The Effectiveness of Combined Wound and Intraperitoneal Local Anesthesia as Pain Relief in Laparoscopic Cholecystectomy: Prospective Case Control Study

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ABSTRACT

Background*: Postoperative pain is the main obstacle for safe rapid recovery of patients undergoing laparoscopic cholecystectomy (LC).**Aim of the work**: To evaluate the efficacy of Levobupivacaine when injected incisionally and intraperitoneally at the end of the LC. **Methods**: A total of 220 patients, subjected to elective LC, were divided into four Groups. Group I "control" received normal saline both intraperitoneal and at incision site. Group II received Levobupivacaine both intraperitoneal and at incision site. Group III received incisionalLevobupivacaine only. Group IV received intraperitoneal Levobupivacaine only. Dynamic pain by a visual analogue scale (VAS) and cumulative analgesic consumption at 1 h, 6 h, 24 h postoperatively, as well as incidence of side-effects over 48 h after LC was recorded. **Results:**Compared with those in Group I, the dynamic VAS score (VAS-D) 1 h and 6 h and 24h postoperatively, cumulative Pethidine consumption zero, 25g and 50g, and duration of hospital stay in Group II were less (P<0.05 for each). Furthermore, intraperitoneal and incisionalLevobupivacaine exerts more powerful analgesic effect than single usage with intraperitoneal or incisionalLevobupivacaine (P<0.05). Signs of local anesthetic toxicity did not occur. **Conclusions:**Levobupivacaine when injected incisionally and intraperitoneallyat the end of the LC was foundeffective and safe to reduce postoperative pain intensity.*

Keywords*: Laparoscopic Cholecystectomy;Levobupivacaine; Intraperitoneal and Incisional; Pain.*

INTRODUCTION

Over the past years, laparoscopic cholecystectomy have increased significantly.Improved postoperative pain and improved healing time are the main reasons for their wide spread use [(1)].

The pain in LC is derived from several situations: superficial incisional wound pain (somatic), deep intraabdominal pain (visceral) and/or post-laparoscopy shoulder pain (visceral due to phrenic nerve irritation)[(2,3)]. Numerous studies have been done to improve postoperative pain following LC but none has demonstrated consistent efficacy [(4)].

Pain relieve after LC should be multimodaldue to complexity of postoperative pain [(5)]. Pain management in laparoscopic surgery should include the combined use of opioids, non-steroidal anti-inflammatory drugs,and local anesthetic infiltration [(6)]. There are a lot of local anesthetic techniques that have been testedfor the possible analgesic effects in laparoscopic surgery [(1)]. Improving postoperative pain control and quality of hospital stays are the main issues to which continuous work is directed.Several methods have been tested for improving postoperative pain control includingless pneumoperitoneum pressure [(7)], decreasing operative ports numbers [(8)], local anesthetics use at the site of trocar insertion[(9)], local anesthetics injection intraperitoneally[(10)].

Combined wound and intraperitoneal local anesthetics injection to relieve post operative pain after LC have been evaluated [(11)].

There are different mode of local anesthetics (LA) injection in order to relieve pain post LC: either into site of incision, into the periportal fascia, or muscular and parietal peritoneum injection.Incision site injection of LA prevents pain impulses travel from the site of surgical incision to the brain[(1,12,13)]. Peritoneal injection of

LA can occur through the surgical ports. It may be injected over the visceral layer of the peritoneum into the surgical bed or under the diaphragmto decrease the frequency of shoulder pain[(14)].

Bupivacaine,levobupivacaine, lidocaine, and ropivacaine have been injected into the peritoneum with different doses to achieve analgesia after LC [(15-18)]. A combined use of local anesthetic both into the peritoneum and in the incisionsite to achieve analgesia has been evaluated in many studies. Bisgaard et al. infiltrated ropivacaine or saline both into the peritoneum and in the incision site, and they found that this regimen dramatically reduced pain at the incision site during the first 3 post operative hours [(19)]. These findings were also proved in LC [(20)].

Aim of the work:

To evaluate the efficacyof Levobupivacaine when injected incisionally and intraperitoneallyat the end of the LC in decreasing the postoperative pain and postoperative analgesic usage.

PATIENTS AND METHODS

A prospective case control study was done during one year period. The participants were adult patients who were indicated for elective LC. About 220 consecutive patients who subjected to LC at the Department of Surgery in the Assiut University Hospital and Cairo University Hospitalswere enrolled. All participants providedwritten, and informed consent about use of anesthetics for pain relief.

Inclusion criteria:

Patients who were undergoing LC for symptomatic gall stone disease aged from 18 to 60 years old and also classified as American Society of Anesthesiology (ASA) 1and 2.

Exclusion criteria:

Patient refusal, patients having acute cholecystitis, laparoscopic converted to open surgery, ASA Grade 3 and 4 and patients with contraindications to Levobupivacaine use. Patient received immunosuppressive drug therapy within previous 6 months; had an immunosuppressive condition; had undergone chemotherapy within the previous 6 months; or had insulin-dependent diabetes mellitus (i.e., type 1 diabetes) were also excluded.

Discharge from the hospital was the primary endpoint. Between the groups, we compared the clinical features, laboratory data, operative outcomes, pain score, and the amount of analgesic required. The hospital stay was defined as the number of days between the operation and the actual date of hospital discharge. Surgical mortality was defined as death occurring within 1 month of surgery.

In the operating room, an IV line was secured in non-dominant upper limb using an 18 gauge IV cannula and a crystalloid infusion was started. Pre-induction monitors were electrocardiogram (ECG), noninvasive blood pressure (NIBP) measurement and pulse oximeter for peripheral oxygen saturation (SPO2).

After evaluation to meet the inclusion and exclusion criteria, each of the 220 patients was randomly included into 1 of 4 Groups (55 patient for each).

- **Group I:** included patients who received a local wound andintraperitoneal saline (control Group).
- **Group II:** included those who received both local wound and intraperitoneal local anesthetic (0.25 Levobupivacaine).
- **Group III**: included patients who received local wound anesthetic at the end of LC only.
- **Group IV**: included those who received an intraperitoneal local anesthetic only (0.25 Levobupivacaine).

LC protocol:

Two authors (An Anesthesia Team), administered general anesthesia to all 220 patients by using the same protocol. Before the start of the cholecystectomy, the LC patients in Group II, IV received 5 mg/kg of 0.5% bupivacaine in 200 mL of 0.9% normal saline as an intraperitoneal infusion into the operative field (i.e., infusion after the saline loading test and before carbon dioxide insufflation). Bupivacaine was administered in 2 separate 100-mL infusions while the patient lay in the Trendelenburg position. The first infusion was administered in the right subdiaphragmatic region and the second infusion was administered in the left subdiaphragmatic region. Patients in Groups III and I received 200 mL of 0.9% normal saline as the intraperitoneal infusion of the operative field before the start of surgery. All infusion fluid was drained after the completion of the LC. The LC patients inGroup II, III received a total of 20 mL

of 0.5% bupivacaine at the port sites immediately after wound closure (6 mL at the epigastric port, 6 mL at the umbilical port; and 4 mL at each working port). Patients in GroupsIV and I received a total of 20 mL of 0.9% normal saline at the port sites immediately after wound closure (6 mL at the epigastric port, 6 mL at the umbilical port; and 4 mL at each working port). At the end of surgery, local anesthesia or normal saline was applied to the skin, subcutaneous fascia, and parietal peritoneum through the port sites.

Patient monitoring and testing:

A visual analog scale (VAS) with a 10-cm vertical score ranged from "no pain" to "worst possible pain". The VAS was used to assess postoperative pain when the patient awake in the operating room (approximately 1 h after surgery), at 6 h after surgery, and at 24 h after surgery. The pain score was recorded by 1 of 4 authors who were blinded to the patient groups. Acetaminophen was used for pain relief in the postoperative period. Pethidine was further used as rescue pain relief if acetaminophen did not work well. Pain intensity was estimated by using the VAS and the amount of analgesics used. Biochemical data, operative time, hospital stay, and perioperative complications were recorded.

Ethical Consideration:

Approval from medical ethical committee of Assiut Faculty of Medicine was taken. Each patient gave his/her written consent to participate in the study.

Statistics Analysis:

SPSS software for windows, version 23 (SPSS Inc., Chicago,IL, USA) was used for data analysis. This software name originally stood for Statistical Package for the Social Sciences. Statistical analysis for demographic data, total mean doses of pethidine were done using t-test and chi-square tests. Analysis of variance (ANOVA) was used to compare between the four Groups as regard pain intensity (VAS pain score) 1h, 6h and 24h postoperatively. Data are presented as mean ± SD (standard deviation) or number of patients. A p-value of less than 0.05 was considered significant.

RESULTS

Demographic characteristics:

Of the total of 220 patients assessed for eligibility in the study, there were no significant differences between the four Groups as regard to age, gender, ASA physical status, duration of surgery (Table 1).

Hospital stay:

The percentage of patients with 2 days hospital stay were higher in Group I compared to other Groups but this difference was notstatistically significant (Table 1).

Table (1): Demographic data in study groups

Item	GI	GII	GIII	GIV	P value
Age	46.56±12.71	43.82±11.79	44.60±12.55	44.76±10.86	0.673 NS
Sex:					
▪ Male	13(23.6%)	9(16.4%)	14(25.5%)	17(30.9%)	P=0.354 NS
▪ Female	42(76.4%)	46(83.6%)	41(74.5%)	38(69.1%)	
Operative time	54.29±10.30	58.70±8.22	71.65±15.52	63.09±10.78	P<0.04*
Hospital stay:					
▪ One day	52(94.5%)	55(100%)	54(98.2%)	54(98.2%)	P=0.274 NS
▪ Two days	3(5.5%)	0.0	1(1.8%)	1(1.8%)	

GI: None.
GII: Local &intraperitoneal anesthetics.
GIII: Local wound anesthetics only.
GIV: Intraperitoneal anesthetics only.
NS= Non significant. * Statistically significant. G = Group

Dynamic pain by a visual analogue scale (VAS) and cumulative Pethidine consumption:

As regard toVAS score, we found highly significance difference between different Groups with higher value in Group I "Control" Group than other Groups. As regard mean value of Pethidine needed, it was significantly lower in Group IIthan other Groups (Table 2, Figure 1, 2).

Table (2): VAS in different Groups

Item	GI	GII	GIII	GIV	P-value
VAS 1	5.5±0.2	3.8±0.1	3.9±0.12	5.1±0.12	0.0001
VAS 6	4.4±1.3	3.5±1	3.6±0.2	3.6±0.11	0.0003
VAS 24	2.5±0.07	2.9±0.1	2.4±0.14	1.4±0.13	0.0004
Pethidine	33.7±1.96	5.9±1.5	21.4±2.4	23.6±2.1	0.0001

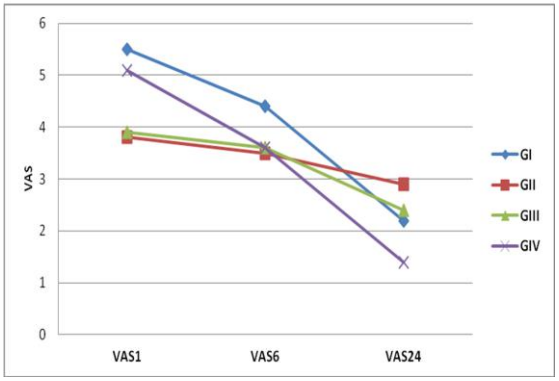

Fig (1): VAS in different Groups

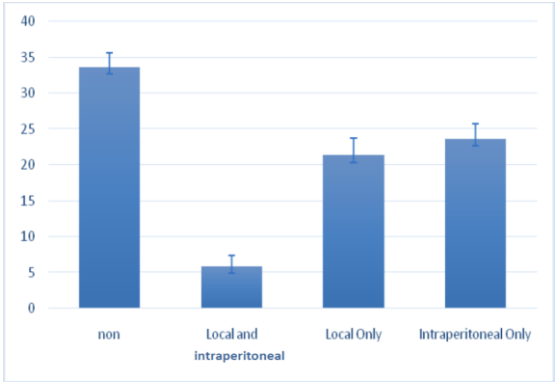

Fig (2): Postoperative total consumption of Pethidine (mg) in each Group

DISCUSSION

Pain after LC is less severe when compared to pain after open cholecystectomy (21), and so patients can be discharged very early after LC surgery. However, LC is not free from pain. Pain after laparoscopic surgery can be transient or persistence for three days [(22)].

Pain after laparoscopic cholecystectomycan be related to multiple factors.It may be related to gall bladder bed, trauma to port sites, nervetraction and irritation,and theuse of cold CO2 to create pneumoperitoneum causing peritoneal irritation by carbonic acid (formed by reaction between CO2 and water). In addition, the pressure created by the pneumoperitoneum and the volume of residual intra-abdominal gas after laparoscopy has been implicated as the cause of shoulder tip and visceral pain [(7, 23, 24)].

As regard to VAS score, we found highly significance difference between different Groups with higher value in Group I "Control" Group than other Groups.

Lower VAS in Group II (Local &intraperitoneal). That means less pain in Group II than other Groups with highly significance difference. This agree with Ortiz and Rajagopalan [(1)] who reported in a study using levobupivacaine, a combination of thismedication both at incisionand into the peritoneum had better analgesia when compared with the use of this drug at one site only [(11)]. The result that incisional and intraperitoneal LA had better effect was also proved in a study using ropivacaine [(25)]. Pappas-gogos et al. [(26)] used ropivacaine both at the trocar site and in the peritoneum under the right hemi diaphragm and showed that LA could be safely used to provide adequate pain relief.

Shivhare et al [(27)] stated that instillation of ropivacaine in the peritoneum is more effective than placebo instillation in reducing postoperative abdominal pain after laparoscopic

cholecystectomy specially at early postoperative hours.

LC is not a procedure without pain. Apredominant complaint after LC is early postoperative pain. This study demonstrated that pain reaches to the peak few hours after the operation, but decreases significantly by the next day, and this proved by pain scores distribution and parenteral analgesics requirement. Incisional pain is more severe than visceral pain and peaks during the initial 48 hours following LC **(18)**.

In conclusion, combined usage of levobupivacaine at the end of the LC both in the peritoneum and at incision site might shorten the time of hospital stay and effectively reduce postoperative dynamic pain scores and cumulative analgesic consumption. This analgesic method have a better safety profile for postoperative patients after LC.

REFERENCES

1. Ortiz J and Rajagopalan S. A Review of Local Anesthetic Techniques for Analgesia After Laparoscopic Surgery. J Minim Invasive Surg Sci. 2014; 3(2): e11310.
2. Megahed HA and Mahmoud IF: Effect of port sites and intraperitonealLevobupivacaine infiltration before or after laparoscope cholecystomy on postoperative pain. Al - AzharAssiut Medical Journal 2015;13 (2):145-149.
3. Bisgaard T, Klarskov B, Rosenberg J, et al. Characteristics and prediction of early pain after laparoscopic cholecystectomy. Pain.2001; 90:261-269.
4. Mitra S, khandewal P, Roberts K, et al. Pain relief in laparoscopic cholecystectomy- a review of the current options. Pain Pract, 2012; 12: 485-496.
5. Bisgaard T, Kehlet H, Rosenberg J. Pain and convalence after laparoscopic cholecystectomy. Ann R CollSurg Engl. 2001;167:84-96.
6. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy; a critical assessment of the evidence. Anesthesiology, 2006; 104 : 835-864.
7. Joshipura VP, Haribhakti SP, Patel NR, Naik RP, Soni HN, Patel B, Bhavsar MS, Narwaria MB, Thakker R. A prospective randomized, controlled study comparing low pressure versus high pressure pneumoperitoneum during laparoscopic cholecystectomy. SurgLaparoscEndoscPercutan Tech. 2009; 19:234–240.
8. Marks J, Tacchino R, Roberts K, Onders R, Denoto G, Paraskeva P, Rivas H, Soper N, Rosemurgy A, Shah S. Prospective randomized controlled trial of traditional laparoscopic cholecystectomy versus single-incision laparoscopic cholecystectomy: report of preliminary data. Am J Surg. 2011; 201:369–372.
9. Liu YY, Yeh CN, Lee HL, Wang SY, Tsai CY, Lin CC, et al. Local anesthesia with ropivacaine for patients undergoing laparoscopic cholecystectomy. *World J Gastroenterol.* 2009;15(19):2376–80.
10. Kahokehr A, Sammour T, Soop M, Hill AG. Intraperitoneal use of local anesthetic in laparoscopic cholecystectomy: systematic review and meta analysis of randomized controlled trials. J HepatobiliaryPancreat Sci. 2010;17:637–656.
11. Louizos AA, Hadzilia SJ, Leandros E, Kouroukli IK, Georgiou LG, Bramis JP. Postoperative pain relief after laparoscopic cholecystectomy. a placebo-controlled double-blind randomized trial of preincisional infiltration and intraperitoneal instillation of levobupivacaine 0.25% SurgEndosc. 2005;19:1503–1506.
12. Alessandri F, Lijoi D, Mistrangelo E, Nicoletti A, Ragni N. Effect of presurgical local infiltration of levobupivacaine in the surgical field on postsurgical wound pain in laparoscopic gynecological surgery. *ActaObstetGynecol Scand.* 2006;85(7):844–9.
13. Cantore F, Boni L, Di Giuseppe M, Giavarini L, Rovera F, Dionigi G. Pre-incision local infiltration with levobupivacaine reduces pain and analgesic consumption after laparoscopic cholecystectomy: a new device for day-case procedure. *Int J Surg.* 2008;6 (Suppl 1):S89–92.
14. Barczynski M, Konturek A, Herman RM. Superiority of preemptive analgesia with intraperitoneal instillation of bupivacaine before rather than after the creation of pneumoperitoneum for laparoscopic cholecystectomy: a randomized, double-

blind, placebo-controlled study. *SurgEndosc.* 2006;20(7):1088–93.
15. Loughney AD, Sarma V, Ryall EA. Intraperitonealbupivacaine for the relief of pain following day case laparoscopy. Br J ObstetGynaecol. 1994;101(5):449–51.
16. Papadima A, Lagoudianakis EE, Antonakis P, Filis K, Makri I, Markogiannakis H, et al. Repeated intraperitoneal instillation of levobupivacaine for the management of pain after laparoscopic cholecystectomy. Surgery. 2009;146(3):475–82.
17. Williamson KM, Cotton BR, Smith G. Intraperitoneallignocaine for pain relief after total abdominal hysterectomy. Br J Anaesth. 1997;78(6):675–7.
18. Kaufman Y, Hirsch I, Ostrovsky L, Klein O, Shnaider I, Khoury E, et al. Pain relief by continuous intraperitonealnebulization of ropivacaine during Gynecologic laparoscopic surgery- a randomized study and review of the literature. J Minim Invasive Gynecol. 2008;15(5):554–8.
19. Bisgaard T, Klarskov B, Kristiansen VB, Callesen T, Schulze S, Kehlet H, et al. Multi-regional local anesthetic infiltration during laparoscopic cholecystectomy in patients receiving prophylactic multi-modal analgesia: a randomized, double-blinded, placebo-controlled study. *AnesthAnalg.* 1999;89(4):1017-24.
20. Lee IO, Kim SH, Kong MH, Lee MK, Kim NS, Choi YS, et al. Pain after laparoscopic cholecystectomy: the effect and timing of incisional and intraperitonealbupivacaine. *Can J Anaesth.* 2001;48(6):545-50.
21. Trondsen E, Reiertsen O, Andersen OK, Kjaersgaard P. Laparoscopic and open cholecystectomy: a prospective, randomized study. Eur J Surg. 1993;159:217–221.
22. Dixon JB, Reuben Y, Halket C, O'Brien PE. Shoulder pain is a common problem following laparoscopic adjustable gastric band surgery. Obes Surg. 2005;15(8):1111–7.
23. Alexander JI, Hull MG. Abdominal pain after laparoscopy: the value of a gas drain. Br J ObstetGynaecol. 1987;94(3):267–9.
24. Sarli L, Costi R, Sansebastiano G, Trivelli M, Roncoroni L. Prospective randomized trial of low-pressure pneumoperitoneum for reduction of shoulder-tip pain following laparoscopy. Br J Surg. 2000;87:1161–1165.
25. Cha SM, Kang H, Baek CW, Jung YH, Koo GH, Kim BG, et al. Peritrocal and intraperitonealropivacaine for laparoscopic cholecystectomy: a prospective, randomized, double-blind controlled trial. *J Surg Res.* 2012;175(2):251-8.
26. Pappas-Gogos G, Tsimogiannis KE, Zikos N, Nikas K, Manataki A, Tsimoyiannis EC. Preincisional and intraperitonealropivacaine plus normal saline infusion for postoperative pain relief after laparoscopic cholecystectomy: a randomized double-blind controlled trial. *SurgEndosc.* 2008;22(9):2036-45.
27. Shivhare P, Dugg P, Singh H, Mittal S, Kumar A, Munghate A. Instillation of Ropivacaine in Postoperative Pain Reduction in Laparoscopic Cholecystectomy.J Minim Invasive Surg Sci. 2014; 3(4): e18009.