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RAPID COMMUNICATION

Tc-99m ciprofloxacin imaging in acute cholecystitis

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Abstract

AIM: To evaluate the efficacy of a new nuclear imaging Infecton (Tc-99m ciprofloxacin) for the diagnosis of acute cholecystitis.

METHODS: Sixteen patients thought to have acute cholecystitis were included in this study. The diagnosis of acute cholecystitis was made based on clinical symptoms and ultrasonographic and pathologic findings.

RESULTS: The 16 patients were composed of 12 acute and 4 chronic cholecystitis patients. Twelve patients with acute cholecystitis were image-positive, including one false-positive. Four patients with chronic cholecystitis were image-negative, of whom three were true-negative. This nuclear imaging had a sensitivity of 91.7%, a specificity of 75%, a positive-predictive value of 91.7%, and a negative-predictive value of 75%.

CONCLUSION: Tc-99m ciprofloxacin imaging is easy to perform and applicable for the diagnosis of acute cholecystitis.

Key words: Acute cholecystitis; Diagnosis; Tc-99m ciprofloxacin nuclear imaging

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INTRODUCTION

Acute cholecystitis is one of the most common and major complications of gallstones. In most cases, the diagnosis of acute cholecystitis is made by ultrasonography and/or biliary scintigraphy. Although biliary scintigraphy has superior diagnositic accuracy compared with ultrasonography, ultrasonography is extensively used for the diagnosis of acute cholecystitis[1].

Ultrasonography is a useful diagnostic method for acute cholecystitis. It can identify gallstones and abnormalities of the biliary tree, such as ductal dilatation, gallbladder wall thickening, or pericholecystic fluid. But the sensitivity of the ultrasonography is low for sludge, common bile duct stone, and severe inflammation of the gallbladder. The biliary scintigraphy is a non-invasive examination and demonstrates the anatomical structure and function of the liver, gallbladder, biliary tree and duodenum. Although it is highly sensitive and specific for the acute cholecystitis, it is not applicable to emergent or seriously ill patients because it requires longer time of examination.

In this study, we introduced the Tc-99m ciprofloxacin (Infecton) scan in the diagnosis of acute cholecystitis. This radiopharmaceutical consists of the synthetic broad-spectrum quinolone antibiotic, ciprofloxacin, linked to the radiochemical technetium-99m. Ciprofloxacin is a broad-spectrum, commonly used antibiotic and active against both gram-positive and gram-negative bacteria. The main aim of this study was to evaluate the efficacy of Tc-99m ciprofloxacin imaging for the diagnosis of acute cholecystitis.

MATERIALS AND METHODS

Sixteen patients diagnosed as having acute or chronic cholecystitis based on the clinical and ultrasonographic findings were included in this study. The diagnosis of acute cholecystitis was made according to the clinical symptom, leukocytosis (> 10000/mm^3), wall thickening on the ultrasonography and the pathologic findings. The ultrasonographic criteria for the diagnosis of acute cholecystitis were a positive Murphy's sign, gallbladder wall thickness > 4 mm and gallbladder-measuring > 5 cm in length. All patients gave their informed consent.

We used a custom-formulated Tc-99m ciprofloxacin kit. Two miligrams of ciprofloxacin were mixed with stannous tartrate as a reducing agent in a 10 mL sterile serum vial, and dissolved on a vortex-gene (a shaker) for

Table 1 Clinical diagnosis of acute cholecystitis and ^{99m}Tc-Ciprofloxacin imaging results

		Clinical diagnosis of acute cholecystitis	
		Positive	Negative
^{99m}Tc-infecton	Positive image	11	1
	Negative image	1	3

3 min. Fifteen millCurie of Tc-99m were added to the vial, and incubated for 30 min at room temperature. The resultant radiopharmaceutical had a radiochemical purity of 98% and the complex was radiochemically stable over 8 h. We injected 370 MBq (10 mCi) of Tc-99m ciprofloxacin intravenously. Single photon emission computerized tomography (SPECT) images of the abdomen were obtained at about 1 h after injection.

We analyzed the correlations between the histological findings of the gallbladder, clinical findings and nuclear imaging.

RESULTS

The patients were composed of 4 males and 12 females with age ranging from 22 to 69 years. Twelve images were positive, and four were negative. No adverse reactions occurred following the administration of the radiopharmaceuticals to the patients.

All 16 patients underwent surgical intervention with laparoscopic or open cholecystectomy. Twelve patients were diagnosed as having acute cholecystitis based on clinical symptoms, radiological and pathological reports, and 4 patients diagnosed as having chronic cholecystitis.

Normal images showed high uptake in the kidneys with excretion to urinary bladder and moderate uptake in the liver and spleen. No uptake was observed in the bone or bone marrow. Abnormal images showed diffuse uptake at the sites of gallbladder (Figure 1). Of the 12 positive images, 11 were diagnosed as acute cholecystitis (Figure 1), one positive image was considered false-positive which had been on antibiotics for 5 d and acute inflammation subsided at the time of imaging. Of the 4 negative images, 3 were diagnosed as chronic cholecystitis (Figure 2) and 1 was diagnosed as acute cholcystitis (Table 1).

From these results, it was calculated that this imaging had a sensitivity of 91.7% (11/12), a specificity of 75% (3/4), a false-positive value of 25% and a false-negative value of 8.3% for detecting acute cholecystitis. We found that this imaging had a positive-predictive value of 91.7%, and a negative-predictive value of 75%.

DISCUSSION

As for the causes of acute cholecystitis, acute calculous cholecystitis occupies 90%-95% while acute acalculous cholecystitis covers the remaining 5%-10%[2]. Up to now, ultrasonography and hepatobiliary scintigraphy are considered the most useful diagnostic tests. Ultrasonography is the initial diagnostic method of choice for biliary tract disease, especially in critically-ill patients.

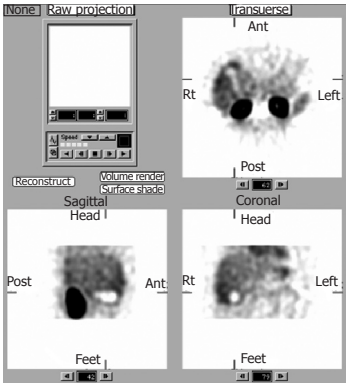

Figure 1 Tc-99m ciprofloxacin images showing increased uptake in the area of the gallbladder wall.

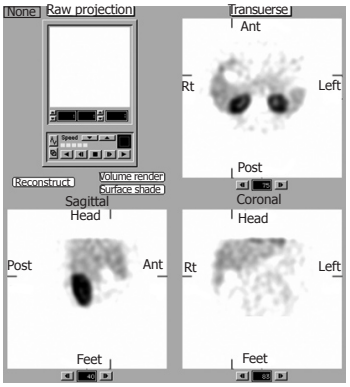

Figure 2 Tc-99m ciprofloxacin images showing no uptake in the gallbladder.

Ultrasonography is 90%-95% sensitive for gallstones. But the sensitivity of ultrasonography is low for sludge, common bile duct stone and severe inflammation of gallbladder[3]. The computed tomography is frequently used in the evaluation of biliary tract disease and other suspected intra-abdominal pathology. It is less useful than ultrasonography in evaluation of gallstone due to its lower sensitivity for gallbladder or common bile duct stones[4,5]. Yet, it is useful in evaluating complications of gallstone diseases. The diagnostic value of biliary scintigraphy is significantly superior to that of ultrasound for acute cholecystitis[1]. The biliary scintigraphy is commonly used to diagnose acute cholecystitis or bile leak after cholecystectomy. But non-visualization can also occur with prolonged fasting or chronic cholecystitis[5,6]. Furthermore, biliary scintigraphy requires longer time of the examination.

In patients with acute cholecystitis, bacterial infection is common. Enteric organisms such as *Escherichia coli*, *Enterococcus* and *Klebsiella* are commonly cultured[7,8]. Bacterial infection of the gallbladder can progress to gallbladder empyema, and gallbladder perforation may lead to a pericholecystic abscess or generalized peritonitis. Tc-99m Infecton is absorbed by various bacteria, including *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus aureus*. The ciprofloxacin is taken and bound specifically by living bacteria where it inactivates DNA gyrase[9].

Tc-99m Infecton consists of the synthetic broad-spectrum antibiotic ciprofloxacin linked to the radiochemical technetium-99m[10]. Ciprofloxacin is a broad-spectrum commonly available and active against both gram-positive and gram-negative bacteria. Tc-99m

Infecton appears to retain the property of concentrating in live bacteria. The uptake is specific, because it is not concentrated in dead bacteria or sterile abscess. But the bacteria resistant to ciprofloxacin still bind to Tc-99m Infecton. This suggests that it is likely to detect infective lesions with a high specificity[11-13]. The early Tc-99m Infecton images show predominantly renal activity as this agent is excreted through this route to the bladder. There is some blood pool activity in the liver and spleen, which is reduced in the delayed images. No activity is noted in normal bone marrow, bone, muscle or soft tissues[11].

Radiolabelled leukocyte imaging (WBC imaging) is currently the main method used for imaging for infection. They can be labeled with indium 111 (^{111}In) using either oxine or tropolone as a chelating agent or technetium 99 (^{99m}Tc) using hexamethylpropyleneamineoxime (HMPAO) as a chelating agent. The technique has the disadvantage that although it is very specific for detecting inflammatory foci, it can not distinguish between infective and non-infective inflammatory conditions[14]. An initial study of the comparison between Tc-99m Infecton and leukocytes radiolabelled with ^{111}In or Tc-99m Infecton has shown that Tc-99m Infecton is more clinically effective and specific for bacterial infection[9].

Tc-99m Infecton imaging gave a higher sensitivity (84%), specificity (96%), and accuracy (90%) compared with white-blood-cell imaging (sensitivity 81%, specificity 77%, and accuracy 79%)[9]. The high positive predictive value is of practical importance, as a positive Infecton image confirms a diagnosis of bacterial infection with a high degree of certainty[13], and was reported to be effective for the diagnosis of many other diseases such as prostatitis, pelvic inflammatory disease and seminal vesiculitis[15-17].

Tc-99m Infecton has several advantages over conventional methods of radiolabelled white-cell imaging. First, Tc-99m Infecton does not require handling of blood or blood products during preparation, thus reducing risks of hepatitis B and HIV infection. Second, Tc-99m Infecton is packaged as a kit and is technically easier and less laborious than radiolabelling white blood cells. Third, this method is independent of the white-cell status of the patient and, thus, more advantageous in evaluating leukopenic patients. Finally, because Tc-99m Infecton is not uptaken by bone marrow, the agent can identify infection in the spine and proximal parts of the limbs[9].

The early Tc-99m Infecton images show predominantly renal activity as this agent is excreted through this route to the bladder. There is some blood pool activity in the liver and spleen, which is reduced in the delayed images. No activity is noted in normal bone marrow or bone, muscle or soft tissues. The normal gastrointestinal tract bacterial flora does not show the uptake of injected Tc-99m Infecton due to the biological barriers preventing access to the intravenous agent[11,13]. The gallbladder may be seen occasionally and some bowel activity may occur in the delayed images[13].

Since only a tracer dose of ciprofloxacin (2 mg, only one two-hundredth of a single intravenous therapeutic dose of ciprofloxacin) is used in the labeling process, the risk of side effects from the Infecton was expected to be very low, if any[11-13]. No adverse effects were observed in response to the intravenous injection of Tc-99m Infecton and the technique is easy to practise.

The diagnosis of acute acalculous cholecystitis by either ultrasonography or biliary scintigraphy is more difficult than the diagnosis of acute calculous cholecystitis[6]. If the diagnosis of acute acalculous cholecystitis is still unclear after ultrasonography or CT, biliary scintigraphy may be used. However, the false-positive results (absent gallbladder filling without acute inflammation) are frequent[5]. In such cases, this imaging will play an important role in diagnosing acute acalculous cholecystitis.

The use of Tc-99m Infecton has obvious advantage of better images and shorter time to diagnose as compared with hepatobiliary scintigraphy, which requires more time by 2-8 h and sometimes has non-visualization of the gallbladder with prolonged fasting or chronic cholecystitis when Tc-99m ciprofloxacin imaging is not affected.

In conclusion, Tc-99m ciprofloxacin imaging is easy to perform and applicable in diagnosing acute calculous and acalculous cholecystitis.

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