Journal of Medicine and Medical Sciences Vol. 10(1) pp 84-90, March, 2019
DOI: http:/dx.doi.org/10.14303/jmms.2019.5
Available online http://www.interesjournals.org/JMMS

Full Length Research Paper

Laparoscopic cholecystectomy in hepatitis C liver cirrhosis patients

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ABSTRACT

Introduction: With this increase in the prevalence in viral C hepatitis, surgeons now more frequently encounter cirrhotic patients with symptomatic gallstones. Now, when such patients required cholecystectomy, it is performed laparoscopically. However, an abdominal pain, especially radiating to the right shoulder, nausea and vomiting in the postoperative period due to pneumoperitoneum using carbon dioxide gas. The use of c drainage tube after uncomplicated LC in patients without liver cirrhosis, which is supposed to prevent such postoperative events, is an issue of considerable debate. Aim of the work is to evaluate our experience of LC in hepatitis c liver cirrhosis patients from surgical, anesthesia and surgical intensive care aspects. We conducted a prospective, randomized, double blind study to determine the effect of placing of drains after LC in hepatitis c liver cirrhosis patients on the incidence of postoperative pain, nausea and vomiting.

Patients and methods: Forty-four patients with non-complicated chronic calcular cholecystitis and liver cirrhosis were recruited for the study during the period from February 2017 to December 2018. They electively operated upon at the department of general surgery of Theodor Bilharz Research Institute (TBRI) using the laparoscopic technique. The patients were randomly subdivided into two equal groups Group-I (n=22); suction drains will be placed in the sub-hepatic region (Morison's pouch) and Group-II (n=22), no drains will be placed. Demographic data, preoperative variables, duration of surgery, postoperative shoulder tip pain, vomiting and analgesics requirement evaluated and recorded.

Results: Operative times were not statistically significant of both groups. Drain group I had a significant lower shoulder tip pain and analgesic requirement at post-operative 6 and 12 hours but that was higher after 12 hours, than Group II. The overall incidence of nausea/vomiting was more in group without drain than in drain group which was statistically significant. Patients in Group I had a longer stay in hospital as compared to Group II that was statistically significant.

Conclusion: The routine use of abdominal drain after elective uncomplicated laparoscopic cholecystectomy in patients with liver cirrhosis because its role in reducing post-operative nausea/vomiting is not justified. It increases post-operative pain and hospital stay. Selective use of drain is reasonable if there is a surgical indication like potential bile leak.

Keywords: laparoscopic cholecystectomy, viral C liver cirrhosis

INTRODUCTION

Due to this increase in the prevalence in viral C hepatitis in our country, surgeons frequently encounter cirrhotic patients with symptomatic gallstones. Invariably in the past, when such patients required cholecystectomy; it was performed by an open approach which is associated with greater operative time, blood loss and prolonged hospital stay, as compared with those performed laparoscopically. Several studies have reported the efficacy and safety of Laparoscopic Cholecystectomy (LC) in cirrhotic patients. However, abdominal pain, especially radiating to the right shoulder, nausea and vomiting is witnessed

in 30% of patients in the postoperative period due to pneumoperitoneum using carbon dioxide gas (Morino et al., 2000; Puggioni et al., 2003; Ji et al., 2005; Leandros et al., 2008; Hamad et al., 2010; Chmielecki et al., 2012 and Bessa et al., 2011). The use of prophylactic drainage tube in LC to avoid bile and blood collection requiring subsequent treatment; is supposed to prevent such postoperative events. Surgeons keep being divided to drain or not to drain and its impact on postoperative pain (Nursal TZ et al. 2003; Capitanich P et al. 2005; Mrozowicz A et al. 2006; Picchio M et al. 2014 and Uchiyama K et al. 2007). Controlling pain in hepatic patients is crucial and the use of analgesics is hazardous as they have altered drug metabolism with increased risk for over or under-sedation. Improper pain management can precipitate renal failure or provoke hepatic encephalopathy. Thus, the technique that can minimize postoperative pain and decrease the need for postoperative analgesics should be considered (Bessa SS et al. 2011; Nursal TZ et al. 2003 and Sharma A et al. 2016). Aim of the work is to evaluate our experience of LC in hepatitis C liver cirrhosis patients from surgical, anesthesia and surgical intensive care aspects with special emphasis on the effect of placing of drains on the incidence of postoperative pain, nausea and vomiting.

MATERIALS AND METHODS

Patient selection

The study was conducted in the General Surgery Department, at Theodor Bilharz Research Institute after approval by the Research Ethical Committee and written informed consents were obtained from all patients before participation in this trial. Forty-four patients were recruited for the study during the period from February 2017 to December 2018. Patients were of both sexes with non-complicated chronic calcular cholecystitis and liver cirrhosis. Liver cirrhosis related to hepatitis C viral infection diagnosed in all patients on clinical, biochemical, serum virus titers and histopathology findings. They electively operated upon at the department of general surgery of Theodor Bilharz Research Institute (TBRI) using the laparoscopic surgical technique. After the preoperative clinical evaluation and routine laboratory investigations including serum albumin, serum bilirubin and Prothrombin time (PT) and serum levels of Aspartate aminotransferase (AST), Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP); all patients classified according to American Society of Anesthesiologists (ASA) score, Childe-Pughe-Turcotte (CPT) classification. Inclusion criteria involved physical status classification; groups II or III of American Society of Anesthesiologists (ASA) and age between 25 and 60 years and a Childe-Pughe-Turcotte (CPT) classification of liver disease class A or B. Patients excluded from the study were those older than 60 years, with ASA-IV or more, Childe-Pughe-Turcotte (CPT) class C. Those patients with previous laparotomy, severe or refractory ascites, acute cholecystitis, acute pancreatitis or choledocholithiasis, those who required additional surgery, BMI of $\geq$ 40 kg/m^2 and research refusal also excluded. One patient with unclear anatomy suffered of intraoperative bleeding from the gall bladder fossa; which required conversion to open technique was excluded from the study. Patients with preoperative international normalized ratio (INR)>1.5 received fresh-frozen plasma. Those with a preoperative platelets count <50,000/mm^3 were given platelet transfusions.

Surgical technique

Standard laparoscopic cholecystectomy performed to all patients with technical modifications suitable for such patients. They involve avoidance of varices during trocar placement, avoidance of excess traction on the gall bladder and avoidance of dissection at the periportal area. The patients were subdivided at the beginning of the study, into two equal groups using sealed envelope technique just after completion of the surgery before trocar removal; Group-I (n=22); suction drains will be placed in the sub-hepatic region (Morison's pouch) and Group-II (n=22), no drains will be placed. Careful closure of port site wounds performed.

Anesthesia technique

The most recent up to date recommendations regarding anesthetic management of patients with liver disease undergoing surgery were adopted. In the induction room, an intravenous access was established via 18 gauge cannula a preload of 500 ml Ringer acetate was given slowly with no premedication. All monitors were attached electrocardiogram (EKG), pulse oximetry (SpO_2), non-invasive blood pressure (NIBP). 100% Oxygen supplementation (5-l min^{-1}) via a face mask was applied for 5 minutes before intubation. Anesthetic induction was obtained via IV fentany 11.5l g/kg followed by Propofol titration (10 mg every five seconds) until loss of conscious which was confirmed with loss of verbal response. Ventilation was then established via a face mask using oxygen/air mixture (FiO_2=0.5) after injection of IV Atracurium as a muscle relaxant in an intubating dose of 0.5 mg.kg^{-1} for 3 minutes until adequate curarizaion is established. Endotracheal intubation was done and IPPV using a closed circuit was then established using Isoflurane in a mixture of oxygen/air (FiO_2=0.5) providing end-tidal carbon dioxide tension ($PETCO_2$) 35-40 mmHg.

Intraoperative continuous monitoring of heart rate (HR), non-invasive blood pressure (NIBP), pulse oximetry (SpO_2), skin temperature (T), end-tidal carbon dioxide ($PETCO_2$) and anesthesia gas analysis (%insIso,

%ETIso) were monitored and recorded throughout the whole procedure. Any decline in heart rate HR or MAP ≥ 20% of the preoperative values treated with IV atropine or ephedrine respectively. After completion of the surgical procedure, patients were reversed using intravenous injection of Neostigmine 0.05 $mg.kg^{-1}$ and atropine 0.02 $mg.kg^{-1}$ to reverse residual neuromuscular blockage which was followed by extubation and transfer to the post anesthetic care unit (PACU). After fulfilling an Aldrete score of greater than or equal to 9, patient were discharged from PACU to an intermediate care unit for 24 h.

Assessment

Demographic data, preoperative variables, duration of surgery and postoperative course were recorded analysed. HR, NI-MAP, and SpO_2 were recorded during the immediate postoperative period at 15 and 30 min, and at discharge from the PACU. Adverse events particularly postoperative shoulder tip pain and/or vomiting at 24-48 h postoperatively recorded. Post-operative pain analgesics requirement was evaluated and recorded at first 6 h, at 12 hand 24 h postoperatively. Liver function tests were assessed at 24 h postoperatively. Patients will be asked to rate their satisfaction after leaving the PACU with the anesthesia and analgesia received using a seven-point Likert-like verbal rating scale, where 1=extremely dissatisfied, 2=dissatisfied, 3=somewhat dissatisfied, 4=undecided, 5=somewhat satisfied, 6=satisfied, and 7=extremely satisfied.

Statistical analysis

Results were expressed as mean, mean ± standard deviation (SD) or number (%). Comparison between categorical data [number (%)] was performed using Chi square test. According to test of normality, comparison between different variables in the two groups was performed using either unpaired t test or Mann-Whitney U test whenever it was appropriate. p value ≤ 0.05 was considered significant. The data was analysed using SPSS version 16.0 and Microsoft Excel 2007.

RESULTS

The overall mean patient age was 43.6 years (range 34-64 years). 33 were females (75%) and 11 were males (25%). Age, gender and CPT class distribution was comparable in both groups of the study. The randomization was biased by the need of putting a drain in some of the cases against the closed envelope method choice started at the beginning of the study if there is a worry about potential bile leak, bearing in mind that drain placement, provides a false sense of security. So, this study is only a retrospective cohort analysis.

No intra-operative bile leakage occurred in both groups apart from one patient in group-II in which an accessory duct was found at the gall bladder hepatic bed where closed using an intra-corporeal stitch. None of the patients was converted to open cholecystectomy. HR, NI-MAP, and SpO_2 during the immediate postoperative period at 15 and 30 min, and at discharge from the PACU were satisfactory in all of the patients. Operative time (mean, range) was not statistically significant of both groups 70.0 (52-80) *vs.* 62. 6 (55-65) minutes, (p=0.65) (Table 1).

Table 1. Preoperative data of the study groups.

Data	Group-I (n=22)	Group-II (n=22)
Age (mean, range) yrs.	39.9 (34-61)	41.6 (36-64)
Male/female ratio	20-February	16-June
Childe-Pughe-Turcotte (n, %)		
class I	13	12
class II	9	10
class III	0	0

There was no postoperative mortality. None of patients required postoperative blood transfusion. Postoperative complications were trocar site hematoma (one), port site infection (two) and postoperative ascites (two) of the patients (Table 2).

Table 2. Post-operative findings of the study groups, significant at p-value <0.05, insignificant at p-value >0.05.

Post-operation	Group-I (n=22)	Group-II (n=22)	p-value
Shoulder Tip Pain (n, %)			
6 hours	5 (22.7%)	9 (40.9%)	0. 056*
12 hours	6 (27.2%)	10 (45.5%)	0. 055*
24 hours	12 (54.5%)	3 (13.6%)	0.010**
Analgesia requirement			
Time for 1st dose (Mean ± SD) (h)	6.16 ± 1.73	1.72 ± 0.67	0.010**
6 hours (n, %)	16 (72.6%)	22 (100%)	0. 152*
12 hours (n, %)	15 (68.2%)	20 (90.9%)	0. 155*
24 hours (n, %)	11 (50.0%)	3 (13.6%)	0.010**
Post-operative nausea/vomiting (n, %)			
6 hours (n, %)	8 (36.3%)	16 (72.6%)	0.002**
12 hours (n, %)	6 (27.2%)	12 (54.5%)	0.002**
Postoperative complications (n, %)			
Trocar site hematoma	1 (4.5%)	0 (0%)	0.001**
Ports sites infection	1 (4.5%)	1 (4.5%)	0

Postoperative ascites	0 (0%)	2 (9.0%)	0.001**
Hospital stay (mean) days	3.56	1.5	0.001**
Satisfaction score (mean)	4.9	6.1	0. 055*

Drain group I had a significant lower shoulder tip pain at 6th and 12th post-operative hours. After 12 hours, group-I had higher shoulder tip pain than group-II (Table 2). Analgesic requirement was higher in group-II up to 12 hours after which it was higher in group I. Mean value time for 1st dose analgesia requirement for group-II was statistically significant shorter than in drain groups I. Number of patients required analgesia 6 and 12 hours in drain group I was not statistically significant greater compared to group-II ($p<0.005$, <0.001 respectively). However, the difference was statistically significant at the postoperative 24 hours (Table 2). The overall incidence of nausea/vomiting was more in group without drain than in drain group which was statistically significant (Table 2).

Patients in group-I had a longer hospital stay as compared to group-II that was statistically significant. Most of patients were discharged after 24-48 hours except six patients of group-I (four required more pain control for further 24 hours, one patient with bile leakage which stopped spontaneously after 3 days and one patient of with continuous ascites fluid leakage post-operatively which stopped under medical treatment after 4 days). There were two cases of mild wound infection unrelated to the use of a drain. No statistically significant liver function derangement happened in both groups (Table 3).

Table 3. Pre- and postoperative liver function tests of the study groups.

	Group-I (n=22)			Group-II (n=22)		
Parameters	**Preoperative**	**24 hours Postoperative**	**p-value**	**Preoperative**	**24 hours Postoperative**	**p-value**
Albumin (g/dL)	3.21 ± 0.81	3.01 ± 0.5	0.06*	2.91 ± 0.81	3.01 ± 0.3	0.07*
Bilirubin	1.22 ± 1.3	1.02 ± 1.29	0.12*	0.71 ± 0.28	0.73 ± 0.52	0.1*
AST (IU/L)	34.5 ± 5.0	69.5 ± 1.5	<0.001**	24.63 ± 8.1	52.01 ± 8.1	0.004**
ALT (IU/L)	39.8 ± 7.2	67.5 ± 8.0	0.006**	24.50 ± 7.5	44.91 ± 1.8	0.005**
ALP (IU/L)	93.2 ± 52.6	83.2 ± 72.2	0.087*	73.2 ± 5.6	83.2 ± 2.2	0.08*
Prothrombin Time	--	10 ± 0.9	0.09*	10 ± 2.0	11 ± 0.9	0.07*
Results are expressed as mean ± standard deviation. Significant at p-value <0.05, insignificant at p-value >0.05.						

DISCUSSION

Specific advantages of laparoscopic cholecystectomy in patients with cirrhosis in Child-Pugh class A, B, without evidence of significant portal hypertension and severe coagulopathy, include less blood loss, shorter operative time the absence of wound infection, a lower rate of postoperative hepatic failure and shorter length of hospitalization. Finally, laparoscopic surgery reduces the risk of viral contamination of the surgical staff (Morino et al., 2000; Puggioni et al., 2003; Ji et al., 2005; Leandros et al., 2008; Hamad et al., 2010; Chmielecki et al., 2012 and Bessa et al., 2011). Routine abdominal drainage after uncomplicated laparoscopy cholecystectomy in patients without liver cirrhosis is an issue of considerable debate (Nursal et al., 2003; Capitanich et al., 2005; Mrozowicz et al., 2006; Picchio et al., 2014 and Uchiyama et al., 2007). Reason for draining is to detect early bile or blood leak and allow CO_2 that had been insufflated during laparoscopy to escape via the drain site thereby decreasing shoulder tip pain and post-operative nausea and vomiting (Rossi S et al. 2008 and Imani F et al. 2011). On the other hand, some studies showed no difference in post-operative nausea /vomiting/pain between drain and no drain group (Bessa et al., 2011; Nursal et al., 2003 and Sharma et al., 2016). A meta-analysis of six randomized trials revealed that postoperative pain scores were significantly higher in the drainage group both at 6-12 h and at 12-24 h after surgery. No difference was found with regarding the incidence of sub-hepatic collection and drainage procedures (Antoniou et al., 2014). Our study was conducted to assess the effect of drain in uncomplicated laparoscopic cholecystectomy in patients with liver cirrhosis on post-operative pain, nausea and vomiting.

In this study, the average operative time in the two groups was statistically insignificant which is consistent with other studies (Uchiyama et al., 2007; Antoniou et al., 2014 and Tzovaras et al., 2009). Shoulder tip pain and analgesic requirement was lower in drain group in first post-operative 12 hours than the group without drain. However after 12 h, it showed higher shoulder tip pain and analgesic requirement

than the group without drain which are consistent with some studies (Uchiyama et al., 2007; Bessa et al., 2011; Antoniou et al., 2014 and Tzovaras et al., 2009). Authors agree about what was supposed that less shoulder tip pain in initial hours is due to the drain removes retained CO_2 which causes diaphragmatic stretch and phrenic nerve neuropraxia but, its increased incidence beyond 24 hours is due that drain irritates the diaphragm (Koivusalo et al., 1996 and Bhattacharjee et al., 2017).

Consistently with all our studies, there were more incidences of nausea/vomiting in group without drain than in drain group which was statistically significant. The proposed mechanisms of increasing nausea/ vomiting are increased cerebral blood flow and intra peritoneal acidosis due to insufflated CO_2. Drains placed in sub-hepatic space acts as a conduit for the escape of retained CO_2 which lead to less post-operative nausea/vomiting as seen in present study as well as other studies (Nursal et al., 2003; Capitanich et al., 2005; Mrozowicz et al., 2006; Picchio et al., 2014 and Uchiyama et al., 2007; Rossi et al., 2008; Imani et al., 2011 and Sharma et al., 2016). However, other methods were found to reduce the incidence and severity of postoperative nausea, vomiting and intensity, frequency of right shoulder pain such as: the gasless LC or LC under low-pressure pneumoperitoneum and their safety, efficacy, near equal operative time and surgeon's satisfaction appear to be comparable with standard-pressure pneumoperitoneum (Koivusalo et al., 1996; Bhattacharjee et al., 2017; Vijayaraghavan et al., 2014; Hua et al., 2014; Esmat et al., 2006). Drain group patients had a statistically significant longer hospital stay as compared to the group without drain due to the fact that none of the patient in the drain group could be discharged before removal of the drain.

Authors conclude that the routine use of a drain in elective uncomplicated LC in patients with hepatitis C liver cirrhosis has nothing to offer. It is associated with increased postoperative pain. The consequences of loss of ascites fluid which may occur after surgery are troublesome in those patients. However, it would be reasonable to leave a drain if there is a worry about an unsolved or potential bile leak i.e., imperfect closure of cystic duct or bile staining in the lavage fluid or gall bladder bed bearing in mind that drain placement, although sometimes providing a false sense of security does not guarantee either prevention or treatment of postoperative bile collections, bleeding, or bile peritonitis.

CONCLUSION

LC in hepatitis c liver cirrhosis patients is feasible from surgical, anesthesia and surgical intensive care aspects. The routine uses of abdominal drain because the incidence of post-operative nausea/vomiting is less and not justified as it increases post-operative pain and hospital stay.

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