Clinical Assessment of Differential Diagnostic Methods in Infants with Cholestasis due to Biliary Atresia or Non-Biliary Atresia

Chen DONG (董 琛)[1], Hui-yun ZHU (朱慧云)[1], Yun-chao CHEN (陈云超)[2], Xiao-ping LUO (罗小平)[1#], Zhi-hua HUANG (黄志华)[1#]

[1]Department of Pediatrics, [2]Department of Ultrasound, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China

Summary: The different methods in differentiating biliary atresia (BA) from non-BA-related cholestasis were evaluated in order to provide a practical basis for a rapid, early and accurate differential diagnosis of the diseases. 396 infants with cholestatic jaundice were studied prospectively during the period of May 2007 to June 2011. The liver function in all subjects was tested. All cases underwent abdominal ultrasonography and duodenal fluid examination. Most cases were subjected to hepatobiliary scintigraphy, magnetic resonance cholangiopancreatography (MRCP) and a percutaneous liver biopsy. The diagnosis of BA was finally made by cholangiography or histopathologic examination. The accuracy, sensitivity, specificity and predictive values of these various methods were compared. 178 patients (108 males and 70 females with a mean age of 58±30 days) were diagnosed as having BA. 218 patients (136 males and 82 females with a mean age of 61±24 days) were diagnosed as having non-BA etiologies of cholestasis jaundice during the follow-up period in which jaundice faded after treatment with medical therapy. For diagnosis of BA, clinical evaluation, hepatomegaly, stool color, serum gamma-glutamyltranspeptidase (GGT), duodenal juice color, bile acid in duodenal juice, ultrasonography (gallbladder), ultrasonography (griangular cord or strip-apparent hyperechoic foci), hepatobiliary scintigraphy, MRCP, liver biopsy had an accuracy of 76.0%, 51.8%, 84.3%, 70.0%, 92.4%, 98.0%, 90.4%, 67.2%, 85.3%, 83.2% and 96.6%, a sensitivity of 83.1%, 87.6%, 96.1%, 73.7%, 90.4%, 100%, 92.7%, 27.5%, 100%, 89.0% and 97.4%, a specificity of 70.2%, 77.5%, 74.8%, 67.0%, 94.0%, 96.3%, 88.5%, 99.5%, 73.3%, 75.4% and 94.3%, a positive predictive value of 69.0%, 72.6%, 75.7%, 64.6%, 92.5%, 95.7%, 86.8%, 98.0%, 75.4%, 82.6% and 98.0%, and a negative predictive value of 83.6%, 8.5%, 95.9%, 75.7%, 92.3%, 100%, 84.2%, 93.7%, 100%, 84.0% and 92.6%, respectively. It was concluded that all the differential diagnosis methods are useful. The test for duodenal drainage and elements is fast and accurate. It is helpful in the differential diagnosis of BA and non-BA etiologies of cholestasis. It shows good practical value clinically.

Key words: neonatal cholestasis; biliary atresia; non-biliary atresia etiologies of cholestasis; jaundice

Neonatal cholestasis can be caused by hepatic biliary atresia (BA) and non-BA etiologies[1, 2]. It is one of the most common causes of hyperbilirubinemia in infancy (including neonatal life). The incidence is 1 in 2500 live births according to Guideline for the Evaluation of Cholestatic Jaundice in Infants, etc[3–5]. It is one of the most serious conditions in infancy. Extrahepatic BA is one of the indications of liver transplantation during childhood[6]. It has been reported that 55% of patients who underwent a liver transplantation suffered from BA[7].

Chen DONG, E-mail: dongchen98@163.com
#Corresponding authors, Zhi-hua HUANG, E-mail: Zhhuang@tjh.tjmu.edu.cn; Xiao-ping LUO, E-mail: Xpluo@tjh.tjmu.edu.cn

Due to commonalities in clinical features and liver function results observed in extrahepatic BA and intrahepatic cholestasis causes, it is very difficult to differentiate between the two causes. It is a global problem. Though there are several differential diagnosis methods, few studies were about the clinical assessment of the methods. We evaluated the differential diagnosis so that to discuss the practical, easy and reliable method.

Kasai portoenterostomy is the most important treatment for extrahepatic BA[8]. The prognosis for the disease is closely related to the timing of the surgical intervention. The operation requires early diagnosis of BA[9]. Extending the life expectancy of patients is also very important. More than 80% of extrahepatic BA (EHBA) cases who undergo Kasai portoenterostomy before the 60th day of life, result in a jaundice-free outcome, as compared to only 20%–35% of cases where

the surgery was performed outside that time frame[10].

1 MATERIALS AND METHODS

1.1 Ethics Statement

The study protocol was approved by the Human Ethics Committee of the Department of Pediatrics, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. Written informed consent was obtained from the parents or guardians of all patients before the examinations.

1.2 Patients

This study retrospectively analyzed 396 patients with neonatal cholestasis who were admitted to the Department of Gastroenterology and Infectious Diseases in Pediatrics, between May 2007 and June 2011. The patients meeting the following clinical inclusion criteria were enrolled in this study: (1) existence of jaundice in infancy (including the neonatal period) without remission; (2) pale or light yellow feces; (3) hepatomegaly or hepatic texture change; (4) conjugated hyperbilirubinemia. The clinical follow-up duration exceeded more than one year.

1.3 Differential Diagnosis

Each patient was subjected to liver function testing that included alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin (ALB), total bilirubin (TB), conjugated bilirubin (CB), gamma-glutamyltranspeptidase (GGT), total cholesterol (TC), triglyceride (TG), total bile acid (TBA) and 5'-nucleotidase (5'-NT). Abdominal B-ultrasound and duodenal aspiration were also conducted. In some cases, radionuclide hepatobiliary dynamic imaging, magnetic resonance cholangiopancreatography (MRCP) and pathological examination were conducted additionally.

1.3.1 Clinical Diagnoses The subjects were diagnosed clinically as BA if: (1) The jaundice appeared in infancy (including the neonatal period) without remission. (2) The color of the feces was pale for longer than 15 days. (3) The liver was enlarged more than 3 cm or the texture change was seen.

1.3.2 Serum GGT The subjects were diagnosed as BA if the serum GGT ≥300 IU/L. The subjects were diagnosed as non-BA cholestasis if the serum GGT <300 IU/L[11, 12].

1.3.3 Abdominal Ultrasonography All patients underwent ultrasonography (US) without having been fed for a minimum of 6 h prior to the procedure. A supine position was used for all patients. It was specially noted if there was triangular cord or strip-apparent hyperechoic foci around the portal vein or its branches. US findings of triangular cord (thickness of more than 4 mm, gallbladder length of less than 15 mm, abnormal gallbladder shape, and sub-capsular flow on color Doppler US) were regarded as the diagnostic criteria of BA[13]. Other US observations resulted in the patients being diagnosed as having non-BA etiologies of cholestasis.

1.3.4 Duodenal Fluid Examination The examination was conducted with duodenal intubation (the cannula has obtained a national patent in China: ZL97241165.8) using the following procedure: (1) All the patients had not been fed for a minimum of 4 h prior to the procedure and were offered the treatment of infusion. (2) The patients were sedated orally with chloral hydrate (50 mg/kg) if they were crying or irritable. (3) A right lateral position was used. An assistant restrained the patient's head and a disposable drainage tube, with liquid paraffin applied to its tip, was then slowly inserted by the operator through the right nasal cavity. The tube passed through the nasopharynx and esophagus into the stomach where it was inserted 30–35 cm and gastric fluid outflow was observed. The duodenal intubation tube was then inserted through the pylorus into the duodenum to approximately 40 cm.

This allowed for the color of the duodenal fluid in the tube to be observed. Non-BA etiologies of cholestasis were diagnosed if yellow liquid was observed (The fluid was yellow and positive for bile acid). BA was diagnosed if the yellow fluid could not be collected after discontinuous 24 h or 48–72 h of drainage during which the subject was fed timeously and quantitatively and at the same time it was confirmed by X-ray if the end of the drainage tube was in the middle or lower duodenum. Alternative observations were diagnosed as BA.

1.3.5 Radionuclide Hepatobiliary Dynamic Imaging Before the radionuclide hepatobiliary dynamic imaging examination, each subject was sedated orally with chloral hydrate (50 mg/kg). All the above examinations were performed without the patients having been fed for a minimum of 4 h prior to the procedure. The supine position was used for all patients and they were examined using a single photon emission computed tomography (SPECT) machine (Starcam XP/T400 produced by the GE Co., USA), after intravenous injection of ^{99m}Tc-labeled diethylacetanilide-iminodiacetic acid. The frame rate was 1 frame/60 s and 30 frames in total. The matrix was 128×128. The magnification was 1.33 times. A static image at 1 h post-injection was then acquired. The 2-, 4-, 8-, 12-, and 24-h delayed images were acquired if no distribution of radio-element was found in the intestine at 1 h, so as to observe the anatomical structure and excretory function of the biliary tract. The dynamic imaging was stopped until the radio-element appeared in the intestine. The diagnostic criterion for non-BA etiologies of cholestasis was the observation of the radio-element in the intestine. Normal uptake function with no observation of the radio-element in the intestine was regarded as the diagnostic criterion of BA.

1.3.6 MRCP Before the MRCP examination, each subject was sedated orally with chloral hydrate (50 mg/kg). All MRCP examinations were performed on patients without them having been fed for a minimum of 6 h prior to the procedure. The supine position with the feet-advanced was used for all patients. The studies were performed with a 1.5-T magnetic resonance imaging (MRI) unit (Signal Propeller HD; GE Medical Systems, USA). Images were obtained in both the axial and coronal planes. The routine axial-plane T2-weighted images (TR/TE=3000/80 ms) and T1-images (TR/TE=400/8 ms), with fast-spin echo-accelerated pulse sequence, were obtained. The scan took about 5 min. The extrahepatic central biliary ducts (including the

right, left and common hepatic ducts), common bile duct and gallbladder could be described clearly. The field of view was 34 cm. Images were obtained in both the axial and coronal planes. The echo time was 2000 ms[14].

The following criteria were defined to interpret the MRCP findings. Non-BA cholestasis were diagnosed if the normal left and right hepatic duct, common bile duct and gallbladder were clearly observed. BA was diagnosed if the common bile duct could not be delineated, regardless of whether the gallbladder was present. The MRCP images were interpreted in consensus by two experienced pediatric radiologists, who were blinded to the clinical information.

1.3.7 Hepatic Pathologic Examination 178 patients underwent pathological examination. Liver wedge biopsy specimens (0.5 cm×0.5 cm×0.5 cm) were routinely obtained from 142 patients at the time of operation and the other 36 specimens were obtained by liver biopsy. All specimens were fixed in 10% formalin, embedded with paraffin and stained with HE for immunohistochemistry observation. The specimen samples obtained were reviewed and final diagnosis was made by two pathologists.

All the samples were analyzed with microscopic examination as follows: The degree of hepatocyte giant cell change, the degree of cholestasis of the hepatocyte and bile canaliculi, the degree of inflammation of the hepatocyte and portal area, the degree of biliary cast formation and hyperplasia of intrahepatic bile ducts, the degree of the fibrosis of the portal area and the extra-medullary hematopoiesis (EMH).

The diagnostic criteria of non-BA cholestasis are lobular disarray and inflammatory cells are seen within the portal area, and the bile ductules show little or no alteration[1]. The diagnosis for BA is made if the main pathological changes are bile duct proliferation, bile plugs, portal or perilobular fibrosis and edema, with preservation of the basic hepatic lobular architecture[1].

1.4 Statistical Analyses

Statistical analyses were performed using the IBM SPSS ver. 11.5. To show differences between groups we used a Fisher's exact test and Student's *t* test as indicated. $P<0.05$ was considered significant.

2 RESULTS

2.1 General Data

There were 396 cholestatic infants in the study. 178 patients (108 males and 70 females with a mean age of 58±30 days) were diagnosed as having BA and diagnosis was confirmed by cholangiography or histopathologic examination. 218 patients (136 males and 82 females with a mean age of 61±24 days) were diagnosed as having non-BA cholestasis and the diagnosis was made during the follow-up period in which jaundice faded after treatment with medical therapy. 226 (57.1%) cases including 55 cases of non-BA and 171 cases of BA had pale yellow or pale colored feces. Furthermore, 170 (42.9%) cases including 163 cases of non-BA and 7 cases of BA had normal-colored feces (table 1).

Table 1 Comparison of various diagnostic methods for non-BA etiologies of cholestasis and BA

Methods	Patients (*n*)	Results	Final diagnosis				*P*
			BA (*n*=178)		Non-BA cholestasis (*n*=218)		
			n	%	*n*	%	
Clinical evaluation	396	BA	148	83.1	65	29.8	
		INH	30	16.9	153	70.2	<0.001
Hepatomegaly	396	>3 cm	156	87.6	49	22.5	
		<3 cm	22	12.4	169	77.5	<0.001
Stool color	396	Pale yellow or pale	171	96.1	55	25.2	
		Yellow or light yellow	7	3.9	163	74.8	<0.001
Serum GGT	347	≥300 U/L	115	73.7	63	33.0	
		<300 U/L	41	26.3	128	67.0	<0.001
Duodenal juice color	396	Pale yellow or pale	161	90.4	13	6.0	
		Yellow or light yellow	17	9.6	205	94.0	<0.001
Bile acid in duodenal juice	396	Negative	178	100	8	3.7	
		Positive	0	0	210	96.3	<0.001
Ultrasonography (gallbldder)	396	Absence	165	92.7	25	11.5	
		Presence	13	7.3	193	88.5	<0.001
Triangular cord or strip-apparent hyperechoic foci		Presence	49	27.5	1	0.46	
		Absence	129	72.5	217	99.54	<0.001
Hepatobiliary scintigraphy (radioactivity in the bowel)	347	Absence	156	100	51	26.7	26.7
		Existence	0	0	140	73.3	<0.001
MRCP (gallbladder)	273	Absence	138	89.0	29	24.6	
		Existence	17	11.0	89	75.4	<0.001
Liver biopsy	207	BA	150	97.4	3	5.7	
		INH	4	2.6	50	94.3	<0.001

2.2 Accuracy, Sensitivity and Specificity of Various Diagnostic Methods

In our study, bile acid in duodenal juice showed the highest accuracy (98.0%). Bile acid in duodenal juice and hepatobiliary scintigraphy showed the highest sensitivity (100%). Ultrasonography (triangular cord or strip-apparent hyperechoic foci) showed the highest specificity (99.5%). The results are shown in table 2.

Table 2 Accuracy, sensitivity and specificity of various diagnostic methods for BA and non-BA etiologies of cholestasis

Diagnostic methods	Accuracy for BA and non-BA etiologies of cholestasis		Sensitivity for BA		Specificity for BA	
	n	%	*n*	%	*n*	%
Clinical evaluation	301/396	76.0	148/178	83.1	153/218	70.2
Hepatomegaly	205/396	51.8	156/178	87.6	169/218	77.5
Stool color	334/396	84.3	171/178	96.1	163/218	74.8
Serum GGT	243/347	70.0	115/156	73.7	128/191	67.0
Duodenal juice color	366/396	92.4	161/178	90.4	205/218	94.0
Bile acid in duodenal juice	388/396	98.0	178/178	100	210/218	96.3
Ultrasonography (gallbladder)	358/396	90.4	165/178	92.7	193/218	88.5
Ultrasonography (triangular cord or strip-apparent hyperechoic foci)	266/396	67.2	49/178	27.5	217/218	99.5
Hepatobiliary scintigraphy	296/347	85.3	156/156	100	140/191	73.3
MRCP	227/273	83.2	138/155	89.0	89/118	75.4
Liver biopsy	200/207	96.6	150/154	97.4	50/53	94.3

2.3 Positive and Negative Predictive Values of Various Diagnostic Methods

In our study, ultrasonography (triangular cord or strip-apparent hyperechoic foci) and liver biopsy showed the highest positive predictive values (98.0%). Bile acid in duodenal juice and hepatobiliary scintigraphy showed the highest negative predictive values (100%). The results are shown in table 3.

Table 3 Positive and negative predictive values (PV) of various diagnostic methods in BA and non-BA etiologies of cholestasis

Diagnostic methods	Positive (PV) for BA and negative (PV) for non-BA etiologies of cholestasis		Negative (PV) for BA and positive (PV) for non-BA etilolgies of cholestasis	
	n	%	*n*	%
Clinical evaluation	147/213	69.0	153/183	83.6
Hepatomegaly	156/215	72.6	169/191	8.5
Stool color	171/226	75.7	163/170	95.9
Serum GGT	115/178	64.6	128/169	75.7
Duodenal juice color	161/174	92.5	205/222	92.3
Bile acid in duodenal juice	178/186	95.7	210/210	100
Ultrasonography (gallbladder)	358/396	90.4	165/178	92.7
Ultrasonography (triangular cord or strip-apparent hyperechoic foci)	165/190	86.8	193/206	84.2
Hepatobiliary scintigraphy	156/207	75.4	140/140	100
MRCP	138/167	82.6	89/106	84.0
Liver biopsy	150/153	98.0	50/54	92.6

3 DISCUSSION

Neonatal cholestasis can be caused by BA and non-BA etiologies. BA is a cholangio-destructive disease affecting both the intra- and extra-hepatic biliary tract[15]. The incidence is higher in Japan and China (1 in 9600) than in Europe and the UK (1 in 16000)[16, 17].

A retrospective analysis of 82 infants with cholestasis from January 2009 to April 2013 reported that BA was the most common diagnosis (41%), followed by idiopathic cases (13%), progressive familial intrahepatic cholestasis (PFIC, 10%), cholestasis in preterm infants (10%), α1-antitrypsin (α1-AT) deficiency, Alagille syndrome, portocaval shunts, mitochondriopathy, biliary sludge (all 2%), and others[18].

Not only BA, but some intrahepatic cholestatic disorders such as intrahepatic biliary hypoplasia (Alagille disease), progressive familial intrahepatic

cholestasis, sclerosing cholangitis (primary, neonatal, secondary) and Langerhans cell histiocytosis are all indications for pediatric liver transplantation. Therefore finding a reliable method for early differential diagnosis is an important topic concerned with both pediatrics and surgery.

Detailed history plays a critical role, including the onset and changes of the jaundice, feces color. Moreover, physical examination such as liver and spleen size through palpation, the presence or absence of ascites and so on is important.

The jaundice of the BA patients appeared in infancy (including the neonatal period) without remission and progressively worsened. The cholestasis patients' feces have different colors such as yellow, light yellow, pale yellow or pale. We should consider the diagnosis of BA if the clay-colored feces persist for longer than one week. While a few patients' feces may be yellow within the first few days after birth, and then changed to a clay color. If the liver injury is severe and high levels of bilirubin occur, the bilirubin can seep into the intestinal lumen and the stool will be light yellow or pale yellow. Therefore, it is sometimes not accurate to diagnose the BA based solely on the color of the stool. A retrospective analysis on 62 infants with cholestasis reported that 94.7% of the BA patients' feces were clay colored, as compared to 56.5% of the non-BA etiologies of cholestasis patients[19].

Our study showed that 226 of 396 patients were initially considered to have BA by observing feces color, of which 171 patients were later confirmed as BA and 55 patients did not have BA. The diagnostic accuracy by feces color was 84.3% with 96.1% of sensitivity and 74.8% of specificity.

GGT is usually elevated during cholestasis. BA usually presents with a high GGT. While non-BA cholestasis patients sometimes present with normal or low GGT[1].

In this study, bile samples were collected through duodenal dynamic drainage testing. The color of the bile and the presence of bile acid in duodenal fluid were recorded so as to confirm an unobstructed bile duct. This was applied to the differential diagnosis of BA and non-BA etiologies of cholestasis.

The color of the drainage is similar to that of the feces of the patients. The drainage regardless of the different colors such as yellow, light yellow, pale yellow or pale is observed. The first two colors directly prove that the bile duct is unobstructed. The latter two colors result from severe edema, necrosis, apoptosis of the hepatocyte, cholestasis of bile canaliculi, impaired bile drainage or BA. Bile samples should be collected dynamically and continuously. The concentration of bile acid should be measured. BA should be excluded if only bile acid is observed in the duodenal fluid.

It is reported that the diagnostic sensitivity for duodenal dynamic drainage testing was 97.3%, the specificity was 93.7%, the negative predictive value was 92.3%, and the positive predictive value was 98.5%[20].

Our study showed that the diagnostic sensitivity for bilirubin-positive duodenal drainage was 90.4%, specificity was 94.0%, and accuracy was 92.4%. The diagnostic sensitivity for bile acid-positive duodenal drainage was 100%, specificity was 96.3% and accuracy was 98.0%. The results further proved that the method was characterized by its simple, reliable and rapid performance.

Furthermore, we observed that the duodenal fluid of a few non-BA etiologies of cholestasis patients stayed white because of the serious cholestasis of the bile canaliculi, hepatic cell injury and only turned to yellow after treatment for several days to several weeks. Therefore it should be dynamically checked so that to avoid false positive reactivity and false negative reactivity.

A retrospective analysis showed that the sensitivity and the specificity for abdominal B-ultrasound were high. The sensitivity for triangular cord or strip-apparent hyperechoic foci was 87.4%, the specificity was 89.7%, and the accuracy was 86.9%[21]. Our study showed that the sensitivity for triangular cord or strip-apparent hyperechoic foci was 27.5%, the specificity was 88.5%, and the accuracy was 67.2%. The study also showed that if the BA was diagnosed based on the absence of gallbladder, the sensitivity was 27.5%, the specificity was 99.5%, and the accuracy was 67.2%. Thus it was not reliable to diagnose BA based solely on the absence of the gallbladder.

If the healthy liver undergoes ^{99m}Tc-labeled diethylacetanilide-iminodiacetic acid hepatobiliary scintigraphy, ^{99m}Tc-EHIDA can distribute uniformly in the liver after hepatocyte intake. It will then make its way into the bile ducts after a short stay in the liver. Finally it is excreted into the intestine through the biliary system. Intense bowel radioactivity occurs depending on the normal uptake, secretion and excretion function of the liver. The diagnosis of BA is made based on whether there is radioactivity in the bowel. Our study showed that the sensitivity of scintigraphy was 100%, the specificity was 73.3%, and the accuracy was 85.3% in detecting an obstruction[22].

It was reported that MRCP could be used to diagnose neonatal cholestasis. Jaw found that small gallbladders (0.8–1.4 cm) were detected by MRCP on 6 cases of BA diagnosed surgically. Only one patient had a dilated bile duct, while the others' cystic ducts or common hepatic ducts could not be observed. The intrahepatic bile ducts in 2 patients could be partially observed. Larger gallbladders (1.4–4.5 cm) were observed by MRCP on 9 patients with infantile hepatitis. Cystic ducts, common hepatic ducts and intrahepatic bile ducts could be clearly observed, while in the case of an absence of gallbladder, only the cystic duct and the common hepatic duct were observed in MRCP[23].

It is reported that the diagnostic sensitivity for MRCP is 90%, the specificity is 77%, and the accuracy is 82%[24]. Our study showed that the sensitivity of MRCP in detecting an obstruction was 89.0%, the specificity was 75.4%, and the accuracy was 83.2%. The results of the two are comparatively similar. Therefore, a diagnosis of BA should be considered if the cystic duct or common hepatic ducts could not be observed by MRCP. Other methods should be used for differential diagnosis if an isolated and large gallbladder was observed by MRCP[24]. MRCP is influenced by the level of image diagnosis and the age of the patient,

economic conditions, so it is feasible.

Liver biopsy examination has for long been considered as one of the most reliable methods for the differential diagnosis of EHBA and non-BA etiologies of cholestasis[19, 25].

Kahn reported that during the early stage of the diseases course, cholestasis could be seen in the hepatocytes and small bile ducts. Edema of the portal area, bile duct proliferation, and granulocyte and lymphocyte infiltration could occur. Hepatocyte metaplasia to cholangiocytes and connection to the proliferated bile ducts around the portal areas can be observed in some cases. During the late stage, fibrosis could occur in the portal area and its surroundings. Stricture and atresia of the bile ducts and formation of regenerative nodules of hepatocytes could also occur and progress to biliary cirrhosis, fibrosis of extrahepatic bile ducts and proliferation of intrahepatic bile ducts[25]. Before the 40th day of the diseases course, proliferation of bile ducts, fibrosis of the portal area and cholestasis occur. Sixty days later, dilatation of the biliary ducts at the portal area, proliferation of small bile ducts, hyperplasia of fibrous tissue and biliary cirrhosis would occur[26]. Therefore, hepatic pathological findings were chronic inflammation. We should dynamically observe this so as to diagnose BA early. Kahn reported that the diagnostic sensitivity was 88.0%, the specificity was 94.0%, and the accuracy was 92.0%[26]. Our study showed that the sensitivity of pathology in detection of an obstruction was 97.4%, the specificity was 94.3%, and the accuracy was 96.6%, which indicated that some cases require dynamical observation.

By comparison of different diagnostic methods, we believe duodenal fluid examination can determine the presence or absence of bile. It is a reliable differential diagnosis method. It is simple, rapid, safe and economical while it is influenced by drainage technique. Abdominal B-ultrasound can be used to exclude choledochal cysts and stones. The hepatic uptake and excretion function can be determined through ^{99m}TC-EHIDA.

The degree of cholestasis, hepatocyte injury and bile duct proliferation can be observed through a liver biopsy examination.

Therefore, all the differential diagnosis methods are useful. The duodenal juice color and elements test is fast and accurate. It is helpful in the early differential diagnosis of BA and non-BA etiologies of cholestasis. Cholangiography and histopathologic examination are reliable for the differential diagnosis of BA and non-BA etiologies of cholestasis.

Conflict of Interest Statement

The authors have indicated that they have no potential conflicts of interest to disclose.

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