RADIOIMMUNOASSAY FOR SERUM GASTRIN IN SINGAPORE CHINESE

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SYNOPSIS

Fasting serum gastrin was determined by radioimmunoassay with the Dianabot kit (Tokyo) in 81 Chinese subjects. The mean fasting serum gastrin level in 43 duodenal ulcer patients (73 pg/ml) was higher than that in 18 control subjects (57 pg/ml) though the difference did not reach statistical significance. These levels fall within the range in Caucasians. The findings support the hypothesis that impaired auto-regulation of gastrin release in patients with duodenal ulcer by low antral pH is a contributing factor in duodenal ulcer diathesis. The mean fasting level in 19 gastric ulcer patients (68 pg/ml) was also higher than in the control subjects, but not significantly so. The infrequency of hypergastrinaemia in these gastric ulcer patients is probably due to associated antral gastritis.

In 1905 Edkins (1) observed that an extract of gastric antral mucosa strongly stimulated gastric acid secretion. It was 60 years later before the active principle, the heptadecapeptides gastrin I & II were isolated, characterised and synthesized (2, 3). When it was shown that gastrin produced by non-beta islet cell tumour of pancreas caused the Zollinger-Ellison Syndrome (4 - 9), it was postulated that subtle differences in levels of circulating gastrin might represent a major contributing mechanism in the development of the less fulminant, more classical duodenal ulcer disease. This hypothesis has been the subject of intensive research following the development of accurate measurement of the hormone by radioimmunoassay (10).

To upgrade our facilities for the study of gastric physiopathology, a gastrin laboratory was set up in 1979. Interesting results might be expected in view of the marked difference in frequency of peptic ulcer disease in the racial groups of South East Asia (11, 12, 13). Our study is an ongoing project and the first paper records the fasting serum gastrin levels in Chinese control subjects and patients with peptic ulcer disease.

METHODS

1. Subjects

Each subject was fasted overnight and a fasting blood sample obtained for serum gastrin estimation. Of the 81 Chinese subjects, 18 were controls, being clinically free of gastrointestinal disease (11 males, 7 females; age range 19 - 60, average 34.7 years); 44 had duodenal ulcer (32 males, 12 females; age range 15 - 97, average 46.1 years); and 19 had gastric ulcer (13 males, 6 females, age range 42 - 88; average 60 years). Peptic ulcer disease in all patients was confirmed by endoscopic examination or at surgical operation.

2. Radioimmunoassay of Serum Gastrin

Sera obtained by immediate centrifuge of blood sample was stored in a freezer at – 16°C. Gastrin concentrations were determined in the serum samples by radioimmunoassay. The reagents for the assay (rabbit antigastrin serum, ^{125}I synthetic gastrin and standard synthetic gastrin) were purchased in kit form from Dianabot Radioisotope lab. Tokyo. The assay was performed as described by the manufacturers of the tests. Unbound antigen was separated by dextran-charcoal adsorption and counted in a G.D. Searle gamma spectro-meter. Standard curve was prepared by plotting percentage of precipitate values upon total activity against gastrin standard curves. The concentration of gastrin in the samples was read from the standard calibration curve. Assay for each sample was done in duplicate.

RESULTS

The results are summarised in Table 1.

Control Subjects

The fasting levels of gastrin in 18 control subjects varied from 25 to 107 pg/ml, with a mean of 57 pg/ml and a standard deviation (SD) of 21. If mean ± 2SD is accepted as including 95% of normal values, then the upper limit of normal in our laboratory is 99 pg/ml.

Duodenal Ulcer patients

The fasting levels of gastrin in 44 duodenal ulcer patients varied from 17 to 210 pg/ml, with a mean of 73 pg/ml and SD of 34. The mean fasting level of 73 pg/ml, although elevated compared to that of control subjects did not reach statistically significant levels according to the *t* test ($P < 0.1 > 0.05$). Of the 44 duodenal ulcer patients, 6 had levels above the normal range, i.e. > 99 pg/ml.

Gastric Ulcer Patients

The fasting levels of gastrin in 19 gastric ulcer subjects varied from 16 to 162 pg/ml, with a mean of 68 pg/ml and SD of 37. The mean fasting level of 68 pg is higher than that in control subjects but the difference was not statistically significant. Of the 19 gastric ulcer patients, 4 had levels above the normal range, i.e. > 99 pg/ml.

Comparison with other series

The basal serum gastrin in Caucasian subjects has been reviewed recently (14). In 21 studies in patients with duodenal ulcer, variable results in five publications could be explained by differences in techniques & methodology. The sixteen reports considered representative are listed in Table II and show that fasting serum gastrin in duodenal ulcer patients vary between 43 to 134 pg/ml as compared to controls in whom the range is between 30.4 and 105 pg/ml. The range of serum gastrin in gastrin ulcer patients from 5 publications (Table III) is from 93 to 285 pg/ml.

DISCUSSION

The levels of fasting serum gastrin vary to some extent amongst laboratories and this may be explained at least in part by difference in methodology. Nevertheless, using the Dianabot radioimmunoassay kit, we found that the levels of serum gastrin in Chinese control subjects (mean 57 pg/ml) and patients with duodenal ulcer (mean 73 pg/ml) fell within the range described for Caucasians (30.4 - 105 pg/ml for controls and 43 - 134 pg/ml for duodenal ulcer group).

Within each laboratory, fasting gastrin levels either showed no significant difference between duodenal ulcer group and control group or significantly higher values in the duodenal ulcer group. We found that the mean fasting levels in Chinese duodenal ulcer patients (73 pg/ml) was higher than that in the control group (57 pg/ml) though the difference did not reach statistical significance. The somewhat higher level of fasting gastrin in the duodenal ulcer group was due to six of the 44 patients having levels above the normal range of 99 pg/ml in our laboratory. None of these patients were suspected to have the Zollinger-Ellison syndrome as the basal gastrin levels did not approach the very high levels (frequently exceeding 1000 pg/ml) diagnostic of the syndrome (32; 33).

Duodenal ulcer patients as a group are gastric acid hypersecretors and the Chinese patients are no exception (34). Lower levels of gastrin would be expected if the normal inhibition of gastrin release by low antral pH was functional. Furthermore, increased sensitivity of the parietal cell mass to pentagastrin in patients with duodenal ulcer disease has been demonstrated (35). Thus impaired autoregulation of gastrin release in patients with duodenal ulcer disease by low antral pH and increased sensitivity to stimulation of acid secretion would appear to be major contributing factors to duodenal ulcer diathesis (28, 35) and our findings in Chinese patients support this hypothesis.

Fasting gastrin level in gastric ulcer patients have been usually reported to be moderately elevated compared to control subjects (see Table III) and this may be explained by hypochlorhydria and diminished acid inhibition favouring gastrin release. The release of gastrin may however be impaired if gastric ulcer is associated with antral gastritis. Our finding was that the mean fasting serum gastrin level of gastrin ulcer patients (68 pg/ml) was higher than that in control

TABLE 1
MEAN FASTING SERUM GASTRIN LEVELS IN CHINESE SUBJECTS

Subjects	No.	Mean Serum Gastrin (pg/ml)	S.D.	Ulcer versus Control	
				t	p
Control	18	57	21		
Duodenal Ulcer	44	73	34	1.89	NS
Gastric Ulcer	19	68	37	0.82	NS

TABLE II
SERUM GASTRINS IN PATIENTS WITH DUODENAL ULCER

Authors	Normal Subjects		Duodenal Ulcer		
	Gastrins (pg/ml)	No. of subjects	Gastrins (pg/ml)	No. of patients	p Value
Reeder et al, 1970 (15)	63 ± 3	5	106 ± 17	6	$p < 0.05$
Trudeau and McGuigan, 1971 (16)	85 ± 9.8	35	78 ± 6.7	55	NS
Stadil and Rehfeld, 1971 (17)	93	20	76	12	not given
Ganguli and Hunter, 1972 (18)	105 ± 7	113	91 ± 6	27	NS
Isenberg et al, 1972 (19)	67.8 ± 7.8	17	55 ± 5.7	20	NS
Becker, Reeder and Thomson 1973 (20)	84 ± 7	10	129 ± 11	17	$p < 0.05$
Stadil & Rehfeld, 1973 (21)	52 ± 4.6	120	50 ± 2.4	103	NS
McGuigan & Trudeau, 1973 (22)	71 ± 9.4	10	76 ± 7.0	22	NS
Stern & Walsh, 1873 (23)	54 ± 8	8	65 ± 7	9	NS
Reeder, Becker & Thompson 1974 (24)	93 ± 2	21	134 ± 7	12	$p < 0.05$
Wesdorp & Fischer, 1974 (25)	54 ± 9	30	61 ± 7	101	NS
Hansky, Soveny & Korman 1974 (26)	44 ± 5.5	49	51 ± 6.8	53	NS
Gedde-Dahl, 1975 (27)	42 ± 5.5	9	109 ± 24.5	9	$p < 0.02$
Walsh, Richardson & Fordtran 1975 (28)	30.4 ± 4.6	7	34 ± 6	6	NS
Stremple and Elliot 1973 (29)	45 ± 11	32	43 ± 10	67	NS
Byrnes, Lam & Sircus 1976 (30)	75 ± 7.8	10	61.9 ± 5.9	28	NS

TABLE III
SERUM GASTRIN IN PATIENTS WITH GASTRIC ULCER

Authors	Normal Subjects		Patients with Gastric Ulcers	
	Gastrin (pg/ml)	No. of Patients	Gastrin (pg/ml)	No. of Patients
Korman, Soveny & Hansky, 1971	(31) 32 ± 43	93	118 ± 8.1	18
Trudeau & McGuigan, 1971 (16)	85 ± 9.8	35	159 ± 33.6	9
Ganguli & Hunter, 1972 (18)	105 ± 7.0	113	285 ± 31	14
Hansky, Soveny & Korman 1974	(26) 44 ± 5.5	49	114 ± 25.2	15
Wesdorp & Fischer 1974 (25)	54 ± 9	30	93 ± 17	31

subjects (57 pg/ml) but the difference was not significant. Only four of 19 patients with gastric ulcer had levels above the normal range of 99 pg/ml of our laboratory. It might be relevant that the mean age of our gastric ulcer patients was 60 years, considerably higher than in the control subjects (34.7 years). Antral gastritis increases with age (36) and this probably explains the infrequency of hypergastrinaemia in the present series of gastric ulcer patients.

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