

# Analgesic Effect of Intraperitoneal Instillation of Bupivacaine for Postoperative Laparoscopic Cholecystectomy

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## Abstract

**Objective :** To study the effectiveness of intraperitoneal instillation of bupivacaine for postoperative laparoscopic cholecystectomy pain relief, especially specific pain (visceral pain, shoulder pain and epigastric pain).

**Patients and Method :** Eighty ASA (American Society of Anesthesiologists) 1 and 2 patients were randomly assigned to receive either 20 ml of 0.5 per cent bupivacaine (n=39) or the same volume of saline (n=41) instilled under direct vision into the hepatodiaphragmatic space, near and above the hepatoduodenal ligament and above the gall bladder bed at the end of surgery. The intensity of visceral pain, shoulder pain and epigastric pain was assessed at 1, 6, 24 and 48 h after surgery using a visual analogue scale (100 mm VAS) and verbal rating "Prince Henry" pain scale (VRS). The time when analgesia was first required and total analgesic consumption were also recorded. *t*-test, Chi-square, Mann-Whitney U test and Kaplan-Meier survival analysis were used for statistical analysis.

**Results :** Patient data were similar in the two groups except for body weight. There were no statistical differences between the two groups for the time when analgesia was first required, VAS, VRS and total analgesic consumption.

**Conclusion :** In this study, intraperitoneal instillation of bupivacaine does not show any advantage for postoperative analgesia after laparoscopic cholecystectomy.

**Key word :** Pain, Laparoscopic Cholecystectomy, Bupivacaine

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Laparoscopic cholecystectomy (LC) is a popular technique for treating symptomatic gall stones because it has many advantages over an open technique. Postoperative pain and respiratory complication can be reduced. A reduced analgesic requirement and duration of hospital stay have been reported<sup>(1-3)</sup>. Other advantages include small surgical wounds and a better cosmetic result<sup>(4,5)</sup>. Although there are many advantages as above, some patients still complain of postoperative discomfort such as visceral pain, nausea and vomiting as a result of intra-abdominal inflammation and from the wound<sup>(3)</sup>. Also, diaphragmatic irritation from carbon dioxide pneumoperitoneum can cause shoulder tip pain in 35-60 per cent of LC patients<sup>(6-8)</sup>. Some patients (34%) suffered from symptoms such as dyspepsia or nausea<sup>(9-11)</sup>. Many studies have looked at postoperative pain control using intraperitoneal bupivacaine instillation but some reports showed no advantages over conventional techniques. This study was set up because there is still controversy as to whether this technique is useful.

#### PATIENTS AND METHOD

This study was a randomized, double blind, placebo control trial and was approved by the Ethical Committee of the Faculty of Medicine, Siriraj Hospital, Mahidol University. Written informed consent was obtained from each patient before surgery. Eighty inpatients undergoing elective laparoscopic cholecystectomy for symptomatic gall stones were studied. The exclusion criteria of the study were ASA status of III or greater, arrhythmia and age  $\geq 70$  years. Oral benzodiazepine, diazepam 5 mg or midazolam 7.5 mg were given as premedication 1 hour before induction of anesthesia. The patients were randomly assigned to two groups. Forty-one patients in group A received 20 ml of intraperitoneal saline. Thirty-nine patients in group B were given 20 ml of intraperitoneal 0.5 per cent bupivacaine. Perioperative monitoring included NIBP, EKG, pulse oxymetry and capnography. Fentanyl (1-2 mcg/kg) was administered intravenously just before induction of anesthesia with thiopental (5 mg/kg) and intubation with succinylcholine (1.5 mg/kg). Maintenance of anesthesia was performed with nitrous oxide in oxygen, isoflurane and atracurium for muscle paralysis. 0.5 per cent bupivacaine was infiltrated locally at the skin incision and sheath before trocar insertion. The pneumoperitoneal pressure of CO<sub>2</sub> was strictly limited to 15 mmHg.

The operations were performed by the same surgeon. Following the removal of gall bladder, the

surgeon administered the randomized solution through a trocar pointed to the right subdiaphragmatic area, the gall bladder bed and the hepatoduodenal ligament under direct vision after the gall bladder had been removed and no active bleeding was seen. The patient was placed in the Trendelenburg position for a period of 5 minutes following the injection. At the completion of surgery, 1.2 mg of atropine and 2.5 mg of prostigmine were given to reverse muscle paralysis.

Patients were interviewed concerning postoperative pain. The visual analogue scale (VAS) and the verbal rating "Prince Henry" pain scale (VRS) were used as a postoperative pain indicator at 1, 6, 24 and 48 hours postoperatively. One hundred millimeters of VRS indicated severe pain and no pain is 0 mm on the VAS. The VRS was divided into 5 levels

- 0 = no pain at all
- 1 = no pain when you take a deep breath but pain when you cough
- 2 = pain when you take a deep breath
- 3 = mild pain when lying still
- 4 = severe pain eventhough no movement

A "rescue" dose of, 1-2 mg/kg of pethidine, was given when the patient requested postoperative pain relief.

Information concerning age, sex, weight, ASA classification, diagnosis, operative time, CO<sub>2</sub> pneumoperitoneal period, anesthetic time, complication, medication, VAS, VRS, time analgesia first required, total dosage of pethidine and duration of hospital stay were recorded.

#### Statistical analysis

The *t*-test was used to compare age, weight, the time of surgery, CO<sub>2</sub> pneumoperitoneum and anesthetic time. Gender, ASA classification and diagnosis were compared using the Chi-square test. The Mann-Whitney U test was used to analyse VRS and VAS at 1, 6, 24 and 48 hour postoperative periods. Kaplan-Meier survival analysis was used to compare the time of first analgesic requirement. Statistical significance was taken at a *p*-value of less than 0.05.

#### RESULTS

Eighty patients were randomized and distributed to two groups of A (41) and B (39). The demographic data were similar in both groups but

the body weight of the saline group was statistically significantly greater than the bupivacaine group (65.02 and 59.77 kg respectively,  $p$ -value = 0.017) (Table 1). The mean operating time and time of CO<sub>2</sub> pneumoperitoneum were not significantly different (Table 2). The mean values of VRS and VAS 1,6,24 and 48 hour postoperatively were similar (Fig. 1, 2). Although there were no significant differences in the mean time of first analgesic requirement, duration of hospital stay and the total dosage of pethidine, the Kaplan-Meier survival analysis showed a tendency for the request for "rescue" pain relief medication was earlier in saline group than the bupivacaine group (Fig. 3).

## DISCUSSION

Laparoscopic cholecystectomy (LC) is a popular technique for treating symptomatic gall stones

because it produces a less traumatic wound than an open technique. However, some patients are still faced with unpleasant symptoms such as visceral pain, shoulder tip pain, nausea and vomiting especially during the first 4 hours postoperatively<sup>(12)</sup>. Some anesthesiologists have suggested that local anesthetic drug can minimize this. Many studies have been performed to confirm the benefit of lidocaine and bupivacaine instillation. Although some papers showed good results, other have not show any advantages in this technique.

There have been many different techniques used and variety of concentrations and dosages of bupivacaine. Intraperitoneal bupivacaine had been shown to reduce pain after laparoscopic cholecystectomy. Chundrigger T, et al successfully applied 20 ml of 0.25 per cent bupivacaine to the gall bladder bed<sup>(13)</sup> and Berven S, et al used 30 ml of 0.5 per cent

**Table 1. A comparison of demographic data, operative time, pneumoperitoneal time and anesthetic time (mean  $\pm$  SD).**

	Saline group	Bupivacaine group	P-value
Age (year)	52.4 $\pm$ 11.2	50.8 $\pm$ 9.7	0.498
BW (kg)	65.02 $\pm$ 10.8	59.77 $\pm$ 8.3	0.017*
Sex (male : female)	16 : 25	7 : 32	0.067
ASA (I : II)	17 : 24	22 : 17	0.266
Diagnosis (gall stone : other)	39 : 2	36 : 3	0.221
Operative time (min)	57.41 $\pm$ 23.8	51.97 $\pm$ 21.2	0.284
Pneumoperitoneal time (min)	36.37 $\pm$ 19.9	31.49 $\pm$ 19.1	0.266
Anesthetic time (min)	83.85 $\pm$ 25.6	79.46 $\pm$ 24.0	0.432

BW = body weight, ASA = American Society of Anesthesiologists.

**Table 2. The comparison of VAS at 1, 6, 24 and 48 hours postoperatively, VRS at 1, 6, 24 and 48 hours postoperative period, total analgesic requirement in 48 hours postoperatively and postoperative hospitalization (mean  $\pm$  SD).**

	Saline group	Bupivacaine group	P value
VAS at 1 h	33.98 $\pm$ 27.2	31.79 $\pm$ 26.4	0.717
VAS at 6 h	36.46 $\pm$ 28.5	30.00 $\pm$ 20.2	0.248
VAS at 24 h	22.73 $\pm$ 17.5	18.15 $\pm$ 18.0	0.253
VAS at 48 h	11.73 $\pm$ 12.2	11.05 $\pm$ 13.6	0.814
VRS at 1 h	1.83 $\pm$ 1.3	1.51 $\pm$ 1.2	0.257
VRS at 6 h	1.88 $\pm$ 1.0	1.64 $\pm$ 1.1	0.297
VRS at 24 h	1.22 $\pm$ 0.7	1.10 $\pm$ 0.7	0.448
VRS at 48 h	0.71 $\pm$ 0.6	0.74 $\pm$ 0.6	0.770
Total dose of pethidine (mg)	23.05 $\pm$ 25.9	28.21 $\pm$ 41.0	0.501
Postoperative hospitalization (day)	2.27 $\pm$ 0.8	2.15 $\pm$ 0.5	0.472

VAS = visual analogue scale, VRS = verbal rating "Prince Henry" pain scale.

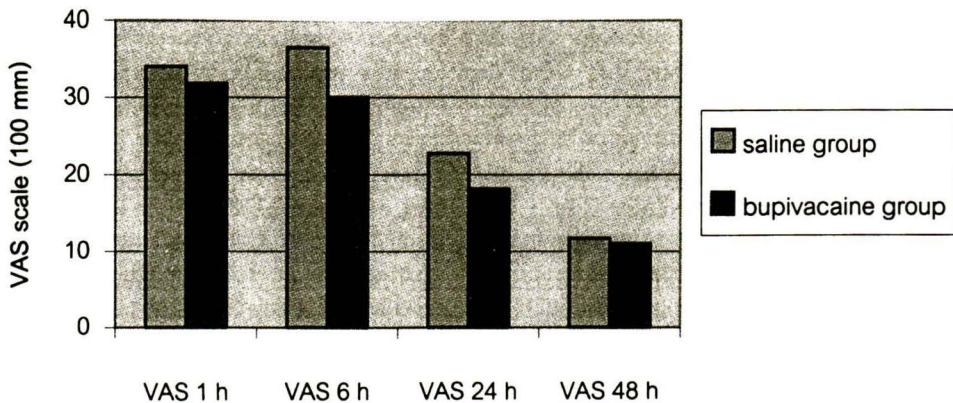


Fig. 1. The comparison of visual analogue scale (VAS) at 1, 6, 24 and 48 hours postoperatively.

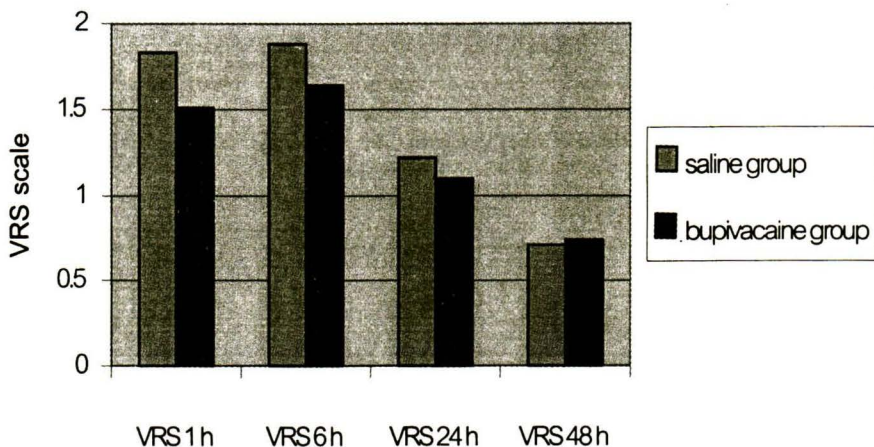
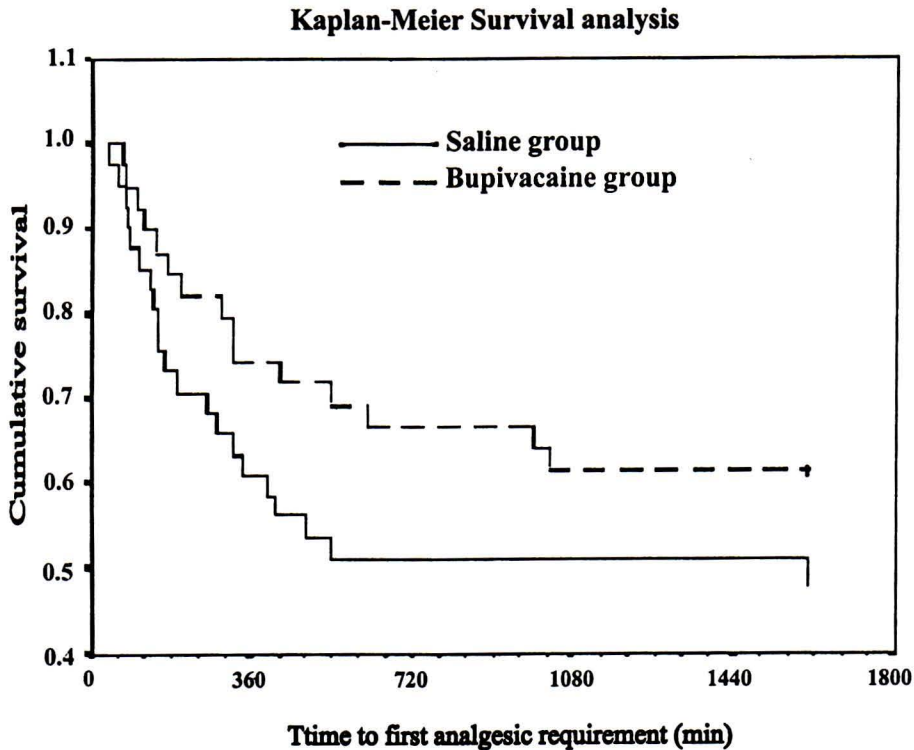


Fig. 2. The comparison of verbal rating "Prince Henry" pain scale (VRS) at 1, 6, 24 and 48 hours postoperatively.

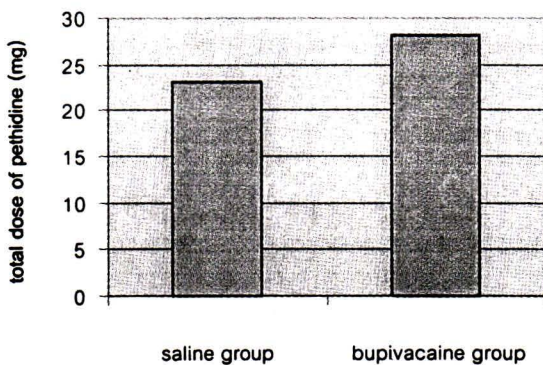
bupivacaine with good results for pain relief<sup>(14)</sup>. On the other hand, Sheinin B, et al<sup>(15)</sup> showed no analgesic effect when they used 100 ml of 0.15 per cent bupivacaine. In addition, Rademaker BMP, et al showed no significant advantages of bupivacaine intraperitoneal instillation<sup>(16)</sup>. The concentration of local anesthetic and the site of administration are important factors affecting the analgesic effect of bupivacaine. Joris J, et al instilled bupivacaine only in the right subdiaphragmatic area which did not produce good pain relief<sup>(12)</sup>. Mraovic B, et al showed effective pain relief when bupivacaine instillation was applied to the hepato-diaphragmatic space, hepato-duodenal ligament and the gall bladder bed<sup>(17)</sup>.

This study applied 20 ml of 0.5 per cent bupivacaine instillation to the right subdiaphragmatic area, hepatoduodenal ligament and gall bladder bed in the Trendelenburg position for 5 minutes under direct vision to ensure absorption of drug. Signs and symptoms of local anesthetic overdose were not found.

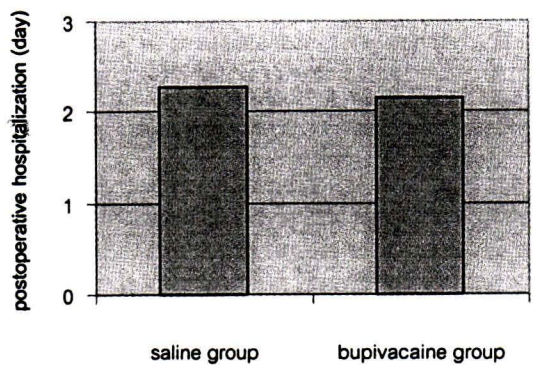
There were no significant differences between the groups with regard to VAS and VRS. However, this analysis using VAS and VRS was weak because the rescue drug (pethidine) can eliminate the pain. We didn't compare the VAS and VRS ie the pain level experience by the patient before we



**Fig. 3.** Kaplan-Meier survival analysis compare time to first analgesic requirement between the Saline group and the Bupivacaine group. X-axis, time of first analgesic requirement; Y-axis, cumulative survival.



**Fig. 4.** Total dose of pethidine each group.



**Fig. 5.** The duration of hospital stay.

gave the rescue drug. We had already decided the exact time to perform a VAS and VRS assessment of the patient's pain and so the primary outcome should be changed to the time analgesia was first required.

Although mean of time of first analgesic requirement of both groups was similar, the Kaplan-Meier survival analysis showed a tendency of group A to request "rescue" drug more quickly than group

B at 360 minutes. If the sample size was four times larger than this, the Kaplan-Meier survival graph would demonstrate a statistically significant difference in the time of first analgesic requirement, but this is not important in clinical practice. We found some patients in group B had no need of the rescue drug at all, perhaps, a high personal pain threshold was a good reason to explain this.

When we compared duration of hospital stay, there was no difference between the groups because all patients wanted to stay until they felt comfortable. We could draw no conclusion from this because of emotional and cultural factors.

### SUMMARY

This study showed no advantage of intraperitoneal instillation of 20 ml of 0.5 per cent bupivacaine for postoperative pain relief in laparoscopic

cholecystectomy. Although the saline group requested rescue drug earlier than the bupivacaine group at 360 minutes this was not statistically significant. The sample size is a big problem because a sample size of 320 patients is needed to demonstrate any statistically significant difference between the groups.

We look forward to seeing a study that can solve the postoperative problems associated with the laparoscopic cholecystectomy procedure.

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## การศึกษาผลระงับปวดหลังผ่าตัดถุงน้ำดีโดยส่องกล้องด้วยการฉีดยาชาเฉพาะที่ บูพิวาเคนเข้าช่องท้อง

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**จุดมุ่งหมาย :** เพื่อศึกษาผลระงับปวดหลังผ่าตัดถุงน้ำดีโดยการส่องกล้องด้วยการฉีดยาชาเฉพาะที่บูพิวาเคนเข้าช่องท้องภายหลังเอาถุงน้ำดีออกแล้ว อาการปวดที่ศึกษาได้แก่ visceral pain, shoulder tip pain และ epigastrium pain

**วิธีการศึกษา :** ได้ศึกษาในผู้ป่วย 80 คนที่ได้รับการผ่าตัดถุงน้ำดีโดยการส่องกล้องที่โรงพยาบาลศิริราช แบบ double blind ได้สุ่มแบ่งผู้ป่วยเป็น 2 กลุ่ม โดยกลุ่มแรกได้รับยาชา 0.5% บูพิวาเคน 20 มล. ในขณะที่กลุ่มที่ 2 ได้รับน้ำเกลือในปริมาณเท่ากัน ฉีดเข้าสู่ช่องท้องบริเวณ hepatodiaphragmatic, hepatoduodenal ligament และ gall bladder bed โดยศัลยแพทย์ผู้ทำการศึกษาได้สอบถามผู้ป่วยหลังผ่าตัดที่เวลา 1, 6, 24, 48 ชั่วโมงหลังผ่าตัดเพื่อประเมินอาการปวด โดยใช้ VAS และ VRS รวมทั้งได้บันทึกเวลาที่ผู้ป่วยได้รับยาแก้ปวด (pethidine) ครั้งแรกหลังผ่าตัดและปริมาณยาแก้ปวดที่ใช้ทั้งหมด

**ผลการศึกษา :** พบว่าข้อมูลของผู้ป่วยทั้งสองกลุ่มไม่มีความแตกต่างทางสถิติ ทั้งค่า VAS, VRS, ระยะเวลาที่ผู้ป่วยได้ยาแก้ปวดครั้งแรกหลังผ่าตัด และปริมาณยาแก้ปวดทั้งหมด

**สรุป :** การฉีดยาชาบูพิวาเคนในช่องท้องหลังผ่าตัดถุงน้ำดีโดยการส่องกล้อง ไม่ช่วยลดอาการปวดหลังผ่าตัด

**คำสำคัญ :** อาการปวดหลังผ่าตัด, การผ่าตัดถุงน้ำดีโดยส่องกล้อง, บูพิวาเคน

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