REEVALUATION OF PAROTID SALIVA TEST IN THE DIAGNOSIS OF PANCREATIC DISORDERS

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SUMMARY

The parotid saliva test was performed in 223 subjects, including 83 patients with pancreatic disorders, 124 with nonpancreatic disorders and 16 healthy persons. The following results were obtained: **1.** An abnormal saliva test was found in 77.1 % of the patients with the pancreatic disorders. **2.** Comparison was made of the parotid saliva test with the pancreozymin-secretin test in regard to diagnostic reliability in 51 subjects, including 28 with pancreatic disorders and 23 with nonpancreatic disorders. The data indicated that, in this series, an abnormal saliva test was 75.0 % accurate in diagnosing pancreatic disorders, whereas positive pancreozymine-secretin test was 71.4 %. **3.** The results of the parotid saliva tests in 9 patients with pancreatic diseases before and after surgery were analysed. The result revealed that the parotid gland function was presumed to return to normal or to be elevated in parallel with the improvement of the pancreatic function or lesions.

RESUMO

Reavaliação da prova da saliva da parótida no diagnóstico das doenças pancreáticas

A prova da saliva, obtida da parótida, foi efectuada em 233 casos, incluindo 83 doentes pancreáticos, 124 com patologia não pancreática e 16 normais. Os resultados obtidos são os seguintes: 1 - Prova anormal em 77,1 % dos doentes com patologia pancreática; 2 - Da correlação da prova da saliva com a prova de Secretina-Pancreozimina, no que se refere ao rigor diagnóstico em 51 casos, incluindo 28 com doença pancreática e 23 com patologia não pancreática. Verificou-se que a prova da saliva anormal tem 75,0 % de rigor diagnóstico nas doenças pancreáticas enquanto que a prova de Secretina-Pancreozimina foi positiva em 71,4 %. 3 - Avaliação da prova da saliva em 9 doentes com patologia pancreática, antes e pós cirurgia, revelou que a função da glândula parótida parece normalizar-se ou elevar-se paralelamente à melhoria da função ou das lesões pancreáticas.

INTRODUCTION

We have developed the parotid saliva test as a screening-test for the diagnosis of pancreatic disorders.[8, 12, 13] The results of our saliva test, however, have been partially confirmed[3, 17, 18] and partially debated.[2, 15, 16]

We have made the parotid saliva test on a larger number of subjects. These findings will be presented hereunder to reevalue the test in the diagnosis of pancreatic disorders. Furthermore, the effectiveness of the test in the diagnosis of pancreatic disorders was studied by comparing the findings with those of the pancreozymine-secretin test and we have analyzed the results of the tests in patients with pancreatic diseases before and after surgery.

MATERIALS AND METHODS

Subjects

As shown in Table 1, the saliva test was performed on 223 subjects, including 83 patients with pancreatic disorders, 124 with nonpancreatic disorders and 16 healthy persons. In 207 patients except for healthy persons, in addition to the application of the entire diagnostic armamentarium, histologic examinations of surgical or biopsy specimens of the pancreas obtained at laparotomy were undertaken in a final attempt to confirm the clinical impression. Table 1 shows the final diagnosis of individual patients studied. In 44 patients with pancreatitis, there were 9 patients with alcoholic pancreatitis, including 4 with pancreatolithiasis, 4 with chronic pancreatitis and one with acute pancreatitis, whereas the etiology of the disease in the remaining 22 patients except 13 patients of satellite pancreatitis with cholelithiasis remained unknown.

The parotid saliva test

Collection of saliva samples: The saliva test was performed in fasted subjects in the morning. With the patient in the lateral position, a saliva-sampling apparatus was attached closely on to the orifice of the parotid on one side and 1 % pilocarpine hydrochloride was injected intramuscularly in a dose of 0.13 mg/kg. After the parotid began secreting, samples of saliva were collected continuously into a graduated test tube for five consecutive 5-minute samples, 25-minutes in total. At the end of the saliva sampling, the patients were given an intramuscular dose of 0.13 mg atropine sulfate per 10 kg of body weight.

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TABLE 1 **Patients examined**

Classification of disorders		Number of cases
Pancreatic disorder group		(83)
Pancreatic cancer		18
Cancer of the papilla of vater		2
Pancreatitis		44
Acute pancreatitis	2	
Chronic pancreatitis	17	
Pancreatolithiasis	7	
Pancreatic cyst	5	
Satellite pancreatitis	13	
Miscellaneous carcinomatous infiltration into the pancreas		18
Lipomatosis of the pancreas		1
Nonpancreatic disorder group		(124)
Gastric cancer		40
Benign gastric diseases		15
Malignant bile duct diseases		7
Benign bile duct diseases		47
Other malignant tumors		7
Others		8
Healthy person		(16)
Total		223

Examination of parotid saliva: The salivary secretion, the concentration of bicarbonate and amylase contents in the consecutive 5-minute saliva samples were determined. The salivary secretion was expressed in units of ml/kg of body weight in 25 minutes. The assay for bicarbonate concentration and amylase level in the parotid saliva were accomplished by the method of Van Slyke[20] and by the procedure as described by Caraway,[1] respectively.

Pancreozymin-secretion test (P-S test)

The P-S test used in the present study is a modification of the standard pancreozymin-secretin test of Sun and Shay.[19] Briefly, the patients were given intravenously a 5--minute infusion of a solution containing pancreozymin (1 u/kg), followed by a 60 minutes infusion of a solution containing secretin (1.2 u/kg). Six fractions were obtained. Each of the last three duodenal drainage fractions obtained during secretin infusion was measured for the total volume, maximum bicarbonate concentration and amylase secretion. The normal values of this test are for volume > 1 ml/kg, for maximum bicarbonate > 85 mEq/l and for amylase secretion > 2,400 u/kg.

RESULTS

Diagnosis

Criteria of diagnosis in saliva test: In a previous paper,[13] we decided that the normal range of salivary output is 0.204 ~ 0.741 ml/kg that of maximum bicarbonate concentration 21 ~ 50 mEq/l and that of amylase content 607 ~ 3,423 u/kg (Table 2). The ranges are from the lowest to the highest values in the nonpancreatic disorder group and healthy person group. Values outside these ranges were defined as abnormal. In addition, the degree of abnormality was expressed as follows: *1.* when only one of these three parameters shows abnormality, +; *2.* when two of these parameters are abnormal, + + and *3.* when all the parameters are abnormal, + + +.

TABLE 2 **Normal range of saliva test**

Salivary output	0.204-0.741 mL/Kg
Maximum bicarbonate concentration	21-50 mEq./L
Amylase content	607-3423 U./Kg

Results of diagnosis: Using these criteria, the correct diagnosis of pancreatic disorder was made in 64 of the 83 patients with pancreatic disorder, an accurancy of 77.1 % (Table 3). Except for two cases in the pancreatic disorder group which showed an abnormally high value of salivary secretion, e. g. hypersecretion, all other cases displaying positive parotid saliva tests had low values for each parameter. In 9 patients with alcoholic pancreatitis, the correct diagnosis was made in 7 patients including one case showing hypersecretion.

TABLE 3 **Degree of abnormality in each disorder group**

Degree of abnormality	Classification of disorders		
	Healthy person (16 cases)	Nonpancreatic disorder group (124 cases)	Pancreatic disorder group (83 cases)
+	0	18	31
+ +	0	1	20
+ + +	0	2	13
Total	0 (0 %)	21 (16.9 %)	64 (77.1 %)

TABLE 4 **Patients examined**

Classification of disorders		Number of cases
Pancreatic disorder group		(28)
Pancreatic cancer		9
the head of the pancreas	3	
the body of the pancreas	2	
the tail of the pancreas	2	
the whole of the pancreas	1	
the processus uncinatus of the pancreas	1	
Cancer of the common bile duct with carcinomatous infiltration into the pancreas		2
Cancer of the papilla of Vater		2
Pancreatolithiasis		4
Chronic pancreatitis		5
Cholelithiasis with satellite pancreatitis		4
Pancreatic cyst		1
Lipomatosis of the pancreas		1
Nonpancreatic disorder group		(23)
Gastric cancer		4
Benign gastric diseases		3
Cholecystolithiasis		2
Choledocholithiasis		2
Cholecystitis		3
Postoperative cholecystectomy syndrome		2
Cancer of the bile duct		2
Idiopathic dilatation of the common bile duct		1
Others		4
Total		51

TABLE 5 **Comparison of the diagnostic accuracy of the parotid saliva test with the P-S test**

	Parotid saliva test			P-S test		
	Patients examined	Patients diagnosed accurately	Accuracy of diagnosis (%)	Patients examined	Patients diagnosed accurately	Accuracy of diagnosis (%)
Pancreatic disorder group	28	21	75.0	28	20	71.4
Nonpancreatic disorder group	23	19	82.6	23	13	56.4
Total	51	40	78.4	51	33	64.7

Parotid saliva test compared with P-S test

As shown in Table 4, 51 patients, including 28 with pancreatic disorders and 23 with nonpancreatic disorders were studied. As shown in Table 5, positive results of the P-S test were 71.4% accurate and those of the parotid saliva test were 75.0% accurate in 28 patients with pacreatic disorders. In 23 patients with nonpancreatic disorders, however, the parotid saliva test was 82.6% accurate, while the P-S test gave far too high a proportion of false positive results. It should be noted that in 6 patients with biliary tract diseases, 3 patients with gastric diseases and one patient with duodenal cancer grave false positive results in the P-S test. As a whole, the parotid saliva test gave an accuracy of 78.4% and the P-S test 64.7%.

Changes of the parotid saliva test before and after surgery

Nine patients, including 2 patients with pancreatolithiasis, 1 with traumatic pancreatic cyst, 1 with pancreatic cyst, 1 with cancer of the duodenal papilla, 1 with cancer of the intrapancreatic bile duct, 1 with cancer of the head of the pancreas, 1 with cancer of the tail of the pancreas and 1 with chronic pancreatitis were examined. In Table 6 individual changes of the parotid saliva test before and after surgery were summarized. In these patients the parotid saliva test was performed before and after surgery and the results were comparatively analysed.

In the present series, the operations for 8 patients were of the type which allowed drainage of the pancreatic duct or the cyst to the intestinal lumen, and one other patient had distal pancreatectomy. It is seen that four patients showed reduction of both parameters, four patients that of one parameter and one patient normal before surgery. Thus, in 8 patients who showed hypofunction before surgery, 5 patients showed normal parotid gland function and one patient abnormally elevated function after surgery. There was concomitant improvement of the symptoms after surgery in these patients.

TABLE 6 **Saliva tests before and after surgery**

Case No.	Name	Age & Sex	Diagnosis	Surgical technique	Results of saliva tests								
					Preop.				Postop				
					Vol. (ml/kg)	HCO_3^- (mEq/L)	Amy. U/kg	Score	Vol. (ml/kg)	HCO_3^- mEq/L	Amy. (U/kg)	Score	Follow-up period
(1)	SS	49 m	Pancreatolithiasis	Pancreaticojejunostomy (side to side)	0.238	16↓	213↓	(—)↓	0.756↑	62↑	1294	(—)↑	21 days
(2)	KN	35 m	Pancreatolithiasis	Pancreaticojejunostomy (side to side)	0.401	17↓	1537	(+)↓	0.605	30	1830	(—)	30 days
(3)	KM	56 f	Cancer of the head of the pancreas	Caudale pancreaticojejunostomy	0.444	18↓	1788	(+)↓	0.292	38	1014	(—)	34 days
(4)	TK	60 m	Cancer of the common bile duct with carcinomatous infiltration into the pancreas	Pancreato duodenectomy	0.406	19↓	1277	(+)↓	0.404	9↓	848	(+)↓	3 months
(5)	TK	54 m	Cancer of papilla Vater	Pancreatoduodenectomy	0.162↓	27	470↓	(++)↓	0.465	46	1443	(—)	38 days
(6)	KH	57 m	Cancer of the tail of the pancreas	Caudale pancreatectomy	0.322	19↓	1505	(+)↓	0.121↓	15↓	360↓	(+++)↓	39 days
(7)	YB	31 f	Pancreatic cyst	Cystojejunostomy (Roux-Y)	0.182↓	19↓	1134	(++)↓	0.484	22	1534	(—)	8 months
(8)	YS	6 m	Traumatic cyst	Cystojejunostomy (Roux-Y)	0.471	20↓	230↓	(++)↓	0.336	28	815	(—)	1 1/12 yrs
(9)	KO	62 m	Chronic pancreatitis with stenosis of the common bile duct	Pancreaticoduodenectomy	0.340	31	1024	(—)	0.393	34	1845	(—)	59 days

COMMENT

Since 1971 we have reported a series of experimental and clinical studies concerning the interrelationship between the pancreas and parotid gland. We have demonstrated experimentally that after a pancreatic lesion is induced, the parotid glands shows atrophic degeneration and hypofunction with dimentions in volume, amylase content and maximal bicarbonate concentration of the parotid saliva.[4, 5, 7, 9, 10] Furthermore, with the recovery of the pancreatic lesion, the parotid glands displayed morphological as well as functional recovery.[6] Conversely, it was demonstrated that with impairment of the parotid glands, the pancreas also was slightly influenced.[14] In an experimental study in parobiotic rats, we have recently demonstrated that a humoral transmission mechanism is participating in the development of an interactive response between the pancreas and parotid glands.[11]

On the basis of these findings, we have developed a parotid saliva test as a screening one for the diagnosis of pancreatic disorders and revealed it was sufficiently reliable and informative to merit extensive clinical trial.[8, 12, 13]

Grimmel et al[3] reported that amylase concentration in the parotid saliva was significantly reduced in patients with chronic pancreatitis compared with normal subjects. Nacchiero et al[17] reported that alterations in parotid secretion might be of value in the diagnosis of chronic pancreatitis, in the evaluation of its severity and might yield information on the duration of the disease as the result of the experiment of dogs with irradiation-induced chronic pancreatitis. Noronha et al[18] in the parotid saliva test with the stimulation of secretin, observed the following results: *1.* pancreatic pathology appears to be associated with decreased salivary flow after secretin. *2.* Only in patients with chronic alcoholic pancreatitis significant changes in the salivary bicarbonate response to secretin were noted. *3.* Basal salivary flow is depressed in non-alcoholic as well as alcoholic pancreatitis. *4.* The salivary response to secretin in patients with alcoholic pancreatic insufficiency shows depressed flow, bicarbonate and protein. And she noticed the pattern of secretion of the parotid appears altered in patients with pancreatic disease with some parallelism between the salivary and pancreatic responses to secretin.

Lankisch et al[15] and Dobrilla et al,[2] on the other hand, reported that the parotid saliva test could not be recommended as a screening test for chronic pancreatitis, according to the results in the parotid saliva test in the diagonis of chornic pancreatitis using application os 2 ml of 10% citric acid to the tongue and intramuscular injection of 1% pilocarpine hydrochloride resplectively.

Therefore, we undertook to revalue the test in the diagnosis of pancreatic disorders on 223 subjects. An abnormal saliva test was found in 77.1% of the patients with pancreatic disorders.

22 cases in 31 cases examined by Lankisch et al[15] and 26 cases by Dobrilla et al[2] who stood against the parotid saliva test, were alcoholic pancreatitis. Only 9 patients in 83 patients with pancreatic disorders examined by us were alcoholic pancreatitis. In 9 patients with alcoholic pancreatitis, the correct diagnosis was made in 7 patients including one case showing hypersecretion in parotid saliva test. As we have experienced only a small number of the patients with alcoholic pancreatitis in parotid saliva test, more clinical and experimental studies will be required in order to judge the practical value of the test in the patient with alcoholic pancreatitis. It can be speculated that an alcoholic pancreatitis takes a peculiar place among other pancreatic disorders, that is, an alcoholic agent may injure the function of the parotid gland as well as the pancreas.

The results of the present study clearly show that both the parotid saliva test and the P-S test give fairly comparable results in the diagnosis, of plancreatic disorders. In this small series, however, the P-S test gave false positive results for 6 patients with biliary tract diseases, 3 with gastric disease and one with duodenal cancer in nonpancreatic disorder group. In the cases with biliary tract disease the P-S test is liable to give false results even if there is no pancreatic disease. In this respect, a lot of research has been done to improve the accuracy of the P-S test and the P-S test has been designed to eliminate so much as possible the bile juice from duodenal drainage. It is also known that the presence of duodenal desease affects the diagnostic values of the P-S test. The results of the present study indicate that the parotid saliva test is as accurate as the P-S test in nonpancreatic diseases. Thus the parotid saliva test is a useful test in predicting both the presence or absence of pancreatic diseases, even in patients with abnormal biliary function or of duodenal diseases.

Comparative analysis of parotid gland functions was made in 9 patients with pancreatic diseases pre and postoperatively. It was seen that 8 patients showed hypofunction of the parotid gland and one patient normal before surgery. In 8 patients showed hypofunction before surgery, 5 patients showed normal and one patient abnormally elevated parotid gland function after surgery. As there was concomitant improvement of the symptoms after surgery, it was presumed that in parallel with the improvement of pancreatic function the parotid gland functions would return to normal or became rather hyperfunctional. It appears to be of importance that, as in animal experiements.[6] The parotid gland function changes also in man in parallel with the changes of the pancreatic lesion or function.

Further studies are needed to evaluate advantages and disadvantages of the parotid saliva test in a variety of clinical settings. On the basis of our experience so far it is concluded that the parotid saliva test, being simple and fast, is sufficiently reliable and informative to merit extensive clinical trial.

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