Corn Oil Emulsion: A Simple Cholecystagogue for Diagnosis of Chronic Acalculous Cholecystitis

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This study investigated the use of a corn oil emulsion as an inexpensive alternative to sincalide in the scintigraphic diagnosis of chronic acalculous cholecystitis (CAC). **Methods:** Thirty patients with abdominal or right upper quadrant pain underwent ^{99m}Tc-disofenin hepatobiliary imaging for 60 min. After gallbladder filling, 30 mL of corn oil emulsion were administered orally to all patients followed by dynamic imaging for an additional 60 min in all patients and for 90 min in 26 patients. Gallbladder emptying kinetics were determined with gallbladder ejection fractions calculated at 30, 60, and 90 min. The results were compared with histopathologic or clinical follow-up data. **Results:** Corn oil emulsion was found to be palatable and free of side effects in all patients. Seven of the 30 patients had histopathologic evidence of CAC, whereas the remaining 23 did not have evidence of gallbladder disease based on clinical follow-up. The 30-, 60-, and 90-min gallbladder ejection fractions were determined to be 25% ± 22% (mean ± SD), 47% ± 28%, and 62% ± 29%, respectively. Receiver-operating-characteristic analysis showed that the 60-min gallbladder ejection fraction best distinguished between CAC and non–gallbladder disease with an area under the curve of 0.963. A 60-min gallbladder ejection fraction of ≤20% had 100% sensitivity, 96% specificity, 88% positive predictive value, 100% negative predictive value, and 97% overall accuracy for the diagnosis of CAC. **Conclusion:** Standardized corn oil emulsion appears to be an adequate and well-tolerated gallbladder stimulant. Based on receiver-operating-characteristic analysis, a 60-min gallbladder ejection fraction of ≤20% using this simple cholecystagogue results in high diagnostic accuracy for CAC.

Key Words: gallbladder; chronic acalculous cholecystitis; corn oil emulsion; cholecystagogue; sincalide

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Sincalide, a cholecystokinin analog (Kinevac; Bracco Diagnostics, Inc.), is a well-established gallbladder stimulant that is widely used in the scintigraphic diagnosis of chronic acalculous cholecystitis (CAC) (*1–4*). Although there is controversy regarding the optimal infusion time and stimulant dose, sincalide is most commonly administered as a 3-min intravenous infusion after gallbladder filling following standard hepatobiliary imaging of about 60 min (*5*). A 30-min infusion period, however, is used at some institutions, including ours, after which the gallbladder ejection fraction (GBEF) is determined. Normal cutoff values for the GBEF after a 3- or 30-min infusion have been established in several studies, and it is generally accepted that a GBEF of <30% is associated with CAC (*6–9*).

The use of sincalide in conjunction with hepatobiliary imaging is an attractive approach for the diagnosis of CAC because of the standardization of this test and the reproducibility of results (*1*). However, one might argue that the infusion of sincalide does not truly represent a physiologic gallbladder stimulant, its intravenous administration is somewhat of an inconvenience compared with an oral agent, and unwarranted side effects could result, particularly with the 3-min infusion (*3*). Instead, the use of a well-defined fatty meal would be more physiologic and, if standardized, may be preferable to sincalide.

Other reasons for the potential use of a well-defined fatty meal include the higher cost of the cholecystokinin analog and the possibility of drug shortages in the future. In fact, up until recently, there had been a temporary unavailability of sincalide that lasted for >1 y (between November 2001 and December 2002) because of technologic transfer delays and supplemental new drug approval requirements (*10,11*). This unavailability prompted several groups to search for alternatives to sincalide.

At our institution, we investigated the use of a corn oil emulsion as a potential alternative. This cholecystagogue was chosen primarily because it is prepared based on a specific formula with a high fat content, hence representing a well-defined fatty meal. In this report, we describe our clinical experience with this simple cholecystagogue in the diagnosis of CAC.

MATERIALS AND METHODS

Patient Selection and Characteristics

Thirty consecutive patients were studied (22 females, 8 males; mean age, 40 y; range, 11–73 y) (Table 1). All patients were

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TABLE 1
Patient Characteristics, GBEF, LP, EP, and ER Results

Patient no.	Age (y)	Sex	Weight (kg)	GBEF (%) 30 min (n = 30)	GBEF (%) 60 min (n = 30)	GBEF (%) 90 min (n = 26)	LP* (min) (n = 30)	EP* (min) (n = 30)	ER* (%/min) (n = 30)	Follow-up
1	12	F	53	29	42	57	1	85	0.7	Gastritis
2	26	F	67	29	52	81	1	89	0.9	Lactose intolerance
3	27	F	58	62	84	90	5	85	1.1	Constipation
4	26	F	52	23	46	71	10	80	0.9	PUD
5	71	M	79	49	65	80	1	56	1.4	Gastritis
6	21	F	63	0	31	41	30	60	0.7	Pregnancy
7	26	F	56	49	60		1	59	1.1	Pregnancy
8	54	F	85	41	96	100	1	60	1.7	GERD
9	73	F	90	24	61		1	59	1.0	Appendicitis
10	62	F	82	59	94	100	2	64	1.6	GERD/gastritis
11	32	M	100	16	45	71	1	89	0.8	Hiatal hernia
12	11	F	48	22	54	51	1	59	0.9	GERD
13	39	F	78	38	49	65	1	59	0.8	Functional bowel disorder
14	46	F	94	24	60	75	10	80	0.9	Hiatal hernia
15	30	M	131	19	44		10	50	0.9	GERD
16	40	M	59	37	70	90	1	89	1.0	Transient pancreatitis
17	33	M	100	4	77	92	1	89	1.0	HIV positive
18	22	F	104	55	82	100	1	79	1.3	GERD
19	33	F	47	85	99	100	1	60	1.7	PUD/fructose intolerance
20	37	F	77	0	42	55	10	80	0.7	Myofascial abdominal pain
21	33	F	72	18	41	58	2	88	0.7	Atypical angina
22	40	F	104	0	1	70	30	60	1.2	CAC
23	46	F	99	0	10	9	10	50	0.2	CAC
24	46	F	95	4	17	23	2	88	0.3	CAC
25	58	M	95	0	22	34	11	79	0.6	Low-grade pancreatitis
26	67	M	74	8	16	17	2	65	0.3	CAC
27	53	F	90	6	11	19	1	86	0.2	CAC
28	40	F	95	16	20	34	1	89	0.4	CAC
29	25	M	185	18	5	25	1	89	0.3	Musculoskeletal pain
30	67	F	107	8	19		1	59	0.3	CAC

*Obtained from 90-min data except in patients 7, 9, 15, and 30, where 60-min data were used.
LP = latent period; EP = ejection period; ER = ejection rate; PUD = peptic ulcer disease; GERD = gastroesophageal reflux disease.

referred for recurrent postprandial abdominal or right upper quadrant pain between January and October 2002 and had a prior ultrasound that did not show evidence of cholelithiasis. Twenty-seven of the 30 patients were outpatients and the remaining 3 were inpatients at the time of the study.

Twenty-nine of the 30 patients had not received any opiods before the hepatobiliary study, with the remaining patient not having had opioids for >24 h before imaging. Patients were excluded from the study if they had not fasted for at least 4 h or fasted for >24 h, were on total parenteral nutrition, took medications that could potentially cause the gallbladder to contract, or had previous biliary or gastrointestinal surgery. In addition, patients with a history of gastroparesis (e.g., diabetic gastroparesis) were excluded because of the potential effect of delayed gastric emptying on GBEF measurements after a fatty meal (*4*).

Corn Oil Emulsion Preparation

Corn oil emulsion was compounded at our institution's pharmacy based on the formula for the historically marketed Lipomul from Upjohn, which was discontinued in 1979 (*12*). Ingredients included corn oil (10 g/15 mL) and saccharin sodium (6.3 mg/15 mL) as well as the addition of an artificial citrus vanilla flavoring to make the emulsion more palatable. The total caloric content of this product (essentially all due to corn oil) was approximately 170 calories per 30-mL patient dose.

Hepatobiliary Imaging and Corn Oil Emulsion Administration

All patients underwent dynamic hepatobiliary imaging in a 20° left anterior oblique view while in the supine position for 60 min (1 frame per minute) using a large-field-of-view γ-camera equipped with a low-energy, all-purpose collimator. The matrix size was 128 × 128.

Imaging was initiated immediately after intravenous injection of 185 MBq (5 mCi) ^{99m}Tc-disofenin (DISIDA/Hepatolite; CIS-US, Inc.). This was followed by ingestion of 30 mL of the corn oil emulsion regardless of the patient's weight over <1 min after gallbladder filling was identified to confirm patency of the cystic duct. All 30 patients then underwent imaging for an additional 60

min and 26 of the 30 patients underwent imaging for a total of 90 min.

GBEF Calculation

A tight region of interest (ROI) was visually drawn over gallbladder activity on a computer on the images acquired before the administration of the corn oil emulsion. The gallbladder activity in sequential views after administratioin of the oral corn oil emulsion was then expressed as a percentage of the starting value or total counts within this ROI. These data were used to generate a gallbladder emptying time–activity curve with all values decay-corrected so that a GBEF could be calculated as follows:

$$\text{GBEF}\ (\%) = \frac{(\text{gallbladder counts}_{max}) - (\text{gallbladder counts}_{min})}{(\text{gallbladder counts}_{max})},$$

where gallbladder counts_{max} and gallbladder counts_{min} = the maximum and the minimum number of gallbladder counts, respectively.

Receiver-Operating-Characteristic (ROC) Analysis

ROC curve analysis was performed using MedCalc statistical software (MedCalc Software). This was used to determine the diagnostic accuracy of the GBEF measurements at various time points (i.e., 30, 60, and 90 min) for CAC by comparing the GBEFs with the final patient outcome based on histopathologic findings or clinical follow-up of at least 6 mo. In addition, ROC analysis was used to determine the optimum cutoff GBEF for the diagnosis of CAC, defined by the point on the ROC curve with the minimum distance from the 0% false-positive rate and 100% true-positive rate.

RESULTS

Corn Oil Emulsion Tolerability

Corn oil emulsion was found to be palatable and free of side effects in all patients.

Histopathologic and Clinical Follow-Up Findings

Of the 30 patients studied, 7 had evidence of CAC histopathologically documented at surgery (cholecystectomy) as chronic inflammation and no evidence of stones. Three were reported to have Rokitansky–Aschoff sinuses, and 1 had fibrosis. The remaining 23 patients did not have any evidence of gallbladder disease based on clinical follow-up of at least 6 mo. Their symptoms were ultimately explained by other causes or diseases, such as gastritis, gastroesophageal reflux disease, hiatal hernia, fructose intolerance, pregnancy, low-grade pancreatitis, and so forth (Table 1).

Gallbladder Emptying Kinetics and GBEF After Corn Oil Emulsion Administration

Figure 1 shows 2 representative examples of gallbladder emptying time–activity curves, one in a patient with histopathologic evidence of CAC and the other in a patient with no follow-up evidence of any gallbladder abnormalities.

Table 1 shows the GBEFs at various time points (i.e., 30, 60, and 90 min) as well as the latent period (LP), ejection period (EP), and ejection rate (ER) after administration of corn oil emulsion in all patients. LP was defined as the time (in minutes) from the beginning of corn oil emulsion ingestion to the beginning of gallbladder emptying, EP as the time (in minutes) from the beginning to the end of gallbladder emptying, and ER as the percentage of GBEF divided by the EP (%/min).

The 30-, 60-, and 90-min GBEFs (mean ± SD) in all 30 patients were found to be 25% ± 22% (range, 0%–85%),

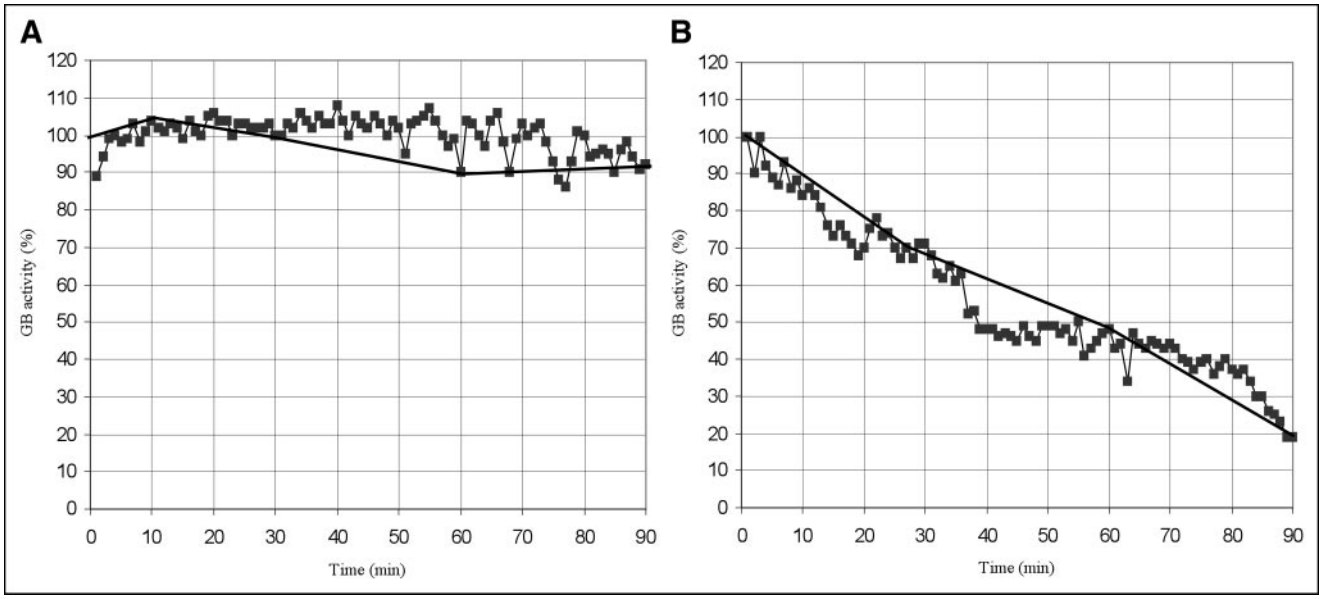

FIGURE 1. Gallbladder time–activity curves show change in gallbladder activity over time. (A) Abnormal time–activity curve shows 0% clearance of activity by 30 min, 10% by 60 min, and 8% by 90 min. (B) Normal time–activity curve with 29% clearance by 30 min, 52% by 60 min, and 81% by 90 min.

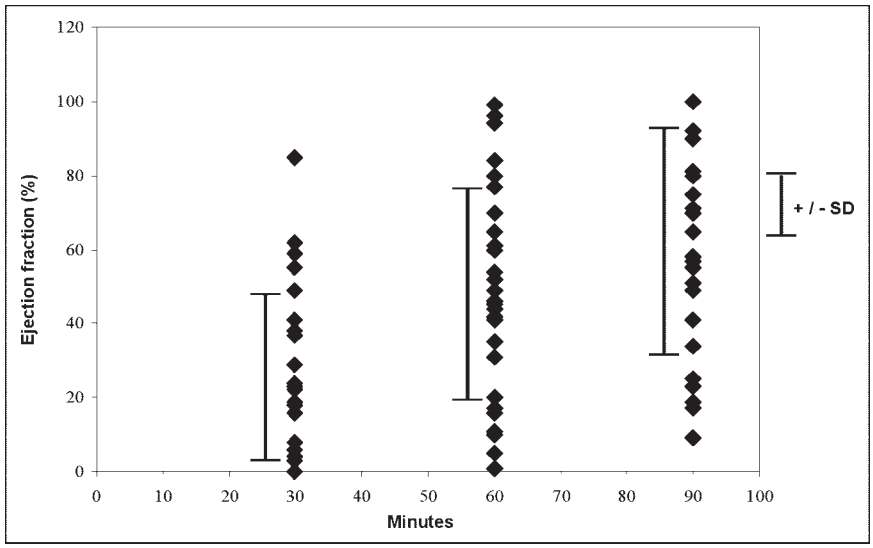

FIGURE 2. Raw data distribution of 30- and 60-min GBEFs in 30 patients and 90-min GBEFs in 26 patients including mean ± SD bar shown at each measurement. Differences in mean 30-, 60-, and 90-min GBEFs between 2 groups of patients (normal vs. CAC) were statistically significant ($P < 0.007$).

47% ± 28% (range, 1%–99%), and 62% ± 29% (range, 9%–100%), respectively (Fig. 2).

The 30-, 60-, and 90-min GBEFs (mean ± SD) in the 7 patients with histopathologic evidence of CAC were 6% ± 6% (range, 0%–16%), 13% ± 7% (range, 1%–20%), and 29% ± 22% (range, 9%–70%), respectively, compared with 30% ± 22% (range, 0%–85%), 57% ± 24% (range, 5%–99%), and 72% ± 23% (range, 25%–100%) in the 23 patients with no evidence of CAC. Differences in the 30-, 60-, and 90-min GBEFs between the 2 groups of patients were statistically significant ($P < 0.007$).

No correlation was found between body weight and the 30-, 60-, or 90-min GBEF in the 23 patients with no evidence of CAC ($r = -0.21$ to -0.39; P = not significant) despite considerable variability in the patients' body weight (range, 47–185 kg; median = 78 kg).

The LP, EP, and ER in all patients were 5 ± 8 min (mean ± SD; range, 1–30 min), 73 ± 14 min (range, 50–89 min), and 0.9%/min ± 0.4%/min (range, 0.2%/min–1.7%/min), respectively. However, it should be noted that the gallbladder was still emptying even at 90 min in 15 of the 26 patients imaged for 90 min after the fatty meal and at 60 min in all 4 patients imaged for only 60 min. This was apparent by the continued downward slope of the gallbladder time–activity curve at 90 or 60 min after the meal in these patients, suggesting that gallbladder emptying was not complete when data acquisition was terminated. Because the EPs and ERs could be determined only based on the available 60- or 90-min imaging data, the EP is underestimated in these patients. On the other hand, assuming that the rate of gallbladder ejection was relatively stable soon after the beginning of the EP, the estimated ERs in these patients are unlikely to be significantly different from their true ERs had imaging been performed until the end of gallbladder emptying.

Correlation Between GBEFs and Final Diagnoses

Figure 3 shows the distribution of the 30-, 60- and 90-min GBEF measurements in the 2 groups of patients: those with evidence of CAC and those without evidence by histopa-

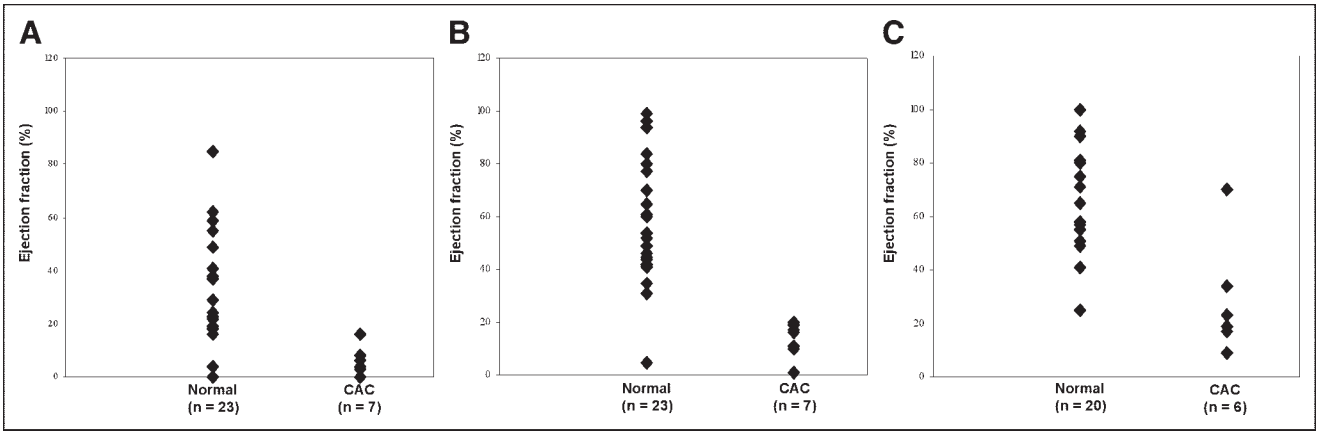

FIGURE 3. Raw data distribution of GBEFs for study subjects at 30 min ($n = 30$) (A), 60 min ($n = 30$) (B), and 90 min ($n = 26$) (C) classified according to whether they did or did not have CAC on final diagnosis.

thology or follow-up. Figure 3 shows that the GBEF measurements at each time point (i.e., the 30-, 60-, and 90-min GBEFs) provided reasonably good separation between patients in the 2 groups. The 60-min GBEF appears to give the best separation between both groups. We also noted that all patients with subsequent evidence of CAC had 30- or 60-min GBEFs that were clearly below the clinically commonly used cutoff GBEF of 35% used with cholecystokinin studies. The 90-min GBEFs were also below this cutoff in these patients, except for 1 patient who had a 90-min GBEF of 70%. This patient had 30- and 60-min GBEFs of 0% and 1%, respectively. A decision was made by the surgeon to perform cholecystectomy in this patient based on clinical work-up and signs and symptoms of CAC in conjunction with the very low 30- and 60-min GBEFs.

To further investigate the diagnostic accuracy of the 3 GBEF measurements (i.e., 30-, 60-, and 90-min GBEFs) for CAC, ROC curve analysis was used (Fig. 4). This analysis showed that the area under the ROC curve was largest for the 60-min GBEF (0.963; 95% confidence interval [CI] = 0.821–0.995), followed by the 90-min GBEF (0.925; 95% CI = 0.751–0.989), and then the 30-min GBEF (0.863; 95% CI = 0.689–0.960). The difference in the area under the ROC curve between the 30- and 60-min GBEF was statistically significant ($P = 0.04$). However, the differences between the 30- and 90-min GBEF and the 60- and 90-min GBEF areas under the ROC curves were not statistically significant (i.e., $P = 0.4$ and $P = 0.5$, respectively). Overall, the data suggest that the 60-min GBEF provides the highest diagnostic accuracy for CAC, although the 90-min GBEF was statistically similar. The 30-min GBEF was clearly inferior in this respect.

ROC curve analysis provided the optimum cutoff or criterion for diagnosing CAC for each of the ROC curves representing the 30-, 60-, or 90-min GBEF measurements. As shown in Figure 4, a 60-min GBEF of ≤20% was associated with 100% sensitivity (95% CI = 100%–100%) and approximately 96% specificity (95% CI = 78%–99%) for the diagnosis of CAC. The positive and negative predictive values (PPV and NPV) and accuracy for diagnosing CAC at this cutoff were 88%, 100%, and 97%, respectively. For the 30-min GBEF, a value of ≤16% was also associated with 100% sensitivity (95% CI = 100%–100%) but only about 78% specificity (95% CI = 56%–93%). The PPV, NPV, and accuracy at this cutoff were 85%, 100%, and 80%, respectively. A 90-min GBEF of ≤34% was associated with about 83% sensitivity (95% CI = 36%–97%) and 95% specificity (95% CI = 75%–99%). The PPV, NPV, and accuracy at this cutoff were 71%, 95%, and 77%, respectively. Thus, a 60-min GBEF of ≤20% appears to provide the highest accuracy for differentiating between patients with and without CAC among the various cutoffs identified.

DISCUSSION

The purpose of our study was to investigate the potential use of a corn oil emulsion compounded at our institution's pharmacy as an alternative to sincalide to aid in the diagnosis of CAC. The formulation was based on the historically marketed Lipomul, which was discontinued in 1979. Interestingly, Lipomul given in a similar amount (30 mL) as our corn oil emulsion has been investigated previously as a cholecystagogue in a small study with 7 healthy volunteers (*13*). However, to our knowledge, no further studies have been reported on the clinical use of Lipomul in diagnosing CAC. Our study reports on the clinical use of a Lipomul-like agent for this diagnosis in a substantial number of patients.

Gallbladder contraction or the GBEF may be reduced after exogenous hormonal stimulation in situations of either

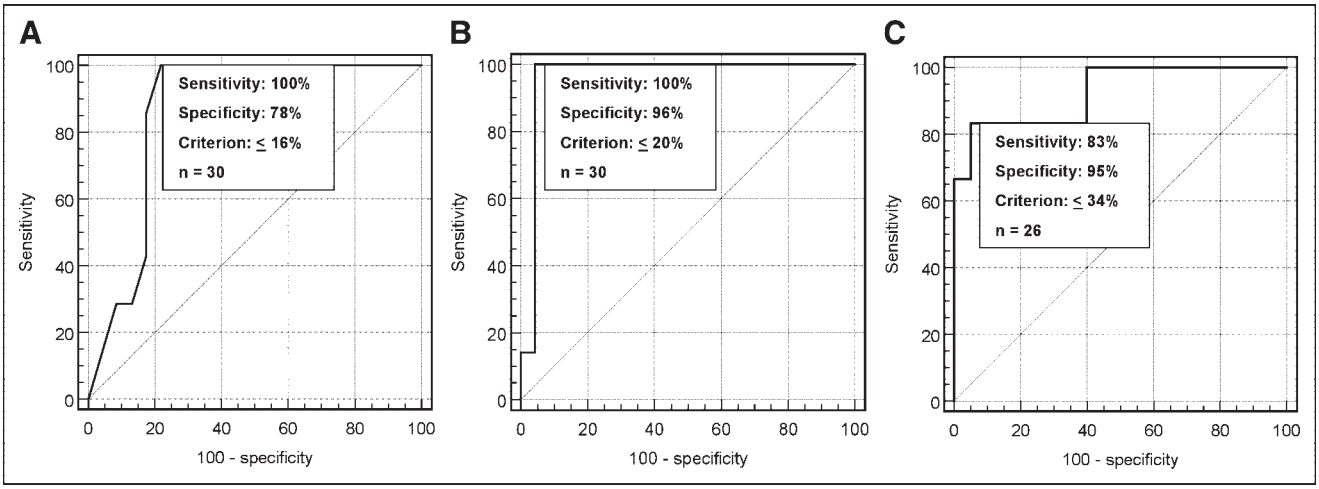

FIGURE 4. ROC curves for GBEF measurements at 30 min (A), 60 min (B), and 90 min (C) with best cutoffs identified for each of 3 measures. Difference in area under ROC curve between 30- and 60-min GBEF was statistically significant ($P = 0.04$). However, differences between 30- and 90-min and 60- and 90-min areas under ROC curves were not statistically significant ($P = 0.4$ and $P = 0.5$, respectively).

calculous or acalculous biliary disease (e.g., CAC, sphincter of Oddi dysfunction), with nonbiliary conditions, or due to drugs (i.e., opioids, ethanol, calcium channel blockers, benzodiazepine, erythromycin), which are known to alter gallbladder contraction (*14,15*). Most patients with abdominal or right upper quadrant pain and a normal GBEF are found to have a nonbiliary cause for their symptoms. The vast majority of those with an abnormally low GBEF are ultimately found to have actual gallbladder disease. Therefore, GBEF evaluation is a very useful tool in excluding or confirming the diagnosis of CAC.

Surgeons are usually reluctant to operate on patients with abdominal or right upper quadrant pain who do not have objective confirmation of chronic cholecystitis by ultrasound. However, it has also been shown that gallbladder dysmotility can produce recurrent abdominal or right upper quadrant pain in patients without sonographic evidence of gallstones (*2,16*). The use of ^{99m}Tc-labeled hepatobiliary imaging, combined with exogenous cholecystokinin infusion or the ingestion of a well-defined fatty meal, to determine GBEF is a noninvasive method of studying biliary dynamics and gallbladder motility. This diagnostic imaging technique helps to identify patients with abnormal gallbladder contractility and function and has a high PPV in diagnosing CAC. This aids surgeons preoperatively in their clinical decision making to determine who may benefit from cholecystectomy (*1,2*). In fact, several investigations have shown a PPV of >90% for CAC when the GBEF is low (confirmed histopathologically and by resolution of symptoms after cholecystectomy) (*7*).

Sincalide, the synthetic C-terminal octapeptide fragment of cholecystokinin, was approved by the Food and Drug Administration in 1976 and is currently the only exogenous cholecystagogue commercially available in the United States (*17,18*). It has been used as a pharmacologic adjunct during hepatobiliary imaging to aid in the diagnosis of CAC after gallbladder filling.

Sincalide is typically administered as an intravenous infusion in a dose of 0.01–0.02 μg/kg, preferably over 1–3 or 30 min. However, more rapid infusions of sincalide, such as 1–3 min, have been shown to produce more clinical side effects in patients depending on the dose. With the longer infusion, GBEFs using this agent have been standardized to be >30%–40% at 30 min depending on the methodology used. Cholecystectomy can be recommended with a high probability of symptom relief in patients with a decreased GBEF (*1,7,9*).

Alternative agents to stimulate gallbladder contraction were developed and used when sincalide became unavailable. Pharmacy-compounded sincalide was advocated, but it was controversial regarding quality control and sterility issues (*10,17*). Various fatty meals were investigated and formulated with the intention of physiologically stimulating duodenal release of endogenous cholecystokinin (*1,4*). These fatty meal stimulants have been used by different institutions in combination with cholescintigraphy to aid in the diagnosis of CAC. They include a lactose-free food supplement (Ensure Plus; Abbott Laboratories) with the lower limit of normal for GBEF determined to be 33% at 60 min, half-and-half milk with GBEF values reported as 24%–95% at 60 min in healthy subjects, and heavy whipping cream with an average normal GBEF reported to be 70% at 75 min (*4,10,11,17,19*).

In this study, we have used a corn oil emulsion preparation based on a specific formula as an alternative to sincalide. Our experience with this standardized fatty meal has been encouraging. Although no nationally available product or universal quality control exists for a product such as this, we found that this simple oil-in-water emulsion was readily and reproducibly prepared by pharmacists at our institution. The corn oil emulsion was also easy to administer over a short period of time and free of side effects in all patients.

Our data show that the gallbladder LP was ≤2 min in the majority (21/30) of patients studied. Little variability was noted with 9 patients having LPs ranging from 5 to 30 min (median, 10 min). This suggests that there were generally no significant problems with gastric emptying of the corn oil emulsion and that its effect on gallbladder contraction occurred fairly soon (i.e., in ≤10 min) after ingestion in the vast majority of patients. However, it is interesting to note that the gallbladder was still emptying even at 90 min after ingestion of corn oil emulsion in 15 of 26 patients imaged for 90 min and at 60 min in all 4 patients imaged for 60 min. This is probably because of continued gastric emptying of the fatty preparation into the duodenum, further stimulating endogenous cholecystokinin release and subsequent gallbladder contraction. Nevertheless, it is noteworthy that maximal gallbladder emptying occurred in <90 min in 11 of 30 patients and that a GBEF of ≥90% was measured in an additional 3 patients at 90 min. In fact, a sufficient gallbladder response with a 60-min GBEF of >20% was seen at 60 min after ingestion of corn oil emulsion in all but 1 patient with no evidence of CAC. The measured 60-min GBEFs in these patients were, in general, somewhat higher (mean ± SD, 58% ± 23%; range, 5%–99%) than those reported by Shafer et al. for 7 healthy volunteers (mean ± SD, 31% ± 11%; range, 16%–42%). This difference is likely due to the relatively small sample size in the study by Shafer et al. (*13*). Most importantly, our data show that regardless of whether maximal gallbladder emptying was reached by 60 or 90 min, the 60- or 90-min GBEF measures provided excellent accuracy for diagnosing CAC.

ROC analysis shows that the 60-min GBEF results in the highest diagnostic accuracy for CAC based on histopathologic or clinical follow-up data. The area under the ROC curve of 0.963 is significantly better than that for the 30-min GBEF. Thus, despite the obvious advantages of being able to diagnose CAC based on the 30-min rather than the 60-min GBEF, the former cannot be recommended for reliable diagnosis of CAC after ingestion of the corn oil

emulsion. However, because of the superb diagnostic accuracy of the 60-min GBEF, and because the 90-min GBEF did not result in any increase in this accuracy compared with this measure, the study can be completed in 1 h after ingestion of corn oil emulsion.

On the basis of ROC analysis, a cutoff 60-min GBEF of ≤20% resulted in very high sensitivity, specificity, and overall accuracy (100%, 96%, and 97%, respectively) for diagnosing CAC. The only patient with a false-positive finding at this cutoff had a GBEF of only 5% and had a final diagnosis of musculoskeletal pain. It is noteworthy that this patient's GBEF increased to only 25% at 90 min; hence, the use of the best cutoff of ≤34% for the 90-min GBEF would still have classified the patient as having CAC.

We explored using a 60-min GBEF cutoff value of <16% to define CAC based on the report of Shafer et al., who found a lower threshold 60-min GBEF of 16% in healthy volunteers (*13*). Our sensitivity would have been only 38%, specificity 95%, and accuracy 80%, which is clearly inferior to the use of a ≤20% cutoff. This highlights the strength of our ROC analysis and may be, at least in part, due to the larger number of subjects included in our study.

As might be expected, based on the values of the areas under the ROC curves, even the best cutoff values for the 30- or 90-min GBEF did not result in higher accuracy compared with the 20% cutoff for the 60-min GBEF. In fact, none of these cutoffs resulted in higher sensitivity or specificity compared with the 20% 60-min GBEF cutoff. The diagnostic accuracy with this cutoff is comparable with that reported for sincalide using a cutoff GBEF of 30%–40% (*8,16*).

Interestingly, cholecystokinin and its various analogs are not used in many nuclear facilities worldwide because of the high cost. Rather, well-defined fatty meals such as those investigated in the United States during the period of unavailability of sincalide were used to evaluate gallbladder contraction. Based on our study, corn oil emulsion may represent an attractive alternative to sincalide, because it is a well-defined fatty meal that is easy to prepare at virtually any institutional pharmacy and is of relatively low cost. At this writing, the average wholesale price of sincalide is $48.72 per vial (usually 1 dose per vial), whereas our hospital pharmacy charges $34.30 for a 100-mL bottle of corn oil emulsion (up to 6 patient doses at <$6.00 per dose).

Even with the current availability of sincalide in the United States, corn oil emulsion may still be preferable in that it is more physiologic, free of side effects, easy to administer, and considerably less expensive. Furthermore, there is no concern that corn oil emulsion might become unavailable in the future. Studies comparing corn oil emulsion with sincalide in the same patients are, therefore, warranted.

Despite the very promising findings of this study, evident by the high diagnostic accuracy obtained with the 60-min GBEF, there are a few limitations. One of these limitations is its retrospective nature. Although the gallbladder emptying kinetics, including GBEF measurements, after ingestion of corn oil emulsion were prospectively evaluated in the studied patients, evaluation of the clinical utility of corn oil emulsion as a cholecytagogue for diagnosis of CAC, the major focus of the current study, was performed in a retrospective fashion. Another limitation is that our study involved only patients with a clinical suspicion of biliary pain, and gallbladder emptying kinetics after ingestion of corn oil emulsion were not determined in healthy control subjects for a more stringent comparison with respective parameters in patients with CAC. This limitation may be relatively minor, however, considering the fact that the mean 60-min GBEF in patients with a clinical suspicion of biliary pain who had no evidence of CAC based on clinical follow-up was in fact even higher than the 60-min GBEFs reported by Shafer et al. in healthy volunteers using Lipomul (*13*). This clearly suggests that these patients were very unlikely to have clinical or subclinical CAC and were in this respect quite similar to healthy control subjects. A further limitation of our study is that the corn oil emulsion dose was not adjusted for body weight to control for the amount of endogenous cholecystokinin release. Although this deficiency did not appear to have any appreciable adverse effect on the accuracy of our approach and no apparent correlation was found between body weight and the GBEF in patients with no evidence of CAC, this is a deficiency for a physiologic study such as this.

CONCLUSION

Gallbladder-stimulated cholescintigraphy is a widely accepted diagnostic test for assessing gallbladder motility and function. Preparing and using a corn oil emulsion based on a specific formula represents a standardized and well-tolerated gallbladder stimulant. A 60-min GBEF of ≤20% using this simple cholecystagogue results in high diagnostic accuracy for CAC that is comparable with that reported for sincalide. Corn oil emulsion may represent an attractive alternative to sincalide, because it is more physiologic, free of side effects, easy to administer, and relatively inexpensive. Studies comparing corn oil emulsion with sincalide in the same patients are, therefore, warranted.

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