Positive correlation between normal serum gastrin concentrations and antral and duodenal G cells

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WR YACOB, ABR THOMSON, RW SHERBANIUK, P HOOPER, LD JEWELL. Positive correlation between normal serum gastrin concentrations and antral and duodenal G cells. *Can J Gastroenterol* 1994;8(4):235-238. It is controversial whether there is a correlation between serum gastrin concentrations and the density of G cells in the antral or duodenal mucosa. In this study, endoscopically obtained antral and duodenal biopsies were stained immunocytochemically for gastrin and the G cells quantitated using an MOP Videoplan computer image analysis system. Studies were performed in 20 patients with acid-peptic disorders (gastric ulcer, n=5; duodenal ulcer, n=10; reflux esophagitis, n=4; and nonulcer dyspepsia, n=1). Correlations between antral and duodenal G cell densities, and basal- and food-stimulated serum gastrin concentrations within the normal range (less than 100 mg/L) – but not in those with elevated gastrin concentrations – support the postulate that alterations in G cell function are important in patients with acid-peptic disorders.

Key Words: Gastric endocrine cells, Gastrin, Immunohistochemistry, Morphometry

Corrélation positive entre concentration normale de gastrine sérique et cellules G antrales et duodénales

RÉSUMÉ : Une certaine controverse règne au sujet d'une corrélation possible entre les concentrations de gastrine sérique et la densité de cellules G dans la muqueuse antrale ou duodénale. Dans cette étude, des biopsies antrales et duodénales colorées à l'endoscopie par méthode immunocytochimique pour y déceler la présence de gastrine et de cellules G quantifiées à l'aide d'un système vidéoplan informatisé d'analyse de l'image. Des épreuves ont été effectuées chez 20 patients atteints de troubles peptiques liés à l'hyperacidité (ulcère d'estomac, n = 5; ulcère duodénal, n = 10; oesophagite de reflux, n = 4; et dyspepsie non ulcéreuse, n = 1). Les corrélations entre les densités des cellules G antrales et duodénales, et les concentrations sériques normales (moins de 100 mg/mL) de gastrine basales et induites par la prise d'aliments (et l'absence de telles corrélations avec des concentrations élevées de gastrine) appuient le postulat selon lequel toute dysfonction des cellules G est importante chez les patients qui souffrent de problèmes peptiques liés à l'hyperacidité.

MORE THAN A DECADE AGO, Stave et al (1) and Royston et al (2) reported a correlation between fasting serum gastrin and antral G cell density. Others (3,4) were not able to confirm this finding. The presence or absence of such a correlation may help to determine whether elevated concentrations of fasting or meal-stimulated serum gastrin are associated with hyperfunctioning or hyperplastic G cells. In the present study we investigated whether a correlation existed between gastric and duodenal mucosal G cell densities, and basal and meal-stimulated serum gastrin concentrations.

MATERIALS AND METHODS

Twenty-six endoscopically obtained antral and duodenal mucosal biopsies (five from five gastrointestinal ulcer subjects, 12 from 10 duodenal ulcer subjects, seven from four gastroesophageal reflux disease [GERD] subjects and two from one nonulcer dyspepsia subject) were stained immunocytochemically for gastrin-secreting G cells. Eleven patients were male and nine were female. The mean ages were: gastrointestinal ulcer patients, 52 years; duodenal ulcer patients, 47 years; GERD patients, 54 years; and nonulcer dyspepsia patients, 54 years. The patients were on a variety of antacid and antisecretory regimens. Endocrine cell counts were obtained using an MOP Videoplan computer image analysis system. Details of the immunocytochemical and

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Figure 1) Correlation between fasting serum gastrin concentrations and antral G cells in 18 cases. $P=0.001$, $r=0.650$

Figure 2) Lack of correlation between fasting serum gastrin concentrations over 100 ng/L and duodenal G cells

Figure 3) Left Correlation between meal-stimulated serum gastrin levels at 30 mins and duodenal G cells in 10 cases. $P=0.04$, $r=0.655$

morphometric studies are available (unpublished data).

STATISTICAL ANALYSIS

All analyses were based on the square roots of the cell counts. A theoretical argument suggested that on this scale the variance would remain nearly constant as the mean changed. Plots of the data showed that the distributions of the root counts were fairly symmetric.

The authors examined the relationship between root counts of duodenal and gastric G cells and serum gastrin levels. Multivariate regression of duodenal and gastric G cells on basal and meal-stimulated serum gastrin levels examined the possible correlation between these variables. The strength of relationships between G cell densities and serum gastrin levels was measured by the Pearson correlation coefficient.

RESULTS

Analysis was carried out on 23 biopsies ($n=18$ patients: five gastrointestinal ulcer, nine duodenal ulcer, three GERD and one nonulcer dyspepsia) taken from patients whose fasting serum gastrin levels were less than 100 ng/L (normal range 0 to 100). A highly significant correlation (Figure 1) was found between basal (fasting) serum gastrin concentrations and the antral G cell densities ($r=0.65$, $P=0.001$; multi-

Figure 4) Correlation between meal-stimulated serum gastrin concentrations at 60 mins and antral G cells in 11 cases. $P=0.035$, $r=0.637$

Figure 5) Correlation between meal-stimulated serum gastrin concentration at 120 mins and antral G cells in 13 cases. $P=0.011$, $r=0.677$

variate test statistics, $P=0.001$). There was no correlation between fasting serum gastrin and duodenal G cell numbers (Figure 2).

Measured at 30 mins (Figure 3), meal-stimulated serum gastrin concentrations were positively correlated with duodenal, but not with antral, G cell densities in the 10 cases where values had not exceeded 100 ng/L ($r=0.655$, $P=0.04$, multivariate test statistics, $P=0.12$). At 60 mins (Figure 4), meal-stimulated serum gastrin concentrations correlated with antral G cell densities in the 11 cases where values were within the normal fasting range ($r=0.637$, $P=0.035$, multivariate test statistics, $P=0.10$). Two hours after meal-stimulation (Figure 5), serum gastrin concentrations were correlated with antral G cell densities ($r=0.677$, $P=0.011$, multivariate test statistics, $P=0.04$) in 13 cases processed.

DISCUSSION

This study confirms earlier findings (1,2) of a correlation between fasting serum gastrin concentrations and antral G cell density; this study also provides the novel demonstration of a positive correlation between meal-stimulated serum gastrin levels, and antral and duodenal G cell densities. It is

important to stress that the positive correlation was limited to the circumstances in which gastrin levels were within normal limits.

Normally rising meal-stimulated serum gastrin levels remaining within normal values correlated positively with antral and duodenal G cell densities at different times during testing (Figures 3-5).

The presence of this correlation only when serum gastrin values were within normal limits provides strong evidence for the concept of G cell hyperfunction (as opposed to G cell hyperplasia) in patients with acid-peptic disorders. The pathophysiological mechanism(s) of G cell hyperactivity remain speculative. Theoretically, enhanced gastrin release could be a result of increased G cell stimulation or sensitivity to certain stimuli, and/or defective inhibition due to diminished acid inhibition or disturbance in somatostatin release or synthesis (5,6).

While a few duodenal ulcer patients with basal hypergastrinemia have marked antral G cell hyperplasia (7-9), it is still controversial whether this represents an end-point in a continuum in peptic ulcer disease or whether it is a separate pathogenetic entity (10,11). Significant G cell hyperfunction, how-

ever, has been ascribed to a subgroup of duodenal ulcer patients with hypergastrinemia and acid hypersecretion (12). Recently, Cooper and co-workers (13) suggested that enhanced gastrin response to feeding in these patients is due to increased sensitivity to amino acid stimulation rather than defects in acid inhibitory mechanisms. The demonstration in this investigation of a positive correlation between G cell densities and basal and stimulated serum gastrin concentrations, when the latter were within the normal range (0 to 100 ng/L), indicates that higher serum gastrin values are not due to increased G cell numbers. It also suggests that a stable G cell population is capable of adapting to physiological and pathological stimuli.

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