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Secretin Half-Life in Cirrhotics with High Secretory Volumes to a Secretin Test (40680)

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Patients with hepatic cirrhosis frequently exhibit pancreatic and biliary hypersecretion in response to exogenous secretin (1–3), but the mechanism is unknown. One of the proposed explanations for this phenomenon is prolonged secretin stimulation resulting from impaired catabolism by an abnormal liver (4). A role for the liver in the catabolism of secretin has been suggested by the work of Chey *et al.*, who demonstrated inactivation of this hormone by rat liver *in vitro* (5).

It was the purpose of this study to determine whether or not patients with biopsy-proven cirrhosis and secretin-induced pancreatic and biliary hypersecretion exhibit abnormal secretin catabolism as reflected by an alteration in its disappearance rate ($t_{\frac{1}{2}}$).

Materials and methods. Four chronic alcoholic males (age 42–54) who had biopsy-documented hepatic cirrhosis and were clinically free of ascites were selected. All had been recently evaluated with routine liver function tests, BSP retention studies, creatinine clearance, serum amylase, and albumin (Table I). These studies were compatible with a mild to moderate degree of hepatic functional impairment and normal renal function. All patients underwent a standard secretin test of pancreatic function using intravenous injection of one unit of GIH secretin per kilogram body weight. Each patient had a pancreatic secretory volume greater than 4.9 ml/kg-hr (mean 7.8 ml/kg-hr) with normal values for this laboratory being less than 4.6 ml/kg-hr. Although peak bicarbonate concentration was less than 80 meq per liter in two patients, peak bicarbonate output was normal in all, being greater than 20 meq/hr (Table I).

Five volunteers who were clinically free of hepatic, renal, and pancreatic disease and whose weight approximated that of the cirrhotic subjects were selected as controls.

GIH secretin at a dose of one unit per kilogram was administered intravenously for 1 hr by constant infusion. Blood samples were obtained before the infusion, at 15-min intervals during the infusion, and at 2-min intervals for 20 min after completion of the infusion. Serum secretin concentrations were determined by a previously described sensitive and specific radioimmunoassay (6). Regression equations were determined from plateau infusion and postinfusion secretin levels after subtracting the basal (or preinfusion) values. The natural logarithm of the adjusted postinfusion values was used in linear regression analysis against time to determine the slope (K) of the regression line. The half-lives were calculated using the formula, $t_{1/2} = \ln \frac{1}{2}/-K$ (7).

The relationship of body weight to disappearance half-life was examined in each cirrhotic subject by linear regression analysis. In addition, the relationships of renal function (creatinine clearance), liver function (BSP retention), and pancreatic function (secretory volume, bicarbonate output, and bicarbonate concentration) to disappearance half-life in the cirrhotic subjects were also examined.

Results. Preinfusion and plateau mean secretin levels were similar in each group, being 53.2 and 678 pg/ml, respectively, for the cirrhotic group and 46 and 717 pg/ml, respectively, for the controls. In both groups plateau secretin levels were obtained within 30 min after starting the infusion and were maintained until the infusion was discontinued.

The cirrhotic group had a mean secretin half-life of 2.74 ± 0.31 (SEM) min (Fig. 1). The healthy volunteers showed a mean half-life of 2.72 ± 0.41 (SEM) min which was not significantly different from that of the cirrhotic patients ($P > 0.1$) (Table II).

Individual values for disappearance half-life were compared with parameters of hepatic, renal, and pancreatic function and weight by linear regression analysis. There was no correlation between secretin half-life and either BSP retention ($r = -0.09771$), creatinine clearance ($r = -0.45664$), peak bicarbonate concentration ($r = 0.76428$),

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TABLE I. LABORATORY DATA OF THE FOUR PATIENTS WITH CIRRHOSIS

Test	Mean	Range
Secretin test		
Volume	7.82 ml/kg-hr	(4.92–10.2)
Peak HCO_3–	77 meq/liter	(54–107)
HCO_3– output	43.5/meq-hr	(20.6–55.5)
Serum amylase	85 units	(35–134)
Liver function		
BSP (%)	14%	(4–34)
Serum albumin	3.7 g%	(3.1–4.3)
Prothrombin time	11.3 sec/10.9 control	(10.6–12.6)
Renal function		
Creatinine clearance	93.7 ml/min	(77–116)

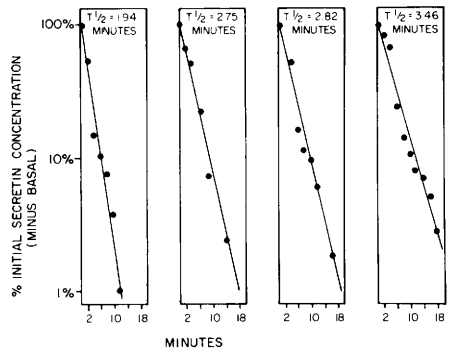

FIG. 1. Linear regression curves plotted from the logarithm of the postinfusion secretin concentrations minus basal expressed as a percentage of the initial concentration at time 0 (x axis) with time in minutes shown on the y axis.

peak bicarbonate output (r = −0.55869) or volume (r = 0.31994). However, when secretin half-life was compared to weight a negative correlation was found (r = −0.91354).

Discussion. The mean secretin half-life values obtained in this study of cirrhotics and healthy volunteers are similar to values reported for canine subjects (8, 9) and to values which we have previously reported in man (6).

We found a negative correlation between secretin disappearance half-life and body weight in the cirrhotic group. This result differs with the findings of Khalil *et al.* (10) which showed a positive relationship in healthy animals. Although the method which they reported for calculating half-lives differs from the usual method used in this report, it does not explain the differing results (personal communication). Other explanations include (i) dissimilar animal species, (ii) dissimilar hepatic and pancreatic function in the two reports, and (iii) small study sample sizes.

The fact that the mean secretin-half lives of the patients with cirrhosis were not significantly different from those of our healthy controls suggests that mechanisms other than altered secretin catabolism are responsible for the hypersecretion seen in response to a secretin test in cirrhotic patients. These results are consistent with recent experimental evidence that the liver may not be a site of significant degradation of either endogenous or exogenous secretin (9). Other potential explanations for pancreatiocobiliary hypersecretion in cirrhosis include:

(i) pancreatic and/or biliary ductal hyperplasia resulting in a larger volume response to a standard secretin stimulus (11),

(ii) an altered pancreatic or biliary secretory threshold to exogenous secretin,

(iii) secretin-induced release of a pancreatic secretory agonist with liver-dependent catabolism, or

(iv) dissociation of biologic and immunoreactivity.

Identification of the mechanisms responsible for the pancreatic and biliary hypersecretion seen in response to exogenous secretin in cirrhotics will require further investigation.

TABLE II. SECRETIN HALF-LIVES IN FOUR PATIENTS AND FIVE HEALTHY CONTROLS AND r VALUES OBTAINED FROM THE LINEAR REGRESSION ANALYSIS

	$t_{1/2}$ (min)	r
Patient		
1	2.75	0.94246
2	3.46	0.98023
3	1.94	0.98140
4	2.82	0.93162
Mean	2.74 ± 0.31 (SEM) min	
Controls		
1	2.77	0.92300
2	2.13	0.96693
3	2.05	0.92911
4	2.37	0.93256
5	4.27	0.99464
Mean	2.72 ± 0.41 (SEM) min	

[a] Using Student's t test for unpaired samples, the mean half-life for the patients does not differ from control (t = 0.41915; $0.7 > P > 0.6$).

Summary. The hypothesis of prolonged secretin half-life was examined in four cirrhotic patients who had pancreatic and biliary hypersecretory responses to exogenous secretin. The mean serum half-life of secretin from these patients was 2.74 ± 0.31 (SEM) min and did not differ significantly from a group of five healthy volunteers whose secretin half-life was 2.72 ± 0.41 (SEM) min ($P > 0.1$). In addition, the secretin half-lives correlated inversely with body weight in the cirrhotic patients. These data are consistent with the hypothesis that mechanisms other than altered secretin disappearance half-life are responsible for the hypersecretion seen in response to a secretin test in cirrhotic patients.

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