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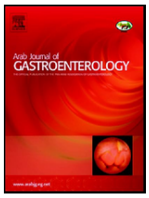

Original article

Efficacy and safety of cholangioscopy guided laser lithotripsy for difficult bile duct stones – A prospective study from a tertiary care centre in Eastern India

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ABSTRACT

Background and study aims: Endoscopic sphincterotomy combined with endoscopic papillary balloon dilatation, mechanical lithotripsy or both, are effective modalities for the ex- traction of difficult common bile duct (CBD) stones. However, approximately 5–15% of cases are still difficult to treat. In the present study, we have evaluated the safety and efficacy of single- operator cholangioscopy guided laser lithotripsy (LL) for difficult to treat CBD stones.

Patients and methods: Consecutive patients undergoing LL for the extraction of difficult CBD stones were enrolled in the study. The primary outcomes were related to the efficacy of the procedure in terms of ductal clearance and safety in terms of complications.

Results: During the 36 months, 764 patients presented for biliary stone extraction. Most of the patients, 683 (89.4%), had a successful stone extraction with standard techniques. Thirteen patients (1.7%) were not suitable for endoscopic therapy or did not consent for endoscopic therapy, and were referred directly for surgical treatment. Sixty-seven patients (8.8%) were included in the study. Cholangioscope was able to reach the stone in all the cases but one. Complete ductal clearance was achieved in 61 (91%) patients. Complications were encountered in 8 (11.9%) patients. All patients were asymptomatic at one-month of follow-up.

Conclusion: LL is a highly effective and safe procedure with minimal and transient complications.

Introduction

Endoscopic sphincterotomy (ES) combined with endoscopic papillary balloon dilatation (EPBD), mechanical lithotripsy (ML), or both are modalities for the extraction of common bile duct (CBD) stones [1]. However, approximately 5–15% of cases are still difficult to treat [2–5]. Such stones are generally large, multiple, stacked, square-shaped, impacted (wider in diameter than the bile duct), located proximal to a stricture, or associated with Mirizzi syndrome. They are difficult to extract by the above-mentioned methods, hence considered to be difficult bile duct stones [6]. These stones may require a more invasive surgical approach. High-risk patients, such as the elderly or those with serious comorbidities, are difficult to treat with the surgery. Laser lithotripsy (LL) provides an alternative non-surgical treatment for such patients.

Intraductal lithotripsy involves two essential components. The first component requires visualization of the CBD and localization of the stone by the cholangioscopy. Cholangioscopy also assists the positioning of the laser probe for accurate targeting of the stone and adequate CBD visualization to avoid duct injury. The second component involves laser fragmentation of the stone under direct cholangioscopy visualization. In the present study, we have evaluated the safety and efficacy of single-operator cholangioscopy guided LL for difficult to treat CBD stones.

Patients and methods

This is a prospective single-center study from a tertiary care teaching institute of Eastern India. Consecutive patients with difficult bile duct stones visiting our institute from May 2016 to May 2019 were enrolled in this study. The study was approved by the ethical committee of the insti- tute. Patients referred to our institute for stone extraction from other centers were also enrolled. All patients had magnetic resonance cholangiopancreatography (MRCP)

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before intervention in order to delineate the anatomy, shape, and number of stones. MRCP was not mandatory in patients referred from other hospitals with failed stone extraction and having a cholangiogram available with them. Difficult CBD stones were defined as stones that were not amenable to retrieval by ML with or without EPBD. Patients with Mirizzi syndrome and impacted stones were also included. Exclusion criteria involved patients with stones that were managed by conventional measures, patients with distorted anatomy, bleeding diatheses, malignant biliary strictures, or portal hypertension. Patients with multiple large stones with intact gall bladder having stone where endoscopist considered surgery (cholecytectomy with choledochotomy) as a better option were also excluded. However, patients with history of cholecystectomy having multiple large CBD stones were included for LL. Informed and written consent was obtained from all patients before the procedure.

All patients received prophylactic antibiotics before the procedure. Procedures were performed in the prone position without endotracheal intubation or mechanical ventilation, using sedation with intravenous propofol with continuous monitoring, administered by an anesthesiologist. After using the standard cannulation techniques and outlining the CBD stones, wire-guided biliary sphincterotomy was performed or extended (if considered inadequate). This was followed by sphincteroplasty by the EPBD up to the diameter of the distal CBD in all the patients. After biliary sphincterotomy, stone removal was attempted with a stone retrieval balloon, extraction bas- ket, or ML whenever considered possible. When the above techniques failed or not regarded as suitable, the 10Fr cholangioscope (SpyGlassTM DS Boston Scientific, Marlborough, United States) was introduced through the 4.2 mm working channel of a therapeutic duodenoscope into the CBD under the endoscopic vision to target the CBD stone. Cholangioscope was reused 3–4 times after proper disinfection.

We used LITHOTM (35 W, Quanta System, Italy) laser therapy system, which uses holmium laser technology and laser fiber (Proflex TM laser fiber 273, InnovaQuartz LLC, USA) which is 0.021 in. in diameter (Fig. 1). The laser fiber was inserted through the 1.2 mm working channel of the cholangioscope. Laser parameters used included: Energy: 0.8–1.5 J, Rate: 8–15 Hz, Power: 8 – 15 W was used.

Fig. 1. Laser lithotripsy system.

Laser bursts of < 5 s of duration were applied under continuous saline irrigation to fragment the target stone, which was removed with conventional extraction devices (Fig. 2). In cases where complete stone clearance was not achieved, a straight plastic biliary stent was inserted until definitive stone clearance. Rectal indomethacin to prevent post ERCP pancreatitis was administered to high-risk individuals without any contraindications to nonsteroidal anti-inflammatory drugs.

The study outcomes included the clinical success of the procedure, which was defined as the ability to visualize, target, and achieve clearance of the CBD stone. The incidence of adverse events (AEs), including post ERCP pancreatitis as defined by the Cotton criteria, was also observed [7]. All patients were monitored for at least 4 h following the procedure and were followed for at least one month, with subsequent visits to our outpatient department as needed. Descriptive statistics were used to describe the results. The results were presented as mean (SD) or median and/or range.

Results

During the 36 months period, 764 patients presented for biliary stone extraction. Most of the pa- tients, 683 (89.4%), had a successful stone extraction with standard techniques. Thirteen patients (1.7%) were not considered for the endoscopic therapy as 9 patients had CBD stones with two or more stones measuring > 2 cm in diameter along with gall bladder stone. Remaining 4 patients did not consent, for the endoscopic therapy and were referred for surgical treatment. One patient was excluded because of portal hypertension. Thus, 67 patients (8.8%) were included in the study.

Table 1 shows details of the patients, stone, intervention, and adverse event characteristics. The mean (±SD) age of the patients was 42.5 (±14.22) with a range of 21–88 years. Thirty-seven (55.2%) patients were male. The mean size (±SD) of the stone was 20.4 (±5.3) mm with a range 12–35 mm. The most frequent location of the stone was CBD, which was seen in 40 (59.7%) patients, followed by common hepatic duct/ hilum in 14 patients (20.9%), 12 (17.9%) patients had cystic duct stones and the least common was an intrahepatic stone in a single patient (1.5%). Twenty patients (29.8%) had failed prior stone extraction in centers elsewhere and were referred to our institute for stone extraction. EPBD and/or ML had failed to facilitate stone extraction in 42 patients (62.7%). Of the remaining 25 patients, 13 (19.4%) had impacted stones, and 12 (17.9%) patients had Mirrizzi syndrome.

The mean time (±SD) for lithotripsy (calculated from the time of insertion of cholangioscope into the bile duct upto its removal) was 15.04 (±7.5) with a range of 5.16 – 35.31 min. LL was started during the initial ERCP in 39 (58.2%) patients and 28 (41.8%) patients during the second attempt. The cholangioscope was able to reach the biliary stone in all cases, but one, as there was a tight CBD stricture distal to the stone. Complete ductal clearance was achieved in 61 (91%) patients, of which 48 (78.7%) of patients had ductal clearance in the first attempt, and 13 patients (21.3%) required multiple (2–4) attempts. Mean ductal clearance was achieved in 1.4 LL (±0.6) sessions. Six patients (8.9%) who had unsuccessful ductal clearance were referred to undergo surgery. Five of these six patients had multiple large stacked CBD stones, and all of them after the initial suboptimum LL session were referred to undergo surgery. One patient had a tight CBD stricture, distal to the impacted stone. In this patient, even after two settings of biliary stent exchange, cholangioscope was difficult to insert and hence was referred for surgery.

AEs were encountered in 8 of 67 (11.6%) patients. Two patients developed mild acute pancreatitis; three patients had sphincterotomy site bleed, which was controlled with balloon tamponade, adrenaline injection, or both. Transient fever (>100 degrees Fahrenheit) was

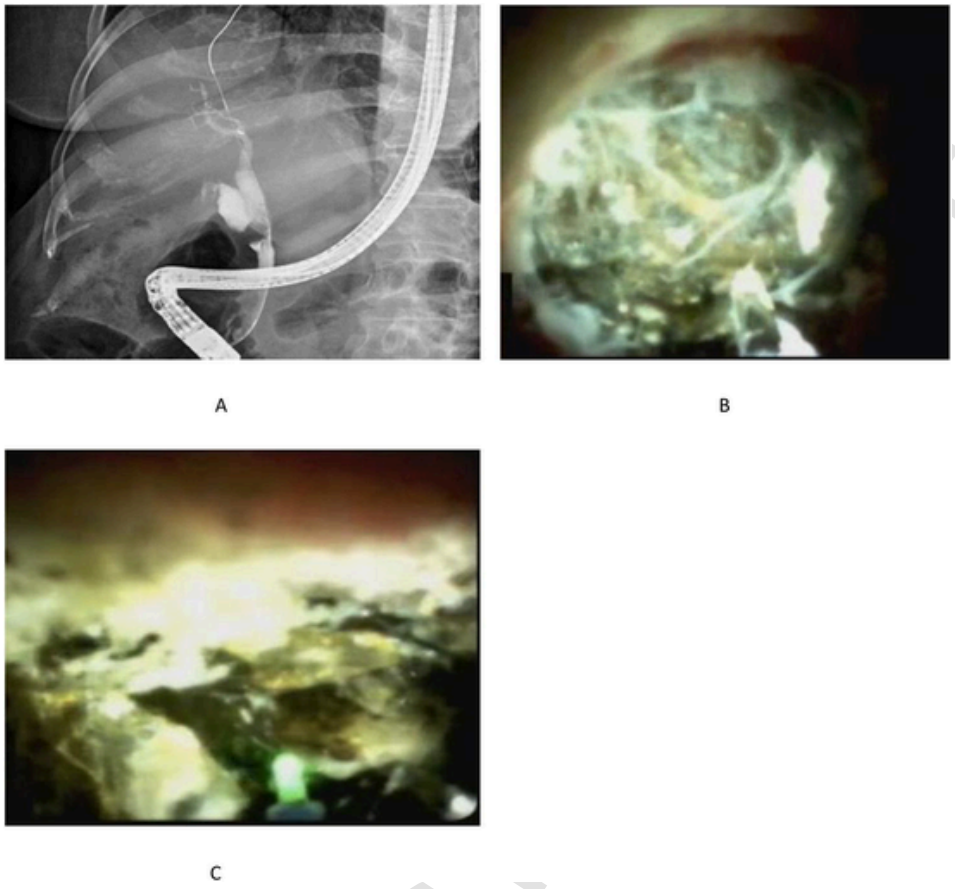

Fig. 2. A) Cholangiogram showing Mirizzi Syndrome. B) A cholangioscopic image of an impacted CBD stone undergoing lithotripsy. C) Fragmentation of the stone after laser lithotripsy.

noted in 3 patients. All the patients were asymptomatic at one month of follow up.

Discussion

Difficult CBD stones often present as a technical challenge for stone extraction during ERCP. Interventions like ML and EPBD may not be a very effective therapy for these types of stones. ERCP with conventional techniques achieves complete endoscopic stone removal in 86% to 90% of the cases. However, as the size of the stone increases the likelihood of success with conventional techniques decreases. Success rate decreases in the range of 68% to 79%, in large (>1 cm) and difficult CBD stones [8–10]. There are very few modalities available for the extraction of such difficult bile duct stones such as extracorporeal shock-wave lithotripsy (ESWL), cholangioscopy assisted LL or electrohydraulic lithotripsy (EHL) and surgical exploration of the CBD [11,12].

In a comparative study, cholangioscopy assisted LL was found to be more effective (97% versus 73%), safer and less time consuming than ESWL for fragmentation of the CBD stones [13]. ESWL of CBD stones requires several sessions usually, and the probability of injury to surrounding tissues due to shock-wave was also significant. Furthermore, a subsequent ERCP is required for the extraction of the fragmented stones. A systematic review showed that LL had a higher ductal clearance rate (95.1%) than EHL (88.4%) and ESWL (84.5%; $P < 0.001$). Moreover, the stone fragmentation rate for LL was also higher (92.5%) than for EHL (75.5%) and ESWL (89.3%; $P < 0.001$). The AEs rate for EHL (13.8%) was significantly higher than the patients treated with ESWL (8.4%) or LL (9.6%; $P = 0.04$) [14].

The present study reports the safety and efficacy of cholangioscopy guided LL of difficult bile duct stones and their subsequent extraction. The complete bile duct stone clearance was achieved in 91% of patients. Multiple (2–4) LL attempts were required in 19% of patients, while one at- tempt was sufficient to achieve complete ductal clearance in 71.6% of patients. AEs were noted in 11.9% of patients, which were mild in severity and were managed conservatively, with all patients been asymptomatic at a one-month follow-up. Previously reported bile duct stone clearance rates with the use of LL varied from 64% to 97.4%. AEs reported in previous studies varied from 0% to 23.1%0.4 [15–21]. Various studies have reported success rate of 69% to 81% clearance rate in one session for lithotripsy of difficult CBD stones [4,18,19,22].

We also emphasize that the 4-way 30 degrees tip deflection of the SpyGlass DS cholangioscope enabled easier cannulation, clear visualization, and precise stone targeting for the LL. In our practice, we do not preload the LL fiber into the working channel before cannulation. As contrary to a previous study, we rarely find resistance to pass the LL fiber across the tip of the duodenoscope [6]. One must also be careful to avoid the LL fiber tip too close to the stone, as it causes a drilling effect without apparent stone fragmentation. It is advisable to keep LL fiber 1–2 mm away from the stone to achieve maximum impact. We also observed that all stones could be fragmented, either cholesterol or pigmented stones, supporting the existing data on laser lithotripsy [23]. In the present study, we did not evaluate the cost of the procedure. We reused cholangioscope 3 to 4 times with disinfection in between the procedures. Similarly, we

Table 1
Patients, stone, intervention, and adverse event data.

Median Age (Range)	42.5 (21–88) years
Gender, male n (%)	37 (55.22%)
Previous Cholecystectomy, n (%)	21 (31.34%)
CBD Stone Characteristics	
· Mean Size ± SD (Range)	20.4 ± 5.3 mm (12–35 mm)
· Stone size, n (%)	
12–20 mm	16 (23.88%)
20–30 mm	40 (59.7%)
>30 mm	11 (16.42%)
· Location:	
CBD	52 (59.7%)
CHD/Hilum	14 (20.9%)
Cystic Duct	12 (17.9%)
Intrahepatic Stones	1 (1.5%)
• Impacted stones, n (%)	13 (19.4%)
· Number of stones, mean (range)	1.8 (1–8)
· Multiple stones present, n (%)	45 (67.16%)
Interventions, n (%)	
· Prior Intervention	42(62.7%)
EPBD	6 (8.95%)
Failed ML	5 (7.46%)
Failed Combined EPBD and ML	31 (46.26%)
· No Prior Intervention	25 (37.3%)
Stone clearance	
· First attempt, n (%)	48 (71.65%)
· Subsequent attempts, n (%)	13 (19.4%)
· Failure	6 (8.95%)
· Mean session, (Range)	1.4 (2–4)
Adverse Events	
· Overall n, (%)	8 (11.94%)
Acute Pancreatitis	2
Bleeding	3
Transient Fever	3

used LL fibers multiple (50–60) times after careful sterilization. The LL fiber (Proflex TM laser fiber 273, InnovaQuartz LLC, USA) used in the present study was 4.3 m long. So if after the procedure, it is noted that the tip of LL fiber is damaged, a 3–4 mm portion of the tip is cut and reshaped using the ceramic scissors.

There are distinct limitations to the present study. It evaluates a single modality of LL for difficult bile stones at a high-volume institute. These results cannot be generalized for low-volume centers with limited experience in the management of difficult bile duct stones. In this prospective study, there was no control group or randomization to compare with the other modalities of stone extraction. We cannot infer regarding the use of this modality in patients with intrahepatic bile duct stones. In conclusion, this study demonstrates the high efficacy and safety of SpyGlass DS cholangioscopy guided LL for difficult to treat biliary stones. It shows the technical feasibility, with a high rate of success for ductal clearance with a low and mild AEs.

Note: The preliminary work of this manuscript was presented as an abstract in the Asia Pacific Digestive Week, 2019.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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