Anatomical delineation of the biliary tree during laparoscopic cholecystectomy by intracholecystic injection of methylene blue

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Background
Many factors have been incriminated in occurrence of bile duct injuries during laparoscopic cholecystectomy (LC). Misidentification of the anatomy and lack of surgeon's experience seems to be preliminary; however, many techniques were used to avoid such injuries.
Aim of the work
To asses feasibility of delineation of biliary tree by intracholecystic injection of methylene blue (MB) during LC.
Patients and methods
A prospective study had been conducted in Ain Shams University Hospitals between January 2019 and January 2020. The study included 60 patients who presented to outpatient department (OPD) with abdominal ultrasound showing chronic calcular cholecystitis and all underwent intracholecystic injection of MB during LC.
Results
As regards MB delineation of different parts of gall bladder and biliary tract component, gall bladder delineation occurred in all patients (100%), whereas cystic duct delineated in 80% of patients (48/60) and common bile duct (CBD) delineated in 41.7% of patients (25/60) as general and separate assessment of each element alone with no detected cases of bile duct injury. There was significant increase in CBD delineation in patients with single stone and thin-walled gall bladder. Extravasation of dye from the gall bladder into the abdominal cavity occurred and this led to anatomical misidentification and significant prolongation of operative time (extra time was needed for irrigation and suction).
Conclusion
The technique by which the MB is injected into the lumen of gall bladder to delineate the cystic duct and CBD is feasible, cheap, and performed without any radiation exposure and without using special equipment. By this technique, no cases of biliary injury were detected; however, critical view of safety remains the gold standard surgical technique to prevent bile duct injury.

Keywords:
biliary tree, laparoscopic cholecystectomy, methylene blue

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Introduction

It has been recognized that the treatment of symptomatic gallstones is removal of the gall bladder (GB), not because it contains stones, but because it causes them. For over 100 years, the technique of cholecystectomy required a generous abdominal incision to provide sufficient light and exposure to perform the operation safely. In the late 1980s, with the technology of improved optics, the technique of laparoscopic cholecystectomy (LC) was introduced and widely adopted by practicing general surgeons [1].

Many factors have been incriminated in occurrence of bile duct injuries (BDIs) during LC. These are mainly anatomical misidentification, anatomical variations, surgeon's experience, technical difficulties, poor visualization of the operative field, and acute and chronic inflammation of the GB [2]. However, misidentification of the anatomy and surgeon's experience seems to be preliminary [3].

Subsequent improvements in the equipment and refinement in technique, as well as improved learning curve in laparoscopic surgery, resulted in a progressive decrease of the incidence of these injuries. Nevertheless, global incidence of CBD injury has remained fairly

constant around 0.5%, as reported by various meta-analysis studies over a 15-year period [4].

There are different modalities that have been described for intraoperative assessment of biliary anatomy during LC such as intraoperative cholangiography (IOC) and laparoscopic ultrasound (LUS) [5].

Sari *et al.* [6] described a technique by which the methylene blue (MB) is injected into the lumen of GB to delineate the cystic duct (CD) and common bile duct (CBD). This technique seems easier to perform, without any radiation exposure and less time consuming than conventional IOC.

MB has a 120-year long history of diverse applications, both in medical treatments and as a staining reagent [7].

Aim of the work

The aim of our work is to assess feasibility of delineation of biliary tree by intracholecystic injection of MB during LC.

Patients and methods

This is a prospective study that had been conducted in Ain Shams University Hospitals in the period between January 2019 and January 2020 after obtaining informed consent from all patients. Sixty patients were included who presented to general surgery clinic with abdominal US document revealing that they are suffering from chronic calcular cholecystitis, and all underwent intracholecystic injection of MB during LC.

All patients were assessed by the following.

History taking

Detailed history for all patients especially the history of any medical problem such as diabetes mellitus (DM), hypertension, liver disease, and jaundice was taken. A designed sheet was fulfilled for every patient to document these data and past history of previous treatment either medical or surgical.

All patients had symptoms of chronic calcular cholecystitis, for example, pain in the right hypochondrium referred to right shoulder or epigastric pain sometimes referred to back. Some patients (e.g., diabetic patients) are asymptomatic and stones were discovered accidentally during abdominal US that was done for other indications.

Clinical examination

General and local examinations were done to exclude calcular obstructive jaundice and acute calcular cholecystitis.

Investigations

Laboratory workup: hematologic and biochemical tests: complete blood count, coagulation profile, fasting blood glucose, hemoglobin A1C for diabetic patients, renal function tests and liver function tests. Abdominal US was taken to show site and size of GB stones, GB size, GB wall thickness, and any associated pathology as CBD dilatation, CBD stones, or other hepatobiliary-pancreatic pathology.

Magnetic resonance cholangiopancreatography (MRCP) was done in patients with history of elevated alkaline phosphatase and gamma GT (GGT) to exclude stone or stricture in CBD.

Inclusion criteria

(1) Patients having chronic calcular cholecystitis and candidates for LC.
(2) Male and female sex.
(3) Age from 18 to 65 years.

Exclusion criteria

(1) Any associated hepatobiliary-pancreatic pathology (e.g., cirrhotic liver or acute pancreatitis).
(2) Calcular cholecystitis with obstructive jaundice.
(3) Acute calcular cholecystitis.
(4) GB tumors.
(5) Patient unfit for surgery.
(6) Pregnant females.

Consent

Detailed explanation of the procedure and its outcome and possible complications was included in an informed consent and signed by all included patients before operation.

Surgical technique

The GB fundus was grasped and held tight toward the anterior abdominal wall. The GB fundus was punctured by aspiration or Veress needle that was introduced through the abdominal wall.

All the bile in the GB was aspirated and 50% diluted MB equal to the amount of aspirated bile was injected slowly into the GB. To prevent bile leakage, the GB fundus was held tight anteriorly during the withdrawal of the needle and a grasper introduced through the right (anterior axillary line [AAL]) trocar was

applied immediately to the puncture site and was held throughout the operation.

To open the triangle of calot, the Hartmann pouch grasped and retracted caudally and to the right. Using a curved (Maryland) dissector through the main operating trocar, the peritoneal layer overlying the GB–CD junction was peeled away. The neck of the GB was dissected away from its attachment and the GB–CD junction can now be seen clearly from all directions.

No structure was clipped or divided until this "critical view of safety" (CVS) was achieved where only two structures were clearly entering into the GB and the base of the liver can be visualized through the dissected triangle of calot. Once identified, the CD was dissected to allow the safe placement of three clips and milked toward the GB to push any stones present into the GB.

The artery was located in relation to the duct and usually runs parallel to it. The cystic artery is usually anatomically related posterior to the CD node. A posterior branch of cystic artery may be encountered and should be sought to avoid troublesome bleeding. Once fully dissected, the CD and artery were controlled with clips and divided.

Dissection was done until the GB fundus was attached by a thin strip of peritoneum. Using the GB as a handle to maintain exposure, the area of dissection was carefully examined for bleeding or bile leak, with particular attention paid to the clipped CD and artery stumps. After hemostasis was assured, the final attachment to the GB was divided and the GB was placed above the right lobe of the liver without removing the grasping forceps.

A heavy grasping forceps was introduced through the epigastric port to grasp the neck of the GB. Under direct vision, the GB was extracted. In some cases, the fascia and skin incisions needed to be enlarged to retrieve the GB. A drain was left in the subhepatic space and exteriorized through the right lateral trocar site.

Evaluation

The evaluation is based on delineation of the GB, CD, and CBD, thick or thin wall GB, with multiple or single stones, postoperative complications, and operative time.

Statistical analysis

The data were collected, tabulated, and statistically analyzed. Description of quantitative variable was done as mean and SD, and qualitative data as frequency. The results were considered significant (S) with $P \leq 0.05$, whereas being nonsignificant (NS) with P value more than 0.05. Analysis of data was done using IBM SPSS software (Statistical Program for Social Science version 21).

Results

This study included 60 patients with chronic calcular cholecystitis who underwent LC with intracholecystic injection of MB dye.

This study included 60 patients with chronic calcular cholecystitis who underwent LC with intracholecystic injection of MB dye, the mean age for the patients was 41.05 years, most of those patients were females (50/60) (83.3%), whereas males were 16.7% (10/60) as shown in Table 1.

As regards classification of patients according to GB characteristics, number of gall stones and GB wall thickness are shown in Table 2.

As regards MB delineation of different parts of GB and biliary tract component, GB delineation occurred in all patients (100%), whereas CD delineated in 80% of patients (48/60) and CBD delineated in 41.7% of patients (25/60) as general and separate assessment of each element alone.

Combination of structures delineated by MB; GB, CD, and CBD were delineated in 41.7% of patients (25/60), whereas GB and CD were delineated together without CBD in 80% of patients (48/60) as shown in Table 3 and Figs. 1 and 2.

Table 1 Demographic data of study candidates

	No.=60
Age	
Mean±SD	41.05 ± 7.77
Range	25–60
Sex	
Female	50 (83.3%)
Male	10 (16.7%)

Table 2 Gall bladder characteristics of study candidates

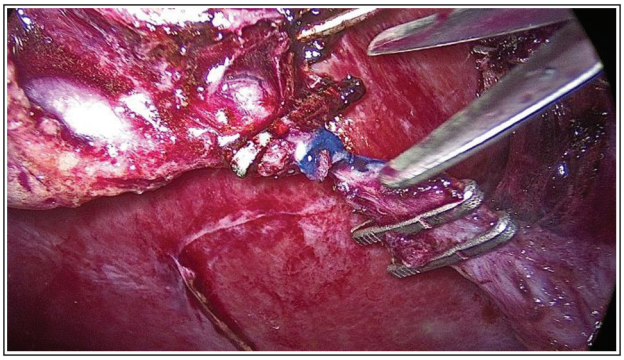
	No. (%)
Stone *N*	
Multiple	42 (70.0%)
Single	18 (30.0%)
Gall bladder wall thickness	
Thick	36 (60.0%)
Thin	24 (40.0%)

Table 3 Methylene blue delineation

Methylene blue delineation	No. (%)
Gall bladder	60 (100.0%)
Cystic duct	48 (80.0%)
CBD	25 (41.7%)
Gall bladder only	12 (20%)
Gall bladder + cystic duct	48 (80.0%)
Gall bladder + cystic duct + CBD	25 (41.7%)

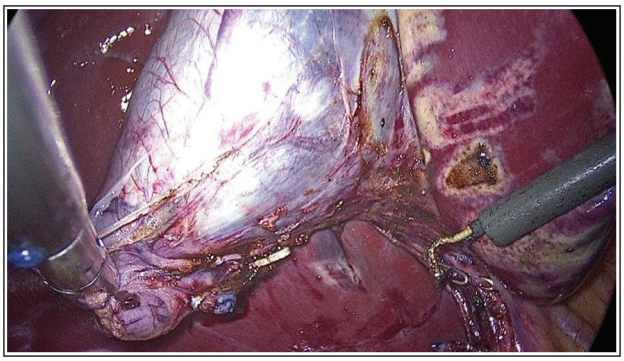
CBD, common bile duct.

Figure 1



Cystic duct stump delineated.

Figure 2



Gall bladder and cystic duct stump delineated.

As regards the relation between number of gall stones and MB delineation, single stone patients showed statistically significant difference in CD and CBD delineation in comparison with multiple stones patients as shown in Table 4.

As regards the relation between GB wall thickness and MB delineation, thin-walled GB patients showed statistically significant difference in CD and CBD delineation in comparison with thick-walled GB patients as shown in Table 5.

As shown in Table 6, the hospital stay postoperatively for all patients was 1 day, whereas the mean operative time was 68.9 min. Dye spillage was important factor causing highly significant prolongation in operative time as spillage occurred in 6 of 60 patients with mean operative time 92.50 min, whereas in 90% of patients (54/60) with no dye spillage, the mean operative time was 66.35 min as shown in Table 7.

As regards perioperative insults and complications, no biliary injury, hemorrhage, missed stone, or reaction to dye was recorded among study patients, whereas only nine patients reported that bluish discoloration of the urine lasted for only 12 h postoperatively as shown in Table 8.

Discussion

LC represents the gold standard treatment for GB stones; open cholecystectomy (OC) is performed only rarely, because LC confers advantages such as a shorter hospitalization period, more rapid return to normal activities, reduced postoperative pain, and good cosmetic outcomes [8,9].

An inexperienced surgeon; severe, acute, or chronic gallbladder inflammation; fatty surgical sites; excessive

Table 4 The relation between number of gall stones and methylene blue delineation

Methylene blue delineation	Stone *N*		Test value	*P* value	Sig.
	Multiple No. (%)	Single No. (%)			
Gall bladder	42 (100.0)	18 (100.0)	NS	NS	NS
Cystic duct	30 (71.4)	18 (100.0)	6.429	0.011	S
CBD	9 (21.4)	16 (88.9)	23.592	0.001	HS

CBD, common bile duct.

Table 5 The relation between gall bladder wall thickness and methylene blue delineation

Methylene blue delineation	Gall bladder wall thickness		Test value	*P* value	Sig.
	Thick No. (%)	Thin No. (%)			
Gall bladder	36 (100.0)	24 (100.0)	NS	NS	NS
Cystic duct	25 (69.4)	23 (95.8)	6.267	0.012	S
CBD	3 (8.3)	22 (91.7)	41.143	0.000	HS

CBD, common bile duct.

Table 6 Hospital stay and operative time

	No.=60
Hospital stay (day)	
1 day	60 (100.0%)
Operative time (min)	
Mean±SD	68.97 ± 14.04
Range	45–100

Table 7 Relation between dye spillage and operative time (min)

Operative time (min)	Spillage of dye		Test value	*P* value	Sig.
	No No.=54	Yes No.=6			
Mean±SD	66.35 ± 12.02	92.50 ± 7.58	−5.191	0.001	HS
Range	45–95	80–100			

Table 8 Perioperative insults and complications

Perioperative insults	No. (%)
Biliary injury and biliary leak	
No	60 (100.0)
Yes	0 (0.0)
Spillage of dye	
No	54 (90.0)
Yes	6 (10.0)
Bluish discoloration of urine	
No	51 (85.0)
Yes	9 (15.0)
Hemorrhage	
No	60 (100.0)
Yes	0 (0.0)
Missed stone in CBD	
No	60 (100.0)
Yes	0 (0.0)
Reaction to dye	
No	60 (100.0)
Yes	0 (0.0)

CBD, common bile duct.

bleeding; aberrant or rare anatomy; and/or the application of inappropriate surgical techniques may increase the likelihood of BDI [5].

Less common causes of BDI or biliary leakage include inappropriate closure of the CD, choledochal damage after tenting, the opening of superficial intrahepatic bile ducts after deep dissection of the liver bed and inappropriate use of electrocautery [8,10]. However, the most frequent cause of BDI is anatomical misidentification, particularly by inexperienced surgeons [11].

The incidence of BDIs is two times greater when compared with OC. BDI, either in classic open or LC, may necessitate several consecutive operations and invasive procedures, causing fear and anxiety to all surgeons [2].

The development of BDIs after LC is not common but a serious complication resulting in long-term morbidity [12]. When the literature is reviewed, the incidence of BDIs in LC is between 0, 3, –0, and 6% [13], which may be considered an acceptable percentage and result in secondary biliary cirrhosis with considerable financial burden [14]. Higher incidence of biliary tree injuries has also been reported. In United States, 600 000 cases of LCs are performed annually. When this number is taken into consideration, it will be clearly understood that the economic problem caused by even small (0, 3–0, 6%) rates of BDIs cannot be underestimated [15].

There are different modalities that have been described for intraoperative assessment of biliary anatomy during LC such as IOC, LUS, and cholangioscopy [5].

All the previous procedures suffered many obstacles, such as prolongation of the operative time, use of specific equipment, radiation exposure, and need for expert surgeon and/or expert radiologist. Therefore, Sari *et al.* [6] described a technique by which the MB is injected into the lumen of GB to delineate the CD and CBD. This technique seems easier to perform, without any radiation exposure and less time consuming than conventional IOC and cheap without any reported hypersensitivity reaction.

Our study included 60 patients with chronic calcular cholecystitis who underwent LC with intracholecystic injection of MB dye; the mean age for patients was 41.05 years, and most of those patients were females (50/60) (83.3%), whereas males were 16.7% (10/60).

Sari *et al.* [6]reported that 37 patients were female (mean age 45 years) and 9 patients were male (mean age 52 years).

In our study, 70%of patients were with multiple gall stones (42/60), whereas 30% of patients were with single gall stone (18/60) and as regards GB wall thickness, 60% of patients were with thick-walled GB (36/60), whereas 40% of patients were with thin-walled GB (24/60). As regards MB delineation of different parts of GB and biliary tract component, GB delineation occurred in all patients (100%), whereas CD delineated in 80% of patients (48/60) and CBD delineated in 41.7% of patients (25/60). In the relation between GB wall thickness and MB delineation, thin-walled GB patients showed statistically significant difference in MB delineation in comparison with thick-walled GB patients and that delineation was better in single stone than multiple ones.

Abdelaziz [16] reported that 16 patients (27%) had single stone, whereas 44 patients (73%) had multiple stones.

Abdelaziz [16] reported that all GBs were painted, whereas 56 CDs were painted (93%), which is significantly important, whereas CBD and common hepatic ducts were painted in 38 patients (63%). Comparing single with multiple stones patients, it was found that 16 patients (100% of those who had single stone) were painted, whereas 40 of 44 patients who had multiple stones (90.9%) had their CD painted. Those who had their CD not visualized had their GB wall thickened in ultrasonographic preoperative evaluation. Regarding CBD and hepatic ducts painting, only 38 patients (63%) had their ducts painted. Comparing single with multiple stones patients, it was found that 12 patients (31.5%) had single stone, whereas 26 patients (68.5%) had multiple stones. The ducts were not painted in 22 patients (37%), 4 had single stone (19%) and thick GB wall, whereas 18 patients (81%) had multiple stones and 12 of them had thick wall GB, whereas the other 6 had thin wall GB. From these results, it is clear that failure of painting the CBD is more in thick wall GB.

Elmaghraby *et al.* [17] reported that all gallbladder were delineated (100%), 46 CDs were delineated (92%), whereas 19 CBDs were delineated (38%). These results are different from the results obtained by Sari *et al.* [6] who used the same technique. Forty-six patients underwent LC by "MB dye injection" technique. They found that the GB, CD, and ductus choledochus were painted with MB in 43 cases but only the GB and the proximal CD were visualized in 3 cases [6].

In our study, six patients (10%) were reported to have dye extravasation either after injection or duration disection of GB from liver bed without any consecutive complications but because MB is excreted by the kidneys, the patients should be informed of the possibility of blue urine in the early postoperative period, which already occurred in nine cases (15%).

Elmaghraby *et al.* [17] reported that in nine cases (18%), extravasation of dye from the GB into the abdominal cavity occurred during injection of dye, removal of needle from GB, or during removal of GB from its bed. These results are different from the results obtained by Sari *et al.* [6] who used the same technique. They found that five cases (11%) had extravasation of dye from the GB.

In this study, the hospital stay postoperatively for all patients was 1 day, whereas the mean operative time was 68.9 min. Dye spillage was important factor causing highly significant prolongation in operative time as spillage occurred in 6 of 60 patients with mean operative time 92.50 min, whereas in 90% of patients (54/60) with no dye spillage, the mean operative time was 66.35 min.

Elmaghraby *et al.* [17] showed that the operative time from skin incision up to skin closure of the trocars' sites ranged from 45 to 90 min with mean 64.6 ± 12.73 min. It was found that operative time in patients with extravasation of dye ranged from 75 to 90 min with mean 81.67 ± 5.0 min, whereas in patients without extravasation of dye ranged from 45 to 80 min with mean 60.85 ± 10.66 min (P value<0.001); so, there is statistically significant prolongation of operative time in patients with extravasation of dye.

Elmaghraby *et al.* [17] showed that the hospital stay postoperatively was 1 day in all patients. This result is consistent with the result obtained by Sari *et al.* [6] who used MB injection technique. All patients were discharged the day after the operation, whereas the mean hospital stay was 1.2 days, and was 2.43 days in a study done by Priego *et al.* [18] on 1849 patients.

There was no biliary injury in our cases. This result is consistent with the results obtained by Sari *et al.* [6] and Elmaghraby *et al.* [17]

In 1995, Strasberg *et al.* [19] described the "CVS" approach. Although CVS is not an imaging modality, it is the operative technique that plays a major role in establishing the anatomical orientation of the bile ducts during LC.

There are not many studies on the use of blue dye injection technique because of the more recent methods of intraoperative assessment of biliary anatomy during LC as IOC, laparoscopic ultrasonography, and cholangioscopy; however, the use of this method is of fundamental benefit in small hospitals with limited resources to train young surgeons.

Conclusion

The technique by which the MB is injected into the lumen of GB to delineate the CD and CBD is feasible, cheap, and performed without any radiation exposure and without using special equipment. By this technique, no cases of biliary injury were detected. There was significant increase in CBD delineation in patients with single stone and thin-walled GB. Extravasation of dye from the GB into the abdominal cavity may occur and this leads to anatomical misidentification

and significant prolongation of operative time (extra time was needed for irrigation and suction); however, CVS remains the gold standard surgical technique to prevent BDI.

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Conflicts of interest
No conflict of interest.

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