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Evaluation of the use of laparoscopic-guided cholecystocholangiography and liver biopsy in definitive diagnosis of neonatal cholestatic jaundice

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ABSTRACT

Background: Once it is established that a jaundiced infant has direct hyperbilirubinemia, the principal diagnostic concern is to differentiate hepatocellular from obstructive cholestasis. Traditional tests such as ultrasonography, percutaneous liver biopsy and technetium 99 m hepatobiliary iminodiacetic acid (HIDA) scan are often not sufficiently discriminating. Definitive exclusion of biliary atresia (BA) in the infant with cholestatic jaundice usually requires mini-laparotomy and intra-operative cholangiography. This approach has many drawbacks because those sick infants are subjected to a time-consuming procedure with the probability of negative surgical exploration. **Aim of the Study:** The aim of this study was to determine the feasibility of laparoscopic-guided cholecystocholangiography (LGCC) and its accuracy and safety in the diagnosis of BA and thus preventing unnecessary laparotomy in infants whose cholestasis is caused by diseases other than BA. **Patients and Methods:** Twelve cholestatic infants with direct hyperbilirubinemia subjected to LGCC (age, 7–98 days; mean, 56 days) after ultrasound scan and (99 mTc) HIDA scan and percutaneous liver biopsy failed to provide the definitive diagnosis. **Results:** One patient had completely absent gall bladder (GB) so the laparoscopic procedure was terminated and laparotomy was done (Kasai operation). Four patients had small size GB; they underwent LGCC that showed patent common bile duct with atresia of common hepatic duct, so laparotomy and Kasai operation was performed. Seven patients had well-developed GB, LGCC revealed patent biliary tree, so laparoscopic liver biopsies were taken for histopathology. Five of those patients had neonatal hepatitis, and two had cholestasis as a complication of prolonged TPN. No perioperative complications or mortalities were recorded. **Conclusion:** When the diagnosis neonatal cholestasis remains elusive after traditional investigations, LGCC is an accurate and simple method for differentiating BA from hepatocellular causes.

Key words: Biliary atresia, laparoscopy, neonatal cholestatic jaundice

INTRODUCTION

Neonatal cholestasis is generally defined as prolonged conjugated hyperbilirubinemia that occurs in neonatal period and lasting more than 2 weeks.[1-3] The clinical presentation varies little irrespective of the aetiology.[4] Early definitive diagnosis is an important step because success rate of surgical intervention, if required, is inversely proportionate to the age of the patient. This is particularly relevant in extrahepatic biliary atresia (BA).[3-5]

For definitive diagnosis in patients with prolonged cholestasis, a series of investigations are needed.[2,4,6] Ultrasonography, hepatobiliary scintigraphy, endoscopic retrograde cholangiopancreatography (ERCP) and fine needle or true cut needle liver biopsy are usually performed.[7-11] Despite all these investigations the exact diagnosis my remain elusive and minilaparotomy

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is mandatory to perform open cholangiogram and liver biopsy to reach the final diagnosis. In the era of laparoscopy, this surgical exploration can be omitted and replaced by a minimally invasive procedure.[3] Laparoscopic cholecystocholangiography is an alternative option in such doubtful cases.[3-5]

The aim of this study is to evaluate the feasibility, safety and accuracy of laparoscopic-guided cholecystocholangiography (LGCC) in our institution in the diagnosis of questionable cases of neonatal cholestatic jaundice.

PATIENTS AND METHODS

This study was conducted in paediatric surgery departments in Asser central hospital and Abha Maternity and children hospital in Saudi Arabia during the period from February 2013 to October 2015. The study included 12 infants with prolonged, more than 2 weeks, conjugated hyperbilirubinemia (total bilirubin <5 mg/dl and the conjugated fraction was more than 1 mg/dl or total bilirubin was more than 5 mg/dl with the conjugated fraction more 20%). Their ages ranged from 7 to 98 days, mean 56 days. They were referred from paediatric medical department and neonatal intensive care unit to exclude BA. All patients were thoroughly investigated by detailed biochemical and metabolic workup, repeated abdominal US scan and radioisotope biliary excretion scan. However, extrahepatic BA could not be differentiated from other causes of neonatal cholestasis. Diagnostic laparoscopy was performed for all cases of this study and LGCC was done once the gall bladder (GB) was visualised. Liver biopsies were taken in all cases at the end of the procedure.

Under general anaesthesia, pneumoperitoneum (6–8 mmHg) was created by open Hasson technique through an infraumbilical small incision using a 5 mm trocar and cannula. The liver and GB were visualised using 5 mm, 30° camera. When the GB was atretic and the liver appeared greenish brown, coarse irregular with a rounded inferior edge, we progressed directly to laparotomy and surgery. When the GB was present with reasonable size, two 5 mm trocars were inserted to execute cholangiography laparoscopically to prove or disprove the patency of intra- and extra-hepatic biliary system. The second trocar was inserted at the left hypochondrium, and the third trocar was inserted one cm below the second one [Figure 1].

Under direct vision, a cannula 16 gauge was inserted through the skin of right hypochondrium into the GB [Figure 2]. The contrast material, diatrizoate 50% (3,5-diacetamido-2,4,6-triiodobenzoic acid), was injected through the cannula and serial X-ray films were taken [Figure 3]. If the biliary system was occluded, with no passage of dye into the extrahepatic biliary tract, the case was diagnosed as BA, and we proceeded to laparotomy and surgery. However, if the dye passed freely through the upper and lower biliary tract, the procedure was terminated by taking a liver biopsy from the lower edge of the liver for histopathological diagnosis.

RESULTS

Twelve cholestatic infants with direct hyperbilirubinemia underwent laparoscopic exploration under general anaesthesia after the other investigations failed to provide a definitive diagnosis, and they were managed according to the findings. One patient had completely absent GB, so the laparoscopic procedure was terminated and laparotomy was done (Kasai operation). Four patients had small size GB; they underwent LGCC that showed patent common bile duct with atresia of the common hepatic duct, so laparotomy and Kasai operation was performed. Seven patients had well-developed GB, LGCC revealed patent biliary tree, so laparoscopic liver biopsies were taken for histopathology. Five of those patients had neonatal hepatitis, and two had cholestasis as a complication of prolonged TPN [Table 1]. No perioperative complications or mortality were observed in the patients of this study.

DISCUSSION

The evaluation of infants with suspected BA is challenging because no single pre-operative investigation enables the diagnosis to be made with certainty. Liver

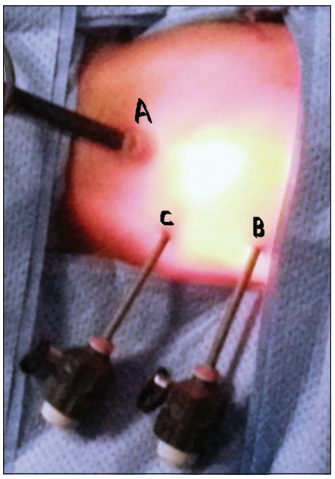

Figure 1: Sites of laparoscopic ports. A - for camera, B and C - for working instruments

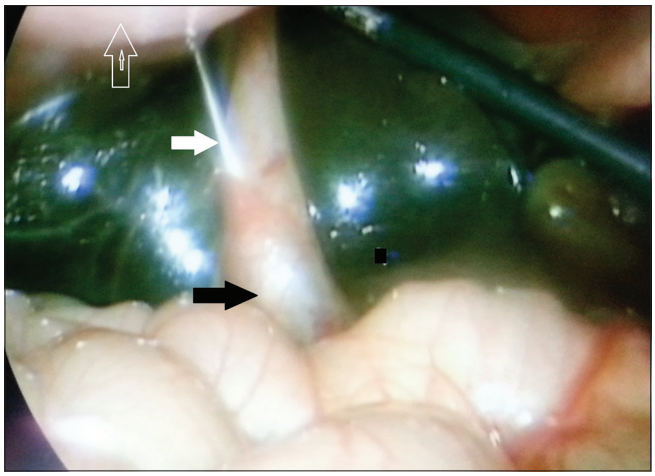

Figure 2: Laparoscopic view. Empty arrow - anterior abdominal wall, white arrow - cannula 16 gauge, black arrow - gall bladder

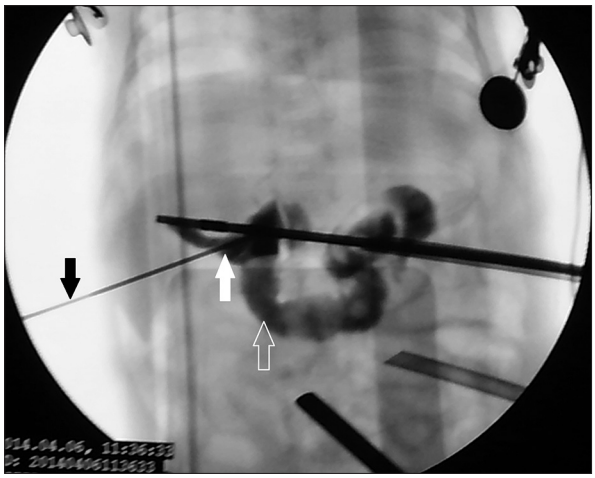

Figure 3: LCCG. Black arrow - 12 gauge cannula, white arrow - gall bladder, empty arrow - duodenum

biochemistry assessment, biliary radionuclide excretion scanning, magnetic resonance cholangiography, endoscopic retrograde cholangiography, percutaneous needle liver biopsy and laparoscopy can all be helpful, but their results are not individually diagnostic. The diagnosis of BA is usually suggested after results of several of these investigations (typically including liver biopsy) have been reviewed, and the diagnosis is confirmed at laparotomy.[12]

The triangular cord sign and a combination of three gallbladder features, namely, length <19 mm, an irregular wall and an indistinct mucosal lining (the so-called gallbladder ghost triad)–is diagnostic for BA. However, Infants with no US evidence of BA will require further investigations to establish the cause of their conjugated hyperbilirubinemia.[12-15]

The sensitivity and specificity of scintigraphy in detecting obstruction ranges from 83% to 100% and 33% to 100%, respectively. This wide range is reflected in the variation in its use by different centres.[10] Non-visualisation of the gallbladder or lack of excretion can occur in patients without BA.[8] Pre-treatment for 5 days with phenobarbital (5 mg/kg/day) increases the accuracy of this test by enhancing isotope excretion.[9] However, in most cases the use phenobarbital will delay the diagnosis and does not obviate the need for liver biopsy. Scintigraphy adds little to the routine evaluation of the cholestatic infant, but may be of value in determining patency of the biliary tract, thereby excluding BA. However, it should never be relied upon solely to make a diagnosis in neonatal cholestasis.[10]

In spite of the usefulness of a new paediatric duodenoscope (PJF Endoscope; Olympus Corporation of America, is a Japan-based manufacturer of optics,

Table 1: Intraoperative findings and procedures

Number of patients (total 12)	Finding of laparoscopic exploration	LGCC findings	Procedure
1	Absent GB	Not needed	Laparotomy and Kasai operation
4	Small size GB	Patent common bile duct and atresia of common hepatic duct	
7	Normal size GB	Normal biliary tree	Laparoscopic liver biopsy

GB: Gall bladder, LGCC: Laparoscopic guided cholecystocholangiography

established on 12 October 1919, Its global headquarters are in Shinjuku, Tokyo, Japan.) in the diagnosis of neonatal cholestasis, the rate of successful cannulation of the common bile duct in neonates and young infants is often lower than in adults, ranging from 27% to 95% in various reports.[16,17] Experience of the endoscopists may account for a large part of the variability. In addition, ERCP usually conducted in tertiary centres where the majority of the ERCPs are performed by one experienced operator.[18]

Although percutaneous liver biopsy appears to be the definitive diagnostic test in differentiation between BA and neonatal hepatitis, there are many instances where the biopsy reports are equivocal with marked overlap.[3,19,20] Before the introduction of laparoscopy, laparotomy for cholangiography and liver biopsy was the only available option in infants with prolonged cholestasis in whom neonatal hepatitis could not be differentiated with laboratory, radiologic and histopathological investigations. Although it is an effective method for differentiation, it carries high risk of wound complications.[3] Recently, laparoscopy with laparoscopic-guided cholangiography is a very useful tool used in accurately diagnosing infants with conjugated hyperbilirubinemia, and in avoiding

unnecessary laparotomies performed on these critical babies.[3,21] Nevertheless, CO_2 pressure more than 6–8 mm of Hg in newborn can cause reopening of the left to right shunt leading to hypoxemia, so pneumoperitoneum must be maintained between 6 and 8 mm of Hg during the procedure with close monitoring to keep CO_2 level below 35.[3]

CONCLUSION

LGCC is feasible, safe and simple diagnostic modality for questionable cases of neonatal cholestasis. It provides an opportunity for early and definitive diagnosis; as a result, it saves a lot of time searching for nonsurgical causes and avoiding unnecessary laparotomy in these critical babies.

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Conflicts of interest
There are no conflicts of interest.

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