

## Role of ERCP in the era of laparoscopic cholecystectomy for the evaluation of choledocholithiasis in sickle cell anemia

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cholangiography. Sequential endoscopic sphincterotomy and stone extraction followed by LC is beneficial in these patients. Endoscopic sphincterotomy may also prove to be useful in these patients as it may prevent the future development of biliary sludge and bile duct stones.

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**Key words:** Sickle cell anemia; Cholelithiasis; Choledocholithiasis; Laparoscopic cholecystectomy; Cholangiography; Endoscopic retrograde cholangiopancreatography

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### Abstract

**AIM:** To evaluate the role of endoscopic retrograde cholangiopancreatography (ERCP) for choledocholithiasis in patients with sickle cell anemia (SCA) in the era of laparoscopic cholecystectomy (LC).

**METHODS:** Two hundred and twenty four patients (144 male, 80 female; mean age, 22.4 years; range, 5-70 years) with SCA underwent ERCP as part of their evaluation for cholestatic jaundice (CJ). The indications for ERCP were: CJ only in 97, CJ and dilated bile ducts on ultrasound in 103, and CJ and common bile duct (CBD) stones on ultrasound in 42.

**RESULTS:** In total, CBD stones were found in 88 (39.3%) patients and there was evidence of recent stone passage in 16. Fifteen were post-LC patients. These had endoscopic sphincterotomy and stone extraction. The remaining 73 had endoscopic sphincterotomy and stone extraction followed by LC without an intraoperative cholangiogram.

**CONCLUSION:** In patients with SCA and cholelithiasis, ERCP is valuable whether preoperative or postoperative, and in none was there a need to perform intraoperative

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### INTRODUCTION

Sickle cell anemia (SCA) is one of the commonest hemoglobinopathies in the Eastern Province of Saudi Arabia with a sickle cell trait frequency of about 25% and a sickle cell disease frequency of about 2% in some areas<sup>[1,2]</sup>. One of the common complications of SCA is cholelithiasis and choledocholithiasis. The prevalence of cholelithiasis in patients with SCA is variable, ranging from 17% to 55%, but the frequency increases with age<sup>[3-5]</sup>. In the Eastern Province of Saudi Arabia, an overall frequency of cholelithiasis of 19.7% was reported in children with SCA. This frequency however, increased to 36% in those 15-18 years of age<sup>[6]</sup>. The incidence of choledocholithiasis in patients with SCA undergoing cholecystectomy was reported to be around 30%<sup>[7,8]</sup>. In the past, and based on this high incidence of common bile duct (CBD) stones, routine intraoperative cholangiography (IC) was recommended during cholecystectomy as this may necessitate

CBD exploration<sup>[7]</sup>. This however is not the case in the era of LC. Laparoscopic IC and CBD exploration, although feasible, is not easy to perform, requires expertise, and may be time-consuming. Add to this the possibility of converting a LC into an open one once CBD stones are diagnosed and found to be difficult to retrieve laparoscopically. The question now is whether routine laparoscopic IC is necessary for patients with SCA undergoing LC.

## MATERIALS AND METHODS

Two hundred and twenty four patients with SCA underwent endoscopic retrograde cholangiopancreatography (ERCP) as part of their evaluation for cholestatic jaundice (CJ). Their medical records were reviewed for: age at diagnosis, sex, indication for ERCP, hemoglobin (Hb) electrophoresis, liver function tests, including total and direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase, and abdominal ultrasound. The indications for ERCP were divided into 3 categories based on ultrasound findings: (1) patients with CJ and normal ultrasound; (2) patients with CJ and dilated bile ducts on ultrasound; and (3) patients with CJ and CBD stones on ultrasound. All ERCPs were performed in the radiology department using Olympus TJF 240 or JF 260 side-viewing duodenoscopes under general anesthesia, with nasotracheal intubation for children less than 10 years old, and under deep sedation using meperidine (1 mg/kg) and diazepam (midazolam) (0.1-0.2 mg/kg) for those above 10 years of age. The ampulla of Vater was cannulated with tapered or regular catheters and the biliary ducts were visualized under fluoroscopy using Hexabrix (320 mg diluted to 50%). Appropriate radiographs were obtained and, where indicated, sphincterotomy was performed using a 5F sphincterotomy (Olympus); bile duct stones, if found, were extracted with a basket, balloon extractor or mechanical lithotripter.

## RESULTS

There were 144 male and 80 female patients, mean age 22.4 years (range, 5-70 years). Mean HbS was 76.8% (range, 64.7%-92.3%); their mean HbF was 20.4% (range, 5.1%-34.0%); mean total bilirubin was 224 mg/L (range, 55-395 mg/L); mean direct bilirubin was 134 mg/L (range, 40-263 mg/L); mean alkaline phosphatase was 486 IU/mL (range, 81-1189 IU/mL; normal: 50-136 IU/mL); mean ALT was 234.3 IU/mL (range, 50-761 IU/mL; normal: 30-50 IU/mL) and mean AST was 206.3 IU/mL (range, 63-317 IU/mL; normal: 15-37 IU/mL). The indications for ERCP were: CJ only in 97 patients, CJ and dilated bile ducts on ultrasound in 103, and CJ and CBD stones on ultrasound in 42. In those with CJ only, ERCP revealed CBD stones in 18 (18.6%), and the ampulla of Vater was edematous and inflamed in 4, suggestive of recent stone passage. In those with CJ and dilated bile ducts, ERCP revealed CBD stones in 48 (46.6%), and inflamed edematous ampulla in 8. In those with CJ and CBD stones, ERCP revealed stones in 22 (52.4%), and the ampulla was inflamed

and edematous in 4. In total, CBD stones were found in 88 (39.3%) patients, and there was evidence of recent stone passage in 16. Fifteen of these were post-cholecystectomy patients, who had endoscopic sphincterotomy and stone extraction. The remaining 73 had endoscopic sphincterotomy and stone extraction followed by LC without an IC. Two (2.3%) patients developed minor bleeding from the sphincterotomy site. This was controlled with local diluted adrenaline injection. Two (2.3%) developed transient mild pancreatitis.

## DISCUSSION

In the general population with cholelithiasis the incidence of CBD stones has been reported as 5%-15% whereas in those with SCA it ranges from 18% to 30%<sup>[7-10]</sup>. Because of the high incidence of choledocholithiasis in patients with SCA, routine IC was advocated<sup>[7]</sup>. With the recent advances in LC, exclusion of CBD stones is of great importance. This is specially so in patients with SCA who frequently present with CJ and are known to have a high incidence of cholelithiasis and choledocholithiasis. There are those who advocate routine laparoscopic IC to delineate the anatomy and to detect CBD stones<sup>[11-16]</sup>. Lillemoe *et al*<sup>[17]</sup> on the other hand advocate the selective use of laparoscopic cholangiography. Although laparoscopic IC is feasible, it has several disadvantages. It requires operators who are experienced in laparoscopic surgery, it is not technically easy, and it is known to increase the operative time. It also makes it difficult to decide, when CBD stones are diagnosed and difficult to retrieve, whether to convert the operation to open or wait and do a post-LC ERCP. Add to this a 20%-25% false positive rate of IC that may lead to unnecessary CBD exploration or conversion to open cholecystectomy<sup>[16]</sup>. In a prospective study of CBD calculi in patients undergoing cholecystectomy, Nathanson *et al*<sup>[18]</sup> found choledocholithiasis in 3.4%, and concluded that laparoscopic IC would result in unnecessary interventions in 50% of patients who had either false positive results or subsequently passed the stones. Another study in 343 patients who underwent LC concluded that routine IC should be discouraged in view of the low yield and significant rate of false positive results<sup>[19]</sup>. However, Targarona *et al*<sup>[20]</sup> stated that the choice of diagnostic and therapeutic strategies for CBD stones should depend on local circumstances and available expertise. We found ERCP to be valuable both for the diagnosis and management of CBD stones in patients with SCA who were scheduled to have LC, or in those who presented with retained CBD stones following LC. Our policy is that all SCA patients with cholelithiasis who have a dilated CBD on ultrasound, biochemical evidence of obstructive jaundice (elevated alkaline phosphatase, elevated total bilirubin of more than 50 mg/L), or a history of pancreatitis either alone or in combination, and those who have choledocholithiasis detected on ultrasound, should undergo ERCP to confirm and extract the stones, followed by LC. We, like others, support a policy of preoperative ERCP for those with risk factors for CBD stones followed by LC<sup>[21,22]</sup>. However, magnetic resonance

cholangiopancreatography and or endoscopic ultrasound, if available, should replace ERCP as a diagnostic method to detect CBD stones as this will reduce the number of negative ERCPs and avoid the risks and complications of ERCP particularly for those with dilated CBD without stones.

In conclusion, considering the high incidence of CBD stones in patients with SCA, it is important to exclude them as a cause of CJ whether pre- or post-cholecystectomy. This is specially so in the era of LC. Laparoscopic IC, although feasible, is not easy to perform, is time-consuming, requires expertise, and may necessitate conversion to open surgery if CBD stones are identified. We found ERCP valuable in this regard whether pre- or post-LC, and in none of our patients was there a need to perform laparoscopic IC. Sequential endoscopic sphincterotomy and stone extraction followed by LC is beneficial in these patients<sup>[23,24]</sup>. Since we started using ERCP, none of our patients required CBD exploration and all CBD stones, whether diagnosed preoperatively or postoperatively, were managed by endoscopic sphincterotomy and stone extraction. Endoscopic sphincterotomy may also prove to be useful in these patients as it may prevent the future development of biliary sludge and bile duct stones.

## COMMENTS

### Background

Cholelithiasis and choledocholithiasis are common in patients with sickle cell anemia, and it is important to exclude choledocholithiasis in those undergoing cholecystectomy. In the past and at the time of open cholecystectomy, routine intraoperative cholangiography (IC) was part of the operative procedure as they have a high incidence of choledocholithiasis. The question now is whether routine laparoscopic IC is necessary for patients with Sickle cell anemia (SCA) undergoing laparoscopic cholecystectomy.

### Research frontiers

Common bile duct (CBD) stones were found in 88 (39.3%) of 224 patients and there was evidence of recent stone passage in 16. Fifteen of these were post-laparoscopic cholecystectomy patients and had endoscopic sphincterotomy and stone extraction. The remaining 73 had endoscopic sphincterotomy and stone extraction followed by laparoscopic cholecystectomy without IC.

### Innovations and breakthroughs

Laparoscopic IC, although feasible, is not easy to perform, is time-consuming, requires expertise, and may necessitate conversion to open surgery if bile duct stones are identified. We found endoscopic retrograde cholangiopancreatography (ERCP) valuable whether pre- or post-laparoscopic cholecystectomy and in none of our patients was there a need to perform laparoscopic IC. Sequential endoscopic sphincterotomy and stone extraction followed by laparoscopic cholecystectomy are beneficial in these patients. Since we started using ERCP, none of our patients required CBD exploration and all CBD stones whether diagnosed preoperatively or postoperatively were managed by endoscopic sphincterotomy and stone extraction. Endoscopic sphincterotomy may also prove to be useful in these patients as it may prevent the future development of biliary sludge and bile duct stones.

### Applications

All patients with SCA and cholelithiasis who have a dilated CBD on ultrasound, elevated alkaline phosphatase, elevated total bilirubin of more than 50 mg/L, or a history of pancreatitis either alone or in combination, and those who have choledocholithiasis detected on ultrasound should undergo ERCP to confirm and extract stones followed by laparoscopic cholecystectomy. However, magnetic resonance cholangiopancreatography and or endoscopic ultrasound should replace ERCP as a diagnostic method to detect CBD stones as this will reduce the number of negative ERCPs and avoid the risks and complications of ERCP particularly for those with dilated CBD without stones.

## Terminology

ERCP: Endoscopic retrograde cholangio pancreatography. SCA: Sickle cell anemia, a hereditary hemoglobinopathy resulting from a single change of one amino acid, valine instead of glutamic acid of the hemoglobin B-chain. This will lead to a change in the shape of red blood cells causing their adherence together, blocking the small blood vessels and their hemolysis.

## Peer review

The authors discussion of routine cholangiography in patients with SCA with high suspicion of choledocholithiasis is highly appreciated.

## REFERENCES

- 1 Clancey JK, Allen BW, Rogers DT, Smith LS, Aber V, Mitchison DA. Comparison of machine and manual staining of direct smears for acid-fast bacilli by fluorescence microscopy. *J Clin Pathol* 1976; **29**: 931-933
- 2 Al-Awamy BH. Sickle cell anemia, its clinical manifestations and their management. *Saudi Med J* 1987; **9**: 553-562
- 3 Rennels MB, Dunne MG, Grossman NJ, Schwartz AD. Cholelithiasis in patients with major sickle hemoglobinopathies. *Am J Dis Child* 1984; **138**: 66-67
- 4 Sarnaik S, Slovis TL, Corbett DP, Emami A, Whitten CF. Incidence of cholelithiasis in sickle cell anemia using the ultrasonic gray-scale technique. *J Pediatr* 1980; **96**: 1005-1008
- 5 Adekile AD. Experience with cholelithiasis in patients with sickle cell disease in Nigeria. *Am J Pediatr Hematol Oncol* 1985; **7**: 261-264
- 6 Al-Salem AH, Qaisarruddin S, Al-Dabbous I, Bhamidipati P, Abusair H, Amman H, Al Jam'a A. Cholelithiasis in children with sickle cell disease. *Pediatr Surg Int* 1996; **11**: 471-473
- 7 Al-Salem AH, Nangalia R, Kolar K, Qaisarruddin S, Al-Dabbous I, Al-Jama A. Cholecystectomy in children with sickle cell disease. Perioperative management. *Pediatr Surg Int* 1995; **10**: 472-474
- 8 Ware RE, Schultz WH, Filston HC, Kinney TR. Diagnosis and management of common bile duct stones in patients with sickle hemoglobinopathies. *J Pediatr Surg* 1992; **27**: 572-575
- 9 Gholson CF, Sittig K, McDonald JC. Recent advances in the management of gallstones. *Am J Med Sci* 1994; **307**: 293-304
- 10 Vicari P, Gil MV, Cavalheiro Rde C, Figueiredo MS. Multiple primary choledocholithiasis in sickle cell disease. *Intern Med* 2008; **47**: 2169-2170
- 11 Flowers JL, Zucker KA, Graham SM, Scovill WA, Imbembo AL, Bailey RW. Laparoscopic cholangiography. Results and indications. *Ann Surg* 1992; **215**: 209-216
- 12 Ware RE, Kinney TR, Casey JR, Pappas TN, Meyers WC. Laparoscopic cholecystectomy in young patients with sickle hemoglobinopathies. *J Pediatr* 1992; **120**: 58-61
- 13 Tagge EP, Othersen HB Jr, Jackson SM, Smith CD, Gayoso AJ, Abboud MR, Laver JL, Adams DB. Impact of laparoscopic cholecystectomy on the management of cholelithiasis in children with sickle cell disease. *J Pediatr Surg* 1994; **29**: 209-212; discussion 212-213
- 14 Holcomb GW 3rd, Olsen DO, Sharp KW. Laparoscopic cholecystectomy in the pediatric patient. *J Pediatr Surg* 1991; **26**: 1186-1190
- 15 Newman KD, Marmon LM, Attorri R, Evans S. Laparoscopic cholecystectomy in pediatric patients. *J Pediatr Surg* 1991; **26**: 1184-1185
- 16 Fletcher DR, Hobbs MS, Tan P, Valinsky LJ, Hockey RL, Pikora TJ, Knuiman MW, Sheiner HJ, Edis A. Complications of cholecystectomy: risks of the laparoscopic approach and protective effects of operative cholangiography: a population-based study. *Ann Surg* 1999; **229**: 449-457
- 17 Lillemoe KD, Yeo CJ, Talamini MA, Wang BH, Pitt HA, Gadacz TR. Selective cholangiography. Current role in laparoscopic cholecystectomy. *Ann Surg* 1992; **215**: 669-674; discussion 674-676
- 18 Nathanson LK, O'Rourke NA, Martin IJ, Fielding GA,

- Cowen AE, Roberts RK, Kendall BJ, Kerlin P, Devereux BM. Postoperative ERCP versus laparoscopic choledochotomy for clearance of selected bile duct calculi: a randomized trial. *Ann Surg* 2005; **242**: 188-192
- 19 **Korman J**, Cosgrove J, Furman M, Nathan I, Cohen J. The role of endoscopic retrograde cholangiopancreatography and cholangiography in the laparoscopic era. *Ann Surg* 1996; **223**: 212-216
- 20 **Targarona EM**, Bendahan GE. Management of common bile duct stones: controversies and future perspectives. *HPB (Oxford)* 2004; **6**: 140-143
- 21 **Robertson GS**, Johnson PR, Rathbone BJ, Wicks AC, Lloyd DM, Veitch PS. Factors predicting outcome after selective ERCP in the laparoscopic era. *Ann R Coll Surg Engl* 1995; **77**: 437-443
- 22 **Barwood NT**, Valinsky LJ, Hobbs MS, Fletcher DR, Knuiman MW, Ridout SC. Changing methods of imaging the common bile duct in the laparoscopic cholecystectomy era in Western Australia: implications for surgical practice. *Ann Surg* 2002; **235**: 41-50
- 23 **Al-Salem AH**, Nourallah H. Sequential endoscopic/laparoscopic management of cholelithiasis and choledocholithiasis in children who have sickle cell disease. *J Pediatr Surg* 1997; **32**: 1432-1435
- 24 **Gholson CF**, Grier JF, Ibach MB, Favrot D, Nall L, Sittig K, McDonald JC. Sequential endoscopic/laparoscopic management of sickle hemoglobinopathy-associated cholelithiasis and suspected choledocholithiasis. *South Med J* 1995; **88**: 1131-1135

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