Hiroshima Journal of Medical Sciences
Vol.35, No.4, 343~346, December, 1986
HIJM 35-50

Antral Somatostatin Contents and Acidity of Gastric Juice in Normal Subjects and Patients with Duodenal Ulcer

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(Received September 3, 1986)

Key words: Duodenal Ulcer, Antral somatostatin, Acidity

ABSTRACT

The antral somatostatin contents were investigated in biopsy specimens of the antrum from normal subjects and patients with duodenal ulcer. There was good correlation ($r=0.77044$) between antral somatostatin contents and maximal acidity in normal subjects, but the correlation between antral somatostatin contents and maximal acid output was not significant ($r=0.254367$). This result may indicate that antral somatostatin content is regulated by intragastric pH in normal subjects. On the other hands, no correlation was observed between antral somatostatin contents and acidity or acid output in patients with duodenal ulcer.

Therefore the impaired regulation of acid on antral somatostatin contents could be one of the important factors in the pathogenesis of duodenal ulcer disease.

It has been shown that the release of gastrin is inhibited by acidification of gastric luminal content in normal subjects[12]. Somatostatin, which inhibits gastrin release[3], was identified in D cells of antrum[1], and was stimulated to release by acidification of stomach[8]. The purpose of this study was to see if somatostatin play a role in acid inhibition of gastrin release.

METHOD

Thirty-five normal subjects, 27 male and 8 female, ranging in age from 14 to 40 (mean ± SD; 23.0 ± 5.5 years) and 39 patients with duodenal ulcer, 28 male and 9 female, ranging in age 14 to 63 (mean ± SD; 36.3 ± 12.6 years) were studied. Normal subjects were patients who visited Hiroshima University Hospital, proved endoscopically normal and secreted gastric juice more than lower limit of normal range[7]. Duodenal ulcer was endoscopically diagnosed and combined gastroduodenal ulcer was excluded from this study.

After an overnight fast, biopsy specimens were obtained endoscopically using Olympus gastroduodenalfiberscope GIF series. Three specimens, each of which was about 4 mg in weight, were taken from the lesser curvature of the antrum, and were immediately frozen with liquid nitrogen. The specimens were homogenized in 3 ml of 2N acetic acid, boiled in a bath for 10 min, and then centrifuged at 2800rpm at 4°C for 15 min. The supernatant was lyophilized and resuspended in 2 ml of 0.01M pH7.4 phosphate buffered saline containing 0.5% bovine serum albumin (Sigma Co. USA).

Somatostatin was determined by a specific radioimmunoassay as previously described[9]. Somatostatin antiserum was made by immunizing rabbit with synthetic somatostatin 14 (purchased from Peptide Institute Inc., Osaka)

Table 1. Gastric acid secretion, antral somatostatin contents and serum gastrin levels in normal subjects and patients with duodenal ulcer.
Results are presented as mean ± SD. BAC; basal acidity (mEq/liter),BAO; basal acid output (mEq/hr), MAC; maximal acidity (mEq/liter), MAO; maximal acid output (mEq/hr), AS; antral somatostatin contents (ng/mg), SG; serum gastrin (pg/ml)

	Normal	Duodenal Ulcer	
Age	23.0 ± 5.5 (35)	36.3 ± 12.6 (39)	$p<0.01$
BAC	56.50 ± 32.92 (26)	59.08 ± 8.14 (39)	ns
BAO	2.93 ± 2.70 (35)	5.16 ± 4.03 (39)	$p<0.01$
MAC	110.20 ± 24.24 (35)	105.97 ± 17.64 (39)	ns
MAO	17.38 ± 6.64 (35)	22.76 ± 6.93 (39)	$p<0.01$
AS	2.23 ± 1.42 (35)	0.63 ± 0.46 (37)	$p<0.01$
SG	70.6 ± 45.4 (35)	94.1 ± 58.0 (36)	$p<0.1$

conjugated with bovine serum albumin by carbodiimide. The antiserum did not cross react with gastrin, secretin, insulin, glucagon, caerulein and substance P. Tyr^1-somatostatin was iodinated by lactoperoxidase method. The sensitivity of the assay was 3 pg/tube, and intra- and interassay coefficent of variation were 6.8% and 13.7%, respectively. Gastrin was determined by radioimmunoassay as previously described[10].

Gastric acid secretion test was performed in all subjects. After an overnight fast, the gastric juice was collected for 1 hr for the determination of basal acidity (BAC) and basal acid output (BAO), and after intramuscular injection of tetragastrin (4 μg/Kg body weight), the gastric juice was collected every 10 min for 1 hr to determine the maximal acidity (MAC) and maximal acid output (MAO).

The results were presented as mean ± SD. Differences between means were assessed by the Students' t test. Correlation between different variables was estimated by linear regression analysis.

RESULTS

1. Antral Somatostatin Contents, Serum Gastrin Levels and Gastric Acid Secretion

The antral somatostatin contents of patients with duodenal ulcer (0.63 ± 0.46 ng/mg) was significantly lower than that of normal subjects (2.23 ± 1.42 ng/mg). There was no significant difference between normal subjects and patients with duodenal ulcer in basal serum gastrin levels. BAO and MAO were significantly increased in patients with duodenal ulcer than that of normal subjects. However the acidity of normal subjects in basal state and also after stimulation with tetragastrin (BAC and MAC) were similar to those of duodenal ulcer (Table 1).

2. Correlation between Antral Somatostatin Contents and Gastric Acid Secretion

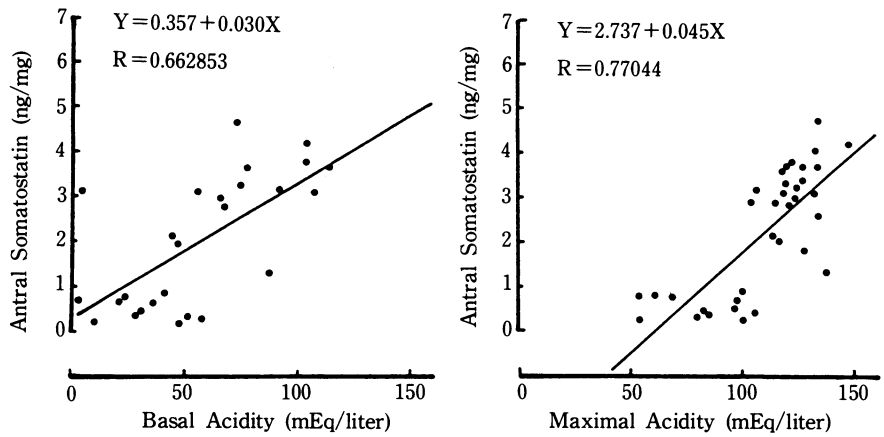

Fig. 1. Relationship between antral somatostatin contents and basal acidity, and between antral somatostatin contents and maximal acidity in normal subjects.

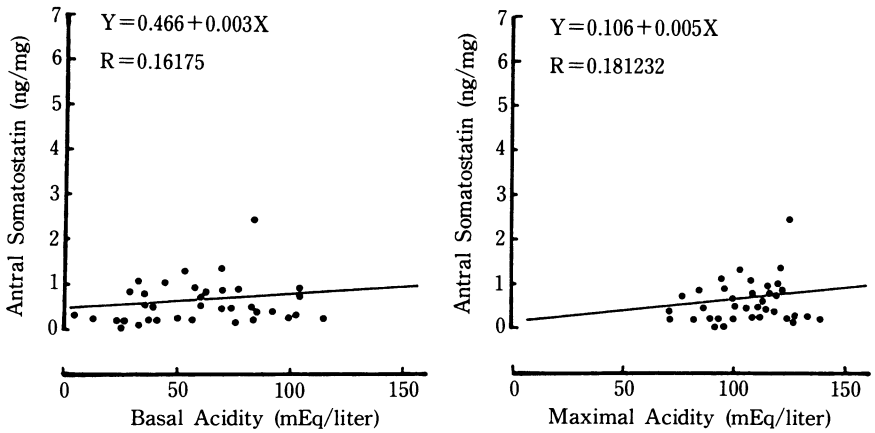

Fig. 2. Relationship between antral somatostatin contents and basal acidity, and between antral somatostatin contents and maximal acidity in patients with duodenal ulcer.

In normal subjects, antral somatostatin contents correlated with the acidity of basal state and after stimulation ($r=0.662853$ $p<0.01$, $r=0.77044$ $p<0.01$), while in patients with duodenal ulcer there was no correlation (Fig. 1, Fig. 2). In patients with duodenal ulcer and also in normal subjects no relationship was observed between antral somatostatin contents and basal or tetragastrin stimulated acid output (Table 2).

Table 2. Coefficients of correlation (CC) between antral somatostatin contents and gastric acid secretion, and serum gastrin levels. Abbreviations are same as Table 1. ** $p<0.01$

	Normal		Duodenal Ulcer	
	n	CC	n	CC
AS-BAC	26	0.662853**	37	0.16175
AS-BAO	35	0.270171	37	0.102108
AS-MAC	35	0.77044 **	37	0.181232
AS-MAO	35	0.254367	37	0.271052
AS-SG	35	−0.127166	36	−0.132556

DISCUSSION

The factors which influence the content of antral somatostatin have not been established. Previously we have shown that atrophic gastritis accompanied the reduction of antral somatostatin contents[9]. In this study the subjects were consisted of patients who secreted gastric juice above normal range, as to exclude the influence of atrophic gastritis on somatostatin contents. It was revealed that antral somatostatin contents were positively correlated with acidity of gastric juice in normal subjects, and suggested that antral pH affect the antral somatostatin contents. The influence of intragastric pH on hormone release from the endocrine cell of the stomach was established in G cell[6,13]. Long-term hypochlorhydria or achlorhydria, as seen in pernicious anemia[6], does result in elevation of serum gastrin level, and causes hyperplasia of G cells[13]. As to somatostatin, Schusziarra et al[8] demonstrated the release of this peptide the gastroepiploic vein in dogs after intragastric instillation of 0.1N HCl. Other authers[4] also reported stimulatory influence of low intragastric pH on somatostatin release into antral vein in experimental animals. Arnold et al[2] demonstrated that there was no relationship between the number of D cells and acid output, but showed that G cell/D cell ratio was decreased in gastrinoma patients, and speculated that a low intragastric pH not only stimulate somatostatin release but also the growth of the D cells. Morphological investigation has demonstrated that D cell touches neighboring G cell in the antral mucosa[5]. When antral pH decreased, it acts on D cell to stimulate somatostatin release, and then gastrin release from G cell may be inhibited in normal subjects.

In the duodenal ulcer patients no relationship existed between antral somatostatin contents and acidity, in contrast to normal subjects. The fasting serum gastrin level of duodenal ulcer patients (94.1 ± 58.0 pg/ml) was increased more than that of normal subjects (70.6 ± 45.4 pg/ml), although there was no significant differ-

ence. It has been reported that serum gastrin response stimulated by test meal are increased in duodenal ulcer patients[10,11]. Walsh et al[12] have shown that the inhibition of gastrin release at a gastric luminal pH of 2.5 was significantly less in duodenal ulcer patients than in normal subjects. The defect of autoregulation of gastrin release in duodenal ulcer may be caused by impaired correlation of antral somatosatin contents and gastric acid concentration.

From these findings it was suggested that the intragastric pH govern the antral somatosatin contents in normal subjects and the impairment of this correlation could be one of important factors in the pathogenesis of duodenal ulcer disease.

REFERENCES

1. **Arimura, A., Sato, H., Dupont, A., Nishi, N. and Shally, A.V.** 1975. Somatostatin; abundance of immunoreactive hormone in rat stomach and pancreas. Science **189**: 1007—1009.
2. **Arnold, R., Hülst, M.V., Neuhof, C.H., Schwarting, H., Becker, H.D. and Creutzfeldt, W.** 1982. Antral gastrin-producing G-cells and somatostatin-producing D-cells in different states of gastric acid secretion. Gut **23**: 285—291.
3. **Bloom, S.R., Mortimer, C.H., Thorner, M.O., Besser, G.M., Hall, R., Gomez-Pan, A., Roy, V.M., Russell, R.C.G., Coy, D.H., Kastin, A.J. and Shally, A.V.** 1974. Inhibition of gastrin and gastric acid secretion by growth-hormone release-inhibiting hormone. Lancet **2**: 1106—1109.
4. **Gustavsson, S. and Lundqvist, G.** 1978. Participation of antral somatostatin in the local regulation of gastrin release. Acta Endocrinol. **88**: 339—346.
5. **Larsson, L.I.** 1980. Gastrointestinal cells producing endocrine, neurocrine and paracrine messengers. Clin. Gastroenterol. **9**: 485—516.
6. **McGuigan, J.E. and Trudeau, W.L.** 1970. Serum gastrin concentrations in pernicious anemia. N. Engl. J. Med. **282**: 358—361.
7. **Miyoshi, A., Ohe, K., Inagawa, T., Inoue, M., Uraki, S., Tatsugami, M., Noguchi, A., Onda, M., Yokoya, H. and Shirakawa, T.** 1980. A statistical study on the age distribution of gastric secretion in patients with peptic ulcer. Hiroshima J. Med. Sci. **29**: 21—28.
8. **Schusdziarra, V., Harris, V., Conlon, M. and Arimura, A.** 1978. Pancreatic and gastric somatostatin release in response to intragastric and intraduodenal nutrients and HCl in the dog. J. Clin. Invest **62**: 509—518.
9. **Sumii, K., Fukushima, T., Hirata, K., Matsumoto, Y., Sanuki, E., Tsumaru, S., Sumioka, M., Miyoshi, A. and Miyachi, Y.** 1981. Antral gastrin and somatostatin concentrations in peptic ulcer patients. Peptides **2 Suppl. 2**: 281—283.
10. **Sumii, K., Yokoyama, Y., Matsui, Y., Kikkawa, N., Hidaka, T., Suenaga, K., Ohe, K. and Miyoshi, A.** 1979. The increased antral gastrin content and its release in response to test meal in patients with duodenal ulcer. Hiroshima J. Med. Sci. **28**: 221—227.
11. **Walsh, J.H.** 1979. Pathogenetic role of the gastrins, p. 181—198. *In* J.F. Rehfeld (ed.), Gastrin and the Vagus, Academic Press, London.
12. **Walsh, J.H., Richardson, C.T. and Fordtran, J.S.** 1975. pH dependence pf acid secretion and gastrin release in normal and ulcer patients. J. Clin. Invest **55**: 461—469.
13. **Yalow, R.S. and Berson, S.A.** 1973. Further studies on the nature of immunoreactive gastrin in human plasma. Gastroenterology **60**: 203—214.