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# Intraperitoneal Analgesia for Laparoscopic Cholecystectomy: Bupivacaine versus Bupivacaine with Tramadol

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## ABSTRACT

*The type of pain after laparoscopic surgery differs considerably from that seen after laparotomy. Whereas laparotomy results mostly in parietal pain, patients after laparoscopic cholecystectomy complain more of visceral pain results from the stretching of intraabdominal cavity, peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity. Intraperitoneal (IP) administration of some drugs can be effective for pain relief after laparoscopic surgery. The purpose of this study was to assess the effects of intraperitoneal application of bupivacaine or bupivacaine in combination with tramadol on pain relief after laparoscopic cholecystectomy. After informed written consent and local ethic committee approval, ninety patients of ASA I and II grade undergoing elective laparoscopic cholecystectomy for cholelithiasis were recruited in the study. At the end of laparoscopic cholecystectomy 30 patients in each group received 50 mL saline 0.9% (group C), bupivacaine 0.25% (group B) or bupivacaine 0.25% with tramadol 100 mg (group T). VAS pain was estimated at 30 minutes, 1, 2, 4 and 24 hours after surgery. Postoperative analgesic requires were also assessed. Pain scores were significantly lower in group receiving the IP bupivacaine with tramadol and bupivacaine compared to saline group. Intraperitoneal applications of these drugs reduced consumption of supplementary postoperative analgesic medication. Intraperitoneal administration of bupivacaine with tramadol and bupivacaine are simple to use and effective in a reduction of pain after laparoscopic cholecystectomy. In our study we found no differences between bupivacaine with tramadol and bupivacaine in postoperative VAS score and analgesic requirements.*

**Key words:** intraperitoneal analgesia, tramadol, bupivacaine, laparoscopic cholecystectomy

## Introduction

Laparoscopic cholecystectomy results in less pain compared to open cholecystectomy, but pain still exist in most of the patients and they often require postoperative opioid treatment.

The type of pain after laparoscopic surgery differs considerably from that seen after laparotomy. Whereas laparotomy results mostly in parietal pain, patients after laparoscopic cholecystectomy complain more of visceral pain results from the stretching of intraabdominal cavity, peritoneal inflammation and phrenic nerve irritation caused by residual carbon dioxide in the peritoneal cavity<sup>1</sup>.

Some investigators have asserted that intraperitoneal administration of local anesthetics and opioids<sup>2-8</sup> is effective method of reducing the pain. However other investigators did not find any analgesic efficacy of IP adminis-

tration of local anesthetics<sup>9-11</sup>. There is few data in literature on analgesic effect of intraperitoneal administration of local anaesthetics in combination with opioid for laparoscopic cholecystectomy<sup>4,5,12</sup>.

Laparoscopic cholecystectomy is commonly performed procedure for treating symptomatic gallstones. This study was designed to examine the efficacy of intraperitoneal administration of tramadol, as weak opioid, with bupivacaine, long-lasting local anesthetic, for pain relief after laparoscopic cholecystectomy.

## Patients and Methods

After informed written consent and local ethic committee approval, ninety patients of ASA I and II grade

**TABLE 1**  
PRESENTATION OF DEMOGRAPHIC CHARACTERISTICS AND SUPPLEMENTARY POSTOPERATIVE MEDICATIONS

	Group C (n=30)	Group B (n=30)	Group T (n=30)
Sex ratio (F:M)	18:12	20:10	17:13
Age <sup>a</sup> (years)	54.6 ± 11.1	51.1 ± 12	56.1 ± 12
Body weight <sup>a</sup> (kg)	74.8 ± 11.5	77.2 ± 12	76.2 ± 12
Duration of operation <sup>a</sup> (min)	75.2 ± 22	78.8 ± 19	76.8 ± 17.5
Supplementary postoperative medication (number of patients)			
NSAID	28*	7	5
opioids	26*	0	0

F – female, M – male, NSAID – nonsteroidal anti-inflammatory drugs, <sup>a</sup> – mean ± SD, \* – p<0.05

undergoing elective laparoscopic cholecystectomy for cholelithiasis were recruited in the study. Any patient with contraindications to tramadol or bupivacaine was excluded from the study. Patients were also excluded if there were complications during operation or the operation had to be converted to an open cholecystectomy. Standard operative method was used as described<sup>13</sup>. A questionnaire was completed for each patient, giving demographic, perioperative and postoperative details.

This was prospective, randomized, double-blinded study with 30 patients in each group.

All patients received same anesthetic technique. They were premedicated with midazolam (7.5 mg orally) 30 minutes before surgery. General anesthesia was induced by intravenously administration of sufentanil (0.15–0.3 µg/kg), propofol (2.5–3 mg/kg) and rocuronium (0.6 mg/kg) and was maintained with a mixture of 1.5–2 vol % isoflurane, oxygen and air. Minute ventilation was adjusted to keep end-tidal pCO<sub>2</sub> at 4.5–5.5 kPa.

At the end of the surgery, the patients allocated to Group C received 50 mL of saline, those allocated in group B received 50 mL of 0.25% bupivacaine and patients allocated in group T received 50 mL of bupivacaine 0.25% with 100 mg of tramadol into the hepatodiaphragmatic space, near and above the hepato-duodenal ligament and above the gall bladder bed under direct vision. The test solution were drawn into the coded syringes and given to surgeons who did not know their content.

After surgery all patients stayed in PACU for two hours. In PACU postoperative pain was assessed using 100 mm visual analog scale (VAS). VAS was recorded at admission, 0.5, 1 and 2 hours after admission. Supplemental analgesic medication was available upon request and was recorded at the above intervals. In PACU intravenous nonsteroidal anti-inflammatory analgesic (NSAID; diclofenac, 75 mg i. v.) were used for pain scores less than 3 and opioids (pethidine 1 mg/kg i.m.) for pain scores above 3. The drugs were administrated on demand by an experienced recovery nurse with no knowledge of perioperative analgesia administration.

All enrolled patients completed the study. Results are expressed as mean ± SD. Data were analyzed by two-way analysis of variance. Demographic data were studied us-

ing Student's t-test. Pain score were compared using the Kruskal-Wallis and Mann-Whitney U-test. Results were considered to be statistically significant at the 5% critical level (p<0.05). Data were analyzed with statistical program Statistica for Windows version 7.1 (StatSoft Inc, Tulsa, USA).

## Results

Ninety patients completed the study. There were no significant differences in patients' demographics data (Table 1). Supplementary postoperative analgesic consumption was compared between groups (Table 1). According to postoperative VAS pain score in PACU NSAIDs or opioids were administrated. Twenty eight patients in group C received NSAID as supplementary analgesic medication while in group T five and in group B seven patient requested same drugs (Table 1). Twenty six patients in group C received opioid analgesia after surgery while in group B and group T no one received opioids (p<0.05) (Table 1).

Statistically significant differences (p<0.05) were found in pain intensity between group C and T and group C and B 30 minutes, 1, 2 and 4 hours after surgery (Figure 1). We found no statistically significant difference in pain scores between group B and group T. At 24 postoperative hour's pain were reduced significantly in all groups (Figure 1).

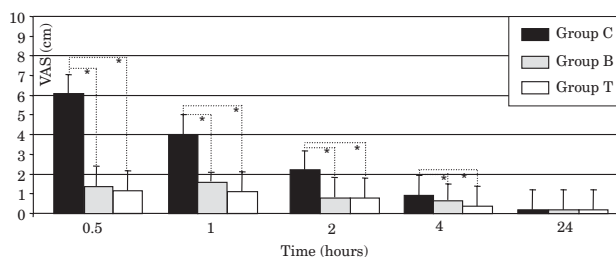


Fig 1. The effect of intraperitoneal bupivacaine and bupivacaine with tramadol on pain using visual analog scale (VAS) at 0.5, 1, 2, 4 and 24 hours after surgery. Values are mean ± SD. \*p<0.05 was considered statistically significant.

## Discussion

We found that IP administration of bupivacaine with tramadol as well as bupivacaine have same potency to reduce postoperative pain during first four hours after laparoscopic cholecystectomy. In general the intensity of pain was mild to moderate. A controversy exists over the effectiveness and clinical value of intraperitoneal local anesthetics or opioids treating pain after laparoscopic cholecystectomy. The reason for these variations in result could be differences in the high variable study protocols<sup>4,12</sup>.

Over a decade there have been controversy data about analgesic benefit of bupivacaine administered intraperitoneally after laparoscopic cholecystectomy. Some investigators<sup>3,6–8</sup> found that IP bupivacaine was effective in pain reduction, while others<sup>9,10</sup> showed that it did not attenuate pain following laparoscopic surgery. The reasons for these variations in result is not known, but the time of injection, site of injection, as well as concentration of local anesthetics could play important role<sup>4,5,8,14</sup>. In our study we found that IP bupivacaine is effective in pain control during early postoperative period after laparoscopic cholecystectomy.

Our work also highlights the analgesic effect of intraperitoneally administered bupivacaine with tramadol after laparoscopic cholecystectomy. As bupivacaine, which in our and some other studies<sup>3,6–8,14</sup> reduce pain after laparoscopic cholecystectomy, we found that bupivacaine with tramadol to be as well effective after laparoscopic cholecystectomy.

Memis et al.<sup>15,16</sup> showed that intraperitoneal administration of bupivacaine with tramadol and bupivacaine is very effective in the early postoperative period in patients undergoing laparoscopic tube ligation and in total abdominal hysterectomy.

Tramadol's analgesic effect can be explained by its dual mechanism of action where it blocks the reuptake of norepinephrine and 5-hydroxytryptamine at the  $\alpha_2$  adrenergic receptor level<sup>17</sup>. Its mode of action is thought to be dorsal horn of spinal cord or in the brain. Tramadol could also have a local effect when given intraperitoneally after laparoscopic surgery, which adds to the effect from systemic uptake and action in central nervous system.

## Conclusion

In our study we found no differences between bupivacaine with tramadol and bupivacaine in postoperative VAS score and analgesic requirements.

Application of bupivacaine with tramadol and bupivacaine intraperitoneally attenuated pain after laparoscopic cholecystectomy. Addition of tramadol to local anesthetics for intraperitoneal analgesia merit further study in patients undergoing laparoscopic cholecystectomy.

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## INTRAPERITONEALNA ANALGEZIJA KOD LAPAROSKOPSKE KOLECISTEKTOMIJE: BUPIVAKAIN NASPRAM BUPIVAKAINA S TRAMADOLOM

## SAŽETAK

Bol nakon laparoskopske kolecistektomije značajno se razlikuje od boli nakon laparotomije. Dok kod laparotomije prevladava parijetalna bol bolesnici nakon laparoskopske kolecistektomije žale se na visceralnu bol. Svrha ove studije

bila je procjena učinkovitosti IP aplikacije bupivakaina ili bupivakaina u kombinaciji sa tramadolom na bol nakon laparoskopske kolecistektomije. U studiju je uključeno 90 bolesnika predviđenih za elektivnu laparoskopsku kolecistektomiju. Na kraju laparoskopske kolecistektomije kod 30 bolesnika iz svake grupe IP je aplicirano po 50 mL: fiziološke otopine (grupa C), bupivakain 0,25% (grupa B) ili bupivakain 0,25% sa 100 mg tramadola (grupa T). Procjena boli putem vizualne ocjenske ljestvice (VAS score) bilježila se nakon 30 minuta, 1, 2, 4 i 24 sata nakon operativnog zahvata. Postoperativna analgetska potraživanja su također bilježena. Intenzitet boli bio je značajno manji u grupi koja je IP dobila bupivakain s tramadolom ili bupivakain u odnosu na grupu koja je dobila fiziološku otopinu. IP aplikacijom bupivakaina samog ili u kombinaciji sa tramadolom značajno se smanjila postoperativna analgetska potražnja. U našoj studiji nije nađena statistički značajna razlika između IP aplikacija bupivakaina sa tramadolom i bupivakaina glede postoperativne procjene boli i analgetskih potraživanja.