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Biliary Pain in Postcholecystectomy Patients without Biliary Obstruction

A Prospective Radionuclide Study

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Biliary pain without obvious biliary obstruction is common in postcholecystectomy patients. We studied 20 symptomatic patients with episodes of biliary-type pain after cholecystectomy (all having undergone endoscopic retrograde cholangiography), and in 18 asymptomatic postcholecystectomy controls. We performed quantitative hepatobiliary radionuclide analysis with dimethyl-imidodiacetic acid. From a series of 90 dynamic images at 1-min intervals using a gamma camera coupled to a computer, time–activity curves were produced in regions of interest in the liver, intrahepatic biliary tree, common duct, and heart, from which quantitative biliary excretion indexes were obtained. The results demonstrate a biliary kinetic dysfunction in patients with postcholecystectomy pain without morphological abnormalities.

KEY WORDS: postcholecystectomy pain; biliary kinetics; hepatobiliary scintigraphy; HIDA.

In postcholecystectomy patients, the occurrence of abdominal pain is common in the years following the surgery (1, 2). When clinical findings or abnormal liver-function tests suggest biliary pathology, an endoscopic retrograde cholangiography (ERC) is usually carried out and often shows biliary obstruction. However, when there is no anatomical obstruction, endoscopic sphincterotomy (ES) is often performed assuming sphincter of Oddi dysfunction (SOD) (3). The purpose of this study was to evaluate in such patients whether an anomaly of the biliary flow could be demonstrated by using a noninvasive quantitative dynamic heptobiliary scintigraphy (HBS). We also evaluated the diagnostic value of several scanning parameters of biliary flow described in the literature.

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MATERIALS AND METHODS

Subjects. We studied patients who had previously undergone cholecystectomy more than one year ago, without any hepatic dysfunction or jaundice at the time of the study and without previous endoscopic or surgical sphincterotomy. None had renal or cardiac pathology (Table 1).

Control Group. We studied 18 subjects with no evidence of biliary dysfunction, either symptomatically or by chemical evaluation since their cholecystectomy. All showed normal hepatic enzymes and a recent normal hepatobiliary ultrasonography. ERC was performed only on two of them and was found to be normal.

Symptomatic Group. ERC had been performed on 1500 patients in a three-year period at our hospital. Of these, 20 (Table 1) had a recent typical biliary-type pain for less than three months (defined as pain originating in the epigastrium and/or right hypochondrium, and radiating to the right side of the abdomen and/or the back) and no anatomical obstruction, such as biliary stones, pancreatitis, stenosis, or tumors. Biliary excretion was appreciated using ERC at 30–45 min: 10 patients had delayed biliary excretion. The maximal diameter of the common bile duct was 1.7 ± 0.6 cm (mean ± SD). ERC was followed by HBS one to two days later. With respect to controls and symptomatic patients, there were no significant differ-

TABLE 1. CLINICAL DATA

	Controls, mean ± SD (range)	*Patients, mean ± SD (range)*
Number of patients	18	20
Age (yr)	62 ± 16 (37–90)	64 ± 14 (34–88)
Previous cholecystectomy (yr)	14 ± 9 (1–34)	9.0 ± 7 (1–31)
Abnormal hepatic enzymes	0 patient	13 patients

ences in age and time interval since cholecystectomy (Wilcoxon test, $P < 0.01$). Seven patients underwent ES after HBS.

Scintigraphy Protocol. Scintigraphy was performed after fasting for at least 8 hr. Subjects were placed in the supine position under a large-field gamma camera (Acticamera, Sopha Medical) with a standard parallel-hole collimator. The camera field enclosed the heart, liver, and a large part of the abdomen. A rapid intravenous bolus of 5–10 mg of *N*-2,6-dimethylphenylcarbamoylmethyl imidodiacetate (HIDA) (4), labeled with 110–200 MBq technetium-99m (Cis Bio International), was injected. Images were obtained for 90 min at a rate of 1 min/image and then analyzed by computer (S4000, Sopha Medical). Analog images were also recorded every 5 min. An additional 1-min image was recorded 2 hr after the injection.

Correction for technetium decay was made, and regions of interest (ROIs) were traced out, one with the total liver (TH), one encircling the liver and biliary tree outline (HB), and two other excluded large ducts of the right lobe (RL) and left lobe (LL). Other ROIs were drawn over the common duct (CD) and digestive tract (D). Time–activity curves were generated. All hepatic curves were smoothed. CD activity curves were corrected point by point by subtracting the adjacent parenchymal background activity.

Parameters Studied. The parameters studied were those usually described in the literature, some obtained from one of the hepatic curves, others from the one or more different curves.

Parameters obtained from hepatic curves are: the time-maximum (Tm) for each hepatic curve: TmRL, TmLL, TmTH and TmHB; the percentage of the maximal activity at 90 min (TH_{90}) for the total liver: TH_{90} = (TH Activity at 90 min/THm)*100; the total hepatobiliary mean time: MTTH = Σ(THi*ti)/(ΣTHi), where THi was the activity at time ti.

Parameters obtained from other curves are: the excretion percentage of the common duct during the second hour: EC_{120} = 100*(CD60 − CD120)/CD120; and the time of entry into the duodenum (TD).

Statistical Analysis. For each parameter, symptomatic patients and controls were compared by using a nonparametric test (Wilcoxon W). The results obtained in the control group were used to determine the normal values; a baseline value was defined as the mean of the control values plus or minus one standard deviation.

TABLE 3. PARAMETERS CALCULATED FROM OTHER CURVES

	EC_{120}	*TD (min)*
Controls	53*	20
Standard deviation	21*	5
Patients	128†	48
Standard deviation	146†	21
FP	2*	4
FN	5†	1
P	NS	0.001

*N = 11.
†N = 12.

RESULTS

The mean HBS excretion index was decreased in symptomatic patients (Tables 2 and 3). Slowing of the biliary excretion seen by HBS was well correlated with delayed biliary excretion at ERC. TmTH and TmHB had very similar values in every patient. The TD was higher than 1 hr in only three symptomatic patients. A higher value of CD activity was observed at 120 than at 60 min in only six of 11 symptomatic patients (eight controls and nine symptomatic patients were not available for studying at 120 min).

TABLE 2. PARAMETERS CALCULATED FROM HEPATIC CURVES

	Time-maximum (min)				*Excretion index*	
	TmRL	*TmLL*	*TmTH*	*TmHB*	*TH_{90}*	*MTTH (min)*
Controls	18	22	24.4	24	39	40.4
Standard deviation	4	6	4.5	4	10	1.7
Patients	22	36	44	46	67	46.1
Standard deviation	6	19	20	16	22	2.7
FP*	3	2	4	4	3	1
FN†	12	7	3	3	3	1
P	0.01	0.001	0.001	0.001	0.001	<0.001

*FP: number of controls above baseline value (1 SD of mean).
†FN: number of patients not within calculated baseline.

Three symptomatic patients constantly had values close to the controls. No ready explanation was available for one of these. In the other two, 3-year follow-up clinical and biological data suggest that the migration of a stone and/or irritable bowel syndrome rather than sphincter dysfunction was probably the cause of the pain. All of the seven symptomatic patients who had undergone to ES showed good results with a decrease or disappearance of symptoms with two to five years' delay; scintigraphic reevaluation of biliary flow in four of these seven patients has shown improvement in HBS indexes.

The more discriminant indexes were TmTH (or TmHB), TH90, MTTH, and TD. In our population, values above the baseline for more than two of these parameters were identified in all of our symptomatic patients (except the three, discussed above) and all but one controls.

DISCUSSION

We studied cholecystectomy patients with biliary-type pain unexplained by ERC, suggesting of SOD. ES is proposed to be a treatment for SOD, but it has a complication rate of about 7% (1). Nevertheless, the diagnosis of SOD is difficult (4). Evaluation of delayed biliary excretion using ERC is not a sensible parameter. Endoscopic manometry has been shown to be a sensitive method for measuring choledocal sphincter pressure (5, 6), but this technique can be difficult to perform and requires experience (moreover, unlike the HBS, it is not available in many centers). Biliary scintigraphy is noninvasive (6, 7), and in the case of common hepatic duct obstruction (9–12), visual analysis is sufficient (2, 13) and easily identifies biliary block. In the cases of incomplete obstruction, several studies have proposed different parameters whose methodology requires computer analysis (14–18). The mean values of our control subjects were moderately higher than those reported in the literature using the same tracer (19, 20), but the selection of controls was different.

For the majority of the indexes studied, we found a significant difference between control and symptomatic patients' mean values. This consisted of slowing of biliary flow and tracer retention. It was identifiable at the level of the common duct, of the whole liver, and, for half of the symptomatic patients, up to the level of the peripheral biliary ductules and/or the hepatocytes (19), particularly in the left lobe. The indexes were well correlated with biliary delay at ERC.

We found an overlap of results between controls and symptomatic patients in all of the indexes. This is easily explained for symptomatic patients with dysfunction without detectable obstruction. These indexes have good specificity but poor sensitivity for the diagnosis of SOD (21). For this reason, we chose a normal baseline value equal to the mean of the control plus or minus one standard deviation. MTTH [principally dependent on the liver-to-bile rate constant (8)], TmTH (or TmHB), TH90 were good indexes with few overlaps between symptomatic patients and controls. TD was also of good accuracy in our postcholecystectomized patients, as has been previously reported (16).

Although the same common duct activity at 2 hr as at 1 hr is reported to be a useful sign in identifying SOD (2, 13, 22), it was not a constant finding in our symptomatic patients and was only a sign of a significant obstruction. The calculation of the time at which CD activity decreases to 50% of maximum (16) is imprecise because of the significant and rapid fluctuations of CD activity. In addition, emptying of half of the maximal CD activity did not occur prior to 90 min in half of the controls. For similar reasons, we did not calculate indexes of CD clearance (14). The size of the common duct is not a reliable parameter (21), and furthermore, it is poorly assessed by HBS (10, 23).

Our results show that HBS differentiated symptomatic patients from controls, clearly identifying a poor biliary excretion and delay caused by SOD. For a postcholecystectomy patient with biliary-type pain, for a reasonable cost (9), HBS can detect and quantify biliary excretion pathology, even when anatomical obstruction is not shown by ERC. These results, based on clinical classification of the patients, should stimulate other studies on the value of scintigraphy in patients with atypical abdominal pain. In such patients, suspected of SOD, scintigraphy could be performed in the absence of the sufficient data to recommend endoscopic sphincterotomy.

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