Influence of the gallbladder on serum bile acids

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SUMMARY Serum bile acids (SBA) were studied after a standard fatty meal in patients with gallbladder disease. Early postprandial bile acid values were found to be greater in patients with non-functioning gallbladders. Higher postprandial SBA values were found after cholecystectomy. Serum bile acid measurements were of no value in the assessment of gallbladder function.

Serum bile acid (SBA) concentrations are known to be increased in patients with liver disease,¹ and the measurement of SBA has been advocated in the evaluation of liver disease.² Because bile acids undergo an enterohepatic circulation³ disease of the gallbladder intestine and portal circulation might also be expected to influence SBA. The purpose of this study was to evaluate the influence of the gallbladder on SBA in order to assess any role SBA values may have in monitoring gallbladder function.

Patients and methods

Patients who had been investigated for upper abdominal pain were studied. Six were found to

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have "non-functioning" gallbladders after an oral cholecystogram and intravenous cholangiogram. Seven patients were similarly identified as having functioning or poorly functioning gallbladders which contained gallstones. Seven healthy subjects acted as controls.

After fasting serum samples had been obtained, each subject was given a fatty meal consisting of 40 ml of Prosparol (an emulsion containing 50% arachis oil) in 160 ml of water. Further samples were taken at 15 minute intervals for 2 h. A second sequence was obtained in 9 of these subjects 6 months after cholecystectomy.

Radioimmunoassay methods⁴ were used to measure conjugates of cholic acid, and chenodeoxycholic acid. Differences between groups were compared for significance with Student's *t* test.

Table 1 Sequential SBA concentrations after fatty meal in patients with gallbladder disease (mean $\pm$ SD (μ mol/l))

	Time (min)								
	0	15	30	45	60	75	90	105	120
<i>Cholyl conjugates</i>									
Controls	0.46 $\pm$ 0.17	0.49 $\pm$ 0.13	1.01 $\pm$ 0.38	1.90 $\pm$ 1.10	2.44 $\pm$ 1.37	2.74 $\pm$ 1.56	2.78 $\pm$ 0.93	3.00 $\pm$ 2.15	3.39 $\pm$ 2.46
Non-functioning gallbladder	0.72 $\pm$ 0.46	0.97*** $\pm$ 0.33	1.95** $\pm$ 0.84	2.57 $\pm$ 1.17	3.10 $\pm$ 2.20	2.58 $\pm$ 1.96	2.28 $\pm$ 1.47	2.82 $\pm$ 2.14	2.13 $\pm$ 1.89
Gallstones	0.51 $\pm$ 0.17	0.56 $\pm$ 0.12	1.13 $\pm$ 0.57	1.40 $\pm$ 0.90	2.14 $\pm$ 0.77	2.60 $\pm$ 1.36	3.23 $\pm$ 1.47	3.33 $\pm$ 2.37	3.47 $\pm$ 2.60
<i>Chenodeoxycholyl conjugates</i>									
Controls	0.86 $\pm$ 0.50	0.84 $\pm$ 0.24	1.64 $\pm$ 0.50	2.57 $\pm$ 1.58	4.68 $\pm$ 2.37	5.00 $\pm$ 3.95	5.51 $\pm$ 2.55	4.59 $\pm$ 2.82	5.22 $\pm$ 3.63
Non-functioning gallbladder	1.43 $\pm$ 1.30	1.60* $\pm$ 0.80	3.25* $\pm$ 2.00	4.60 $\pm$ 3.60	4.88 $\pm$ 3.38	3.82 $\pm$ 2.67	3.45 $\pm$ 2.20	4.25 $\pm$ 3.57	3.70 $\pm$ 2.70
Gallstones	0.97 $\pm$ 0.52	1.10 $\pm$ 0.55	1.80 $\pm$ 0.90	2.23 $\pm$ 1.45	3.70 $\pm$ 1.18	3.82 $\pm$ 1.80	5.30 $\pm$ 2.48	4.36 $\pm$ 2.39	4.78 $\pm$ 2.54

* $p < 0.05$.

** $p < 0.02$.

*** $p < 0.005$.

Table 2 Sequential SBA concentration after fatty meal in patients before and after cholecystectomy (mean $\pm$ SD (μ mol/l))

	Time (min)								
	0	15	30	45	60	75	90	105	120
<i>Cholyl conjugates</i>									
Preop	0.55	0.76	1.49	1.93	2.71	2.30	2.24	1.52	1.43
	± 0.32	± 0.28	± 0.86	± 1.20	± 1.90	± 1.80	± 1.33	± 0.96	± 0.59
Postop	0.90	1.20	2.06	2.50	2.90	3.40	3.10	3.35*	2.93*
	± 0.60	± 0.59	± 0.62	± 0.53	± 0.90	± 1.20	± 1.57	± 1.72	± 1.68
<i>Chenodeoxycholyl conjugates</i>									
Preop	1.00	1.30	2.40	3.08	4.30	3.00	3.89	2.58	2.50
	± 0.75	± 0.69	± 1.60	± 1.88	± 2.75	± 2.19	± 2.99	± 1.60	± 0.98
Postop	1.80	2.20	3.68	4.70	5.00	6.00	5.10	6.00*	4.60*
	± 1.20	± 1.08	± 0.80	± 0.96	± 1.60	± 2.70	± 2.96	± 3.20	± 1.80

* $p < 0.05$.

Results

POSTPRANDIAL PROFILES IN PATIENTS WITH GALLBLADDER DISEASE

Serum bile acid values are summarised in Table 1. There was little difference in the concentrations of both primary bile acid conjugates between the control groups, and patients with gallstones and poorly functioning gallbladders. Patients with non-functioning gallbladders had higher values during the first hour, and lower values thereafter. Surprisingly whereas there was no significant difference between the groups at zero time, SBA values were significantly higher at 15 and 30 min after the meal in patients with non-functioning gallbladders compared to the other two groups. The mean times at which peak values for cholic and chenodeoxycholic acids were noted were 83 and 90 min in the control group, 70 and 75 min in patients with non-functioning gallbladders, and 96 and 100 min in patients with gallstones. A large overlap was noted between groups.

POSTPRANDIAL PROFILES BEFORE AND AFTER CHOLECYSTECTOMY

Serum bile acid values are given in Table 2. For both conjugates mean values were greater after cholecystectomy and the difference between pre- and post-operative specimens became greater as the study progressed and became significant ($p < 0.05$) at 105 min and 120 min.

Discussion

Serum bile acids are influenced by a number of variables including pool size, gallbladder contraction, intestinal transit, intestinal absorption, hepatic blood flow, and first pass clearance. The influence of many of these factors will become greater immediately after a meal. Thus it is not surprising that whereas fasting SBA bile acid values fall within a

narrow range, the range of values becomes progressively large after meals. The scatter was even greater after 2 h in the few subjects in whom samples were collected for 4 h. This confirms our previous findings⁵ and emphasises that postprandial bile acid values should be interpreted with caution. The wide scatter between normal individuals might be expected to mask differences due to gallbladder disease, and clearly SBA values are of no use in the assessment of gallbladder function.

The higher early postprandial values in subjects with non-functioning gallbladders might reflect the larger component of the pool within the enterohepatic circulation under those circumstances and a greater contribution of a gastric phase of biliary tract emptying. No difference was observed between the control group and those with functioning gallbladders and gallstones, although greater postprandial gallbladder emptying has been described in the latter situation.⁶

The concept of a non-functioning gallbladder as defined in this study is unlikely to be absolute, and it is probable that part of the bile acid pool is retained in the gallbladder in the preoperative group. The larger circulating bile acid pool may account for the higher late postprandial values found in the post-operative group.

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