Salivary Amylase and Pancreatic Enzymes in Sjögren's Syndrome


Concentrations of immunoreactive trypsin (IRT) and pancreatic and salivary amylase activities were measured in 22 patients with primary Sjögren's syndrome (SS) and in 13 patients with secondary SS. Nineteen of the 22 patients with primary SS had above-normal IRT, and six had above-normal pancreatic amylase activity. Six of the 13 patients with secondary SS had above-normal IRT; none had above-normal salivary amylase activities. Serum IRT and pancreatic amylase were correlated significantly (r = 0.7; p <0.0001). Above-normal values for IRT and pancreatic amylase were more frequent in patients who had SS for longer than 10 years, but were not related to the presence of salivary gland autoantibodies or to salivary amylase activity. We conclude that the concentration and activity of pancreatic enzymes are frequently abnormal in SS; that the abnormality is greater and more frequent in patients with primary SS; and that it increases with the duration of the disease.

Additional Keyphrases: isoenzymes · trypsin · rheumatoid arthritis · systemic lupus erythematosus

Sjögren's syndrome (SS) is characterized by progressive destruction of the salivary and lacrimal glands by a chronic inflammatory process (1, 2). This leads to a decrease in salivary flow, dryness of the mouth and eyes, and sometimes other exocrine disturbances. SS is classically subdivided into two groups: primary SS (or sicca syndrome), where exocrine disturbances occur in isolation, and secondary SS, where a well-characterized disorder of connective tissue is also present. This clinical subdivision is supported by clinical, immunological, and immunogenetic differences between the two groups.

Two previous studies suggested that concomitant abnor-

References

CLIN. CHEM. 33/2, 305–307 (1987)
malities in exocrine pancreatic function may occur in SS (3, 4). One study included a small number of patients with primary SS, the majority of the rest having concomitant rheumatoid arthritis (RA) (3). The other did not relate the abnormalities of pancreatic function to the duration of the disease or to autoimmune abnormalities in the patients (4). Both studies relied on traditional pancreatic function tests, which are tedious and time consuming.

We have previously shown that the measurement of pancreatic enzymes trypsin, amylase, and lipase in serum provides a sensitive index of subclinical abnormalities in pancreatic function, including diabetes mellitus (6), cystic fibrosis (7), and iron overload (8). We therefore undertook a comprehensive study of changes in the pancreatic enzyme concentrations/activity in serum of subjects with primary or secondary SS, and the possible effect of (a) associated autoimmune abnormalities and (b) the duration of disease.

**Patients and Methods**

**Patients**

Thirty-five patients with SS were included in this study. Nine had RA, four had systemic lupus erythematosus (SLE), and 22 had primary SS according to standard criteria (9).

All patients had symptoms of xerophthalmia and xerostomia. The diagnosis of SS was based on documentation of keratoconjunctivitis sicca and evidence of salivary gland involvement (9); keratoconjunctivitis sicca was judged present by (a) decreased tear flow rate by Schirmer's test (less than 10 mm of wetting of the paper strip in 5 min) and (b) abnormal staining of the cornea and conjunctiva with rose bengal dye. Xerostomia was judged present by (a) lack of pool of saliva under the tongue and (b) decreased stimulated salivary flow rate. Exclusions recently proposed by Fox et al. (10), e.g., pre-existing lymphoma and sarcoidosis, were strictly adhered to.

The findings of a full clinical examination of each patient were recorded, including presence or absence of salivary gland swelling and evidence of any clearly definable connective-tissue disorder. Primary SS was diagnosed only in the absence of a recognizable connective-tissue disorders such as SLE, scleroderma, or mixed connective tissue disease. None of the patients included in this study had an impaired renal function: the concentration of urea in plasma was <6.5 mmol/L and creatinine was <120 μmol/L.

**Controls**

The control group comprised 100 normal subjects (60 men, 40 women), ages 18–60 years.

**Methods**

Blood samples were obtained from all these patients; the serum was separated and frozen at −20 °C. Rheumatoid factor and antinuclear factor were assayed in all sera. The concentrations of immunoreactive trypsin (EC 3.4.21.4; IRT) and the activities of pancreatic and salivary amylase (EC 3.2.1.1) isoenzymes in serum were also measured. IRT was measured with a specific radioimmunoassay kit (Hoechst, Hounslow, U.K.), as previously described (9). Pancreatic and salivary isoamylases were measured by an enzymatic method based on a kit (Phadebas; Pharmacia, Uppsala, Sweden), as previously described (11).

Statistical comparisons were by Student's t-tests, linear regression analysis, and χ² tests.

**Fig. 1. Immunoreactive trypsin (IRT) concentrations in 35 patients with Sjögren's syndrome (SS) and 100 controls**

The mean ± SD indicated for each group differ significantly (p <0.0001)

**Results**

Twenty-five of the 35 patients investigated had above-normal IRT concentrations (see Figure 1). Of the 22 with primary SS, 19 had an increased concentration of IRT. Five of nine patients with RA and SS had increased IRT, but only one of four with SLE did. The mean (±SD) IRT concentration in SS patients (0.55 ± 0.1 mg/L) was significantly greater than that in controls (0.27 ± 0.07 mg/L, p <0.001).

Pancreatic amylase was increased in seven patients, six of whom had primary SS, the seventh being one of the nine patients with RA. The mean pancreatic amylase (148 ± 68 U/L) in SS patients was not significantly different from that in controls (130 ± 45 U/L).

Salivary amylase activity was subnormal in six patients; all except one had primary SS and one had RA. Five of these patients with low salivary amylase had increased IRT; only two had above-normal pancreatic amylase activity. Four of the six patients with subnormal salivary amylase had had SS longer than 10 years.

There was a highly significant correlation between IRT concentration and pancreatic isoamylase activity (r = 0.70, p <0.0001), but no correlation between salivary isoamylase and IRT or between salivary and pancreatic isoamylase. The presence of salivary gland swelling and salivary gland antibodies, rheumatoid factor, or antinuclear antibody was not related to increases in IRT concentrations. The mean (±SD) IRT in patients who had had SS longer than 10 years was significantly greater (0.65 ± 0.15 mg/L) than in patients with SS for less than 10 years (0.49 ± 0.12 mg/L, p <0.01). Four of eight patients with SS longer than 10 years had extremely high IRT (0.7 mg/L) concentrations, but only five of 28 patients with SS for less than 10 years had markedly increased IRT.
Discussion

We found that a majority of patients with SS—both primary and secondary—had increased concentrations of IRT. Pancreatic isoamylase was also increased in seven patients. This study indicates variable pancreatic damage in SS, and confirms the abnormality we have previously demonstrated in patients with primary biliary cirrhosis and SS (5).

Lymphocytic infiltrations of the exocrine glands and acinar tissue damage are often observed in patients with SS. Exocrine pancreas may be similarly affected, which may account for the frequent subclinical pancreatic involvement in this disorder. A recent report (17) showed the presence of humoral autoimmunity to pancreatic duct cells in SS, indicating the involvement of autoimmune mechanisms in the pathogenesis of subclinical exocrine insufficiency.

None of the patients who had an increase in the concentration of IRT had clinical pancreatitis. Rather, the increase of IRT in these patients is a marker of subclinical pancreatic damage/abnormality, which we have previously observed in patients with cystic fibrosis (7) or thalassemia major with iron overload (8), in the elderly (13), and after steroid administration in large doses (14). The fact that the frequency of above-normal concentrations of IRT is greater than that of above-normal pancreatic isoamylase activity is probably due to the fact that the radioimmunoassay of IRT measures both trypsinogen and trypsin, whereas the pancreatic isoamylase assay measures the enzyme activity only. Damage to the acinar cells probably allows the proenzyme to leak into blood in larger quantities than the activated enzyme. Nevertheless, the highly significant correlation between IRT and pancreatic isoamylase in these patients is interesting, as is the observation that early damage of the pancreas may result in hypersecretion of pancreatic juice into the duodenal lumen (15).

The frequency of above-normal values for IRT and pancreatic amylase was greater in patients with primary SS than in those with secondary SS, probably because of the stage in the natural history of the "exocrine pathology" at the time of presentation. Patients with RA and primary biliary cirrhosis may be likely to present at earlier stages of "exocrine pathology."

We were surprised to see the low prevalence of subnormal salivary isoamylase activity in a disease characterized clinically by salivary hyposecretion. We had anticipated a greater frequency of abnormal salivary isoamylase. Apparently a low salivary isoamylase in serum occurs only late in the disorder: four of the six patients with depressed activities of salivary isoamylase had had SS longer than 10 years. Subnormal salivary isoamylase values were associated with increased IRT in five patients. Salivary amylase was increased only in one patient, who also had an increase in pancreatic isoamylase and markedly increased IRT. We also find it interesting that IRT and pancreatic and salivary amylase were not related to any of the clinical features or autoantibodies studied, but there was a correlation between the duration of the disease and pancreatic and salivary abnormalities.

In conclusion: SS is associated with frequent pancreatic abnormality that is independent of the extent of salivary gland abnormality but dependent upon the duration of the disease.

We thank Mrs. W. C. Dick and S. Blair for help and advice and Mrs. P. Dale for preparing the manuscript.

References