Clinical Significance of Chronic Hyperamylasemia

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A longitudinal study of patients with persistent hyperamylasemia was carried out to evaluate the clinical significance of this condition. Twenty-five outpatients were studied by means of serum amylase, isoamylase (wheat germ-inhibition method), and lipase determination; macroamylase detection; and abdominal ultrasonography over a one-year period. Cellulose acetate electrophoresis was carried out to validate the wheat germ-inhibition tests; the results of the two assays were closely correlated, except in three patients with macroamylasemia. At the time of the study, none of the patients had evident signs or symptoms of pancreatic disease. At initial evaluation, wheat germ test demonstrated an elevation of only salivary isoamylase in 16 patients, of both pancreatic and salivary isoenzyme in two, and only pancreatic isoamylase in six patients (three with macroamylasemia). Normal salivary and pancreatic isoenzymes were found in one patient. Serum lipase was elevated in only one patient who had a mixed hyperamylasemia with predominantly pancreatic isoamylase. At the 12-month follow-up, hyperamylasemia had disappeared in six cases and salivary isoamylase elevation in three; pancreatic isoamylase remained abnormally high in all eight patients in whom it was elevated at initial evaluation, and lipase was abnormally high in three patients with elevated pancreatic isoamylase. Of the five patients with true pancreatic hyperamylasemia, one had a juxtagastric duodenal diverticulum, one showed a slight ultrasound alteration of the pancreas, and one had a past history of acute pancreatitis. In our study, most cases of chronic hyperamylasemia were of nonpancreatic origin. In the patients with elevated pancreatic isoamylase, there was no clinical evidence of pancreatic damage, although a subclinical pancreatic involvement could not be excluded in some.

KEY WORDS: chronic hyperamylasemia; serum isoamylase; serum lipase; ultrasound.

It is well known that hyperamylasemia can be detected not only in exocrine pancreatic diseases, but also in other digestive and nondigestive diseases (1). An increase in serum amylase may be due to an elevation of either the pancreatic isoenzymes or those that are nonpancreatic in origin, the latter being referred to as salivary, since the salivary glands are their primary source. In some cases, hyperamylasemia is due to elevated serum concentrations of both the pancreatic and the salivary fractions, or it may be due to the presence of macroamylase (2).

Despite the fact that hyperamylasemia is often unrelated to the pancreas, patients are frequently diagnosed as having pancreatic disease on the basis of this finding, even when there is no clinical evidence of pancreatic damage. As a result, they may undergo unnecessary, invasive, and expensive diagnostic procedures in search of an improbable pancreatic disease.
At present, several techniques are available for determining serum concentrations of the isoamylases which help to formulate a diagnosis in patients with hyperamylasemia (3–7). Nonetheless, the reason for this finding sometimes remains unclear, particularly in those patients whose hyperamylasemia is persistent and not associated with clear signs of pancreatic disease. In order to better understand the clinical significance of hyperamylasemia, especially in these latter patients, we carried out a one-year prospective study of patients with chronic elevation of serum amylase of unclear origin, by performing serum isoamylase and lipase assays and ultrasonographic evaluation of the pancreatic gland.

MATERIALS AND METHODS

The study subjects were 25 white outpatients (11 men and 14 women, average age 52 years, range 24–75) with chronic hyperamylasemia, which had been present for at least four weeks (mean duration three years, maximum 20 years) prior to the start of this investigation. The presence of abdominal pain in 22 and alcohol abuse in three had raised the suspicion of a pancreatic disease; this was the reason for the original serum amylase assay and, due to the finding of hyperamylasemia, also the reason for the referral of these patients to us by general practitioners or gastroenterologists. Sera were obtained from all patients after an overnight fast and stored at −20 °C until the enzyme assays were done, within two weeks of collection.

Serum amylase activity was determined according to the Phadebas chromogenic method (Pharmacia, Uppsala, Sweden) and isoamylase activities by means of a rapid assay widely used in clinical practice (Phadebas Isoamylase Test, Pharmacia). This latter test utilizes a wheat protein that inhibits salivary isoamylase 100 times more effectively than pancreatic isoamylase (8). Serum isoamylase activity also was determined by cellulose acetate electrophoresis, according to a method described elsewhere (9), in order to validate the results of the inhibitory assay. In this study, the reported isoamylase results refer to those determined by wheat germ inhibition. Serum lipase was measured by means of a turbidimetric method using triolein, colipase, and sodium desoxycholate (Boehringer Mannheim, Mannheim, Germany) (10). Macrroamylasemia was detected by both electrophoresis, which shows a characteristic streaking of amylase fractions in this condition (4, 11), and PEG-6000 precipitation technique (12). All patients were interviewed and examined by the same researchers (M.V. and R.P.) throughout the entire observation period. In addition to enzyme assays, an abdominal ultrasound and a blood screening were performed at the beginning of the study, the latter including determinations of nitrogen, creatinine, glucose, transaminases, gammaglutamyltranspeptidase, alkaline phosphatase, bilirubin (total and indirect reacting fractions), total protein, albumin, globulin, cholesterol, triglycerides, calcium, and blood cell count. After 1, 6, and 12 months, patients were reexamined and serum pancreatic enzyme determinations repeated. The patients whose original abdominal sonograms were abnormal had this test repeated at the end of the study. In patients with pancreatic hyperamylasemia, evaluation included serum CEA and CA-19-9 determinations, and, in addition, CT scan was performed in one case, ERCP in two, upper gastrointestinal x-ray series in two, pancreateolauryl test in two, and fecal chymotrypsin in two.

The normal reference ranges of serum enzymes were established on a total of 246 healthy asymptomatic subjects (144 men and 102 women, average age 42 years, range 17–88) recruited from laboratory and medical staff, blood donors, and subjects undergoing a routine medical check-up. In these control subjects, serum amylase, isoamylase, and lipase values did not show a normal or log-normal distribution. For this reason, we used the 2.5th and 97.5th percentiles as the limits of the reference ranges, which were as follows: amylase, 109–392 IU/liter, number of healthy controls studied (N) = 193; pancreatic isoamylase by wheat germ assay, 27–256 IU/liter, N = 193; by electrophoresis, 45–211 IU/liter, N = 83; salivary isoamylase by wheat germ assay, 17–261 IU/liter, N = 193; by electrophoresis, 53–232 IU/liter, N= 83; lipase, 8–197 IU/liter, N = 53. These reference ranges are similar to those reported in other studies (13–15).

Only patients with serum amylase higher than 430 IU/liter were included in this study. This value is well above the 406 IU/liter which is the highest value of amylase observed in healthy controls.

Statistical analysis was carried out using the Spearman rank correlation test.

RESULTS

Final diagnoses of the patients studied were as follows: irritable bowel syndrome in 11, biliary disease in eight (cholelithiasis in five and postcholecystectomy syndrome in three), hyperlipidemia in seven, hepatic disease in five (cirrhosis in three, chronic hepatitis in one and steatosis in one), cardiovascular disease in five, alcohol abuse (daily intake >80 g) in three, partial gastrectomy in two, colon diverticulosis in two, urogenital tract disease in one, esophagitis in one, functional dyspepsia in one, juxtapapillary duodenal diverticulum in one, rectal polyp in one, ulcerative colitis in one, colostomy in one, and diabetes mellitus in one. During the observation period, abdominal pain was present in 18 of the 25 patients, but in none of the cases was it typical of pancreatic disease.

The wheat germ-inhibitory test results were found to be closely correlated with those of the electrophoretic determinations. Regarding the predominance of pancreatic or salivary isoamylase, agreement was observed between the two tests in 88 of the 100 assay pairs performed. The remaining