Indocyanine green direct injection into gallbladder during laparoscopic cholecystectomy: a safety method to outline biliary anatomy

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Received: 22 April 2023
Revised: 10 May 2023
Accepted: 21 May 2023
Published: 11 August 2023

The Egyptian Journal of Surgery 2023, 42:549–553

Background
One of the most frequently done operations in digestive surgery is the laparoscopic cholecystectomy (LC). Despite several safety precautions and guidelines, iatrogenic bile duct damage (BDI) during LC still occurs at a very high incidence. Fluorescence of biliary system may minimise surgical difficulties that might emerge owing to unintended harm to the common bile duct.
Methods
We outline a technique for directly injecting Indocyanine Green (ICG) into the gallbladder to clarify the architecture of the cystic duct and common bile duct. Fifty patients who underwent elective laparoscopic cholecystectomy participated in the study, which was a randomised controlled clinical trial. Patients who had intraoperative direct injection of ICG into the gallbladder were chosen at random using closed envelope technique, then using near-infrared fluorescence (NIF) imaging during LC) and controls (who underwent standard LC technique) Twenty five patients in each limb. Patients were studied pre-operative, intraoperative & postoperative. 50 patients in all, 25 of whom received LC with intracholecystic ICG injection, and 25 of whom underwent standard LC without the use of ICG, were included in our study.
Results
ICG dye was successful to delineate extrahepatic biliary anatomy well in 20 cases out of 25, while without ICG, 9 cases out of 25 were without clear delineation of common bile duct intraoperative even if cystic duct was clear enough to avoid complications in both groups . Operative Time average in cases with ICG-assisted LC was 78±15.0 min which was less than the average of time consumed in LC without ICG to dissect cystic duct and visualize critical view of safety, 101±11.87 min
Conclusion
Direct gallbladder ICG infusion enables quick extrahepatic biliary system imaging and clarifies the dissection, increasing protection against BDI and reducing intraoperative dissection time.

Keywords:
common bile duct injury, direct injection, fluorescence cholangiography, indocyanine green, laproscopic cholecystectomy

Egyptian J Surgery 42:549–553

1110-1121

Introduction

With more than a million cholecystectomies carried out in the US each year, laparoscopic cholecystectomy (LC) is one of the most frequently done operations in digestive surgery. Despite several safety precautions and suggestions, the prevalence of iatrogenic bile duct injury (BDI) during LC is still rather high, ranging from 0.2 to 1.5% in different publications, significantly higher than original reports, and associated with considerable morbidity and death [1]. Due to accidental damage to the common bile duct, surgical problems may be reduced by the fluorescence of biliary structures. In order to establish the architecture of the cystic duct and common bile duct, we present a technique for injecting ICG directly into the gallbladder. The most dreaded LC complication is the BDI. By making the biliary tree easier to see during laparoscopic cholecystectomy, real-time intraoperative imaging using ICG may lower the risk of bile duct damage [2]. Indocyanine Green can be administered intravenously (with a dose of 2.5 mg/ml) or directly into the gallbladder (using a dose of

0.025 mg/ml). In contrast to intravascular injection, the direct approach utilised in this surgical procedure allowed us to execute it as many times as necessary [3]. The extrahepatic biliary tree is preferentially illuminated by intracholecystic ICG injection, which lowers background hepatic noise. By eliminating hepatic fluorescence and improving the bile duct to liver contrast, the Percutaneous Trans-Gallbladder Direct Injection of Indocyanine Green (PTGBD ICG) approach can offer a superior signal-to-noise ratio than intravenous ICG delivery [4]

Patients and methodology

Patients

This prospective randomized clinical study included 50 consecutive patients underwent elective laparoscopic cholecystectomy. Patients were randomized into two groups with 25 in each group. Laparoscopic cholecystectomy with Intracholecystic Indocynine Green (ICG) injection in group (group A) and Standard laparoscopic cholecystectomy in group (group B). All cholecystectomies performed at Kasr Al-ainy Hospital, General Surgery Department, Prof. Dr. Amr Mohamed Abdel-Fattah Ayad Unit (30A) and TBRI-Hospital, General Surgery department, in the age groups of 16 and 75 years, of either sex were included in the study

Surgical method of laparoscopic cholecystectomy

Either the closed Veress needle technique or the open approach is used to create pneumoperitoneum (Hasson's technique).

For the purpose of inserting operational ports through which surgical tools are inserted into the abdominal cavity, LC makes multiple (often 4) tiny incisions in the belly.

The laparoscope is a device that illuminates the abdominal cavity and transmits a magnified picture from inside the belly to a video screen. It also has a video camera and light source at the end. The gallbladder is removed by locating, dissecting, ligating with clips, and cutting the cystic duct and cystic artery. After that, one of the ports is used to remove the gallbladder. Depending on the patient's habits and the surgeon's desire, an infra, intra, or supraumbilical 10 mm telescope is typically utilised at the umbilicus. Another 10 mm trocar is inserted in the epigastrium which is the major right working port for the surgeon. One 5 mm trocar is utilised for gallbladder fundus traction in the right lumbar area, while a second 5 mm trocar is used as the surgeon's left hand working port in the right hypochondrium. A large window is made by anterior and posterior dissection of Calot's triangle with the right hand while Hartmann's pouch is retracted with the left. It's crucial to take a critical eye on safety to avoid bile duct damage.

ICG preparation and direct injection

One ICG vial 25 mg (Fig. 1) is divided into 20 particles under complete aseptic condition, each one 1.25 mg. 1.25 mg of ICG powder dissolved in 3 cm Saline, then every 1 cm diluted by 9 cm Saline to give concentration of approximately 0.04 mg.

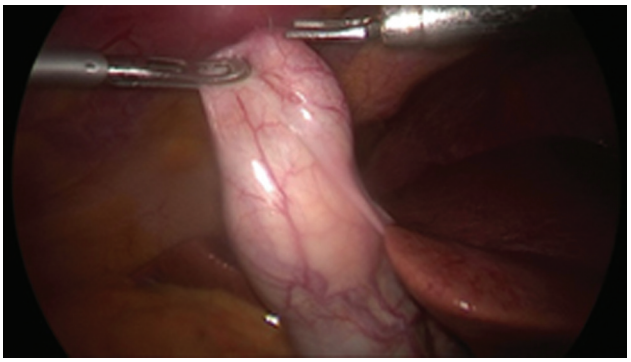
After 4 ports insertion as standard laparoscopic cholecystectomy, fundus of gall bladder traction to the abdominal wall is done using 5 mm trocar in right lumbar region.Spinal Needle (Black 22gauge, OD 0.72 mm, ID 0.46) is inserted in epigastric region through abdominal wall under vision to reach fundus of gallbladder and inserted. About 10 cm bile is aspirated from the gallbladder, then 10 cm of the diluted dye is injected under visualization of NIR fluorescence light switching with white light, then the needle is taken off, followed by clipping of its site pore to avoid spillage of the dye & loss of obvious field (Fig. 2).

A large window is made by anterior and posterior dissection of Calot's triangle with the right hand while Hartmann's pouch is retracted with the left. With careful dissection of the cystic duct and the common bile duct and accurate delineation of the confluence of the cystic duct and CBD utilising NIR fluorescent light switching with white light, a critical perspective of safety is attained (Fig. 3). Through a 10 mm epigastric port, the cystic duct

Figure 1

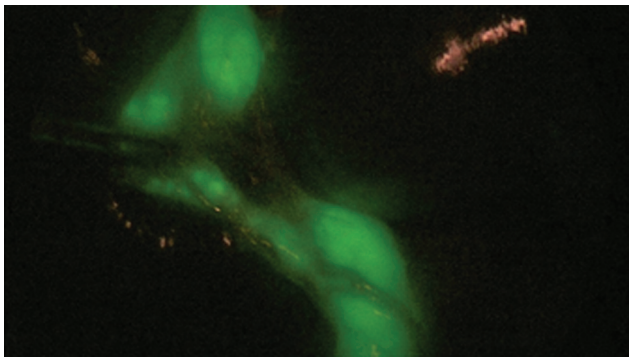
Verdye Indocyanine Green Diagnostic Indocyanine Green (ICG).

Figure 2



Spinal Needle is inserted in epigastric region through abdominal wall under vision to reach fundus of gallbladder and inserted.

Figure 3



Good delineation of confluence between cystic duct & CBD by using the NIR fluorescence light.

and cystic artery are clipped. Usually, the epigastric or umbilical port is used to remove the gallbladder.

The operative time is recorded from the beginning of the first incision until closure of the final wound. Patients are discharged on the first postoperative day.

Operative time, spillage of dye, delineation of common bile duct, drain insertion, postoperative hospital stay, complications and biliary injury are analyzed.

Near-infrared fluorescent light

In all cases, a laparoscopic system (KARL STORZ GmbH & Co. KG, Tuttlingen, Germany) was employed. The high-end full-HD camera system (IMAGE 1 SPIESTM, KARL STORZ) attached to a laparoscope with a 30° field of view and 10 mm diameter and fitted with a special filter for the best detection of NIR fluorescence and white light without manual switching produces the image. Excitation light for both the visible and NIR spectrums is provided by the strong xenon light source (D-LIGHT P SCB, KARL STORZ). The surgeon uses a pedal to manage the transition from conventional light to NIR (53). A system of expert image improvement (IMAGE 1 SPIESTM system, KARL STORZ GmbH & Co. KG, better visualisation in both standard and NIR light)., Tuttlingen, Germany) which offers adjustable visualization modalities that can be selected according to surgeon's preferences [5].

Results

In our study, we found that ICG dye was successful to delineate extrahepatic biliary anatomy well in 20 cases (80%) out of 25, while without ICG, about 9 cases out of 25 was without clear delineation of CBD intraoperative even if cystic duct was clear enough to avoid complications in both groups .There was spillage of ICG dye in 6 cases out of 25 due to different technical errors, led to failure of delineation of CBD in 4 of them. Operative Time average in cases with ICG assisted LC was 78±15.0 min which was less than the average of time consumed in LC without ICG to dissect cystic duct and visualize critical view of safety, 101±11.87 min There was no need for drain insertion in 17 cases out of 25 cases underwent ICG assisted LC, while only 10 cases out of 25 cases underwent LC without ICG didn't need drain insertion. All cases in both groups discharged day one postoperative with no detected complications.

Discussion

ICG was first created by Kodak Research Labs in 1955 for use in photography and was later given clinical use approval in 1956. The dye has no known metabolites, is nontoxic, and is nonionizing. In this prospective randomised study, we describe a novel technique for injecting ICG directly into the gallbladder to visualise biliary anatomy and analyse the length of the procedure, dye spillage, the delineation of the common bile duct, the placement of a drain, the length of the hospital stay following the procedure, complications, and biliary injury in two groups—one receiving ICG-assisted laparoscopic cholecystectomy and the other not. The extrahepatic biliary system is directly injected, eliminating the IV injection's delay and enabling instantaneous fluorescence. Moreover, the extrahepatic biliary system is highlighted while the liver and blood arteries are obscured, increasing visual contrast. Hence, the goal of fluorescence cholangiography is the same as that of intraoperative contrast X-ray cholangiography. Yet, it has a number of benefits, including not requiring radiation, allowing for real-time viewing during dissection, and being totally

handled by the surgeon without the need for further help. Although though unique equipment is needed, it can simply be included into a standard laparoscopic tower. Fluorescent cholangiography has not been demonstrated to reliably detect common bile duct stones, which is a significant drawback. Because of this, it shouldn't take the place of conventional contrast X-ray cholangiography in situations when there is a risk of common bile duct blockage.

In a similar manner, Clara Gené krabec and his coworkers in 2020 compared 20 patients who underwent laparoscopic cholecystectomies with NIF and direct injection of ICG into the gallbladder against 20 patients who underwent 20 consecutive normal cholecystectomies. In 16 (80%) of the patients in the ICG group, fluorescence imaging of the confluence of the Hartmann pouch and the whole cystic duct was accomplished. The ICG group's median surgery time was 65 (50–76) minutes, while the control group's was 55 (45–71) minutes (P=0.113). In none of the groups were there any postoperative problems or bile duct damage [6].

Also, eleven patients who received direct gallbladder ICG injection for NIR-FC during LC were investigated by Claire Graves and his colleagues in 2019. The CD-CBD junction and other extrahepatic biliary architecture were well delineated by fluorescence following direct gallbladder ICG administration. The gallbladder ICG fluorescence also highlights the dissecting plane between the gallbladder and liver [2].

In a 2021 study by Jun Kit Koong *et al.*, individuals who had LC at a single centre were randomly assigned to either conventional LC or Indocyanine Green Fluorescence Cholangiography (ICGFC)-LC. A single surgeon conducted the procedure, and the amount of time it took for the patient to reach Critical View of Safety (CVS) after the gallbladder fundus had been retracted was recorded. A customised scoring system was used to grade and analyse the difficulty level for each procedure (Level 1– Easy to Level 4–Very difficult). 63 individuals were included, and it took an average of 22.3 12.9 min for ICGFC-LC (n=30) and 22.8 14.3 min for traditional LC (P=0.867) to attain CVS. Throughout all difficulty levels, the ICGFC-LC group took less time to complete CVS, but this difference was not statistically significant (P>0.05). No major complication was observed in the study [7].

And by employing a different technique, Man-Ling Jao and his coworkers in 2020 used two methods of indocyanine green administration during surgery: first, direct intracystic administration through Percutaneous Trans-Gallbladder Drainage Tube (PTGBD tube) (5 ml of 12.5 mg ICG) to achieve a critical view of safety, and second, intravenous administration (1 ml of 2.5 mg ICG) to visualise the cystic artery. According to the Tokyo guidelines' diagnostic criteria, two instances who had near-infrared fluorescence cholangiography-guided interval laparoscopic cholecystectomy were identified as having mild acute calculous cholecystitis [4]. With a surgery lasting 84 and 125 min in cases 1 and 2, respectively, both patients had a crucial perspective of safety that could be clearly seen with ICG without any intraoperative or postoperative problems [4].

However, 70 patients, including 29 with and 41 without ICG, underwent laparoscopic cholecystectomy during the investigation when Peter C. Ambe and his colleagues in 2021 performed a retrospective analysis of the data of patients who underwent laparoscopic cholecystectomy with and without ICG in a referral centre for minimally invasive surgery. In the group with and without ICG, they discovered that the median time of operation was 53.0 vs. 54.0 min, and the median length of stay was 2.0 d. In contrast to the group receiving ICG, 2.4% of cholecystectomies without it were converted from laparoscopic to open surgery. No bile duct damage happened in either group [8].

It was found that many technical errors or unskillfulness during gallbladder injection of ICG may lead to spillage of the ICG dye and disturbance of the operative field under NIF imaging which may lead to failure of delineation of CBD by our method. In spite of this, we found that we can complete our work by good dealing with the spillage of the dye and clarify the field using suction instrument and a small gauze. Another cause may lead to failure of the ICG dye to pass into cystic duct and delineate CBD well after its direct injection into gallbladder, even if there is no spillage of dye, is the presence of large stone in Hartmann pouch. We have to clarify that our method was successful, when there was a very narrow cystic duct and with the acute attacks with pericholecystic adhesions, when the dye was injected in a proper manner.

Conclusion

Direct gallbladder ICG infusion enables quick extrahepatic biliary system imaging and clarifies the dissection, increasing protection against BDI and reducing intraoperative dissection time.

Acknowledgements

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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