Technetium-99m BIDA Biliary Scintigraphy in the Evaluation of the Jaundiced Patient

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Biliary scintigraphy using ^{99m}Tc p-butyl acetanilidiminodiacetic acid (BIDA) was performed as part of the diagnostic evaluation on 96 patients with jaundice (serum bilirubin >2 mg/dl) to assess its value in this group of patients. The results of scintigraphy revealed (a) no obstruction to the flow of the scintigraphic agent into the duodenum in 54 patients, (b) delayed appearance of the agent (normal upper limit 60 min) in the duodenum indicating partial obstruction in 22 patients, and (c) complete obstruction of the duct demonstrated by absence of agent in the duodenum in 20 patients. The findings were correlated with the final diagnosis and the overall results show accuracy of 92.7%, sensitivity of 97.3%, and specificity of 89.8%. Biliary scintigraphy was thus found to be useful in differentiating nonobstructive, partially obstructive, and completely obstructive causes of jaundice.

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The differentiation of jaundice due to the hepatocellular disease (medical jaundice) from extrahepatic biliary obstruction (surgical jaundice) is important in planning the appropriate diagnostic and therapeutic procedures.

Currently, there are a number of radiologic techniques available in the investigation of a jaundiced patient. These include: ultrasonography (US), computed tomography (CT), percutaneous transhepatic cholangiography (PTC), and endoscopic retrograde cholangio-pancreatography (ERCP) (*1*). Some of these (PTC and ERCP) are invasive and/or expensive. Furthermore, they delineate anatomic lesions but do not provide a functional evaluation. On the other hand, radionuclide hepatobiliary scanning is a noninvasive study and provides the only means of functional evaluation along with imaging.

In selecting a single screening test which can differentiate medical from surgical causes of jaundice, one has to take into account ease of performance, cost effectiveness, complications associated with the procedure, and degree of accuracy. With the introduction of newer radiopharmaceuticals such as p-butyl acetanilidiminodiacetic acid (BIDA) labeled with technetium-99m (^{99m}Tc), interest in hepatobiliary scintiscanning has increased (*2–4*).

There has not been uniform agreement concerning the diagnostic value of scintiscanning in jaundiced patients (*5–7*). Klingensmith et al. stated that US and hepatobiliary scintigraphy have a complementary role in the evaluation of biliary obstruction (*8*). Their group also suggested that intrahepatic cholestasis can be diagnosed by hepatobiliary scintigraphy (*9*). This study reviews our experience with the use of radionuclide hepatobiliary imaging as a screening procedure in jaundiced patients.

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MATERIALS AND METHODS

During the period March 1, 1979, through April 30, 1983, we studied 96 patients who were clinically jaundiced. All patients were from our institution and included 79 males and 17 females. The age range was 1 mo to 92 yr (mean 52 yr).

The levels of serum bilirubin ranged from 2.1–38.8 mg/dl (normal 0.1–1.1 mg/dl). Excluded from this review were patients who carried a diagnosis of either acute or chronic cholecystitis alone and also patients who have had previous biliary enteric bypass. These have been previously reviewed by one of us (*2–4,10*). In addition to scintiscanning, all patients underwent clinical, chemical, radiologic, and endoscopic evaluations as required. The final diagnosis in each patient was based on the results of all studies noted above and additionally in most patients based on operative findings or needle biopsy of the liver (details in results).

Informed consent was obtained from all subjects. Technetium-99m BIDA was used as scanning agent and was prepared from a commercial kit* and 5mCi of [^{99m}Tc]BIDA was injected intravenously. Using a gamma camera,† images were obtained at 2, 5, 10, 15, 30, 45, and 60 min after the injection and then at 15-min intervals for up to 90 to 120 min. Further scans were obtained at 4 to 6 hr as needed and up to 24 hr if indicated. Each image accumulated 300–500k counts. The details of this technique were previously described (*2,11*).

RESULTS

In a normal scintigram, the liver is visualized at 5 to 10 min after injection of the agent, the gallbladder at ~15–20 min and complete images of the liver, gallbladder, common bile duct, and proximal small bowel are obtained between 25 and 30 min. The criteria used to define extrahepatic biliary obstruction are based on whether the gallbladder and the common bile duct were visualized or not and whether there is radionuclide activity in bowel or not and also the time of appearance of this activity.

The results of scintigraphy in this group were classified into three categories as follows: (a) nonobstructive group (no obstruction to the flow of the scintigraphic agent into the duodenum), 54 patients; (b) partially obstructive (partial obstruction on the basis of delayed appearance of the agent: 60 min or more in the bowel), 22 patients (Fig. 1); and (c) completely obstructive (absence of the scanning agent in the small bowel even after 24 hr), 20 patients (Fig. 2).

In eight patients who were categorized as partial obstruction, in addition to delayed radioactive tracer excretion in bowel, there was a scintigraphic pattern of intrahepatic bile pooling along the area and/or segmental defect in common bile duct (Fig. 3). This characteristic pattern has been previously documented (*12*).

There are two scintigraphic patterns of complete obstruction of the common bile duct. One is that of a fairly rapid hepatic uptake of the tracer by the liver but no visualization of the hepatic ducts, the common duct, gallbladder, or the bowel even up to 24 hr after injection (*13,14*) (Fig. 2). The other pattern is a hyperacute complete common bile duct obstruction, scintigraphic features of which include rapid uptake and visualization of the hepatic ducts, common bile duct, and the gallbladder, but no appearance of activity in the bowel through the 24-hr study period (*15*) (Fig. 4). Only one patient in the study showed this pattern.

The results of scintigraphy were correlated with the final diagnosis (Tables 1, 2, and 3). The following definitions were used: (a) true negative—no obstruction or delay of agent into the duodenum in the scan and no obstruction demonstrated, (b) true positive—obstruction or delay of agent into the duodenum by scan and obstruction confirmed, (c) false positive—obstruction or delay of agent into the duodenum by scan but no obstruction present, and (d) false negative—no obstruction or delay of agent into the duodenum by scan but obstruction present.

Based on the above, the sensitivity of the scan was 97.3%, the specificity was 89.8%, and the overall accuracy was 92.7%.

DISCUSSION

Our results suggest that scintigraphy is useful in the initial evaluation of the jaundiced patient. The differentiation of obstructive from nonobstructive jaundice has been a subject of several conflicting reports (*17–20*). The area of greatest difficulty centers around the fact that at very high levels of serum bilirubin, lack of images may be due to hepatocellular disease (poor hepatic uptake) or extrahepatic biliary obstruction (poor excretion) (*16,21*). In the former situation the tracer remains in the blood pool for a long time and

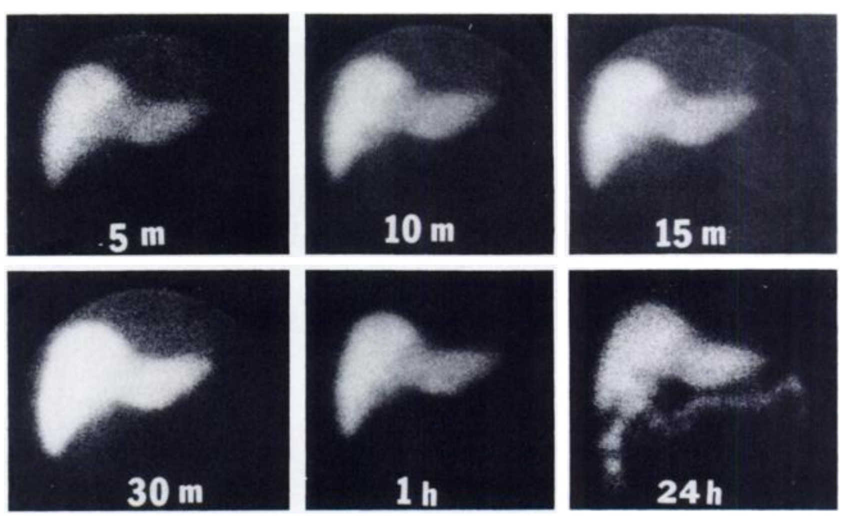

FIGURE 1
Partial obstruction of common bile duct: Fairly rapid radiotracer hepatic uptake and no visualization of bile ducts, gallbladder, and bowel in 5-, 10-, 15-, 30-, and 60-min images; colonic activity seen in 24-hr images but substantial radiotracer remaining in liver at 24 hr, indicating severe partial obstruction

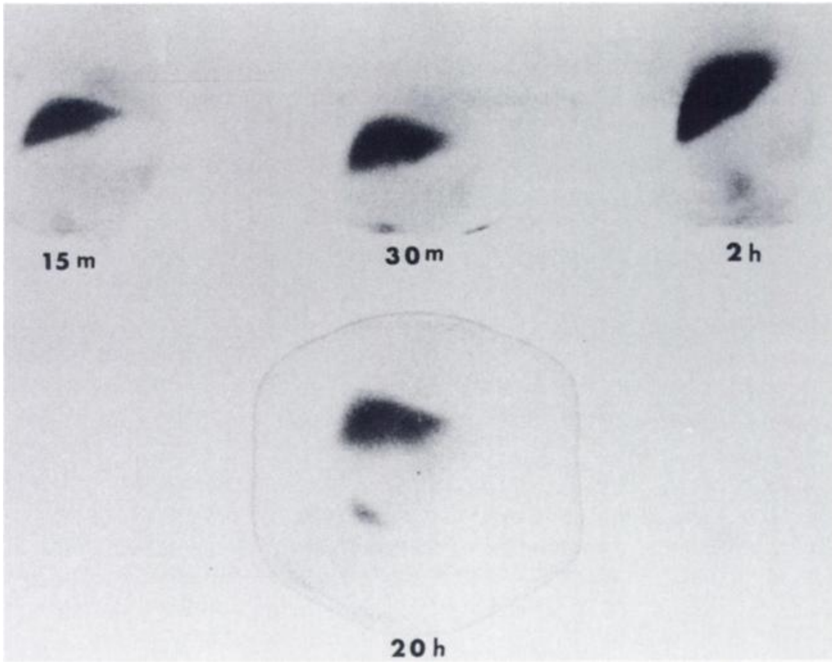

FIGURE 2
Complete obstruction due to biliary atresia in 2-mo-old girl: Radiotracer is rapidly taken by liver but bile ducts, gallbladder, and bowel are persistently not visualized, even in 20-hr image

the biliary tract will not be imaged. However, in patients with very high levels of bilirubin, these results may be equivocal because of dilution of the tracer (*17*).

The scintigraphic patterns associated with biliary obstruction and jaundice are briefly outlined below.

1. In complete obstruction of the common bile duct, there is a fairly rapid hepatic uptake of the tracer, but no visualization of the hepatic ducts, the common duct, gallbladder, or the bowel 24 hr after injection (*13*) (Fig. 1).

2. Hyperacute complete common bile duct obstruction has scintigraphic features that include rapid hepatic uptake and visualization of the hepatic ducts, the common bile duct, and the gallbladder, but no appearance of activity in the bowel through and up to the 24-hr study period (*15*) (Fig. 4). This pattern is very rare because such a patient is usually studied immediately following the onset of the common duct obstruction while the gallbladder is still continuing to reabsorb water. There is an initial imaging of the biliary system while there is net bile flow until the bile is maximally concentrated. Eventually when the pressure in the sys-

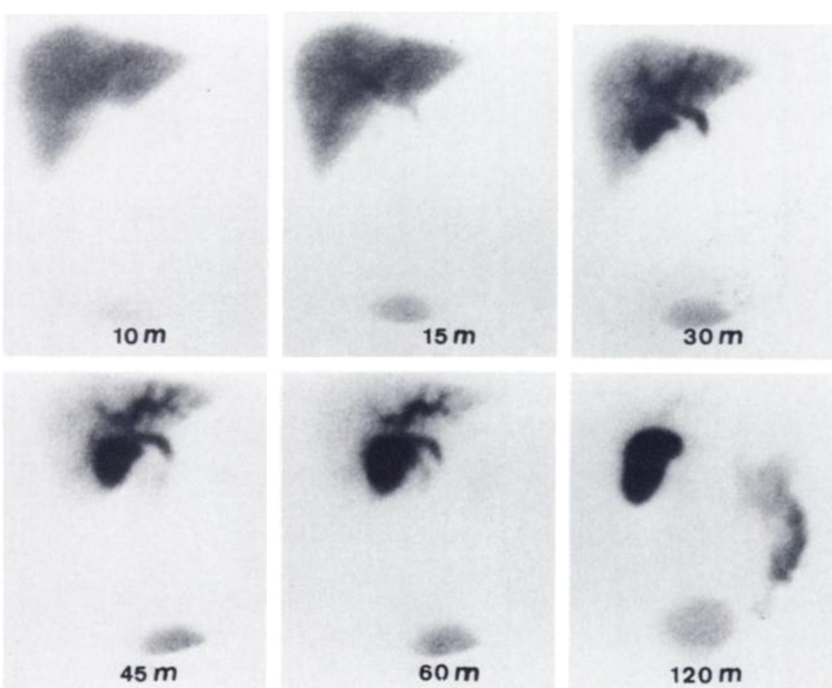

FIGURE 3
Partial obstruction associated with intrahepatic bile pooling and narrowing in common bile duct: Bile pooling seen in 15-, 30-, 45-, and 60-min images; abruptly narrowing common duct seen in 30-, 45-, and 60-min images

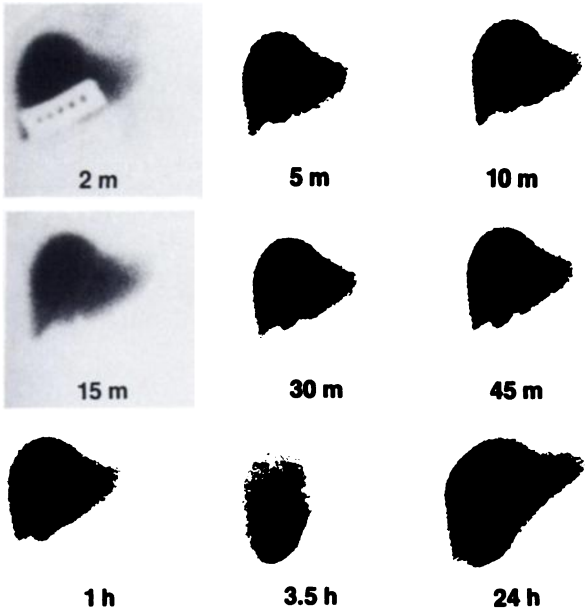

FIGURE 4
Hyperacute complete common bile duct obstruction: Rapid hepatic tracer uptake, in 30-min to 24-hr images and visualization of gallbladder; no bowel activity seen throughout study up to 24 hr

TABLE 1
Nonobstructive Group by Scan

Final clinical diagnosis	No. of patients	Average S. bilirubin (mg/dl)	Confirmation of diagnosis
Alcoholic cirrhosis	12	7.1	Liver biopsy
Alcoholic hepatitis	7	7.7	Liver biopsy
Liver metastasis	8	5.1	Liver biopsy
Drug induced cholestasis	4	8.5	Liver biopsy
Sepsis	4	10.4	Exploratory celiotomy
Hepatitis	4	12.6	Elevated hepatitis B, surface antigen
Liver failure	4	5.9	History
Neonatal hepatitis	2	9.1	Liver biopsy
Sarcoidosis	1	3.6	Liver biopsy
Chronic passive congestion	1	13.5	Liver biopsy
Cirrhosis	1	3.0	Liver biopsy
Hodgkin's disease	1	6.8	Liver biopsy
Cytomegalovirus infection	1	14.3	Liver biopsy
Infected aneurysm	1	6.5	Exploratory celiotomy
Subphrenic abscess	1	2.8	Exploratory celiotomy
Hepatoma	1	11.0	Operation and biopsy
Choledocholithiasis*	1	3.4	Ultrasonography and operation
Total	54		

* False negative.

tem is high, net bile flow will cease and the scintigraphic pattern of complete common duct obstruction will result (*14–16*).

3. The pattern that is seen in patients with biliary atresia includes a delayed hepatic uptake with no visualization of hepatic ducts, common bile duct and bowel throughout the 24-hr period. In those patients who have been pretreated with phenobarbital, this pattern is highly reliable for a diagnosis of biliary atresia and separates this group from those with neonatal hepatitis in whom gstrointestinal excretion is evident (*21*).

4. In intrahepatic cholestasis, there is a rapid hepatic uptake and delayed appearance of activity in the bowel precluding a complete obstruction of the common duct. Since the hepatic function is intact, the scintigraphic pattern is similar to that due to partial obstruction of the excretory mechanism (*21,22*). In our study, there were two patients with drug induced cholestasis who fall into the partially obstructive group and were misdiagnosed. One other patient with alcoholic hepatitis and a serum bilirubin of 20.5 mg/dl was also misdiagnosed as "partially obstructive," probably on the basis of the impaired uptake by the hepatocytes.

5. Hepatic failure. In this group of patients, there is a severely decreased hepatic uptake and persistently high cardiac or blood-pool activity with poor or even nonvisualization of the hepatic ducts, common bile duct, and the bowel. It is virtually impossible to differentiate this condition from partially obstructed or completely obstructed groups (*13*).

Interest in scintigraphy was revived in the mid 1970s with the introduction of new agents which are ^{99m}Tc-labeled derivatives of iminodiacetic acid such as dimethylacetanilidiminodiacetic acid (HIDA) and p-butylacetanilidiminodiacetic acid (BIDA). From past experience, we have noted that using [^{99m}Tc]HIDA, we cannot accurately evaluate patients with serum bilirubin levels above 6 mg/dl whereas [^{99m}Tc]BIDA can be used even with serum bilirubin levels >30 mg/dl (*2*).

Technetium-99m BIDA was used as an investigational drug in this study and has the advantage that more than 95% of this compound is excreted through the bile (*23*). BIDA is protein bound and this high protein binding and hepatic excretion is similar to the manner in which rose bengal is handled by the liver. The amount of renal excretion of BIDA is <5% and is not affected by hepatic function. Other IDA derivatives have a renal excretion in the range of 10–20% of administered dose (*24*). However, in patients with hepatic dysfunction, the proportion of renal excretion increases and the more severe the hepatic dysfunction, the greater the degree of renal excretion (*25*). The higher renal excretion further impairs hepatobiliary scanning and imaging because of the overlap of shadows and effect of the blood pool.

Our study yielded a sensitivity of 97.3%. There was

TABLE 2
Partially Obstructive Group

Final clinical diagnosis	No. of patients	Average S. bilirubin (mg/dl)	Confirmation of diagnosis
Choledocholithiasis	9	6.7	Operation and cholangiogram
Pancreatitis	3	3.1	Laboratory (amylase) and ultrasonography
Common bile duct stricture	2	12.2	Operation and cholangiogram
Pseudocyst—pancreas	1	6.4	Ultrasonography and barium studies
Carcinoma—gallbladder	1	19.5	Operation and biopsy
Leiomyosarcoma—stomach displacing common duct	1	5.6	Operation and biopsy
Drug induced cholestasis*	2	8.1	Liver biopsy
Sepsis*	1	2.2	History, exploratory celiotomy
Gas gangrene abdominal wall*	1	12.4	Physical findings, cultures
Alcoholic hepatitis*	1	20.59	Liver biopsy
Total	22		

*False positive.

only one false negative (2.7%). The patient had a mildly elevated bilirubin with choledocholithiasis and may very well not have had enough extrahepatic obstruction to cause a delay in appearance of the agent into the duodenum. Our false positives consist of six patients (5.76%). These patients had serum bilirubin in the range of 8.0–20.6 mg/dl. The dilution of tracer by retained bile may have caused the delay in imaging of the agent into the duodenum (*17*).

By performing a BIDA scan as the initial procedure in the workup of jaundiced patients, only 10% of the "nonobstructive" group (medical jaundice) of patients would be subjected to further diagnostic workup, whereas 90% would be treated medically after the scan results. In the "obstructive" group (surgical jaundice), all but one patient would have had further appropriate diagnostic studies before their operation. Scintigraphy, therefore, is clearly of benefit as an initial screening procedure. It has the advantages of being noninvasive and it can provide a functional evaluation of the hepatobiliary system in patients with elevated serum bilirubin. It also has the advantages over ultrasonography in these patients because dilated loops of bowel do not interfere with the imaging.

TABLE 3
Completely Obstructive Group

Final clinical diagnosis	No. of patients	Average S. bilirubin (mg/dl)	Confirmation of diagnosis
Carcinoma of pancreas	8	15.5	Operation and biopsy
Biliary atresia (extrahepatic)	7	9.4	Liver biopsy and operation
Common bile duct stricture	1	6.7	Operation
Common bile duct stenosis	1	2.4	Operation
Intra-abdominal mass obstructing common bile duct	1	3.8	Operation
Hemorrhagic pancreatitis	1	15.3	Operation
Primary biliary cirrhosis*	1	13.0	Liver biopsy
Total	20		

*False positive.

As with other noninvasive studies it is not completely infallible. A precise anatomic diagnosis is not feasible with scintigraphy. In equivocal cases, clinical features and appropriate use of other studies, both invasive and noninvasive, become important.

We feel that with a level of accuracy over 90%, biliary scintigraphy warrants serious consideration as a screening test because it offers a safe, simple procedure free from complications, for primary evaluation of jaundiced patients.

In conclusion, biliary scintigraphy is useful as an initial screening tool in differentiating jaundiced patients into nonobstructive, partially obstructive and completely obstructive groups.

FOOTNOTES

* CIS-US, Inc., Lake Success, NY.
† Siemens or General Electric.

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