Idiopathic Gastric Acid Hypersecretion
Comparison with Zollinger-Ellison Syndrome

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Many patients with acid-peptic disease have idiopathic gastric acid hypersecretion defined as a basal acid output >10.0 meq/hr; however, a significant proportion have basal acid outputs >15.0 meq/hr, which is within the range found in Zollinger-Ellison syndrome. Although idiopathic gastric acid hypersecretion is more common than Zollinger-Ellison syndrome, it is important that these two disorders be differentiated because of differences in treatment and natural history. In the present study, we compared 124 patients with idiopathic gastric acid hypersecretion and 137 patients with Zollinger-Ellison syndrome. There were no significant differences with regard to age at diagnosis, history of upper gastrointestinal hemorrhage, nausea, vomiting, and family history of duodenal ulcer and other acid-peptic disease. However, significant differences were observed between patients with idiopathic gastric acid hypersecretion and patients with Zollinger-Ellison syndrome with regard to percentage of males: 77% compared to 64% (P = 0.008), mean serum gastrin: 60 pg/ml compared to 3679 pg/ml (normal <100 pg/ml) (P < 0.001), mean basal acid output: 15.4 meq/hr compared to 47.0 meq/hr (P < 0.001), mean age at onset of symptoms: 33 years compared to 41 years (P < 0.001), mean duration of symptoms before diagnosis: 11 years compared to five years (P < 0.001), percentage with abdominal pain: 67% compared to 82% (P = 0.00004), percentage with diarrhea: 12% compared to 75% (P < 0.000001), percentage with pyrosis: 58% compared to 40% (P = 0.003), percentage with duodenal ulcer: 53% compared to 74% (P < 0.000001), and percentage with esophagitis: 31% compared to 42% (P = 0.0004). The differences in clinical features could be attributed to difference in mean basal acid output, and/or differences in levels of basal acid output used for diagnosis of idiopathic gastric acid hypersecretion (basal acid output >10.0 meq/hr) and Zollinger-Ellison syndrome (basal acid output >15.0 meq/hr). When 45 patients with idiopathic gastric acid hypersecretion and 39 patients with Zollinger-Ellison syndrome with basal acid outputs 15.1–30.0 meq/hr were compared, the main significant differences were with regard to mean serum gastrin: 69 pg/ml compared to 655 pg/ml (P < 0.001), percentage of male gender: 82% compared to 62% (P = 0.03), and percentage with diarrhea: 16% compared to 64% (P = 0.000005). These results indicate that in general patients with idiopathic gastric acid hypersecretion and patients with Zollinger-Ellison syndrome often have similar clinical features that can be difficult to distinguish. However, the increased frequency of diarrhea and female gender should lead to a strong suspicion of Zollinger-Ellison syndrome, which can be distinguished in almost every case by measurement of serum gastrin.

KEY WORDS: idiopathic gastric acid hypersecretion; Zollinger-Ellison syndrome.
IDIOPATHIC GASTRIC ACID HYPERSECRETION AND ZOLLINGER-ELLISON SYNDROME

hypersecretion (1–4), including Zollinger-Ellison syndrome (11, 12). Zollinger-Ellison syndrome is a well-characterized syndrome that is associated with esophageal disease, gastric and duodenal ulcer disease, abdominal pain, and diarrhea; it can be identified by noting gastric acid hypersecretion, an elevated serum gastrin concentration, and a positive response to provocative secretin testing (1, 13). However, less than 1% of patients with gastric acid hypersecretion are estimated to have Zollinger-Ellison syndrome (13, 14), while the majority of all patients have no apparent etiology for their gastric acid hypersecretory states (14, 15). Patients with no apparent etiology for their gastric acid hypersecretory states are classified as having idiopathic gastric acid hypersecretion.

Because of the infrequent utilization of gastric analysis to determine basal acid output in patients with acid-peptic disease, idiopathic gastric acid hypersecretion is frequently not diagnosed and, therefore, poorly characterized with regard to frequency of symptomatic acid-peptic disease and/or mucosal disease, although it is more common than Zollinger-Ellison syndrome (13, 14). It is important that the clinician distinguish these two conditions because they differ in natural history and treatment (1, 14, 16). However, some patients with Zollinger-Ellison syndrome have normal fasting serum gastrin concentrations and negative provocative tests (17), and since idiopathic gastric acid hypersecretion is much more common (13, 14, 16), this would raise the possibility that significant numbers of patients with idiopathic gastric acid hypersecretion might be evaluated for Zollinger-Ellison syndrome, which would involve considerable expense because the evaluation requires multiple serum gastrin concentrations, provocative testing, and detailed imaging studies (1, 13). The purpose of the present study was to compare the clinical features of 124 patients with idiopathic gastric acid hypersecretion with those of 137 patients with Zollinger-Ellison syndrome to attempt to identify clinical parameters that might assist the physician to distinguish these two disorders.

MATERIALS AND METHODS

Idiopathic Gastric Acid Hypersecretion

Patients. From 1985 to 1991 all patients who were being investigated by upper gastrointestinal endoscopy and subsequently diagnosed as having acid-peptic disease and who consented to gastric analysis were prospectively studied to determine basal acid outputs. Patients with Zollinger-Ellison syndrome, renal failure, gastric outlet obstruction, and previous vagotomy or partial gastric resection were excluded from this study. Basal acid output was determined within seven days after the upper gastrointestinal endoscopy. There were 603 patients who had basal acid outputs determined who had clinical symptoms and/or endoscopic evidence of acid-peptic disease. One hundred thirty-four patients were found to have gastric acid hypersecretion, defined as a basal acid output of greater than 10.0 meq/hr (18). Two of those 134 patients were diagnosed as having Zollinger-Ellison syndrome, and the other 132 patients were considered to have idiopathic gastric acid hypersecretion.

Investigations. Basal acid output was performed in the absence of any antisecretory medication for at least 72 hr if antisecretory medication had been started prior to the gastric analysis (19). After a nasogastric tube was inserted into the gastric antrum, the accurate positioning of the tube was confirmed by recovery of greater than 80% of a 30-ml waterload in lieu of fluoroscopy. After the gastric residual was emptied by aspiration, four consecutive 15-min samples of gastric fluid were collected by continuous aspiration. Samples were titrated to pH 7.0 with 0.01 N NaOH and basal acid output was expressed as milliequivalents of acid per hour. Based on our previous studies, a basal acid output of greater than 10.0 meq/hr is considered the definition for gastric acid hypersecretion (18). Zollinger-Ellison syndrome was excluded in all patients with a basal acid output of greater than 10.0 meq/hr by defining a normal baseline serum gastrin concentration (less than 100 pg/ml) and by a normal secretin stimulation test (2 units/kg GIH secretin; Kabi Group, Greenwich, Connecticut) defined as an increase of less than 200 pg/ml in any patient with an elevated gastrin level (17).

Zollinger-Ellison Syndrome Patients

The 137 patients with Zollinger-Ellison syndrome were from a group of patients that are presently being studied at the National Institutes of Health, Bethesda, Maryland. None of the 137 patients with Zollinger-Ellison syndrome had a previous vagotomy or partial gastric resection. The diagnosis of Zollinger-Ellison syndrome required two of the following criteria: a basal acid output of greater than 15.0 meq/hr, an elevated serum gastrin concentration, a positive secretin stimulation test defined as an increase of greater than 200 pg/ml above baseline serum gastrin concentration, or a histological diagnosis for gastrinoma (1, 13, 14, 17, 20). Basal acid output was not determined in one patient because of an esophageal stricture from gastroesophageal reflux disease; however, the diagnosis was histologically confirmed.

Statistics and Informed Consent

The protocol was approved by the Institutional Review Board and written informed consent was obtained from each patient. The correlation coefficient (r) was calculated with a least-squares analysis. Student’s r test and Fisher’s exact test were used for statistical evaluation of data where appropriate, and differences were considered statistically significant when P < 0.05 (21, 22). Unless