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EDITORIAL

Is Morphine Injection Useful in the Scintigraphic Diagnosis of Acute Cholecystitis?

Cholescystectomy is the most common major surgical procedure performed in the United States and approximately 500,000 cholecystectomies are performed each year (*1*). With new techniques such as laparoscopic or ambulatory cholecystectomy, the number of surgical treatments for acute cholecystitis is anticipated to increase.

Biliary colic, acute cholecystitis, and chronic cholecystitis represent the spectrum of gallbladder disease. Acute cholecystitis refers to acute inflammation of the gallbladder due to generally complete obstruction of the cystic duct by an impacted stone or one attempting to pass from the gallbladder through the cystic duct and into the common duct. Acalculous cholecystitis accounts for about 5% of acute cholecystitis and is found in patients with overwhelming sepsis, prolonged starvation, cystic artery occlusion, and prolonged hyperalimentation (*2*).

Although the clinical presentation of acute cholecystitis has been well described, the symptoms can be mimicked by various pathologic conditions. The diagnosis of acute cholecystitis is particularly difficult to establish in critically ill patients. Therefore, surgeons have come to rely on imaging results to confirm or disprove clinical suspicions (*3*). Ultrasound provides information about gallbladder anatomy and shows the presence of stones with relatively high accuracy. Cholescintigraphy with ^{99m}Tc-imminodiacetic compounds is a functional test of the gallbladder and assesses the patency of the cystic duct. The persistent nonvisualization of the gallbladder in the presence of normal excretion into the small intestine is highly suggestive of acute cholecystitis in the symptomatic patient. Chronic cholecystitis is suggested when symptoms have abated and the gallbladder does not visualize. However, failure of the gallbladder to fill can be attributed not only to the obstruction of the cystic duct but also to prolonged fasting, total parenteral nutrition, pancreatitis, hepatocellular disease, alcoholism, and critical illness (*4*). False-positive cholescintigraphy has been reported in more than one-third of the critically ill patients with suspected acute cholecystitis (*3*). The mechanism for nonfilling of the gallbladder in these patients is unclear, but it may be related to altered biliary dynamics and water resorption.

In this issue of *The Journal of Nuclear Medicine*, Fink-Bennett et al. (*5*) report that morphine-augmented cholescintigraphy in 61 patients detects acute cholecystitis with a high degree of accuracy similar to conventional cholescintigraphy, yet only 1.5 hr was required to establish the diagnosis. This confirms the previous reports on the utility of morphine injection in the diagnosis of acute cholecystitis (*6,7*). Recently, Flancbaum and Alden (*8*) also reported that the use of morphine improved the diagnostic accuracy of cholescintigraphy in 68 patients, including 25 critically ill patients, from 43% to 96% and also reduced the false-positive rate from 87% to 5%. These reports include rare instances of false-negative cholescintigraphy anticipated in certain patients with acalculous cholecystitis.

Injection of morphine sulfate (0.04 mg/kg) may produce up to a ten-fold increase in resting common bile duct pressure with the contraction of the sphincter of Oddi (*6*) and thus dislodge a stone from the cystic duct by the increase in pressure resulting in flow of radiotracer into the gallbladder. Fink-Bennett et al. (*5*) demonstrated a "dilated cystic duct sign" (radiotracer within a cystic duct proximal to the obstruction site) and suggested that it is probably prudent not to augment with morphine but to obtain delayed images when a dilated cystic duct sign is present.

The false-positive rate is controversial. Fink-Bennett et al. (*5*) and Flancbaum and Alden (*8*) reported that it is low, although Fig et al. (*9*) have recently shown a rate as high as 60% in a group of seriously ill patients. Rapid biliary to bowel transit of the radiotracer or insufficient quantity of the radiotracer remaining in the hepatocytes seems to be responsible for the false-positive studies. Stasis of the gallbladder with water reabsorption from the

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bile may also cause the gallbladder to become filled with viscous bile. This may prevent entry of the radiocompounds into the gallbladder.

Because hepatic bile flow is determined by the rate at which bile acids are processed through the liver, hepatic bile flow is substantially affected by the size of the bile acid pool. The biliary tract functions as a low-pressure system with slow rates of transductal and transphincteric flow. Small differences in intraluminal pressure between the gallbladder and common bile duct are sufficient to direct flow either into or out of the gallbladder. The partition of bile flow within the common bile and cystic ducts is determined by the relative resistance of the cystic duct and sphincter of Oddi. Common duct flow is solely passive, but the cystic duct may function as a variable resistor that actively regulates flow in and out of the gallbladder. Gallbladder filling is accomplished when a minimally negative pressure gradient exists across the cystic duct. This gradient results in a pressure pump that allows bile to flow into the gallbladder. Gallbladder filling is affected by a number of factors including the rate of hepatic bile secretion, sphincter of Oddi function, cystic duct resistance, serum levels of cholecystokinin and possibly active neural inhibition. The sphincter of Oddi represents a marvelously adaptive structure that has an ejecting as well as occluding function. Sphincter contractions of any type interrupt the passive outflow of the common duct that occurs at a low pressure and cannot enter a distal segment of higher pressure. Morphine causes a marked increase in tonic pressure and amplitude as well as the frequency of phasic contractions of the sphincter of Oddi. Symptomatic partial obstruction at the sphincter of Oddi may cause clinical symptoms referable to the biliary or pancreatic tract. Frequently, organic stenosis of the sphincter of Oddi may be difficult to distinguish from the functional sphincter of Oddi dyskinesia. Moreno et al. (*10*) presented an instance of an unusual perforation of gallbladder during morphine-augmented cholescintigraphy in a patient with a large stone. Whether morphine contributed to the gallbladder perforation is debatable since the gallbladder may be perforated in 10% of patients with acute cholecystitis.

Although morphine-augmented cholescintigraphy may cause false-positive and false-negative results in some patients, depending on various factors, we agree with Fink-Bennett and colleagues that it is a rapid, useful, and relatively safe test in diagnosing the obstruction of cystic duct or excluding the diagnosis of acute cholecystitis especially in critically ill patients or patients with long fasting or parenteral nutrition.

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