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Clinical Significance of Duodenal Bile Acids in Differential Diagnosis for Infantile Jaundice -Duodenal Intubation in Infants with Cholestatic Jaundice-†

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= Abstract = **We evaluated the effectiveness of bile in duodenal fluid collected by intubation from neonates with severe cholestasis to differentiate biliary atresia. Eighty five infants with cholestatic jaundice and acholic stools were studied prospectively from November 1985 to July 1992. Forty nine patients had biliary atresia, 34 neonatal hepatitis, and 2 intrahepatic bile duct paucity. Almost all (47 of 49 infants) of the biliary atresia patients did not show bile in the duodenal fluid and most of the neonatal hepatitis cases (29 of 34 patients) revealed bile in the juice, whereas only 8 of 32 neonatal hepatitis patients demonstrated bowel radio-activity on DISIDA scan. Seventy six of 85 cholestatic jaundice patients could be diagnosed correctly by duodenal intubation bile study, and only 8 of 83 patients could be diagnosed by DISIDA scan only in this study. When DISIDA and duodenal intubation were carried out simultaneously, we could confirm the correct diagnosis in 77 of 83 patients before liver biopsy and operative cholangiogram. During the study, intubation did not cause any complication at all. These data suggest that duodenal intubation must be a superior method for the differentiation of cholestatic jaundice patients, and, moreover, it is simple, rapid and cheap.**

Key Words: *Bile acid, Biliary atresia, Duodenal intubation, Duodenal fluid, DISIDA scan, Neonatal cholestasis*

INTRODUCTION

Differential diagnoses between severe neonatal hepatitis and congenital biliary atresia are often difficult, but early and positive differentiation between biliary atresia and neonatal hepatitis is essential not only to select patients for surgery but also to avoid unnecessary surgery in patients with neonatal hepatitis (Alagille 1979; Wright *et al.* 1981; Markowitz *et al.* 1983; Manolaki *et al.* 1983; Balistreri 1985; Ferry *et al.* 1985). Numerous diagnostic tests have been employed to reduce unnecessary exploration and no single test is considered to be diagnostic except biopsy which is sometimes hard to perform (Poley *et al.* 1978; Fung *et al.* 1985; Schwartz 1985; Tazawa *et al.* 1986; el Tumi *et al.* 1987; Spivak 1988; Treem *et al.* 1988; Torris *et al.* 1990; Burton *et al.* 1990; Maggiore *et al.* 1991). Hepatic scintigraphy is widely used but the absence of intestinal radio-activity can not definitely prove

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the presence of biliary tract obstruction (Dick *et al.* 1986; Cox *et al.* 1987; Spivak *et al.* 1987; Majd *et al.* 1988; Rosenthal *et al.* 1989; Miller *et al.* 1980).

Many authors have been using the absence of bile acids in the duodenal fluid as an indication that bile duct is obstructed completely and that biliary atresia is the likely diagnosis (Hashimoto *et al.* 1978; Greene 1979; Yamashiro *et al.* 1983; Rosenthal *et al.* 1985, 1987, 1989, 1990).

We designed this study to evaluate the usefulness of duodenal intubation in early diagnosis of biliary atresia from cholestatic jaundice infants comparing traditionally used techniques such as DISIDA scan, biopsy and cholangiogram.

We collected duodenal fluid for 24 hours continuously in eighty-five cholestatic jaundice patients with acholic stools from November 1985 to July 1992 (during 80 months). Tc 99m DISIDA scan was also carried out simultaneously to compare the diagnostic accuracy. The prospective study of duodenal fluid interpretation for the presence of bile is superior to DISIDA scan for information which can lead to rapid surgical treatment for biliary atresia.

PATIENTS AND METHODS

Eighty-five infants who had cholestatic jaundice and acholic stools, and who could not be differentiated as biliary atresia or neonatal hepatitis with ease by usual manner were studied (Table 1). The jaundiced patients who had bile pigments in the stool or who had other diseases of cholestasis were not included.

After the initial sampling blood for diagnostic evaluation and securing intravenous lines for fluid and electrolyte replacement, a radiopaque feeding tube (No. 8 French) was positioned fluoroscopically in the second portion of the duodenum. The procedures for duodenal intubations were relatively easy and there were no failures in intubation and location. The intubations themselves were safe and no complications were found. During the 24 hours of duodenal fluid collection, the infants were given nothing by mouth. Duodenal fluid was collected by gravity drainage in glass tubes and specimens were separated into two-hour aliquots. The fluids from the collections were examined for the presence of bilirubin and bile acids by the Ictotest^{R} (Hanil phar. co., Seoul, Korea). Absence of bile in duodenal fluid for twenty four hours was considered negative (no excretion of bile to the duodenum). Tc 99m DISIDA scan was carried out simultaneously. The diagnosis of congenital biliary atresia was made by liver biopsy and/or exploration (intraoperative cholangiogram), and of neonatal hepatitis by liver biopsy, subsequent clinical course and final recovery.

RESULTS

Of the 85 patients with acholic stools and cholestatic jaundice, 49 patients were biliary atresia and 34 were neonatal hepatitis (Table 1).

Most of the bile acid negative duodenal fluids were congenital biliary atresia (47 of the 54 patients) but 5 patients were hepatitis. The bile positive duodenal fluids were mainly neonatal hepatitis (29 of 31 patients), however, to our surprise, two of them were biliary atresia, which were confirmed by intraoperative cholangiogram (Table 2).

DISIDA scan alone could have confirmed

Table 1. Age and sex at the time of diagnosis

	Total	Biliary atresia	Neonatal hepatitis	Intrahepatic duct paucity
Number of patients	85	49	34	2
Mean age (week)	10.85	12.44	8.44	6.29
Male:female	43/42	21/28	21/13	1/1

Table 2. Bile in duodenal fluid

	Total	Biliary atresia	Neonatal hepatitis	Intrahepatic bile duct paucity
Positive	31 (100%)	2 (6.45%)	29(93.55%)	0 (0%)
Negative	54 (100%)	47 (87.04%)	5(9.26%)	2 (3.70%)
Total	85	49	34	2

Table 3. Intestinal excretion in DISIDA scan

	Total	Biliary atresia	Neonatal hepatitis	Intrahepatic bile duct paucity
Excretion (+)	8 (9.64%)	0 (0%)	8 (25.0%)	0 (0%)
Excretion (−)	75 (90.36%)	49 (100%)	24 (75.0%)	2 (100%)
Total	83 (100%)	49 (100%)	32 (100%)	2 (100%)

Table 4. Comparison DISIDA scan with intubation

	Total	Biliary atresia	Neonatal hepatitis	Intrahepatic bile duct paucity	Total
Group A	53(63.87%)	47(88.68%)	4(7.55%)	2(3.77%)	53(100%)
Group B	22(26.50%)	2(9.09%)	20(90.91%)	0(0%)	22(100%)
Group C	1(1.20%)	0(0%)	1(100%)	0(0%)	1(100%)
Group D	7(8.43%)	0(0%)	7(100%)	0(0%)	7(100%)
Total	83(100%)	49	30	2	83

group A: bile (−) in duodenal intubation and Intestinal excretion (−) in DISIDA scan
group B: bile (+) in duodenal intubation and Intestinal excretion (−) in DISIDA scan
group C: bile (−) in duodenal intubation and Intestinal excretion (+) in DISIDA scan
group D: bile (+) in duodenal intubation and Intestinal excretion (+) in DISIDA scan

hepatitis in only 8 of the 32 neonatal hepatitis patients. Although we could not find any false positives, we could not differentiate severe hepatitis from atresia by means of DISIDA scan alone in most of the cases (75 of 83 patients). Confirming the intestinal radio-activity by DISIDA scan was useful in excluding biliary atresia, but it may make for a lot of unnecessary surgical procedures without other confirmatory diagnostic studies (Table 3).

Forty seven of 49 biliary atresia patients showed absence of bile in duodenal fluid and intestinal activity in DISIDA scan at the same time. Four of 30 neonatal hepatitis patients did not demonstrate bile secretion in both methods.

Duodenal intubation was superior to DISIDA scan in distinguishing hepatitis from atresia. In 20 of the 30 neonatal hepatitis cases, intestinal activities were not found in DISIDA but bile was noticed in the duodenal fluid. Only in one case of hepatitis, did DISIDA show the activity despite the absence of bile in the duodenal juice (Table 4).

Interestingly we found two intrahepatic bile duct paucity patients. They looked like biliary atresia in both duodenal intubation and DISIDA scan.

DISCUSSION

Our study demonstrates that detection of the bile in duodenal juice from duodenal intubation is a simple and accurate method to

assess infants with cholestasis (Greene *et al.* 1974; Hughes *et al.* 1980). The duodenal intubation itself was carried out with ease without complications (Hashimoto *et al.* 1978). Visually yellow colored duodenal fluid collected via the duodenal intubation indicated the presence of bile in the intestinal lumen. However, we experienced a few unexpected cases: when we prescribed cholestyramine before intubation, the juice looked slightly yellow, but Ictotest was negative. We found no more yellow duodenal fluid after the discontinuation of cholestyramine. We can confirm previous reports that yellow pigmented duodenal fluid obtained by string test indicates the presence of bile in the duodenum. However the absence of bile in the duodenal juice does not absolutely indicate biliary atresia, it only indicates impairment of bile flow. In our cases only 87% of negative-bile patients were biliary atresia.

In this study, we have been surprised to find bile positive biliary atresia by duodenal intubation. The duodenal fluid was not only yellow colored but also positive by Ictotest. The bile free succus entericus may be yellow and may contain bilirubin in some degree when a patient has high serum bilirubin levels (Hashimoto *et al.* 1978). The Ictotest, we used, can not differentiate bile acid from bilirubin. We think that this yellow color must be leaked or escaped bilirubin from the intestinal mucosae. A more precise method which can check only bile acid such as chromatography may be more desirable.

The string test for the collection of duodenal fluid may not be superior to intubation (Korman, 1990). By string test we could collect only small amounts and could not see the fluid color till the removal of the string. Moreover it must be hard to estimate the suitable time for duodenal fluid collection. We can stop duodenal fluid collection as soon as we find bile in it or we can prolong the collection time on suspicion of severe hepatitis.

The present study demonstrates the utility of the simultaneous administration of duodenal juice collection and hepatobiliary scintigraphy. No one test can actually differentiate extrahepatic and intraheptic causes of cholestasis in all patients (Jaw *et al.* 1984; Hussein *et al.* 1991). When we interpreted only duodenal juice collected by duodenal intubation, we could not differentiate biliary atresia and hepatitis in only 7 cases of the 85 cholestasis. In conjunction with DISIDA scan, we missed only 6 patients (2 biliary atresia and 4 neonatal hepatitis). They were confirmed by liver biopsy or cholangiogram. We could differentiate 8 cases from 32 true neonatal hepatitis in this study when only DISIDA scan results were used. The lower accuracy of DISIDA scan resulted from the fact that only severe neonatal hepatitis cases which were not easily distinguished from biliary atresia were sampled in this study.

In summary, the results of the present study suggest that duodenal intubation and analysis of bile acid in the duodenal juice is a useful maneuver in the initial evaluation of patients with obstructive jaundice and acholic stools. It is a simple, rapid, cheap, and relatively accurate method to evaluate neonatal jaundice. Most important of all, you don't need complicated expensive facilities.

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