USE OF INTRAVENOUS INDOCYANIN GREEN TO DELINEATE BILIARY TREE ANATOMY AND CYSTIC ARTERY ANATOMY IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Laparoscopic cholecystectomy is at times difficult. Intra operative cholangiogram is cumbersome. Advances in fluroscent imaging laparoscopically using intravenous Indocyanin green is an emerging modality which may make delineating bile duct anatomy easier. The aim of this study was to present our experience with indocyanin green fluroscence imaging in delineating common bile duct, common hepatic duct from cystic duct along with cystic artery in patients undergoing laparoscopic cholecystectomy. Thirteen patients undergoing laparoscopic cholecystectomy were injected with Indocyaninn green 15 minutes before the patients were induced for surgery. High definition camera connected to a 30 degree 10 mm scope with lens and light source emitting both visible and near infra-red (NIR) light (KARL STORZ GmbH & Co. KG, Germany) was used to visualize the biliary tree. And intraoperative ICG was injected to look for cystic artery and hepatic arteries. Real time images were obtained which showed biliary anatomy and cysic artery course. There were no adverse effects of ICG insertion. And the extrahepatic biliary anatomy and cystic artery were visible in all the 12 cases. In conclusion, use of ICG in laparoscopic surgery is safe and simple. The delineation of the biliary anatomy is good. Larger studies are needed to determine its use in laparoscopic cholecystectomy.

KEYWORDS

Indocyanine green,
intraoperative cholamgiogram,
laparoscopic cholecystectomy

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INTRODUCTION

Symptomatic cholelithiasis is a common condition requiring surgery. Laparoscopic cholecystectomy has rapidly become the standard surgical procedure for gallstone disease and is one of the most commonly performed surgical procedures today.[1-3] Despite improvements in imaging and surgical technique bile duct injury remains a significant problem. Aberrant anatomy, difficult surgery and pathology are the classical causes. Mistaking common bile duct for cystic duct is the most common cause.[4-6] Literature points to rates between 0.3 – 0.7%.[6-8] Unclear anatomy remains the most common cause for conversion to open cholecystectomy in patients and is in between 3-5% but rates as high as 10% have been reported.[9,10]

Patients with biliary tract injury have increased morbidity, mortality and an increase in hospital stay. This adds to significant economic costs and decrease in quality of life.[5,11,12] Intraoperative cholangiogram can help delineate the biliary anatomy but it is time consuming and cumbersome. So it has not become a routine. There is need for a simple safe and effective procedure to delniate biliary anatomy.[13-14]

Recently research has focused on using near infra red (NIR) light fluroscence using indocyanin green (ICG) to delineate biliary anatomy. [15-17]

MATERIALS AND METHODS

Patients

Thirteen consecutive patients who presented to surgical outpatient clinic of Nepal Medical College and Teaching Hospital with symptomatic cholelithiasis were included. The exclusion criteria were choledocholithiasis, iodine allergy, hyperthyroidism and hypothyroidism. The use of known medication interfering with hepatic ICG uptake (anticonvulsive medication, pethidine, morphine, nitrofurantoin cyclopropane, sodium bisulfite haloperidol, opium alkaloids, phenobarbital, phenylbutazon, probenicid, metamizole, rifamycin, methadone) was also considered a contraindication for inclusion in the study.

Laparoscopic equipment

In all cases, a laparoscopic system (KARL STORZ GmbH & Co. KG, Tuttlingen, Germany) was used. High definition camera system (IMAGE 1 SPIESTM, KARL STORZ) connected to a laparoscope with 30 degree telescope10 mm diameter equipped with a specific filter for optimal detection of the NIR fluorescence and white light without manual switching. The xenon light source (D-LIGHT P SCB, KARL STORZ) was used to provide both visible and NIR light. Surgeon controlled pedal was used to Switch between standard light and NIR.

Indocyanin green injection

ICG is a negatively charged, amphiphilic, water-soluble but relatively hydrophobic, tricarbocyanine with a molecular mass of 776 Da.[18,19] It has a peak emission at 822 nm when assessed with NIR light. Standard diagnostic procedures use between 0.1 and 0.5 mg/kg. Above 0.5 mg/kg, the incidence of immediate allergic reactions increases.[20] The ICG dye was injected Intravenously 15 min before surgery at the rate of 0.2 mg/kg to allow ICG to concentrate in the bile.[20,21]

For delineation of the vascular anatomy, a small bolus of 0.2 mg/kg was injected in to the veins intraoperatively and laparoscopic light and visualization turned to NIR light.

RESULTS

Informed consent was taken in all the patients. Thirteen patients included in the study were injected with ICG 15 minutes before the surgery was scheduled. All the patients were ASA Grade I and II. One patient was diagnosed with mild fever due to sore throat and postponed. The other 12 were included in the analysis. There were 8 females and 4 males, with a mean age of 35 (range 22-56) years. None of the patients had complications pertaining to cholelithiasis. Since this was a preliminary study patient with comorbid conditions and or other high risk factors were not included in the study. There were no adverse reactions. There were no conversions to open cholecysectomies. Drain was placed in one patient. There was no post operative morbidity or mortality. All the patients were discharged on postoperative day 2. Skin staplers were removed on Day 7 or 8 depending upon out patient clinic days.

The average time from injection to us visualizing during surgery was 31 minutes (25-40 minutes). In all the 12 cases the common bile duct, the common hepatic duct, the cystic duct and the cystic duct CBD junction was visible. (See photos 1 and 2). Cystic artery was also clearly visible in all the twelve cases. Because the time from injection to visualization was quick the liver also appeared substantially fluroscent.

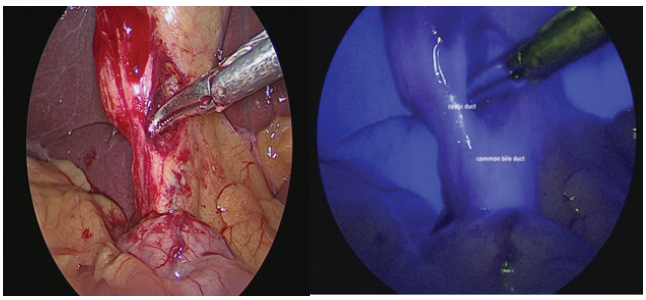

Photo 1: Identification of cystic duct andcommon bile duct using ICG in near infrared light

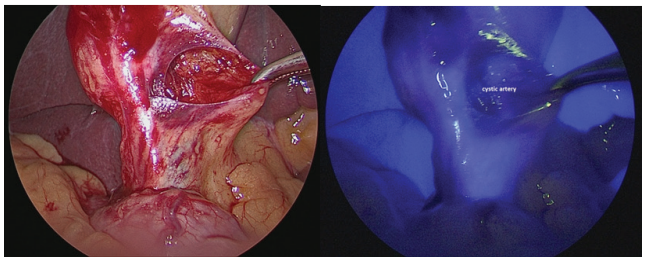

Photo 2: Identification of the cystic artery with injection of ICG in near infrared light.

DISCUSSION

We conducted this study to see the feasibility of using ICG and NIR light fluroscence in delineating the cystic duct and cystic artery anatomy. This would in our view help delineate and thus prevent CBD injury in patients with difficult cholecystectomy.

Use of NIR light and ICG to delineate cystic duct from CBD and cystic artery was successful in all the 12 patients who underwent this procedure. This was possible because 95% of the ICG is captured by the hepatocytes and released in to the bile with in fifteen minutes.[22]

Other studies corroborate our findings with high rates of visualization in patients with uncomplicated cholelithiasis.[23-26]

In patients with deranged liver function there might be a delay in the ICG excretion in to the bile. In these patients earlier injection of ICG or delayed visualization by rechecking during the course of the surgery may be helpful.

Verbeek *et al* in their study have demonstrated optimal visualizationof bileducts to be when the ICG is injected 24 hrs before the surgical procedure. They argue increasing time duration and injection and visualization helps to washout ICG from liver and helps delineate biliary anatomy better.[27]

Studies point out that in dense adhesions due to post inflamatory attacks, post ERCP patients and patient with past history of cholangitis there may be limited visualization because penetration of NIR induced fluroscence is about 1 cm. This may also be the case when the patient has high BMI however studies suggest BMI does not adversely affect visualization.Ankersmit *et al* in a study of 18 patients with complicated cholelithiasis; report better visualization rates with 2nd and 3rd look during surgery. Their visualizations increased from 38% to 72% with repeated visualization.

This is in contrast to other smaller studies which report higher rates of delineation (92%- 100%).[23,28-30]

At present ICG seems to be very effective at visualization of biliary anatomy in uncomplicated cholelithiasis. In patients with complicated cholelithisis with impared liver function and dense adhesion larger studies are required. Our study was limited by a small number of patients and none of our patients had complicated cholelithiasis. Vascular delineation in neurosurgical and ophthalmic procedures is routine and well established. Our study shows visualization of vascular anatomy possible. This may help in difficult cases where we might find finding the cystic artery difficult or when right hepatic artery may be mistaken for cystic artery.

In conclusion, Use of ICG and NIR fluroscence to delineate ductal anatomy is a promising tool which may make intraoperative cholangiogram a much simpler and less cumbersome procedure. It has the potential to become the standard of care for identifying the ducts in difficult cholecystectomies. Larger studies including complicated cholelithiasis and those comparing it with intraoperative cholangiogram are required. The use of near infrared light (NIR) and indocyanin green (ICG) to visualize biliary anatomy may be the future of intraoperative biliary imaging.

REFERENCES

1. Baird DR, Wilson JP, Mason EM *et al*. An early review of 800 laparoscopic cholecystectomies at a university affiliated community teaching hospital. *Am Surg* 1992; 58: 206-10.
2. Soper NJ, Stockmann PT, Dunnegan DL, Ashley SW. Laparoscopic cholecystectomy. The new 'gold standard'? *Arch Surg* 1992; 127: 917-21.
3. National Institutes of Health Consensus Development Conference Statement on Gallstones and Laparoscopic Cholecystectomy. *Am J Surg* 1993; 165: 390-8.
4. Stewart L. Iatrogenic biliary injuries: identification, classification, and management. *Surg Clin North Am* 2014; 94: 297-310.
5. Davidoff AM, Pappas TN, Murray EA, *et al*. Mechanisms of major biliary injury during laparoscopic cholecystectomy. *Ann Surg* 1992; 215: 196-202.
6. Dolan JP, Diggs BS, Sheppard BC, Hunter JG. Ten-year trend in the national volume of bile duct injuries requiring operative repair. *Surg Endosc* 2005; 19: 967-73.
7. Nuzzo G, Giuliante F, Giovannini I, *et al*. Bile duct injury during laparoscopic cholecystectomy: results of an Italian national survey on 56 591 cholecystectomies. *Arch Surg* 2005; 140: 986-92.
8. Tantia O, Jain M, Khanna S, Sen B. Iatrogenic biliary injury: 13,305 cholecystectomies experienced by a single surgical team over more than 13 years. *Surg Endosc* 2008; 22: 1077-86.
9. Sakpal SV, Bindra SS, Chamberlain RS. Laparoscopic cholecystectomy conversion rates two decades later. *JSLS* 2010; 14: 476-83.
10. Trastulli S, Cirocchi R, Desiderio J *et al*. Systematic review and meta-analysis of randomized clinical trials comparing single-incision versus conventional laparoscopic cholecystectomy. 2013; 100: 191-208

11. Zhang WJ, Li JM, Wu GZ, Luo KL, Dong ZT. Risk factors affecting conversion in patients undergoing laparoscopic cholecystectomy. *ANZ J Surg* 2008; 78: 973-6.
12. Machi J, Johnson JO, Deziel DJ *et al*. The routine use of laparoscopic ultrasound decreases bile duct injury: a multicenter study. *Surg Endosc* 2009; 23: 384-8.
13. Massarweh NN, Devlin A, Elrod JA, Symons RG, Flum DR. Surgeon knowledge, behavior, and opinions regarding intraoperative cholangiography. *J Am Coll Surg* 2008; 207: 821-30.
14. Buddingh KT, Nieuwenhuijs VB. The critical view of safety and routine intraoperative cholangiography complement each other as safety measures during cholecystectomy. *J Gastrointest Surg* 2011; 15: 1069-70.
15. Spinoglio G, Priora F, Bianchi PP *et al*. Real-time nearinfrared (NIR) fluorescent cholangiography in single-site robotic cholecystectomy (SSRC): a single-institutional prospective study. *Surg Endosc* 2013; 27: 2156-62.
16. Daskalaki D, Fernandes E, Wang X, et al. Indocyanine green (ICG) fluorescent cholangiography during robotic cholecystectomy: results of 184 consecutive cases in a single institution. *Surg Innov* 2014; 21: 615-21.
17. Ankersmit M, Van Dam A, Rijswijk AS *et al*. Fluorescent Imaging With Indocyanine Green During Laparoscopic Cholecystectomy in Patients at Increased Risk of Bile Duct Injury. *Surgical Innovation* 2017; 24: 245–52
18. Ogawa M, Kosaka N, Choyke PL *et al*. In vivo molecular imaging of cancer with a quenching near-infrared fluorescent probe using conjugates of monoclonal antibodies and indocyanine green. *Cancer Res* 2009; 69: 1268–72.
19. Moody ED, Viskari PJ, Colyer CL. Non-covalent labeling of human serum albumin with indocyanine green: a study by capillary electrophoresis with diode laser-induced fluorescence detection. *J Chromatogr B Biomed Sci Appl* 1999; 729: 55–64
20. Ishizawa T, Bandai Y, Ijichi M, Kaneko J, Hasegawa K, Kokudo N (2010) Fluorescent cholangiography illuminating the biliary tree during laparoscopic cholecystectomy. *Br J Surg* 97: 1369–77.
21. Kawaguchi Y, Ishizawa T, Miyata Y *et al*. Portal uptake function in venoocclusive regions evaluated by real-time fluorescent imaging using indocyanine green. *J Hepatol* 2013; 58: 247–53.
22. Kawaguchi Y, Ishizawa T, Miyata Y *et al*. Portal uptake function in veno-occlusive regions evaluated by real-time fluorescent imaging using indocyanine green. *J Hepatol* 2013; 58: 247-53.
23. Daskalaki D, Fernandes E, Wang X, *et al*. Indocyanine green (ICG) fluorescent cholangiography during robotic cholecystectomy: results of 184 consecutive cases in a single institution. Surg Innov 2014; 21: 615-21.
24. Schols RM, Bouvy ND, Masclee AA, van Dam RM, Dejong CH, Stassen LP. Fluorescence cholangiography during laparoscopic cholecystectomy: a feasibility study on early biliary tract delineation. *Surg Endosc* 2013; 27: 1530-6.
25. Spinoglio G, Priora F, Bianchi PP, *et al*. Real-time nearinfrared (NIR) fluorescent cholangiography in single-site robotic cholecystectomy (SSRC): a single-institutional prospective study. *Surg Endosc* 2013; 27: 2156-62.
26. Schols RM, Bouvy ND, van Dam RM, Masclee AA, Dejong CH, Stassen LP. Combined vascular and biliary fluorescence imaging in laparoscopic cholecystectomy. *Surg Endosc* 2013; 27: 4511-7.
27. Verbeek FP, Schaafsma BE, Tummers QR, *et al*. Optimization of near-infrared fluorescence cholangiography for open and laparoscopic surgery. *Surg Endosc* 2014; 28: 1076-82.
28. Dip F, Roy M, Lo Menzo E, Simpfendorfer C, Szomstein S, Rosenthal RJ. Routine use of fluorescent incisionless cholangiography as a new imaging modality during laparoscopic cholecystectomy. *Surg Endosc* 2015; 29: 1621-6.
29. Boni L, David G, Mangano A, *et al*. Clinical applications of indocyanine green (ICG) enhanced fluorescence in laparoscopic surgery. *Surg Endosc* 2015; 29: 2046-55.
30. Ishizawa T, Bandai Y, Ijichi M, Kaneko J, Hasegawa K, Kokudo N. Fluorescent cholangiography illuminating the biliary tree during laparoscopic cholecystectomy. *Br J Surg* 2010; 97: 1369-77.