Evaluation of indocyanine green-enhanced fluorescence in hepatobiliary conditions in pediatric surgery

Mohamed S. Emam[a], Ahmed A. Youssef[a], Hazem S. Amra[a], Mohammad A. Abd-erRazik[b], Ahmed B. Radwan[a], Tarek Youssef[b], Osama El Naggar[a]

Departments of [a]Paediatric Surgery, [b]General Surgery, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Correspondence to Mohamed S. Emam, MD, Department of Paediatric Surgery, Faculty of Medicine, Ain Shams University, Cairo, Egypt. Tel: +20 111 278 7446; e-mail: mohamedsherif_2010@hotmail.co.uk

Received: 7 February 2023
Revised: 28 February 2023
Accepted: 13 March 2023
Published: 9 June 2023

The Egyptian Journal of Surgery 2023, 42:250–259

Background

Indocyanine green (ICG) is a water-soluble tricarbocyanine dye developed by Kodak Research Laboratories for near-infrared photography in 1955. It was first approved by the Food and Drug Administration in 1956 to study hepatic and cardiac functions in humans. ICG is excited when illuminated by near-infrared light with a wavelength of 778–806 nm. The fluorescence emission is maximal at a wavelength of 832 nm and can penetrate tissue up to 15 mm. This emitted light is then captured with a special camera to be transformed and displayed as visible light.

Aim

This study aimed to evaluate the true extent of ICG application in pediatric patients, whether it is complementary to or replacement of traditional methods and its usefulness in visualizing a anatomy of a biliary system and vascular territory in various organs regarding intraoperative time, postoperative hospital stay and complications at Ain Shams University, Department of Pediatric Surgery.

Patients and methods

A case series was conducted on children with hepatobiliary diseases who were admitted to the Department of Pediatric Surgery of Ain Shams University hospitals. All patients were operated on by ICG-enhanced fluorescence-guided surgery.

Results

In the laparoscopic cholecystectomy group; common bile duct was evident in 75.0% of patients, and cystic duct and common hepatic duct were evident in all patients with no biliary injury in all patients. While in the choledochal cyst group; common bile duct, cystic duct, and common hepatic duct were evident in all patients with no biliary injury. In the biliary atresia group, there was statistically significant differences between preoperative and postoperative liver profiles regarding aspartate aminotransferase, alanine aminotransferase, total and direct bilirubin, alkaline phosphatase, and gamma-glutamyltransferase.

Conclusion

The ICG fluorescence application in pediatric hepatobiliary surgery is feasible and safe with the mentioned doses and timing of administrations. Adequate visualization of ICG fluorescence helped to prevent intraoperative vascular or biliary complications in our study population.

Keywords:
fluorescence, hepatobiliary surgery, indocyanine green, open, whether laparoscopic

Egyptian J Surgery 42:250–259

1110-1121

Introduction

Indocyanine green (ICG) is a water-soluble tricarbocyanine dye developed by Kodak Research Laboratories for near-infrared (NIR) photography in 1955. When illuminated by NIR light with a wavelength of 778–806 nm, ICG is stimulated. Then, using a particular camera, this emitted light is captured to be displayed as visible light [1]. ICG is administered intravenously; it is solely metabolized by the liver and excreted exclusively in the bile at a rate of 18–24% per minute. ICG has been beneficial for visualizing the biliary system and vascular territory in various organs [2].

Although initially ICG was used for clinical trials only, experimental surgery and new surgical techniques have been published by various authors. Whether it is complementary to or replacement of traditional methods is to be determined, but certainly, this is a contrast agent with huge potential [3].

 DOI: 10.4103/ejs.ejs_52_23

Laparoscopic cholecystectomy (LC) is the treatment of choice for symptomatic gallstones in children. The techniques and instruments used in children are similar to those used in adults, but anatomical variations are more common and the abdominal space is more limited. ICG can be a valuable tool in identifying the cystic duct (CD) and common bile duct (CBD) with minimal risk of injury to either the biliary tree or blood vessels [4].

Intraoperative cholangiogram is the gold standard for the diagnosis of biliary atresia (BA) and is usually performed together with Kasai operation [5]. Conventionally, it involves the injection of radio-opaque contrast material into the gallbladder and observes the drainage of contrast in the biliary system. Hirayama *et al.* [6] first reported their experience to use ICG as an alternative in 2015.

The use of ICG is a potential adjunctive for the minimally invasive treatment of choledochal cysts (CC) in children. The adequate treatment of this condition requires careful dissection to avoid vascular and visceral lesions as well as biliary digestive reconstruction according to the morphology of the hepatic duct [7]. The application of this technique allowed for the complete dissection of the cyst without vascular injury, the safe ligation of the duodenal segment of the cyst, and a successful hepaticoduodenostomy [8].

This study aimed to evaluate the usage of ICG in pediatric patients who presented with certain hepatobiliary conditions. Whether ICG usage was a complementary to or replacement of the traditional biliary visualization methods in order to assess the anatomy of the biliary system and vascular territory. The assessment was done regarding intraoperative time, operative vascular and biliary complications, and postoperative hospital stay and complications.

Patients and methods

Study design

A case series, including all pediatric patients presented with one of the three hepatobiliary conditions [namely: gallbladder pathology requiring LC, BA, and CC during 2-year period (from January 2021 to December 2022)]. All patients included in this study were subjected to the following: demographic data collection (age, sex, and biliary condition), clinical history, laboratory, and radiological data recording. Patients were grouped into three groups according to the pathology (group 1 LC, group 2 BA, group 3 CC). Except for BA, all patients were operated on by ICG-enhanced fluorescence-guided minimal invasive surgeries.

Ethical considerations

The study was approved by the ethical committee of the University Hospital authority in February 2021, IBR number: 0006379. Informed written consent was taken from the caregivers before participation in the study.

Preoperative additional preparation for ICG fluorescence usage:

(1) Specific camera system and a specific 0° or 30° laparoscope equipped with a special filter for detection of both NIR light and standard white light (Karl Storzse and Co. KG, Tuttlingen, Germany) were used in all laparoscopic procedures. The specific view mode can be selected by the surgeon through the buttons on the camera head during the initial setting. Switching from white light mode to NIR fluorescence is directly activated by the surgeon through foot-pedal pushing. The visualization of both white and NIR light is enhanced by a professional system of image visualization. In cases of BA, the laparotomy wound was used to insert the same laparoscopic instrument to visualize the biliary and vascular territory then switched on and off as required.
(2) The dose for ICG was 0.25 mg/kg for all indications and extra doses may be given up to 0.4 mgl/kg. ICG vial was diluted with sterile water to create a 2.5 mg/ml solution, and injected through peripheral venous access, after a subcutaneous sensitivity test for 10 min [9]. Regarding the timing of the administration, the ICG solution was administered about 11 h preoperative [10].
(3) LC special considerations: all the patients were operated on under general anesthesia with a nasogastric tube to empty the stomach. A 4-trocars technique was adopted in all patients: a 10-mm camera port was introduced using the open Hasson technique and three 5-mm working ports were placed for the instruments. The critical view of safety (CVS) was defined by three criteria: (a) the hepatocystic triangle was freed of adipose and fibrotic tissue; (b) the lower portion of the gallbladder was separated from the liver in order to expose the cystic plate; and (c) only the CD and the cystic artery entered the gallbladder. The CD was clipped using 5-mm clip appliers with two

clips proximal from CBD and one to two clips distally. The cystic artery was clipped and divided. The gallbladder was then removed from the gallbladder fossa with hook electrocautery and extracted through the umbilical trocar's orifice. ICG-enhanced fluorescence was performed throughout the course of the procedure by switching from bright light image to NIR fluorescence through a foot pedal.

(4) BA/Kasai operation: the patient is placed in a supine position, general anesthesia is introduced, and a pillow is placed under the back to raise the surgical field of the hepatic hilum. A small laparotomy was done just above the gallbladder. An intraoperative cholangiogram was done using ICG-enhanced fluorescence. After confirming the diagnosis of BA by cholangiography, the wound is extended using a right subcostal incision. Our procedure was performed in a manner similar to the original Kasai procedure. Dissection of the fibrous cone (FC) of the porta hepatis (PH) was carried out at the level of the posterior surface of the portal vein, at which point the liver parenchyma cannot be exposed in the PH. ICG-enhanced fluorescence was used to visualize the biliary flow of the hepatic duct at the PH. Hepatoportoenterostomy with Roux-en-Y anastomosis was carried out along with the jejunum taking care to prevent damage to the microbile ducts exposed after dissection of the FC of the PH. Postoperative management in all patients included the same corticosteroid regimen beginning on day 7 (starting at 4 mg/kg/day, with gradual tapering of 1 mg/kg/day over 5 days).

(5) CC/hepaticoduodenostomy: the procedure was carried out under general anesthesia with the patient lying in the supine position with a tilt to the right and head elevation of the operating table. Five ports (5 mm) were used – one in the umbilicus for inserting the scope and four working ports: one in the anterior axillary line for traction on the gallbladder, the second in the midline below the xiphisternum for liver retraction, and two working ports (one in the mid-clavicular line and the other in the midline between the umbilicus and the xiphisternum). After intraoperative cholangiography through the gallbladder using the ICG-enhanced fluorescence, complete excision of the CC. Hepaticoduodenostomy was performed through a wide end-to-side anastomosis, beyond the first part of the duodenum and away from the pylorus, using interrupted absorbable sutures.

Outcome measures

The primary outcome measure was measuring the incidence of vascular or biliary insult during the operative management of these three conditions while using ICG fluorescence. Secondary outcome measures were total hospital stay, postoperative timing to start of oral feeding, and changes in preoperative and postoperative hepatobiliary laboratory profiles after 1 and 6 months in second and third group.

Statistical analysis

Data were collected, revised, coded, and entered into the Statistical Package for Social Science (IBM SPSS, Armonk, NY: IBM Corp), version 20. The qualitative data were presented as numbers and percentages while quantitative data were presented as mean, SDs, and ranges when their distribution was found parametric. The *P* value was considered significant as the following: *P* value greater than 0.05=nonsignificant, *P* value less than 0.05=significant, and *P* value less than 0.001=highly significant.

Results

During the mentioned period we received 14 patients with the three mentioned conditions, they were five males, and nine females. The demographic data of the study population are shown in Table 1.

Regarding the usage of ICG, the used mean dose and mean timing before injections are mentioned in Table 2. Photos projected in the laparoscopic view

Table 1 Distribution of studied sample according to age (years) and sex in different groups (to be noted one of the laparoscopic cholecystectomy cases had laparoscopic splenectomy in the same session)

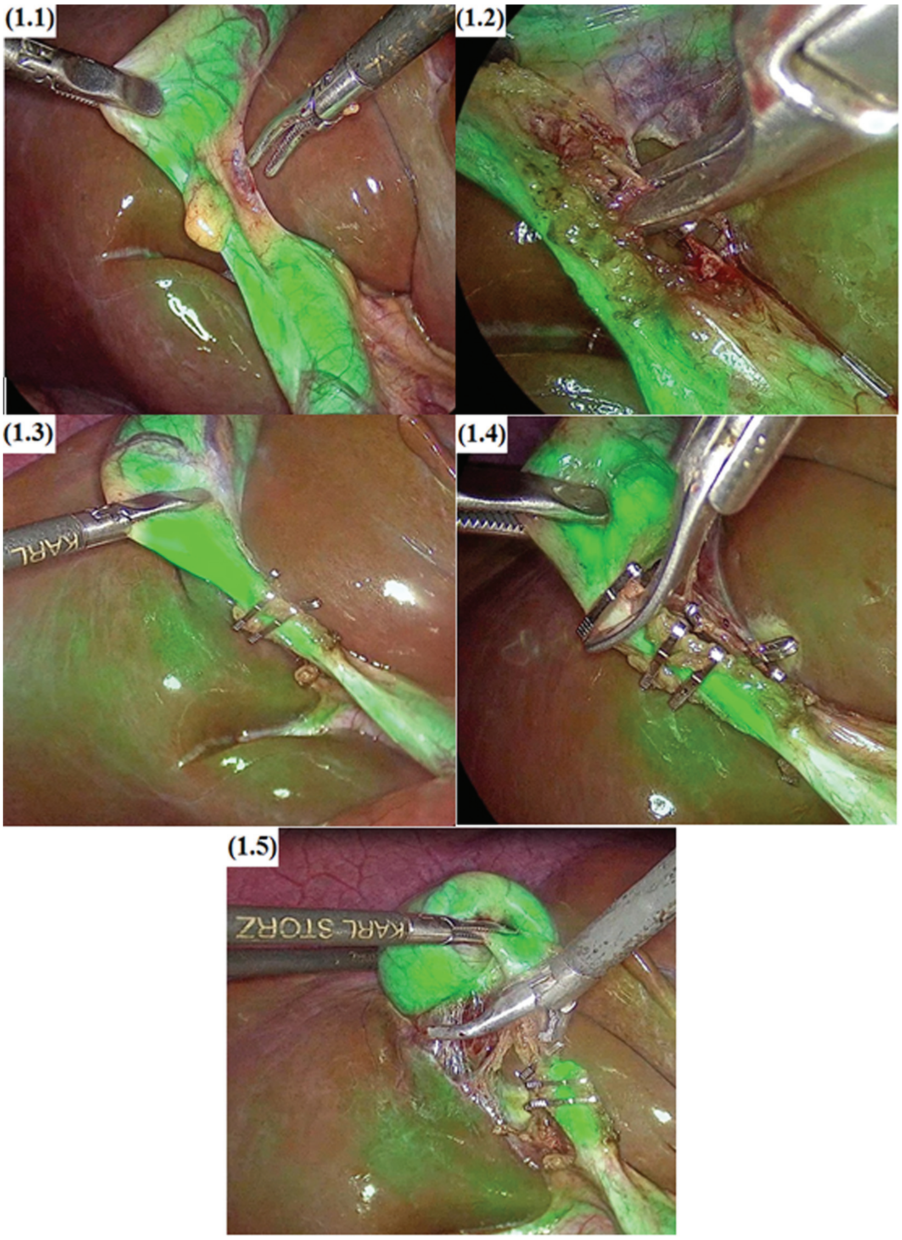
	Laparoscopic cholecystectomy *N*=8 (57.1%)	Biliary atresia *N*=4 (28.6%)	Choledochal cyst *N*=2 (14.3%)
Age (years)			
Mean±SD	11.68±5.48	0.23±0.03	5.25±6.72
Range	4.4–18	0.2–0.25	0.5–10
Sex [*n* (%)]			
Female	6 (75.0)	1 (25.0)	2 (100.0)
Male	2 (25.0)	3 (75.0)	0

Table 2 Indocyanine green dosage (cm), timing of preoperative injection till intraoperative cholangiogram (h)

	Laparoscopic cholecystectomy *N*=8 (57.1%)	Biliary atresia *N*=4 (28.6%)	Choledochal cyst *N*=2 (14.3%)
ICG dosage (cm)			
Mean±SD	3.75±0.46	1.50±0.00	3.00±1.41
Range	3–4	1.5–1.5	2–4
Time of injection (hour preoperative)			
Mean±SD	11.13±0.83	12.00±0.00	11.00±1.41
Range	10–12	12–12	10–12
Intraoperative cholangiogram [*n* (%)]			
Patent with no anomaly	8 (100.0)	0	0
Biliary atresia	0	4 (100.0)	0
Choledochal cyst	0	0	2 (100.0)

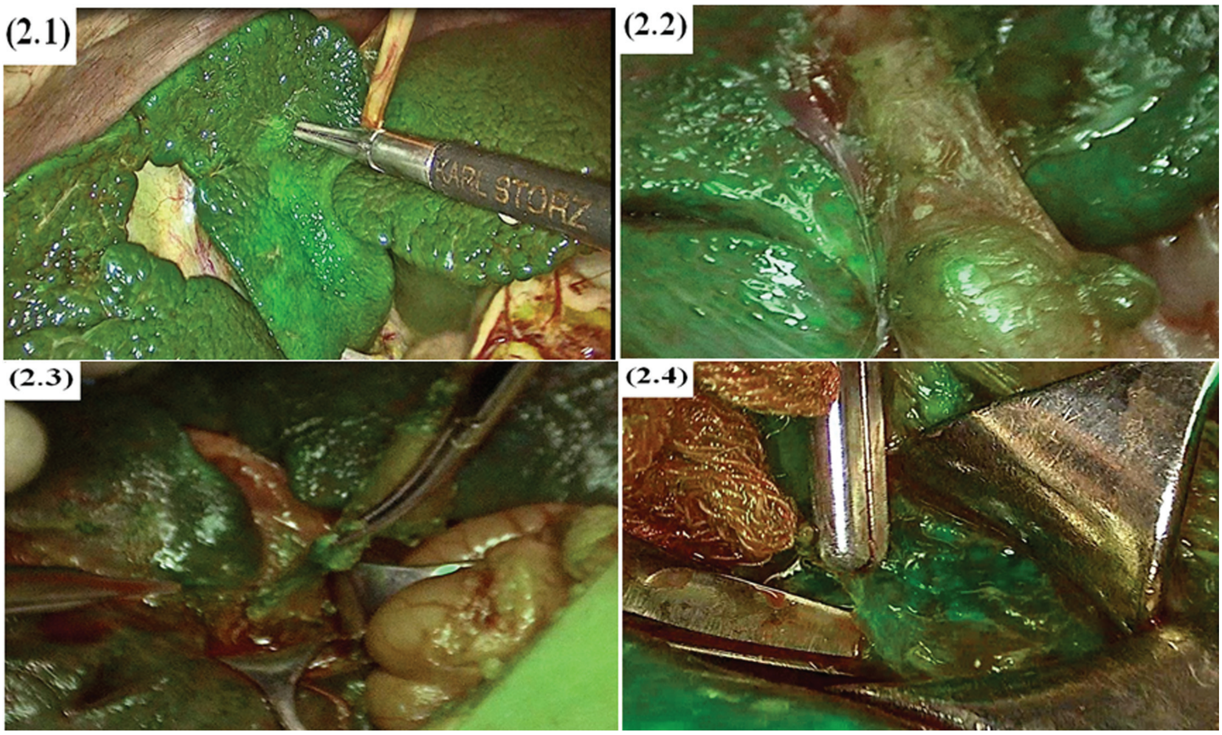
ICG, indocyanine green.

Figure 1



Laparoscopic view of a case from the group of LCs: (a) identification of Calot's triangle before any dissection, (b) dissection of Calot's triangle and clip application over the cystic artery, (c) clip application over the cystic duct, (d) division of the cystic duct, (e) separation of the gallbladder from liver bed. LC, laparoscopic cholecystectomy.

Figure 2



A case from the group of biliary atresia operated for Kasai: (a) uptake of the indocyanine green by the liver, failure of excretion of the dye by the liver (biliary atresia type 3), upon exploration only remnants of the biliary tract was found and operated for Kasai, (b) excision of the biliary remnants, (c) before dissection in the plate, (d) after dissection and preparation for porto enteric anastomosis.

with and without ICG fluorescence are exampled in Figs 1–3.

Regarding clinical data in each group: In group 1, patients presented with recurrent attacks of right hypochondric pain and nonbilious vomiting. Three patients were known cases of spherocytosis and sickle thalassemia. In group 2, patients presented with prolonged neonatal jaundice, clay-colored stool and dark urine. In group 3, patients presented with recurrent attacks of abdominal pain and obstructive jaundice.

Regarding preoperative laboratory data: full liver profile was withdrawn in all patients (aspartate aminotransferase, alanine aminotransferase, gamma-glutamyltransferase, alkaline phosphatase, total and direct bilirubin) showing a marked increase in patients presented with obstructive jaundice in the group of BA as shown in Table 2.

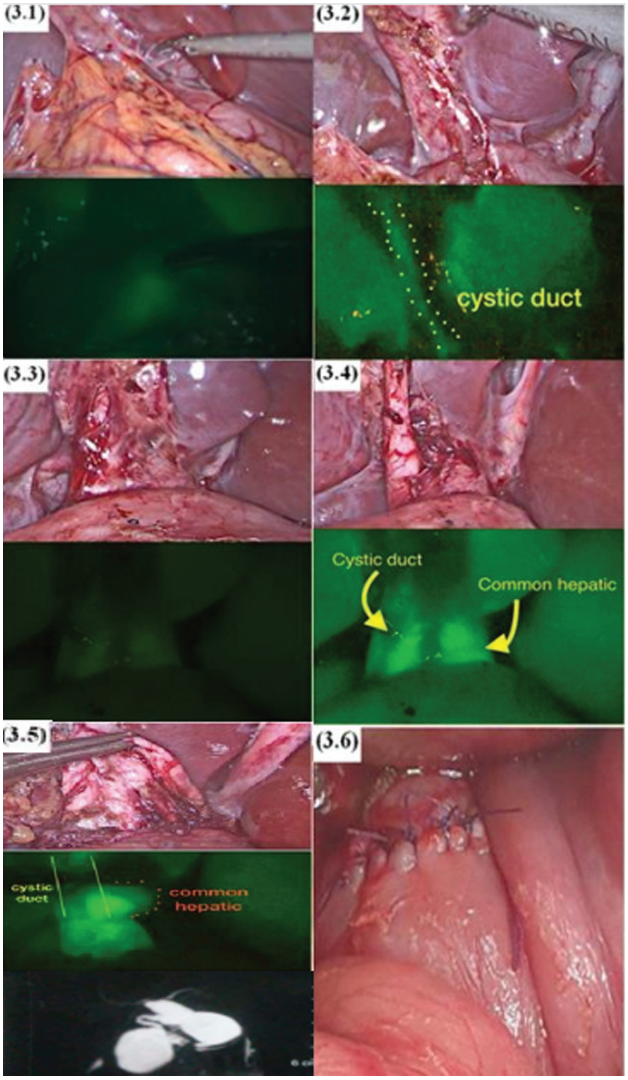
As regards radiological investigation in each group: in the group of calcular gallbladder disease, pelviabdominal ultrasound was done showing calcular gallbladder with average wall thickness and CBD of normal caliber. In the BA group, pelviabdominal ultrasound was done showing a contracted gallbladder with a triangular cord sign seen in one patient. Hepatobiliary iminodiacetic acid scan was done only in one patient showing absent biliary to bowel tracer transit and nonvisualization of the gallbladder up to 6 h.

In the CC group, pelviabdominal ultrasound was done showing a distended gallbladder with dilated intrahepatic biliary radicles and dilated CBD. Tiny gallbladder stones were observed in one of the patients. Magnetic resonance cholangiopancreatography (MRCP) was done showing marked dilatation of the CBD with smooth tapering of its distal end suggesting CC type 4 according to Todani classification.

The preoperatively administered dose of ICG and its timing was mentioned in Table 2. None of our study population suffered from allergic reactions from ICG. Operative time in each group was mentioned in Table 5.

Degree of visualization of the extrahepatic biliary system (CD, common hepatic duct, CBD) has been achieved as shown in Table 3. The beneficial role of ICG usage could be demonstrated in the form of avoiding injury to CBD, CD, CHD, and vascular pedicle in some patients from groups 1 and 3 as

Figure 3



Laparoscopic view of a case from a group of choledochal cysts: (a) before any dissection, (b) identification of cystic duct, (c) choledochal cyst at the confluence of the cystic duct and common hepatic duct, (d) more dissection proximal to expose common hepatic duct, (e) dissection all around the cyst, (f) excision of the cyst and hepaticoduodenostomy was done.

mentioned in Table 3. While group 2 (with BA), as the extrahepatic biliary system was excised, the vascular injury could be avoided in all members of the group.

Groups 2 and 3 patients were followed meticulously in the Hepatology Clinic of the Department of Pediatrics in our hospital with the following changes in preoperative and postoperative liver profiles in Table 4. Table 5 shows the start of enteral feeding data and the postoperative hospital stay.

The mean postoperative follow-up labs in groups 2 and 3 is mentioned in Table 4 showing significantly improved liver profile, especially in group 2.

The pathological assessment of FC in cases of group 2 shows the presence of multiple patent microbile ducts corresponding to the fluorescence in the transected plane at the PH. The histopathological finding of the FC did not include liver parenchyma, indicating that transection had been performed outside of the hepatic capsule.

The histopathological analysis of the excised CC and gallbladder in group 3 showed that the CC was completely excised from the common hepatic duct up to the distal end of the CBD in the duodenum showing a wall of dense collagenous tissue with no evidence of metaplasia lined by columnar epithelium.

Discussion

ICG binds with circulating albumins and lipoproteins and is excreted into the bile almost unaltered following hepatic extraction. With the widespread introduction of LC, the incidence of iatrogenic main bile duct injuries has significantly increased, with incidences

Table 3 Distribution of studied sample according to common bile duct, cystic duct, common hepatic duct, vascular injury, and biliary injury in different groups

	Laparoscopic cholecystectomy [*n* (%)]	Choledochal cyst [*n* (%)]
Common bile duct		
Evident	6 (75.0)	0
Not evident	2 (25.0)	2 (100.0)
Cystic duct		
Evident	8 (100.0)	2 (100.0)
Not evident	0	0
Common hepatic duct		
Evident	8 (100.0)	2 (100.0)
Not evident	0	0
Vascular injury		
No	8 (100.0)	2 (100.0)
Biliary injury		
No	8 (100.0)	2 (100.0)
Yes	0	0

Table 4 Comparison between preoperative and postoperative regarding aspartate aminotransferase, alanine aminotransferase, total bilirubin, direct bilirubin, alkaline phosphatase, and gamma-glutamyltransferase

	Preoperative	1 month postoperative	6 months postoperative	Test value*	*P* value	Significance
Biliary atresia						
AST						
Mean±SD	244.25±100.09	175.00±94.22	140.00±74.39	8.000	0.018	S
Range	142–337	122–316	90–250			
ALT						
Mean±SD	154.75±68.77	129.75±67.03	102.50±56.20	8.000	0.018	S
Range	88–218	64–190	40–150			
Total bilirubin						
Mean±SD	13.25±2.36	7.13±3.11	5.85±2.44	8.000	0.018	S
Range	10–15	2.7–9.7	2.4–8			
Direct bilirubin						
Mean±SD	8.05±1.69	5.18±3.00	3.80±2.12	8.000	0.018	S
Range	5.9–10	0.9–7.9	0.7–5.5			
ALP						
Mean±SD	489.50±274.41	230.00±23.68	192.50±65.51	6.500	0.039	S
Range	329–898	200–256	150–290			
GGT						
Mean±SD	940.75±554.88	595.75±392.03	484.00±327.67	8.000	0.018	S
Range	211–1437	90–1000	80–856			
Choledochal cyst						
AST						
Mean±SD	36.00±9.90	26.50±19.09	22.50±17.68	4.000	0.135	NS
Range	29–43	13–40	10–35			
ALT						
Mean±SD	31.50±24.75	20.50±24.75	19.00±24.04	4.000	0.135	NS
Range	14–49	3–38	2–36			
Total bilirubin						
Mean±SD	2.60±0.28	0.55±0.35	0.45±0.35	4.000	0.135	NS
Range	2.4–2.8	0.3–0.8	0.2–0.7			
Direct bilirubin						
Mean±SD	2.15±0.07	0.20±0.14	0.20±0.14	4.000	0.135	NS
Range	2.1–2.2	0.1–0.3	0.1–0.3			
ALP						
Mean±SD	296.50±146.37	285.00±144.25	205.00±63.64	4.000	0.135	NS
Range	193–400	183–387	160–250			
GGT						
Mean±SD	38.00±16.97	17.50±3.54	13.50±0.71	4.000	0.135	NS
Range	26–50	15–20	13–14			

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, gamma-glutamyltransferase. *P* value greater than 0.05: nonsignificant (NS); *P* value less than 0.05: significant (S); *P* value less than 0.01: highly significant (HS). *Paired *t* test.

ranging from 0.2 to 1.5% [11,12]. New safe LC surgery protocols pay special attention to the prevention of main bile duct lesions, and ICG-assisted NIR cholangiogram is an emerging technique that may increase the visualization of the extrabiliary structures [13,14]. This study aimed to evaluate the usage of ICG application in pediatric patients with certain biliary conditions, either as a complementary to or as a replacement of traditional methods, regarding intraoperative time and complications affection (as a consequence of easier identification of biliary and vascular territory), postoperative hospital stay and at least 6 months follow up. Koong *et al.* [15] demonstrated that an ICG NIR cholangiogram was a safe and helpful tool for residents or new surgeons, on the learning curve of LC in the adult population.

Multiple other studies demonstrated the potential benefits of this fluorescent agent including intraoperative decision improvement, decreased rate of postoperative complications [16], and avoiding stomas [17].

Regarding the doses of ICG reported in the literature, a wide range was noted starting from 0.25 up to 0.5 mg/kg and may reach 10 mg as a fixed dose in adults [9,10]. In our study, the mean±SD ICG dosage (cm) in the LC group was 3.75±0.46, the mean±SD ICG dosage

Table 5 Distribution of studied sample according to operative time (min), blood loss, hospital stay (day), and adverse event related to indocyanine green in different groups

	Laparoscopic cholecystectomy *N*=8	Biliary atresia *N*=4	Choledochal cyst *N*=2
Operative time (min)			
Mean±SD	40.00±23.15	180.00±0.00	165.00±21.21
Range	25–90	180–180	150–180
Blood loss [*n* (%)]			
No	8 (100.0)	4 (100.0)	2 (100.0)
Hospital stay (day)			
Mean±SD	1.13±0.35	5.50±1.00	7.00±1.41
Range	1–2	5–7	6–8
Adverse event related to ICG [*n* (%)]			
No	8 (100.0)	4 (100.0)	2 (100.0)
Start of oral feeding (days)			
Mean±SD	1.25±0.46	3.25±0.5	3.5±0.71
Range	1–2	3–4	3–4

ICG, indocyanine green.

(cm) in the BA group was 1.50±0.00, while the mean ±SD ICG dosage (cm) in CC group was 3.00±1.41.

Also, controversies exist as regards the adequate timing of ICG injection ranging from at least 3 up to 12 h before imaging. Most authors concluded that a prolonged interval of up to 12 h appeared optimal for fluorescence cholangiography [18]. The difference in the contrast between the fluorescence in the liver and the extrahepatic biliary system will not be evident if injected with intervals of less than 3 h. Clearance of the ICG from the biliary system would result in poor visualization if the interval is more than 12 h [19].

In our study, the mean±SD time of injection (hour preoperative) in the LC group was 11.13±0.83, mean ±SD time of injection (hour preoperative) in the BA group was 12.00±0.00, while the mean±SD time of injection (hour preoperative) in CC group was 11.00±1.41.

Regarding the LC group in our study, we noticed adequate visualization of CBD with the usage of ICG fluorescence in 75% of our population with evident CD and common hepatic duct in all patients. Boni *et al.* [9] and Abdelaziz *et al.* [20] reported the successful identification of all the structures of the biliary tree in all adult patients, who underwent LC for biliary stones with high sensitivity and specificity (100%). In a series of adult patients, Ishizawa *et al.* [2] reported CD and common hepatic duct visualization of 100 and 96%, respectively. Broderick *et al.* [21] revealed that overall bile duct injury (BDI) was decreased with the use of an ICG cholangiogram, suggesting that improved visualization of the biliary tree via ICG as the standard of care during LC may decrease the rate of iatrogenic injury.

Authors have reported variations in the visualization ability of ICG in the biliary tree, attributed to many factors; for example, the patient position, the contrast material itself and the surgeons' experience. Improper position aside from a supine position might affect visualization [22]. Different quantities and qualities of contrast materials also play a great role in visualization. Expert surgeons are aware of the possible factors that hinder visualization such as air trapping and inadequate filling and adequate contrast materials [23].

Hirayama *et al.* [6] first demonstrated the absence of fluorescence in the biliary tract and confirmed the diagnosis of BA during the Kasai operation. They suggested that the use of an ICG cholangiogram can better visualize the biliary flow of the hepatic duct at the PH before dissecting the FC, thus a more appropriate level and extent of dissection can be determined. Moreover, it can also be used to evaluate biliary excretion postoperatively by observing the fluorescence of the feces and comparing it to the preoperative value [24].

Hirayama *et al.* [6] demonstrated that the extent of dissection of the FC of the PH, to the baseline of the portal vein, is satisfactory, even with some boring. Hence, it was also recently pointed out that extensive dissection around the outside of the PH can cause damage to the microbile ducts. Nio and Ohi [5] performed hepatoportoenterostomy in accordance with this concept at a level where only a very thin FC remains after dissection. Macroscopically, a thin slice of fibrous remnant remained at the PH after dissection of the FC. These findings suggest that the transection level of the FC of the PH was not too deep from the viewpoint of the analysis of the degree of fluorescence.

Therefore, the recognition of weak fluorescence at the PH after dissection of the FC indicates the presence of bile constituents in the thin slice fibrous remnant, and this finding may also indicate the presence of parent microbile ducts. This was confirmed by collecting the hilar exudate from the transected margin showing fluorescence, this indicates that the exudate was bile. This was in accordant with the histopathological examination of the FC showing microbile ducts [24].

Successful Kasai procedure results in a significant drop in bilirubin level and liver profile, in our BA group, there was a statistically significant difference between preoperative and postoperative tests, denoting marked improvement which could be attributed to the good dissection at PH with satisfactory exposure of microbile ducts. During the period of our study, none of our patients were in need of liver transplantation. The prevalence of long-term complications in the group of BA namely recurrent cholangitis, portal hypertension, coagulopathy, and recurrent hospital admissions were analyzed. Out of four patients with BA, only one patient had recurrent attacks of cholangitis.

García-Hernández *et al.* [8] reported that CC treatment can be complicated due to the modified anatomy caused by biliary dilation and acute pancreatitis. ICG dye facilitated the identification of the CD in Calot's triangle by delimiting the dilation of the CBD from the hepatic artery and the portal vein. Also, defining the anatomy of the dilated CBD in its union with the duodenum facilitated a safe dissection and ligation of the cyst to the intestine, avoiding injury to it [25].

In the CC group in our study, we had a satisfactory visualization of the dilated CBD with ICG fluorescence noted in 100% of our population with evident CD and common hepatic duct.

Apart from an adequate dissection, adequate level of transection of CC is also important to avoid the possibility of developing cholangiocarcinoma, which occurs at various locations, including the remnant of the cyst and intrapancreatic duct. To prevent cholangiocarcinoma during long-term follow-ups, complete excision of the CC without a remnant duct is essential [26].

A third additional benefit of ICG in CC is that: staining with ICG can rule out the existence of an anastomotic leak and confirmed the adequate passage of bile into the intestine [8], the same was noted in our CC patients.

In the group of LC, the operative time ranged from 25 to 90 min which was significantly shorter than non ICG group (53–112 min) reported by Pelizzo *et al.* [27]. The hospital stays ranged from 1 to 2 days with no reported complications. On the other hand, Ozcakir *et al.* [28] reported the occurrence of biliary fistula in one case with the hospital stay of up to 3 days. Also, Zeidan *et al.* [29] reported the occurrence of spillage of bile in 12 (5.9%) patients, as well as wound infection, retained stones, abdominal abscesses, and biloma in nine (4.5%) patients.

In the group of BA, the mean operative time was 180 min which was nearly the same as reported by Xiao *et al.* [30]. The hospital stays ranged from 5 to 7 days with no reported blood loss or bile leakage, contrary to that reported by Sun *et al.* [31] where intestinal obstruction, gastrointestinal bleeding, bile leak, and anastomotic stenosis had occurred in four patients with hospital stay ranging from 12 to 13 days.

In the group of CC, the mean operative time was 165.00±21.21 min which was significantly shorter than non ICG group (214.7±67.95 min) reported by Xuan *et al.* [32]. The hospital stays ranged from 6 to 8 days with no reported vascular injury or biliary spillage. On the other hand, Talini *et al.* [33] reported the occurrence of biliary fistula in one patient out of 13 patients. Also, Xuan *et al.* [32] reported that two patients required blood transfusion and four patients had bile leakage with the hospital stay of up to 12 days.

The limitations of our study were the small sample size; however, these biliary conditions are rare, and we collected as many as these cases were referred to a tertiary center during 2 years period. The lack of a standardized visualization grading system, and lack of quantitative assessment of fluorescence for ICG are still ongoing problems for both the adult and pediatric populations. Also, the high cost associated with purchasing the technology and tools needed for ICG represents an obstacle, especially in developing countries.

Ongoing and future studies hopefully will give firm evidence regarding the clinical and cost-effectiveness of ICG technology that has so many different clinical applications in surgery. Some of them will, undoubtedly, be transformed into the standard of care in the near future [3]. Lymphatic mapping and assessment of blood flow are probably key clinical applications in minimally invasive colorectal surgery, with proven feasibility and safety as well as potential major benefits for the patients. Intraureteral ICG and subsequent visualization under NIR fluorescence seem very promising techniques for primary and secondary prevention against iatrogenic ureteral injury [34].

Conclusion

The ICG fluorescence application in pediatric hepatobiliary surgery is feasible and safe with the mentioned doses and timing of administrations. Adequate visualization of ICG fluorescence may prevent intraoperative vascular or biliary complications.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1 Alander JT, Kaartinen I, Laakso A, Patila T, Spillmann T, Tuchin VV, *et al.* A review of indocyanine green fluorescent imaging in surgery. Int J Biomed Imag 2012; 2012:940585

2 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; 97:1369–1377.

3 Degett H, Andersen H, Gogenur I. Indocyanine green fluorescence angiography for intraoperative assessment of gastrointestinal anastomotic perfusion: a systematic review of clinical trials. Langenbecks Arch Surg 2018; 401:767–775.

4 Ankersmit M, van Dam DA, van Rijswijk AS, van den Heuvel F B, Tuynman JB, Meijerink W. Fluorescent imaging with indocyanine green during laparoscopic cholecystectomy in patients at increased risk of bile duct injury. Surg Innov 2017; 24:245–252.

5 Nio M, Ohi R. Biliary atresia. Semin Pediatr Surg 2000; 9:177–186.

6 Hirayama Y, Iinuma Y, Yokoyama N, Otani T, Masui D, Komatsuzaki N, *et al.* Near-infrared fluorescence cholangiography with indocyanine green for biliary atresia.Real-time imaging during the Kasai procedure: a pilot study. Pediatr Surg Int 2015; 31:1177–1182.

7 Esposito C, Settimi A, Del Conte F, Cerulo M, Coppola V, Farina A, *et al.* Image-guided pediatric surgery using indocyanine green (ICG) fluorescence in laparoscopic and robotic surgery. Front Pediatr 2020; 8:314.

8 García-Hernández C, Cabrera-González H, Carvajal-Figueroa L, Archivaldo-García C, Valero-Mamani RJ, Martinez-Flores RA. Usefulness of indocyanine green fluorescence in laparoscopic resection of choledochal cyst in children. J Pediatr Surg Case Rep 2022; 76:102129.

9 Boni L, David G, Mangano A, Dionigi G, Rausei S, Spampatti S, *et al.* Clinical applications of indocyanine green (ICG) enhanced fluorescence in laparoscopic surgery. Surg Endosc 2015; 29:2046–2055.

10 Boogerd LSF, Handgraaf HJM, Huurman VAL, Lam HD, Mieog JSD, van der Made WJ, *et al.* The best approach for laparoscopic fluorescence cholangiography: overview of the literature and optimization of dose and dosing time. Surg Innov 2017; 24:386–396.

11 Serban D, Socea B, Balasescu SA, Badiu CD, Tudor C, Dascalu AM, *et al.* Safety of laparoscopic cholecystectomy for acute cholecystitis in the elderly: a multivariate analysis of risk factors for intra and postoperative complications. Medicine 2021; 57:230.

12 Gupta V, Jain G. Safe laparoscopic cholecystectomy: adoption of universal culture of safety in cholecystectomy. World J Gastrointest Surg 2019; 11:62–84.

13 van de Graaf FW, Zaïmi I, Stassen LPS, Lange JF. Safe laparoscopic cholecystectomy: a systematic review of bile duct injury prevention. Int J Surg 2018; 60:164–172.

14 Harboe KM, Bardram L. The quality of cholecystectomy in Denmark: outcome and risk factors for 20,307 patients from the national database. Surg Endosc 2011; 25:1630–1641.

15 Koong JK, Ng GH, Ramayah K, Koh PS, Yoong BK. Early identification of the critical view of safety in laparoscopic cholecystectomy using indocyanine green fluorescence cholangiography: a randomized controlled study. Asian J Surg 2021; 44:537–543.

16 Kudszus S, Roesel C, Schachtrupp A, Höer JJ. Intraoperative laser fluorescence angiography in colorectal surgery: a noninvasive analysis to reduce the rate of anastomotic leakage. Langenbecks Arch Surg 2010; 395:1025–1030.

17 Jafari MD, Wexner SD, Martz JE, McLemore EC, Margolin DA, Sherwinter DA, *et al.* Perfusion assessment in laparoscopic left-sided/anterior resection (PILLAR II): a multi-institutional study. J Am Coll Surg 2015; 220:82–92.

18 Matsumura M, Kawaguchi Y, Kobayashi Y, Kobayashi K, Ishizawa T, Akamatsu N, *et al.* Indocyanine green administration a day before surgery may increase bile duct detectability on fluorescence cholangiography during laparoscopic cholecystectomy. J Hepatobiliary Pancreat Sci 2021; 28:202–210.

19 Zarrinpar A, Dutson E, Mobley C., Busuttil RW, Lewis CE, Tillou A, *et al.* Intraoperative laparoscopic near infrared fluorescence cholangiography to facilitate anatomical identification: when to give indocyanine green and how much. Surg Innov 2016; 23:360–365.

20 Abdelaziz A, Anwar H, Muhammed T. Evaluation of the role of indocyanine green fluoroscopy for intraoperative bile duct visualization and prevention of CBD injury during laparoscopic cholecystectomy. Al-Azhar Int Med J 2022; 3:47–51.

21 Broderick RC, Lee AM, Cheverie JN, Zhao B, Blitzer RR, Patel RJ, *et al.* Fluorescent cholangiography significantly improves patient outcomes for laparoscopic cholecystectomy. Surg Endosc 2021; 35:5729–5739.

22 Schlumpf R, Klotz HP, Wehrli H, Herzog U. A nation's experience in laparoscopic cholecystectomy.Prospective multicenter analysis of 3722 cases. Surg Endosc 2019; 8:35–41.

23 Lammert F, Gurusamy K, Ko CW, Miquel JF, Mendez- Sanchez N, Portincasa P, Wang DQH. Gallstones. Nat Rev Dis Primers 2016; 2:1–17.

24 Yanagi Y, Yoshimaru K, Matsuura T, Shibui Y, Kohashi K, Takahashi Y, *et al.* The outcome of real-time evaluation of biliary flow using near-infrared fluorescence cholangiography with Indocyanine green in biliary atresia surgery. J Pediatr Surg 2019; 54:2574–2578.

25 Onishi S, Yamada K, Murakami M, Kedoin C, Muto M, Ieiri S. Co-injection of bile and indocyanine green for detecting pancreaticobiliary maljunction of choledochal cyst. Eur J Pediatr Surg Rep 2022; 10:e127–e130.

26 Madadi-Sanjani O, Wirth TC, Kuebler JF, Petersen C, Ure BM. Choledochal cyst and malignancy: a plea for lifelong follow-up. Eur J Pediatr Surg 2019; 29:143–149.

27 Pelizzo G, Bussani R, De Silvestri A, Di Mitri M, Rosone G, Amoroso S, *et al.* Laparoscopic cholecystectomy for symptomatic cholecystic disease in children: defining surgical timing. Front Pediatr 2020; 8:203.

28 Ozcakir E, Sancar S, Mete KA. laparoscopic cholecystectomy in childhood: a review of twenty-four consecutive cases. Eur Res J 2017; 3:30–34.

29 Zeidan MM, Pandian TK, Ibrahim KA, Moir CR, Ishitani MB, Zarroug AE. Laparoscopic cholecystectomy in the pediatric population: a single-center experience. Surg Laparosc Endosc Percutan Tech 2014; 24:248–250.

30 Xiao H, Huang R, Chen L, Diao M, Li L. The application of a shorter loop in Kasai portoenterostomy reconstruction for Ohi type III biliary atresia: a prospective randomized controlled trial. JSurg Res 2018; 232:492–496.

31 Sun X, Diao M, Wu X, Cheng W, Ye M, Li L. A prospective study comparing laparoscopic and conventional Kasai portoenterostomy in children with biliary atresia. J Pediatr Surg 2016; 51:374–378.

32 Xuan NT, Son NH, Thien HH. Is the laparoscopic choledochal cyst excision and Roux-En-Y hepaticojejunostomy in adults as safe as that in children? Egypt Liver J 2020; 10:1–6.

33 Talini C, de-Carvalho BC, Antunes LA, Schulz C, Sabbaga CC, Avilla SG, *et al.* Choledochal cyst in the pediatric population: experience of 13 Laparoscopic procedures in two years at a single institution. Rev Col Bras Cir 2018; 45:e1854.

34 Esposito C, Alberti D, Settimi A, Pecorelli S, Boroni G, Montanaro B, *et al.* Indocyanine green (ICG) fluorescent cholangiography during laparoscopic cholecystectomy using RUBINA technology: preliminary experience in two pediatric surgery centers. Surg Endosc 2021; 35:6366–6373.