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Liquid Gastric Emptying as an Adjunct to Hepatobiliary Scintigraphy When Using Oral Corn Oil as a Cholecystagogue for Determining Gallbladder Emptying

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ABSTRACT

During times of sincalide shortage, a fatty meal can be used to stimulate gallbladder contraction during hepatobiliary scintigraphy. However, if a patient has an abnormal gallbladder ejection fraction (GBEF), is it chronic cholecystitis or is it inadequate cholecystokinin stimulation due to poor gastric emptying? Hence, simultaneous liquid gastric emptying using 99mTc-sulfur colloid along with corn oil emulsion was initiated as routine practice during the 2014 sincalide shortage in patients evaluated for GBEF. The objective of this study was to retrospectively assess the time course of gastric emptying in these patients, especially with regard as to whether delayed gastric emptying might be a factor in some patients with a poor GBEF.

Methods: Our clinical imaging procedure during the 2014 sincalide shortage consisted of routine 99mTc-mebrofenin hepatobiliary scintigraphy followed by corn oil emulsion and 99mTc-sulfur colloid orally. Dynamic imaging with regions of interest encompassing the gallbladder and the stomach allowed determination of GBEF and of

gastric emptying. For this study, imaging records for 53 consecutive patients undergoing this clinical procedure were reviewed. The time for 1/2 gastric emptying, along with % gastric emptying at the end of imaging, were evaluated in relationship to GBEF.

Results: 17 patients had normal GBEF (74 ± 14%) and satisfactory gastric emptying (31 ± 21 min for 1/2 emptying, 75 ± 14% emptying at end of imaging); 17 patients had normal GBEF (77 ± 17%) in spite of unsatisfactory gastric emptying (only 30 ± 14% emptying at end of imaging); 5 patients had abnormal GBEF (19 ± 9%) and satisfactory gastric emptying (26 ± 19 min for 1/2 emptying, 82 ± 14% emptying at end of imaging), supporting a diagnosis of chronic cholecystitis; 11 patients had abnormal GBEF (26 ± 9%) but also unsatisfactory gastric emptying (only 26 ± 13% emptying at end of imaging), which did offer additional support for a diagnosis of chronic cholecystitis; and 3 patients had borderline GBEF (40 ± 2%) with satisfactory gastric emptying (59 ± 6% emptying at end of imaging).

Conclusion: Simultaneous liquid gastric emptying can provide additional information in the interpretation of GBEF when using a fatty meal as an oral cholecystagogue, especially to help differentiate chronic cholecystitis vs. inadequate cholecystokinin stimulation due to poor gastric emptying.

KEY WORDS: gallbladder ejection fraction; chronic cholecystitis; corn oil emulsion; hepatobiliary scintigraphy; 99mTc-mebrofenin

Sincalide, a synthetic octapeptide of the C terminal (active portion) of the hormone cholecystokinin, is an FDA-approved drug product indicated to stimulate contraction of the gallbladder as assessed by various diagnostic imaging methods(*1*). It is widely used to evaluate gallbladder contraction and emptying (gallbladder ejection fraction) during hepatobiliary scintigraphy(*2-5*). During times of sincalide shortage, alternative approaches are needed. Although some have used compounded sincalide preparations obtained from compounding pharmacies, caution is urged(*6,7*). Alternatively, oral fatty meals can be used to stimulate small bowel release of endogenous cholecystokinin(*7*). During a previous shortage of sincalide, our institution investigated the use of an oral corn oil emulsion as a simple cholecystagogue(*8*). Our corn oil emulsion was compounded by our hospital pharmacy based on the formula for the historically marketed Lipomul® from Upjohn, which was discontinued in 1979(*8*,*9*).

Although oral fatty meals may be useful for confirming normal gallbladder ejection fraction (GBEF), abnormal GBEF remains problematic for interpretation: is it chronic cholecystitis or is it inadequate stimulation by endogenous cholecystokinin due to poor gastric emptying of fat into the small bowel and thus delayed release of endogenous cholecystokinin? Hence, when using corn oil emulsion as an oral cholecystagogue during the 2014 shortage of sincalide, our institution initiated as routine practice the performance of simultaneous liquid gastric emptying using 99mTc-sulfur colloid along with the corn oil emulsion. Dynamic imaging with regions of interest encompassing the gallbladder and the stomach allowed the determination of GBEF and of gastric emptying.

The objective of this study was to retrospectively assess the time course of gastric emptying in patients who had received corn oil as an oral cholecystagogue to stimulate gallbladder contraction,

especially with regard as to whether delayed gastric emptying might be a factor in some patients with a poor GBEF.

METHODS

For this study, imaging records for 53 consecutive patients who had received oral corn oil emulsion and 99mTc-sulfur colloid during hepatobiliary imaging procedures for their clinical care were retrospectively reviewed. In addition to images, these records included time-activity curves for gallbladder emptying and for gastric emptying based on ROIs encompassing the gallbladder and the stomach, respectively.

Briefly, our clinical imaging procedure during the 2014 shortage of sincalide consisted of routine hepatobiliary scintigraphy following injection of 5 mCi (185 MBq) 99mTc-mebrofenin. After about 45 – 60 minutes, the nuclear medicine physician reviewed the images and

determined whether or not to proceed with evaluation of gallbladder emptying. If so, 30 mL (20 g) of corn oil emulsion and 0.5 mCi (18.5 MBq) 99mTc-sulfur colloid were administered orally, immediately followed with 90 mL of water. Dynamic imaging was then performed in the 20^{o} left anterior oblique position for an additional 60-90 minutes, as directed by the nuclear medicine physician. Regions of interest placed around the gallbladder and the stomach allowed the creation of time-activity curves that showed gallbladder emptying and gastric emptying, respectively. GBEF was calculated from the gallbladder time-activity curve as follows:

GBEF = (maximum activity) - (minimum activity) / (maximum activity)

The medical literature suggests that 10 g of fat delivered to the proximal small bowel, which causes release of endogenous cholecystokinin, is generally needed to produce maximal gallbladder

contraction(*5,10*). The administered dose of corn oil contained 20 g, so half of this administered dose is 10 g corn oil. Hence, the time for 1/2 gastric emptying (i.e., the time for 1/2 of the administered dose of 20 g = 10 g corn oil to pass from the stomach into the intestine), along with % gastric emptying at the end of imaging, were chosen by the author as appropriate parameters for evaluation in relationship to GBEF. Greater than 50% gastric emptying during the time of imaging was chosen by the author as indicating satisfactory gastric emptying (i.e., providing delivery of >10 g corn oil into the small bowel). Classification of GBEF as normal, abnormal, or borderline in these patients was accepted as stated in the interpreting physician's dictated report.

Our Institutional Review Board reviewed this proposed retrospective study and deemed it to be a quality control assessment related to performance of a clinical imaging procedure which did not require

approval by the Institutional Review Board nor written informed consent.

RESULTS

Values of GBEF in these patients varied widely, ranging from 6% to 96%. The rates of gastric emptying in these patients also varied widely, with times for 1/2 gastric emptying ranging from 4 minutes to >90 minutes. Similarly, the % gastric emptying at the end of imaging varied widely, ranging from 7% to 95%. Retrospectively, 50 of the 53 patients fell into one of 4 distinct groups: normal GBEF and satisfactory gastric emptying; normal GBEF in spite of unsatisfactory gastric emptying; abnormal GBEF and satisfactory gastric emptying; and abnormal GBEF with unsatisfactory gastric emptying. Three patients had borderline GBEF and satisfactory gastric emptying. Data for these groups are summarized in Table 1.

Representative imaging results for one patient in each of the four groups, as copied from their medical imaging records, are presented in Figures 1-4.

The oral corn oil emulsion was well tolerated in these patients, with no reports of adverse effects.

DISCUSSION

Normal GBEF generally excludes a diagnosis of chronic cholecystitis, whereas an abnormal GBEF is highly suggestive of chronic cholecystitis. However, when using an oral fatty meal as a cholecystagogue, interpretation of abnormal GBEF as being chronic cholecystitis is problematic because the gallbladder could have been inadequately stimulated during the duration of the imaging procedure if there was poor gastric emptying of the fatty meal.

Hence, simultaneous liquid gastric emptying using 99mTc-sulfur colloid can potentially aid in interpretation for this group.

In this group of patients, a minority of patients (16/53) exhibited abnormal GBEF, which is suggestive of chronic cholecystitis. Of these 16 patients, 5 patients had satisfactory gastric emptying, which strongly supports the diagnosis of chronic cholecystis. The other 11 patients had unsatisfactory gastric emptying, which failed to provide additional support for the interpretation of abnormal GBEF being chronic cholecystitis, because the question remains whether the abnormal GBEF was truly due to chronic cholecystitis or was due to inadequate cholecystokinin stimulation. Although simultaneous gastric emptying had limited usefulness in this patient sample overall, it did in fact help support the diagnosis of chronic cholecystitis in a small group of patients.

The normal value for GBEF is difficult to establish because of its wide variation. Reported normal values for GBEF using various doses of sincalide administered over various infusion times have ranged from 30% to 65%(*3,4*). Reported normal values for GBEF from fatty meals are also quite variable, with examples including >20-34% for 30 mL corn oil emulsion (20 g fat)(*8*), ≥24% for 8 ounces/70 kg half-and-half (24 gram of fat)(*11*), ≥ 33% for 8 ounces of Ensure Plus (11.4 grams of fat)(*12*), ≥ 44-51% for 250 mL milk (approximately 8 grams of fat)(*13*), and ≥ 49% for 3 ounces of whipping cream (30 grams of fat)(*14*). Because this study collected GBEF data that were determined and interpreted as part of a routine clinical procedure, each physician was free to use whatever normal value he felt was most appropriate. Hence, for this study, classification of GBEF as normal, abnormal, or borderline in these patients was accepted as stated in the interpreting physician's dictated report.

This study was not intended to evaluate the efficacy of corn oil emulsion for stimulating gallbladder contraction. Nor was it intended to determine the sensitivity and specificity of this clinical procedure. Rather, the focus of this study was limited to the evaluation of gastric emptying as an aid to physicians in interpreting GBEF when using a fatty meal as an oral cholecystagogue. Hence, a limitation of this study was that the physician's interpretation/diagnosis was not confirmed by patient followup/outcome.

Because this study used retrospective data gathered from routine clinical procedures, a further limitation of this study was the lack of an established normal value for interpretation of GBEF. For example, for 3 patients, the interpreting physician dictated that the GBEF was borderline. In spite of this limitation, the majority of GBEF values were clearly normal or clearly abnormal regardless of whatever normal value was used by the interpreting physician (see Table 1).

It is interesting and puzzling that 17 patients had normal GBEF in spite of unsatisfactory gastric emptying. The reason for this was not examined as part of this study and is not known. One reasonable explanation is that is that a loop of bowel may have overlapped the stomach region-of-interest and thereby falsely elevated the counts in that region-of-interest. Another potential explanation is that gallbladder emptying may be induced by the delivery of substantially less than 10 grams of fat into the proximal small bowel. For example, GBEF > 44-51% has been reported when using 250 mL of whole milk(*13*), which contains a total of only about 8 grams of fat. Also, 4 g of fat has been shown to induce substantial, albeit submaximal, gallbladder contraction(*10*). Yet another potential explanation could be the occurrence of intestinal-gastric reflux where corn oil and 99mTc-sulfur colloid are delivered into the intestine but some 99mTc-sulfur colloid and/or 99mTc-mebrofenin is refluxed back up into the stomach. Intestinal-gastric reflux was noted by the

interpreting physician in one patient's imaging report. Regardless of the reason, this is of little concern to the interpreting physician because a normal GBEF generally rules out chronic cholecystitis.

CONCLUSION

Simultaneous gastric emptying using 99mTc-sulfur colloid can provide additional information in the evaluation of GBEF when using a fatty meal as an oral cholecystagogue during 99mTc-mebrofenin hepatobiliary scintigraphy. This may be especially useful in patients with abnormal GBEF to help differentiate chronic cholecystitis vs. inadequate cholecystokinin stimulation due to poor gastric emptying.

ACKNOWLEGMENT

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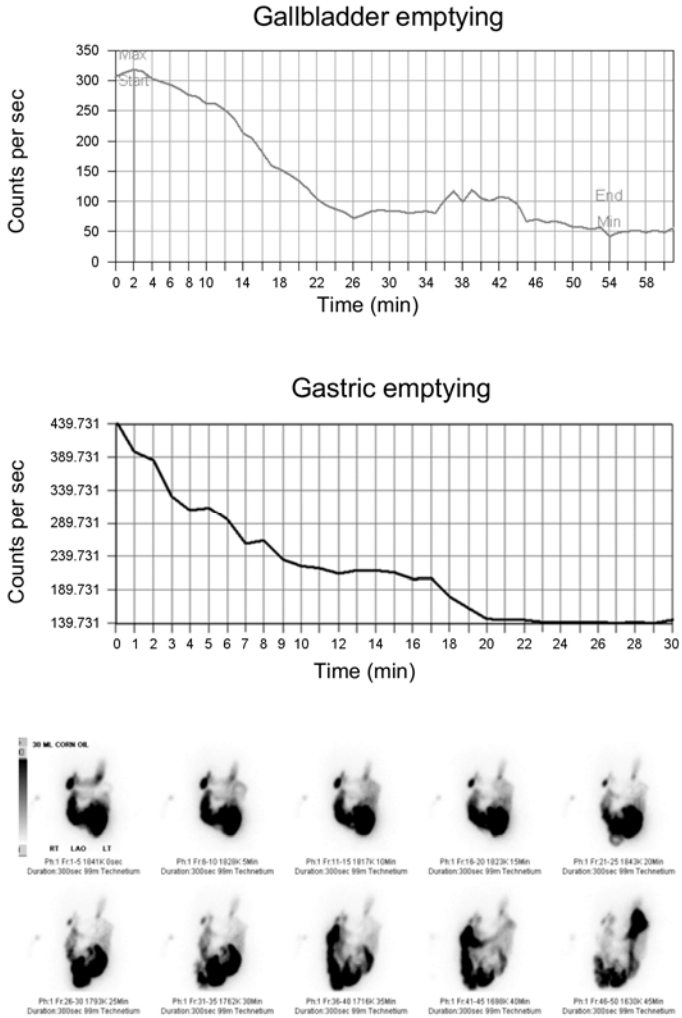

FIGURE 1. Time-activity curves for gallbladder emptying, gastric emptying, and biliary images post corn oil emulsion for a patient with normal GBEF (87%) and satisfactory gastric emptying.

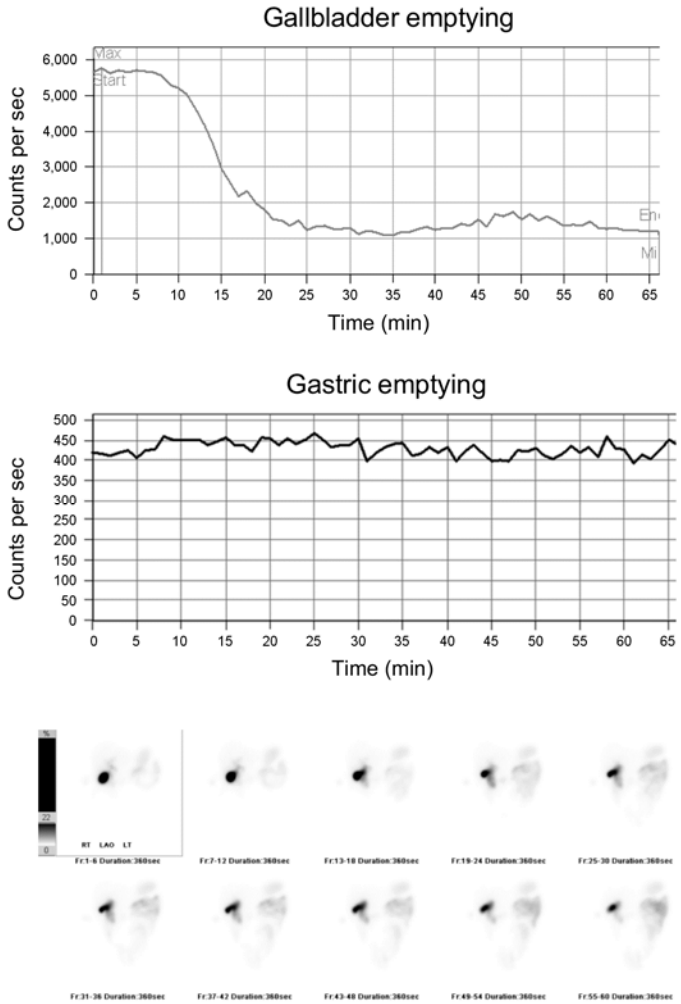

FIGURE 2. Time-activity curves for gallbladder emptying, gastric emptying, and biliary images post corn oil emulsion for a patient with normal GBEF (79%) in spite of unsatisfactory gastric emptying.

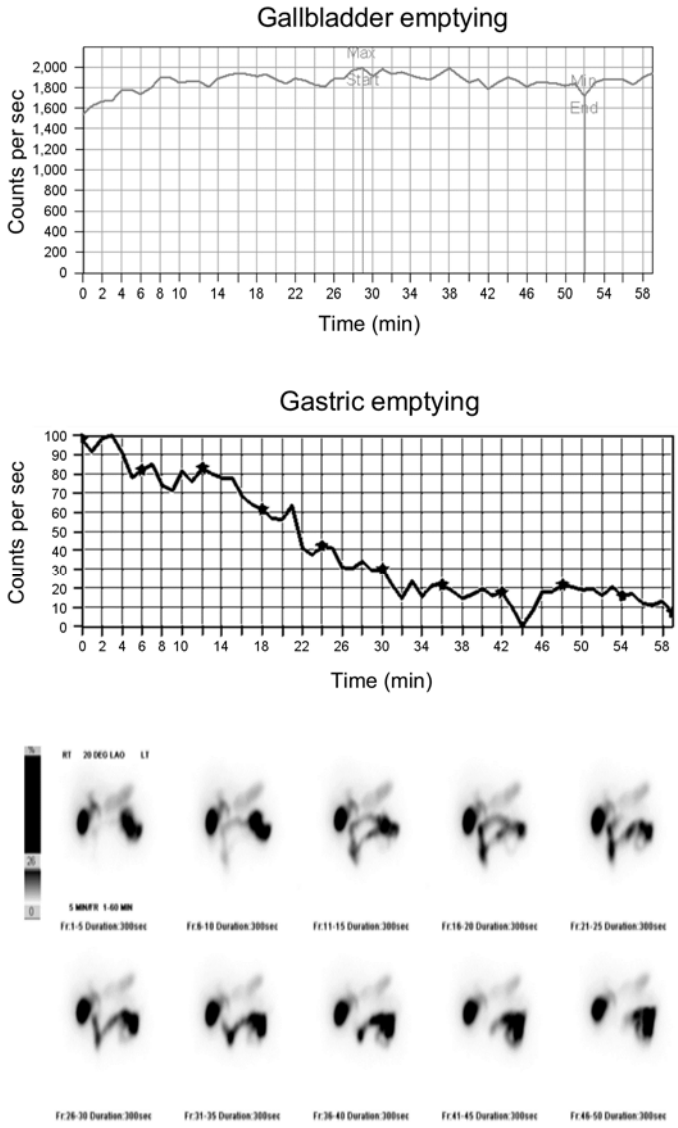

FIGURE 3. Time-activity curves for gallbladder emptying, gastric emptying, and biliary images post corn oil emulsion for a patient with abnormal GBEF (14%) and satisfactory gastric emptying, highly suggestive of chronic cholecystitis.

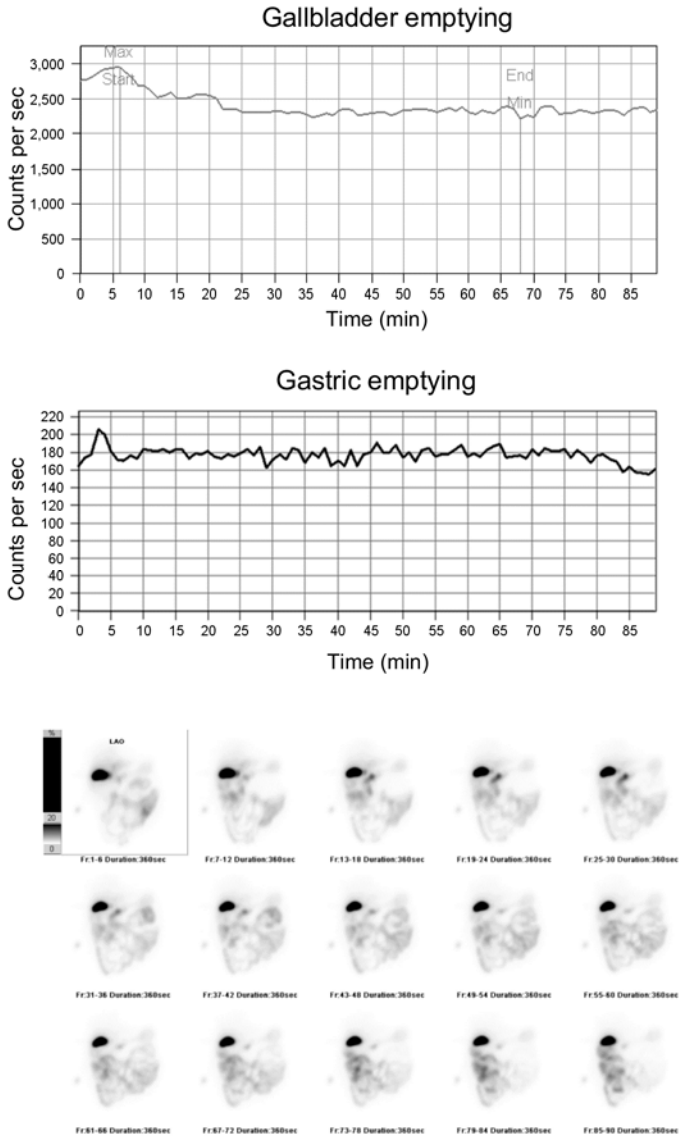

FIGURE 4. Time-activity curves for gallbladder emptying, gastric emptying, and biliary images post corn oil emulsion for a patient with abnormal GBEF (25%) and unsatisfactory gastric emptying, which may be chronic cholecystitis but may be inadequate cholecystokinin stimulation due to poor gastric emptying.

TABLE 1. Results for Gallbladder Ejection Fraction (GBEF) and for gastric emptying (GE) (mean ± SD).

Group	Number of Patients	GBEF (%)	Time for 1/2 Gastric Emptying (minutes)	Gastric Emptying at End of Imaging (%)
Normal GBEF; Satisfactory GE;	17	74±14	31±21	75±14
Normal GBEF; Unsatisfactory GE;	17	77±17	>60-90*	30±14
Abnormal GBEF; Satisfactory GE;	5	19±9	26±19	82±14
Abnormal GBEF; Unsatisfactory GE;	11	26±9	>60-90*	26±13
Borderline GBEF; Satisfactory GE;	3	40±2	34±44	59±6

*1/2 gastric emptying not reached by end of imaging