

The Intravenous Galactose Test as Indicator of the Extent of Fibrosis in Patients with Cirrhosis of the Liver

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The values of the intravenous galactose test in control subjects and in patients with cirrhosis of the liver were compared with some laboratory findings and the extent of fibrosis in liver biopsies. In 10 control subjects the average T/2 value of the galactose test was 13 minutes (range 9' to 15' 30"). In 10 patients with light fibrosis, the values were not significantly different from controls. On the other hand, in 10 patients with severe fibrosis, the fibrotic tissue occupying more than 30 per cent of the liver lobules, a highly significantly prolonged T/2 of the galactose test was found (23 minutes and 23 seconds).

Key-words: Cirrhosis; galactose; liver; liver function tests

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The significance of the intravenous galactose test in the evaluation of liver cell metabolism has been discussed by several authors (1-12). This test shows a decreased elimination of galactose in patients with cirrhosis (1, 2, 9, 12).

The sensitivity of the test in relation to the extent of fibrosis, however, seems to be less known. The purpose of the present paper was to answer this problem by comparing the result of the intravenous galactose test with some other liver function tests and the extent of fibrosis in liver biopsies.

MATERIAL AND METHODS

Liver biopsy and an intravenous galactose test were performed in 25 adults, 6 women and 19 men, average age 55 years (range: 15-70 years). The intravenous galactose test was performed after an overnight fast, and 0.35 g of galactose

per kg body weight was administered during 3-4 minutes, the patient lying quietly in bed. The serum galactose concentrations were determined enzymatically by means of the Kabi reagent (generously provided by Kabi A/S, Stockholm, Sweden), as indicated by de Verdier & Hjelm (3). The upper normal limit of T/2 (time in minutes after which the blood concentration of galactose has dropped to the half) was taken to be 17 minutes (9).

The diagnosis of liver disease was based on clinical and laboratory data including blood counts, serum bilirubin, serum alkaline phosphatase, serum glutamic oxalic, and glutamic pyruvic transaminase activities, total serum protein determination with electrophoresis, and X-ray examination of the stomach and esophagus. A biligraphy was performed when possible. In 19 patients the bromsulphalein 30 minutes retention test was carried out. The prothrom-

Table I. Clinical diagnoses

Groups	No diseases	Chron. alch.	Cirrhosis of the liver	Other diseases	Age, year	No. of patients
Control Students	5				21 (20-22)	5
Patients (normal biopsy)	1	1		3	52 (20-80)	5
Fibrosis						
Light			8	2	52 (15-74)	10
Severe			10		58 (40-88)	10

bin-proconventin time (PP) was determined in all cases (Tables I-IV).

Liver biopsies were obtained by the Menghinis needle in the fasting subjects in the morning. The biopsies were fixed in 4 per cent formalin and stained with hematoxylin and eosin (H+E) for light microscopy.

The extent of fibrosis, as visualized in the biopsies, was evaluated twice by both of us without knowing the names of the patients or the diagnosis. Accordingly the biopsies were classified as: 'normal', no parenchymal changes, 'light fibrosis', the amount of connective tissue occupying less than one-third of the liver lobules, and 'severe fibrosis', the amount of connective tissue occupying more than one third of the liver lobules.

The control group consisted of the patients with the normal biopsies. In addition a control group of 5 healthy male students was used. In these controls an intravenous galactose test was performed as in the patients, but biopsy of the liver was not performed. The total bilirubin was 0.5 mg per cent, and they had never had symptoms indicating liver disease. The Student's t-test was used in testing the significance of differences between means. The coefficient of correlation (r) was determined according to Snedecor (13).

RESULTS

Controls (Tables I-IV). In the 5 healthy male students the average value of T/2 was 12 minutes and 30 seconds, and in the group of 5 patients with dyspepsia the average value of T/2 was 13 minutes and 48 seconds, or not significantly different from that in control students. In the patients the liver biopsy was normal. One patient had elevated bilirubin, but none had a lowered albumin value or increased bromsulphalein retention. The value of PP was higher than 70 per cent in all cases.

Light fibrosis (Tables I-IV). In the 10 patients, 3 women and 7 men, the average value of T/2 was 13 minutes and 43 seconds. In this group three patients had bilirubin values above one mg per cent, whereas one had an albumin value below 2.5 g per cent. Two patients had PP values below 70 per cent, and four out of 7 had a bromsulphalein retention value higher than 9 per cent. In one out of the ten patients the

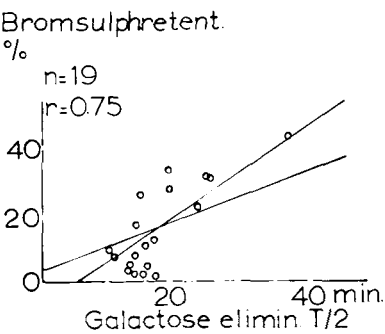


Fig. 1. The correlation between the individual values (open circles) of bromsulphalein retention in per cent after 30 minutes, and the T/2 elimination of galactose, in minutes. The solid lines indicate the regression of b on the x and y axis.

Table II. Laboratory findings

Groups	Hb in g%	ESR in mm/h	Total bilirubin, mg%	Alkal. phosphat., I.U.
Controls:				
Patients (normal biopsy)	12.8 (9.1-16.9)	23 (3-58)	0.8 (0.5-1.4)	32 (13-74)
Fibrosis:				
Light	12.3 (10.8-14.9)	38 (20-102)	0.7 (0.3-1.5)	74 (25-300)
Severe	13.0 (10.2-14.0)	48 (9-97)	3.7 (1.1-11.0)	62 (10-240)

galactose test showed a boarderline value (17.5 min.).

Severe fibrosis (Tables I-IV). In the 10 patients, 3 women and 7 men, the average value of T/2 was 23 minutes and 23 seconds. This value was highly significantly different from that found in patients with light fibrosis. In this group four patients had serum albumin values lower than 2.5 g per cent. The serum bilirubin values were higher than normal in all cases and in nine out of ten patients the PP value was lower than 70 per cent. In all of 6 cases the bromsulphalein retention was increased and none had a normal galactose T/2 value.

Correlation between liver function tests (Fig.

1). A significant correlation was found between the T/2 values of the i.v. galactose test and the bromsulphalein retention. No correlation was found between the values of the serum total bilirubin and the galactose test, or between the values of the alkaline phosphatase and the T/2 values of the galactose test.

COMMENTS

Other authors have shown a prolonged T/2 in patients with severe liver cirrhosis (1, 6, 9, 12). Our observations indicate that the intravenous galactose test does not reveal cirrhosis with light fibrosis, whereas in severe cirrhosis with fibrosis T/2 is significantly prolonged.

The bromsulphalein retention test showed

Table III. Liver function tests

Groups	Total proteins, g%	Albumin, % of proteins	PP, %	Bromsulphalein retention %
Control Students	7.2 (6.5-7.7)	51 (45-56)	84 (72-100)	
Patients (normal biopsy)	6.8 (6.2-8.6)	42 (36-50)	80 (78-120)	4.2 (1-7)
Fibrosis				
Light	7.1 (5.9-8.9)	47 (31-66)	83 (54-100)	12.4 (1-26)
Severe	7.2 (5.8-8.6)	39 (28-50)	42 + (26-74)	32.0 ++ (22-44)

+ Average PP value significantly lower than those in the other groups ($t=5.6$, $p<0.01$)

++ Average value of bromsulphalein retention significantly higher than those of the other groups ($t=4.4$, $p<0.001$).

Number of cases examined = 19.

Table IV. The galactose test, elimination time in minutes (') and seconds (") in controls and patients with liver cirrhosis (fibrosis).

T/2 = half elimination time

Groups of cases	No. of subjects	Values of T/2, minutes	
		Range	Average values
Control			
Students	5	9'-13'45"	12' 30"
Patients	5	12'-15'30"	13' 48"
Fibrosis			
Light	10	10'-16' 5"	13' 43"
Severe	10	19'-30'	23' 23" +

+ The value was highly significantly different from that of the group with light fibrosis (t = 5.6, p < 0.001).

abnormal values in four out of seven patients with cirrhosis demonstrating a light degree of fibrosis in the liver biopsies. This result may indicate that the galactose test may be less sensitive than the bromsulphalein retention test in this series of patients. A significant correlation was, however, obtained between the values of the two tests (Fig. 1). The divergencies between the results can not be explained in this small series of cases. The drop in the PP-values of the blood seemed to occur parallel to the increase in the galactose elimination time.

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