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Plasma Gastrin Levels and Gastric Acid Secretion in Chronic Renal Failure

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Plasma gastrin levels and gastric acid secretion were examined in 17 patients with chronic renal failure on maintenance hemodialysis and 22 normal subjects. Plasma gastrin levels were measured using radioimmunoassay. Gastric analysis was performed by intramuscular injection of tetragastrin (4 μg per kg). Gastroduodenal endoscopy was performed in all patients. Fasting plasma gastrin levels were 421.1±320.8 pg/ml (mean±S.D.), while those of normal subjects were 54.7±51.5 pg/ml. Basal acid output was less than 1.0 mEq/h in 77% of the patients, and one hour acid output was less than 10.0 mEq in 71%. No increase in grastric acid secretion was observed both in basal condition and following tetragastrin stimulation in spite of the presence of hypergastrinemia. None of the patients had peptic ulcer endoscopically, except that one patient had a few erosions on the antral mucosa. Our observations were inconsistent with the former reports from European countries that increased gastric acid secretion and peptic ulcer were more frequently observed in patients with chronic renal failure. These data may suggest that atrophic gastritis preceded the occurrence of renal failure in these patients, or that other factors inhibited the gastric secretion.

(Key Words : Gastrin, Hypergastrinemia, Gastric Acid Secretion, Chronic Renal Failure)

INTRODUCTION

Recent studies have shown that serum gastrin levels are elevated in patients with chronic renal failure (1), (2) as the kidney has a role in the degradation of gastrin (3)～(7). It has been described previously that the high frequency of peptic ulcer and gastric hypersecretion is observed in patients with chronic renal failure on maintenance hemodialysis (8)～(12). But in the renal center of our institute we scarecely see such patients with epigastric distress. Plasma gastrin levels, gastric acid secretion and endoscopic findings of the gastroduodenal mucosa were studied in those patients and normal subjects in this series.

MATERIALS

17 patients with end-stage chronic renal failure undergoing hemodia-

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lysis (12 males and 5 females aged 25–73 years, average 43. 4 years) were studied. Hemodialysis were performed for 15 hours a week in three sessions of equal length with a twin-coil dializer. 22 normal control subjects (aged 19–22 years, average 19. 9) were selected from the healthy male students as volunteer.

METHODS

The collection of blood samples for measuring gastrin was performed on the day of hemodialysis after an overnight fast. Gastric analysis and gastro-duodenoscopy were carried out on the next day or two days after the hemodialysis.

GASTRIC ANALYSIS: Following proper positioning of the tube in the stomach, residual gastric contents were aspirated completely and discarded. Thereafter the basal juice was collected for 60 min. by continuous suction augmented by hand suction at intervals. Then tetragastrin (4 μg. per kg.) was given by intramuscular injection and the gastric juice was aspirated at every 15 min. intervals for the following 60 min. These aspirates were measured volumetrically and titrated with 0. 1 N sodium hydroxide to pH 7. 0. BAO (basal acid output) and OAO (one hour acid output after tetragastrin stimulation) in mEq/h was calculated.

MEASURING OF GASTRIN: Plasma samples were analyzed for gastrin in duplicate with a double antibody radioimmunoassay (13), (14) using synthetic human gastrin (SHG-I, from I. C. I. company, England) as a standard. The antibodies were developed in rabbits by immunization of SHG-I conjugated to bovine serum albumin. Radioiodination of SHG-I was performed through use of a modification of the radioiodination method developed by Hunter and Greenwood (15).

RESULTS

Plasma gastrin levels, gastric acid secretion and gastroduodenoscopic findings in patients with chronic renal failure are summarized in the Table 1. And comparison between normal subjects and patients concerning plasma gastrin levels and gastric acid secretion is shown in the Table 2. The patients with chronic renal failure had significantly ($p<0.005$ by t-test) high gastrin levels (421. 1 ± 320.8 pg/ml, mean $\pm$S. D.) when compared with those of normal subjects (54. 1 ± 41.5 pg/ml). Gastric acid secretion in patients, however, showed rather low values. BAO of the patients 0. 8 ± 0.6 mEq/h (mean $\pm$ S. D.) and was less than 1. 0 mEq/h in 13 (77%) of the patients, while that of normal subjects was 2.6 ± 1.8 mEq/h. OAO of the patients was 7.0 ± 5.0 mEq and was less than 10 mEq in 12 (71%) of the patients, while that of normal subjects was 13.3 ± 6.4 mEq. Table 3 shows plasma gastrin levels and gastric acid secretion in patients, who are classified to two groups according to age (group A : below 40 of age, group B : more than 40 of age). But there was no significant difference between two groups. No significant correlation was noted between fasting plasma gastrin and basal acid output in the patients, as shown in Figure 1. There was also no significant correlation between the severity of the renal damage, as assessed by the concentration of serum-creatinine, and plasma gastrin levels or gastric acid output. None of the patients had peptic ulcer endo-

Table 1. Plasma Gastrin Levels, Gastric acid Secretion and Gastroduodenal Findings in Patients with Chronic Renal Failure Undergoing Hemodialysis

Case No	Age	Plasma Gastrin Levels (pg/ml)	Gastric Acid Secretion		Gastro-Duodenoscopical Findings	Duration of Dialysis at Time of Test (month)	Serum Creatinine, Urea-N, and Ca before Dialysis near Test		
			BAO (mEq/h)	OAO (mEq)			Creatinine (mg/dl)	Urea-N (mg/dl)	Ca (mEq/l)
1	32	320	0.1	14.6	a few erosions	7	14.6	92	4.3
2	73	190	1.2	8.4	no particular findings	6	15.1	130	3.5
3	28	145	0.3	2.5	〃	9	11.3	123	3.5
4	47	160	0.2	3.7	〃	7	17.4	101	4.7
5	55	125	0.3	6.9	〃	9	12.1	154	4.6
6	41	800	0.1	1.3	〃	4	18.4	142	3.2
7	67	1100	0.1	0.1	〃	3	9.8	117	4.2
8	54	250	0.2	17.0	〃	3	18.7	118	4.3
9	45	970	0.1	0.2	〃	36	16.5	136	4.7
10	36	530	0.4	11.1	〃	11	18.4	121	5.2
11	27	94	1.7	7.8	〃	7	23.8	144	4.2
12	31	720	0.4	10.8	〃	7	22.6	150	4.9
13	53	260	0.4	5.4	〃	1	10.6	98	4.4
14	44	155	3.2	8.0	〃	39	22.5	91	5.2
15	50	560	0.1	0.4	〃	2	20.3	143	3.8
16	29	700	0.1	8.1	〃	1	9.4	86	4.2
17	25	80	4.4	12.7	〃	1	13.4	114	4.6

Table 3. Plasma gastrin levels and gastric acid secretion in patients with chronic renal failure

		Group-A (Age<40)	Group-B (Age≧40)
Fasting plasma gastrin(pg/ml)		369.9±259.2	457.0±353.2
Acid secretion	BAO (mEq/h)	1.0±1.5	0.6±0.8
	OAO (〃)	9.7±3.7	5.1±5.0
Average Age		29.7	52.9
Number of cases		7	10

Table 2. Plasma gastrin levels and gastric acid secretion in normal subjects & patients with chronic renal failure

		Normal	Chronic renal failure
Fasting plasma gastrin (pg/ml)		54.1±41.5	421.1±320.8
Acid secretion	BAO (mEq/h)	2.6±1.8	0.8±0.6
	OAO (〃)	13.3±6.4	7.0±5.0
Average age		19.9	43.4
Number of cases		22	17

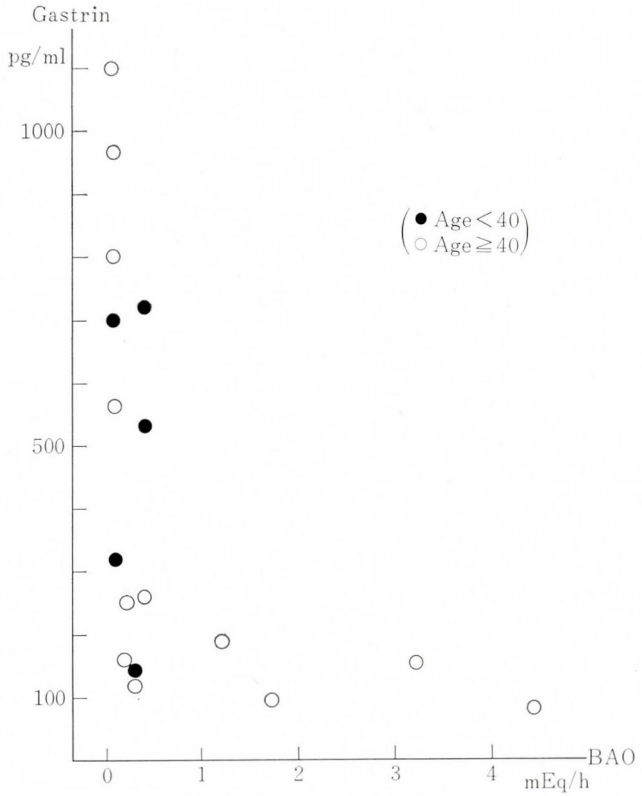

Fig. 1 Plasma gastrin levels and BAO in patients with chronic renal failure

scopically, though one patient had a few erosions on the antral mucosa. And none of the patients complained of epigastric pain or dyspeptic sensation.

DISCUSSION

It is generally agreed that the kidney plays a major role for gastrin degradation or excretion (3)–(7). Jaffe and Newton (3) reported that intravenously administered radiolabelled synthetic human gastrin was concentrated in the renal cortex. According to Clendinnen et al. (4) 40% of renal artery gastrin was extracted and degraded by the kidney when constant intravenous infusion of synthetic human gastrin was performed in dogs. Davidson et al. (5) showed that the dog kidney is an important site for the extraction and degradation of endogenous gastrin induced by the instillation of acetylcholine-sodium bicarbonate into the stomach. Hypergastrinemia in the patients with chronic renal failure is considered to be due to impaired degradation of gastrin by the kidney (1), (2). The uremic patients had shown a return of raised gastrin levels to the normal range after renal transplantation (Korman et al. (1)). Our study has also shown that the plasma gastrin levels are significantly elevated in patients with chronic renal failure. Korman et al. (1) stated that serum gastrin rose proportionately with the degree of renal failure when the serum creatinine levels were used as an index of the degree of renal impairment. Although the patients in our study had similarly severe renal impairment there was no

significant correlation between the severity of the renal damage by use of the same index and plasma gastrin.

Now we have to consider the role of hypergastrinemia for gastric acid secretion in patients with chronic renal failure. There are various reports about this problem. According to some reports increased gastric acid secretion and high frequency of the peptic ulcer was observed (8)～(12), but other reports showed that rather low gastric acid secretion was observed (16), (17). Our study has shown that no increase was observed in gastric acid secretion and none of the patients had peptic ulcer endoscopically. Endoscopy is, as a matter of course, better than barium meals to confirm the existence of gastroduodenal lesions accurately. Hansky et al. (7) reported that there was no clear correlation between acid secretion and serum gastrin levels in their patients with chronic renal failure and the incidence of duodenal ulcer is not higher than in control populations.

Shepherd et al. (8) showed extremely high frequency (53%) of duodenal ulcer with high overnight and basal gastric acid secretion in patients with chronic renal failure on maintenance hemodialysis. They described that the state of some patients resembled that of Zollinger-Ellison syndrome but gastric hypersecretion in their patients differs pathophysiologically from the hypersecretion of the Zollinger-Ellison syndrome in being completely suppressible by secretin (18).

McConnel et al. (9) showed that gastric acid secretion increased progressively during the course of hemodialysis, while it was low at non-dialyzed period. They described that the functional disturbance of gastric secretion in patients with chronic renal failure not receiving dialysis was attributed to gastric mucosal impairement by the factors accompanying the uremia, and hemodialysis, by removing such factors, permitted the improved function of the gastric mucosa and manifestation of an underlying gastric hyposecretory state. In addition they made a comment that the hypersecretion probably depended upon the persistently high concentrations of circulating gastrin, since the abnormally high concentration of circulating immunoreactive gastrin in uremic patients is not affected by hemodialysis (1), (9) and long-continued administration of gastrin exerts trophic effect on the stomach (20). But they did not mention how long duration of hemodialysis at least is necessary to induce the improved function of the gastric mucosa. The patients of our study had hemodialysis in the duration of 1—39 (average 8. 8) months, and there was no clear correlation between gastric acid secretion and the duration of hemodialysis. (Table 1)

Goldstein et al. (10) showed that marked increase in serum calcium was observed during dialysis in one of the patients, who secreted a large volume of gastric juice. Then they described that increased serum calcium may play a role to augment gastric secretory response in some instances. Serum calcium levels seem well related to gastric activity in some cases (21)～(24). In our study serum calcium levels were rather low in all patients as shown in the Table 1.

The above are the reports and opinions of gastric hypersecretion in the patients with chronic renal failure. But we have to consider the cause of rather low gastric secretion observed in our study. It is presumed that low gastric acid secretion is probably due to atrophic change of the gastric

mucosa or gastric mucosal impairement by the factors accompanying the uremia. As atrophic gastritis is so frequent in Japan that it might precede the occurrence of renal failure in this series, although biopsy of gastric mucosa was not performed because the patients had more or less bleeding tendency. Krempien et al. (25) reported that the diminished survival time of differentiated parietal cells with marked alteration of the mucosal barrier was observed in the glandular stomachs of uremic rats.

Schupak and Ferayorni (17) reported that hyposecretion and hypoacidity was the most characteristic feature of the chronicaly hemodialyzed subjects, recognizing the occurrence of peptic diseases. He speculated that factors other than gastric acidity must be implicated in peptic diseases in those patients.

Lieber and Lefevre (16), who reported the low gastric acid secretion in patients with chronic uremia, found that gastric juice ammonia significantly increased in uremia, which may cause low gastric acid. According to Flesher and Gabuzda (26), however, the amount of acid that could be neutralized by ammonia was negligible.

Chey et al. (27) showed that elevated serum secretin levels were observed in patients with chronic renal failure. This report indicates that one of the factors causing low gastric acid secretion in uremic patients may be the suppression by increased serum secretin. Further studies are required to resolve this problem. The kidney is known to be involved in the extraction and degradation of several polypeptide hormones (28)～(32).

2 of 17 patients in our study showed considerably good response to tetragastrin stimulation (OAO : 14. 6 mEq & 17. 0 mEq) in spite of low basal acid secretion (BAO : 0. 1 mEq/h & 0. 2 mEq/h). This fact arouses the supposition that in those patients circulating immunoreactive gastrin could not be always active in gastric acid secretion.

Though there are various reports about gastric acid secretion and complication of peptic ulcer in patients with chronic renal failure, no definitive conclusion can be drawn because of various factors affecting them. Further studies of hormonal, neural, serochemical and histological factors may be required for these problems.

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