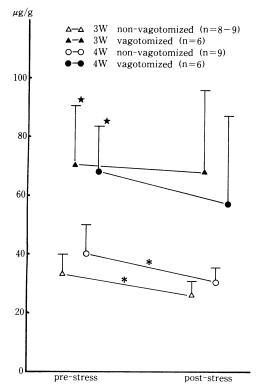


Fig. 1. Changes in gastric mucosal histamine contents on cold restraint for 30 min

- * Significance of the difference between means of the pre- and post-restraint value within each study group (M \pm SD, *p<0.05).
- ★ Significance of the difference between means of the pre-restraint value in the vagotomized and non-vagotomized group within each week ($M \pm SD$, *p<0.05).

dered that the release of both amines was significantly inhibited, considering that the vagus nerve was associated with the release of the amines in the gastric mucosa^{2,3)}. Therefore, a marked increase in the gastric mucosal HA contents in the vagotomized group before stress, as compared with the levels in the non-vagotomized group may be attributed to the inhibition of the release of HA by vagotomy.

On the other hand, there was no significant difference of the 5-HT contents between the vagotomized and non-vagotomized groups. Although it has not been clarified what kind of mechanism induced these results, it may be possible that both the synthesis and release of 5-HT were inhibited by vagotomy, considering that the

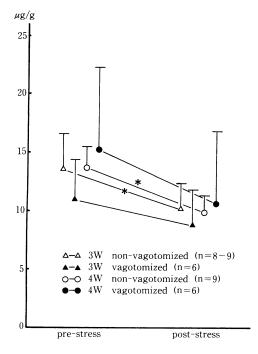


Fig. 2. Changes in gastric mucosal serotonin contents on cold restraint for 30 min

* Significance of the difference between means of the pre- and post-restraint value within each study group $(M \pm SD, *p<0.05)$.

vagus nerve was associated with the synthesis of 5-HT^{1,2)}.

The fact that vagotomy was unable to prevent the onset of AGML completely may suggest a possibility of some other factors than the vagus nerve associating with the release of both amines^{3,6)}, and it may also suggest a possibility that other factors than amines may be associated with the mechanism of onset of AGML in obstructive jaundice.

REFERENCES

- Hutson, D.G., Zeppa, R. and Levine, V. 1969. Effect of vagotomy on the content of serotonin and histamine in the gastrointestinal tract. Surg. Forum 20: 315-317.
- Ikeda, Y. 1980. A pathogenesis of the stress ulcer by biogenic amines. An influence of the stress-induced hypothalamic catecholamine changes on the mucosal amines of the rat stomach. Jap. J. Gastroenterol. Surg. 13: 269-280.
- 3. Izumikawa, F. 1980. Release mechanisms of

- 5-HT from the gastrointestinal tract in rats. Arch. Jap. Chir. 49: 572-594.
- Kodama, O., Takeuchi, H., Ito, N., Tanaka, T., Seikoh, R., Ichiba, Y. and Ezaki, H. 1985. Experimental studies on acute gastric mucosal lesion involved with obstructive jaundice: mainly on the changes of amine contents in the gastric mucosa on cold restraint stress. Hiroshima J. Med. Sci. 34: 75-79.
- Maickel, R.P. and Miller, F.P. 1966. Fluorescent products formed by reaction of indole derivatives and O-phthalaldehyde. Anal. Chem. 38: 1937-1938.
- Reilly, M.A. and Schnyer, R.W. 1972. Effect of glucocorticoids on histamine metabolism in mice. Br. J. Pharmacol. 45: 463-469.
- Senay, E.C. and Levine, R.J. 1967. Synergism between cold and restraint for rapid production of stress ulcers in rats. Proc. Soc. Exp. Biol. Med. 124: 1221-1223.
- 8. Shore, P.A., Burkhalter, A. and Cohn, V.H., Jr.

- 1959. A method the fluorometric assay of histamine in tissues. J. Pharm. Exp. Ther. 127: 182-186.
- Takeuchi, H., Kodama, O., Ito, N., Tanaka, T., Harada, M., Seikoh, R. and Ezaki, H. 1984. Experimental studies on acute gastric mucosal lesion in obstructive jaundice and biliary drainage models with emphasis on the changes of histamine and serotonin in the gastric mucosa. Hiroshima J. Med. Sci 33: 341-347.
- Takeuchi, H., Kodama, O., Ito, N., Tanaka, T., Harada, M., Seikoh, R. and Ezaki, H. 1984. Clinical studies of acute gastric mucosal lesion complicated with obstructive jaundice, particularly regarding the cases on which reduction of jaundice was performed. Hiroshima J. Med. Sci. 33: 425-433.
- Wada, H., Yamatodani, A. and Ogasawara, S. 1977. Systematic determination of biogenic amines. Seitai no Kagaku 28: 215-222.