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Efficacy of Hemopatch® in reducing postoperative bleeding after laparoscopic cholecystectomy: Prospective and multicenter study

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Abstract

Purpose: This study describes the specific use and sealing ability of Hemopatch® in patients undergoing routine laparoscopic cholecystectomy.

Methods: A multicenter, prospective, open-label, non-randomized, control-group comparison was performed to compare the effects of adjunct Hemopatch® in patients undergoing laparoscopic cholecystectomy. The primary endpoint was the reduction of post-operative hospitalization. Secondary endpoints were the amount of post-operative drainage within the initial 6 hours, the total volume of drainage during 72 hours post-operatively, the need for re-operative/re-admission, and reported complications.

Results: one hundred and fifty two consecutive patients were enrolled between March 2016 and May 2018. In 78 (51.3%) of these patients, Hemopatch® was used as an adjunct to surgical hemostasis to obtain hemostasis of the resected areas in the gallbladder bed. The remaining 74 patients (48.7%, the control-group) underwent a standard laparoscopic cholecystectomy using only L-shaped monopolar electrode and clip. No difference was observed between the groups in post-operative hospitalization course and most endpoints, including no surgical re-operations or re-admission in any patient. However, a substantially higher proportion of those in the adjunct Hemopatch® than the control group had no drainage after 6 hours (48.7% [38/78] and 16.2% [12/74], respectively; $p < 0.001$). In an analysis of drained volume, 30.7% (24/78) Hemopatch® cases and 13.5% (10/74) control cases had empty drains ($p = 0.011$). Reported complications occurred in 13.2% of cases, with 11.8% in the Hemopatch® cases and 1.4% in the control group.

Conclusion: These findings suggest that the adjunctive use of Hemopatch® in patients undergoing elective laparoscopic cholecystectomy is safe and easy to utilize and that its sealing ability reduces the amount of post-operative site drainage.

Abbreviations: ASA: American Society of Anesthesiologists; LC: Laproscopic Cholecystectomy; NHS-PEG: Pentaerythritol Polyethylene Glycol Ether Tetra-Succinimidyl Glutarate; US: Ultrasound

Introduction

Laparoscopic cholecystectomy was introduced in the 1980s and is considered the gold standard procedure for gallbladder disease treatment [1,2]. As with all surgical procedures, there is a constant need to modify and refine laparoscopic cholecystectomy operative techniques such that we reduce the risk for complications including those of bleeding.

Hemopatch® Sealing Hemostat (Baxter International, Inc., Deerfield, IL) effectively minimizes the use of mechanical and thermal surgical hemostasis. It is a soft, thin, pliable and flexible pad of bovine-derived collagen that has been coated with pentaerythritol polyethylene glycol ether tetra-succinimidyl glutarate (NHS-PEG). Collagen exposed to blood results in the aggregation of platelets that enable the formation of fibrin [3].

Several studies have demonstrated that the intra-operative use of Hemopatch®, when compared to standard of care or other comparator, improves hemostatic efficacy in patients undergoing different kind of surgery like cardiac [4–6], neurological [5,6], urological [6], and endocrine-related [6] surgical procedures. Overall, the use of Hemopatch® can improve surgical outcomes such as blood loss, need for transfusion(s), complications, and surgical revision reducing hospital stay.

Some studies have evaluated the use of topical hemostatic agents such as Hemopatch® during laparoscopic cholecystectomy [7,8]. However, none have evaluated the effects of Hemopatch® application during routine and non-urgent laparoscopic cholecystectomy. This study described the specific use of Hemopatch® in routine laparoscopic cholecystectomy. This study was designed to evaluate the

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effect and safety of Hemopatch® in patients undergoing laparoscopic cholecystectomy for cholelithiasis and benign neoplasm of gallbladder.

Subjects and methods

Study design

This was a multicenter, prospective, open-label, non-randomized, control-group comparison study of the use of Hemopatch® Sealing Hemostat as an adjunct to surgical techniques. Consecutive patients undergoing laparoscopic cholecystectomy (LC) without energy devices between March 2016 and May 2018 at one of four Department of Surgery in Italy (i.e., Regina Apostolorum Hospital of Albano Laziale in Rome, Cardarelli Hospital of Naples, University Hospital O.O.R.R. of Foggia and A.O.R.N. "SAN PIO" Hospital of Benevento) were eligible for study participation. Inclusion criteria included age between 18 and 75 years, calculosis of the gallbladder, benign neoplasma of the gallbladder, surgical indication for LC, and the provision of written informed consent. Exclusion criteria were coagulopathies, anticoagulant and antiplatelet therapy, American Society of Anesthesiologist (ASA) classification of >3, acute cholecystitis, choledocholithiasis and acute biliary pancreatitis. The research was carried out in accordance with the ethical principles of the Declaration of Helsinki.

The participants were evaluated prior to undergoing the surgical procedure with a detailed medical history and physical examination. They underwent standard laboratory blood chemistry analyses and abdominal ultrasound. During the surgical procedure, participants were managed with either standard hemostatic methods (Group A) or standard hemostatic methods with adjunct Hemopatch® (Group B).

In all participants, a standard four trocar operative technique for LC was performed without the aid of electrosurgical devices. In Group A, the procedure included the use of an L-shaped monopolar electrode. In Group B (adjunct Hemopatch®), the standard LC procedure was performed with the addition of adjunct Hemopatch®. During the surgical procedure in Group B participants, following gallbladder dissection from the gallbladder bed, the Hemopatch® pad was applied using visual guidance following the manufacturer's instructions for use [3]. Hemopatch® was applied with the non-marked white surface placed in contact with the bleeding area. Dry laparoscopic instruments and dry gauze were utilized to protect and introduce the device through the trocar. Contact between the Hemopatch® collagen pad with any blood on surgical instruments, gauze, and gloves was kept to a minimum in order to reduce the affinity of the pad for the blood. A dry gauze was placed and held in place with a gentle, uniform pressure over the entire surface for 2 minutes. After approximately 2 minutes, the gauze was removed, and the gallbladder bed was inspected. In all patients a closed system fall subhepatic drain was left intraabdominally.

Following the surgical procedure, all participants were followed up at regular intervals (6, 12, 24 and 48 hours) by clinical examination. A liver ultrasound (US) was performed on the first postoperative day to diagnose perihepatic fluid, abdominal collection, or hematoma.

The primary endpoint was the reduction of postoperative hospitalization. Secondary endpoints were the proportion of patients requiring re-operation; the amount of postoperative fluid drainage; the occurrence of postoperative hematoma, subhepatic collection, wound infection, and re-hospitalization; and the reduction of postoperative pain.

Statistical methods

The data of the primary and secondary endpoints are expressed as absolute numbers and percentages (%). The results of the two groups in comparison were analyzed using the Pearson's chi-squared test. A p value of < 0.05 was considered to be statistically significant.

Results

Among the 152 surgical participants (102 women and 50 men), standard hemostatic methods were utilized in 74 (48.7%) patients (Group A [standard LC procedure]). The remaining 78 (51.3%) patients underwent the same procedure and technique with the use of adjunct Hemopatch® sealing hemostat to attain hemostasis of the resected areas in the gallbladder bed (Group B). All patients were followed for their entire hospitalization period and no patients were lost to follow-up.

No difference was observed between the two groups with respect to postoperative hospital stay, with the majority of patients in both groups hospitalized for less than 3 days (91% [68/74] Group A [standard LC procedure] and 73% [57/78] Group B [standard LC with adjunct Hemopatch®]). Specifically, most patients were release from the hospital on postoperative day 2 (82.2%, 125/152), with 11.8% (18/152) released on day 3, and 6% (9/152) being release at +3 days. No patient required re-operation or repeat hospitalization related to the procedure.

Substantial differences were observed in drainage amounts (Table 1). The proportion of patients with no (0 mL) drainage during the initial 6 hours postoperatively was significantly higher among those who received adjunct Hemopatch® treatment than those in the control group (48.7% [38/78] adjunct Hemopatch® vs. 16.2% [12/74] control group, $p < 0.001$). The majority of those who received adjunct Hemopatch® exhibited drainage < 50 mL (91% [71/78], with 77% [57/74] of those in the control group having drainage < 50 mL.

All participants had a similar postoperative course, we had no effect on postoperative pain and with no differences in postoperative liver US findings. The postoperative liver US findings were negative in 87.5% (133/152) of all participants with a similar incidence in both groups (66 patients in Group A [standard LC] and 67 patients in Group B [standard LC with adjunct Hemopatch®]). There was one case of hematoma in the adjunct Hemopatch® group. Serous collections were observed in 10.8% [8/74] of those who underwent a standard LC procedure (Group A) and in 12.8% [10/78] of those in the adjunct Hemopatch® group (Group B). General medical complications were reported in 13.2% of participants (1.4% in standard LC group and 11.8% in adjunct Hemopatch® group). These postoperative complications, assessed by Clavien-Dindo classification, consisted of Grade 1 in 19 patients and Grade 3 in only 1 patient.

Discussion

Our findings indicate that the utilization of adjunct Hemopatch® in patients undergoing standardized LC procedures did not result

Table 1. Drainage amounts after 6 hours and volume

	Standard LC Procedure (Group A) n = 74	Hemopatch® Adjunct (Group B) n = 78	*p*-value
Drainage, quantitative after 6 hours, no (%) of patients			
None (0 mL)	12 (16.2%)	38 (48.7%)	$p < 0.001$
≤ 50 mL	45 (60.8%)	33 (42.3%)	
> 50 to ≤ 100 mL	12 (16.2%)	4 (5.1%)	
> 100 mL	5 (6.8%)	3 (3.8%)	
Drainage volume, no of patients			
Empty	10 (13.5%)	24 (30.8%)	$p = 0.011$
Liquid	64 (86.5%)	51 (65.4%)	

in a reduced postoperative hospital stay as compared to those who underwent a standardized LC procedure. In a retrospective review of our protocol, the lack of difference in hospital stay between the adjunct and the standard procedure group may have been related to the performance of liver ultrasound procedures and the scheduling and timing required for the performance of these evaluations. Specifically, patients may have been held in hospital for the performance of this test and due to scheduling difficulties, this may have delayed their drainage removal and subsequent discharge. Notably, the findings in the postoperative liver ultrasound was negative in the majority of cases in each group. Radiologists did detect a collection at the site of the cholecystectomy in a total of 11 adjunct Hemopatch® cases (one case of hematoma, 10 cases of serous collection) and 8 control group cases. This may have been due to the presence of the device on the gallbladder bed with the formation of a gel after its contact with liquid secretions and activation.

The observation of no (0 mL) drainage during the initial 6 hours postoperatively in the Hemopatch® adjunct group is notable and suggestive of its effective sealing ability on both blood capillaries and lymphatic and biliary ducts. A 3-fold higher percentage of adjunct Hemopatch® participants compared to control participants exhibited no drainage (48.7% versus 16.2%, $p < 0.001$). Upon analysis of the quantity of drained material in the postoperative period, our findings indicate that a substantially higher percentage of those in the adjunct Hemopatch® group were without emission of material from the drainage as compared to those in the control group (30.7% versus 13.5%, $p = 0.011$).

Limitations to the generalization of these findings include that it was not designed as a randomized, double-blind clinical trial and that we only enrolled patients who were undergoing elective LC procedures. Further, as stated above, the complexities in scheduling a postoperative ultrasound procedure may have impacted the patients' hospitalization duration. The impact on postoperative drainage and bleeding may have been substantially different with inclusion of a population of patients undergoing more emergent/urgent procedures, those with more acute pathology or coagulopathies, those receiving anticoagulant agents or having other active inflammatory concurrent illnesses that may impact their ability to attain hemostasis. In these cases, the benefits of the sealing ability of Hemopatch® as an adjunct may have been more evident.

In conclusion, despite these limitations, our findings still indicate that adjunct Hemopatch® offers benefits when utilized in patients undergoing standard laparoscopic cholecystectomy. The use of adjunct Hemopatch® is safe and easy to utilize and its effective sealing ability has the potential to reduce the amount of postoperative site drainage in patients undergoing elective laparoscopic cholecystectomy procedures.

Authorship and contributions

Andrea Scarinci carried out the clinical observation studies, participated in data analysis and performed the statistical analysis. Stefano Brun e Francesco Cilurso carried out the clinical observation studies and participated in its design and draft. L. Costigliola, D. Perfetto, A. Travaglino, M. Grillo, G. Di Gioia, G. M. Buonanno participated in the clinical observation studies. Daniele Cavaniglia participated in data analysis. Andrea Liverani e Tatiana Di Cesare conceived of the study and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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Competing interests

The author(s) declare that they have no competing interests.

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