

Pain after laparoscopic cholecystectomy: the effect and timing of incisional and intraperitoneal bupivacaine

[La douleur post-cholecystectomie laparoscopique : l'effet et la chronologie de l'administration de bupivacaine incisionnelle et intrapéritonéale]

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Purpose: To examine the combined preemptive effects of somato-visceral blockade during laparoscopic cholecystectomy (LC).

Methods: One hundred fifty-seven patients under general anesthesia receiving local infiltration and/or topical peritoneal local anesthesia were studied. Patients were randomized to receive a total of 150 mg (0.25% 60 mL) bupivacaine via periportal (20 mL) and intraperitoneal (40 mL with 1:200,000 epinephrine) administration of each. Group A received preoperative periportal bupivacaine before incision and intraperitoneal bupivacaine immediately after the pneumoperitoneum. Group B received periportal and intraperitoneal bupivacaine at the end of the operation. Group C (preoperative) and Group D (postoperative) received only periportal bupivacaine and Group E (preoperative) and Group F (postoperative) received only intraperitoneal bupivacaine. The control group received no treatment. Pain and nausea were recorded at one, two, three, six, nine, 12, 24, 36, and 48 hr postoperatively.

Results: Throughout the postoperative 48 hr, incisional somatic pain dominated over other pain localizations in the control group ($P < 0.05$). The incisional pain of groups A, B, C and D was significantly lower than that of the control group in the first and second hours. The incisional pain of groups A and C was significantly lower than that of the control group in the first three hours.

Conclusion: Incisional pain dominated during the first two postoperative days after LC. Preoperative somato-visceral or somatic local anesthesia reduced incisional pain during the first three postoperative hours. A combination of somato-visceral local anesthetic treatment did not reduce intraabdominal pain, shoulder pain or nausea more than somatic treatment alone. Preoperative incisional infiltration of local anesthetics is recommended.

Objectif : Vérifier les effets préventifs d'un blocage somato-viscéral combiné, réalisé pendant la cholécystectomie laparoscopique (CL).

Méthode : Cent cinquante-sept patients sous anesthésie générale ont reçu une infiltration locale et/ou une anesthésie locale péritonéale topique. Les patients, répartis de façon aléatoire, ont reçu au total 150 mg (0,25 % 60 mL) de bupivacaine administrée par la voie périportale (20 mL) et intrapéritonéale (40 mL avec 1 : 200 000 d'épinéphrine). Les modalités intergroupes sont les suivantes : dans le groupe A, une dose préopératoire périportale avant l'incision et une dose intrapéritonéale immédiatement après le pneumopéritoine ; dans le groupe B, une dose périportale et une intrapéritonéale à la fin de l'opération ; dans les groupes C (préopératoire) et D (postopératoire), seulement une périportale et dans les groupes E (préopératoire) et F (postopératoire), seulement intrapéritonéale. Le groupe témoin n'a reçu aucun médicament. La douleur et les nausées ont été notées à une, deux, trois, six, neuf, 12, 24, 36 et 48 h après l'intervention.

Résultats : Pendant les 48 h d'observation postopératoire, la douleur somatique de l'incision a dominé toute autre douleur chez les patients témoins ($P < 0,05$). La douleur incisionnelle a été significativement plus faible dans les groupes A, B, C et D que dans le groupe témoin pendant les deux premières heures. Elle a aussi été significativement plus faible dans les groupes A et C que dans le groupe témoin pendant les trois premières heures.

Conclusion : La douleur incisionnelle a dominé pendant les deux premiers jours qui ont suivi la CL. L'anesthésie préopératoire somato-viscérale ou somatique locale ont réduit la douleur incisionnelle pendant les trois premières heures postopératoires. Une combinaison d'anesthésiques locaux somato-viscéraux n'a pas réduit la douleur intra-abdominale, la douleur à l'épaule ou les nausées davantage que

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l'anesthésie somatique employée seule. L'infiltration préopératoire d'anesthésique local au site d'incision est recommandée.

LAPAROSCOPIC cholecystectomy (LC) results in less postoperative pain and/or reduced analgesic consumption as compared with open cholecystectomy.¹ Although pain after LC is less intense than after open cholecystectomy, some patients still experience considerable discomfort during the first 24 postoperative hours.² Thus, several interventions have been investigated.³⁻¹⁴ Variable analgesic effects of periportal infiltration of local anesthetics,³⁻⁵ infiltration of the periportal parietal peritoneum,⁶ intraperitoneal spraying above the gall bladder,^{7,8} instillation into the subdiaphragmatic space⁹⁻¹⁴ and into the subhepatic space covering the area of the hepatoduodenal ligament have been reported.⁸ Some of them failed to show analgesic effects.^{9,11-14}

The preoperative analgesic effects of incisional local anesthetics,^{2,4,5} or intraperitoneal local anesthetics^{7,8} have been investigated. Most studies^{2,4,5,8} failed to show a preemptive analgesic effect as compared with postoperative treatment.^{6,15} We are unaware of any study investigating the effects of the combined somato-visceral local anesthetic preemptive blockade after elective LC. Therefore, our study was designed to investigate any differences in the nature of pain after LC and to examine the effects of combined somato-visceral local anesthetic blockade on postoperative pain or nausea.

Methods

We examined the effects of preoperative with postoperative bupivacaine 0.25% 60 mL on pain in 157 inpatients undergoing elective LC in a prospective, randomized study. This study was approved by the local Ethics Committee and informed consent was obtained from all patients. Patients allergic to local anesthetics, as well as those with a history of severe systemic disease, were excluded from the study. Moreover, patients with chronic pain diseases other than gallstone disease were excluded. Patients ASA physical status III or greater and patients who had acute cholecystitis before the operation were also excluded.

One team of surgeons performed all operations. All patients received 5 mg midazolam intramuscularly 30 min before being transferred to the operating room. All operations were performed between 08:30 a.m. and 12:00 noon. Anesthesia was induced using 5 mg·kg⁻¹ thiopentone and 1 mg·kg⁻¹ succinylcholine. After tra-

cheal intubation, general anesthesia was maintained with 1-1.2% isoflurane (end-tidal concentration), oxygen/nitrous oxide (50%/50%). Relaxation was maintained with vecuronium 0.1 mg·kg⁻¹. After the induction of anesthesia, patients were randomly assigned to one of six groups of 22 patients each. The preoperative somato-visceral group (PRE-SV) received preoperative periportal 0.25% bupivacaine (20 mL) 15 min before incision and intraperitoneal 0.25% bupivacaine (40 mL with 1:200,000 epinephrine) immediately after the creation of pneumoperitoneum. The postoperative somato-visceral group (POST-SV) received the same periportal bupivacaine at the end of the operation and intraperitoneal bupivacaine before the trocars were withdrawn. The preoperative-somatic (PRE-S) and postoperative-somatic (POST-S) groups received only periportal bupivacaine and the preoperative-visceral (PRE-V) and postoperative-visceral (POST-V) groups received only intraperitoneal bupivacaine. The control group ($n=25$) received no treatment. The fascia, muscle, preperitoneal space, and the parietal peritoneum were infiltrated (infiltration of four port sites in total, 7 mL each for two 10-mm sites, 3 mL each for the other two 5-mm sites). Intraperitoneal bupivacaine was given as follows: immediately after the creation of a pneumoperitoneum, the surgeon sprayed bupivacaine on the upper surface of the liver and the subdiaphragmatic space to allow it to diffuse into the hepatodiaphragmatic space, near and above the hepatoduodenal ligament and above the gallbladder. This was done using a catheter inserted into the subcostal trocar under direct laparoscopic control. Residual intraperitoneal CO₂ was evacuated carefully at the end of surgery by manual compression of the abdomen with open trocars.

Before the induction of anesthesia, patients were instructed about the use of a 10-cm visual analog scale (VAS: with endpoints 'no pain' and 'worst pain') for the measurement of pain and nausea. Postoperative pain was rated on a VAS at rest.

The time of arrival in the postoperative recovery room was defined as zero hour postoperatively. Pain intensity was measured at one, two, three, six, nine, 12, 24, 36, and 48 hr postoperatively. All patients were admitted in the general ward for two postoperative days. Patients were asked to rate incisional and intraabdominal pain at rest by a comparison of pain severity between the two pain localizations. Incisional pain was defined as superficial pain, wound pain, or pain located in the abdominal wall. Intraabdominal pain was defined as pain inside the abdomen, which may have been deep, dull, and more difficult to localize, and may have resembled biliary colic. Shoulder

pain, and other pain was assessed at rest at the same intervals. The number of patients who experienced nausea and vomiting was assessed during the study period.

On emergence patients were asked, “Do you have any pain?” and given bolus *iv* ketorolac in 30 mg doses if they answered “yes”, followed by an additional ketorolac 30 mg if requested by the patient. For postoperative analgesia, all patients received the following analgesia treatment: *im* ketorolac (30 mg) at eight-hour intervals for 48 hr, additional *iv* ketorolac 30 mg if requested by the patient. Opioids were administered on request (demerol 25 mg *im*) if the patient indicated that he was not satisfied with the level of analgesia that was reached. Only total amounts of requested additional ketorolac or opioids were recorded. Patients were also given metoclopramide 10 mg if they experienced nausea or vomiting, followed by additional metoclopramide 10 mg on request. Supplementary medication required in addition to the standard treatment was recorded.

No patients or observers were informed of the treatment group (preoperative or postoperative). A preoperative sample size calculation determined that a reduction of 3.0 relative to control value in mean postoperative pain score would be detectable using a sample size of 17 patients per group (total of seven groups for ANOVA analysis) for a one-tailed $\alpha=0.05$ and a study power of 0.9. We chose to study a minimum of 20 available patients per group. All data is expressed as means \pm SD except the VAS and requirements of the analgesic which are depicted as median and interquartile range (25–75% confidence intervals). The Chi-square test and Fisher’s exact test (for variables in which there was low frequency in at least one cell) were used to compare the presence of nausea, vomiting, shoulder pain, and other pain. Intergroup comparisons of VAS pain scores and other ordinal data were analyzed using analysis of variance or Kruskal-Wallis one way of variance on ranks. Intragroup comparisons of VAS pain scores during the study period were analyzed using repeated measures analysis of variance or Friedman repeated measures analysis of variance on ranks. Comparison between groups and post-hoc testing was performed using the Dunnett test, Dunn test or Tukey test. A value of $P < 0.05$ was considered to indicate statistical significance.

Results

Demographic data, age, weight, sex, ASA physical status, and duration of surgery were similar in all groups (Table I). One hundred fifty-seven patients gave informed consent. Nine patients were excluded from

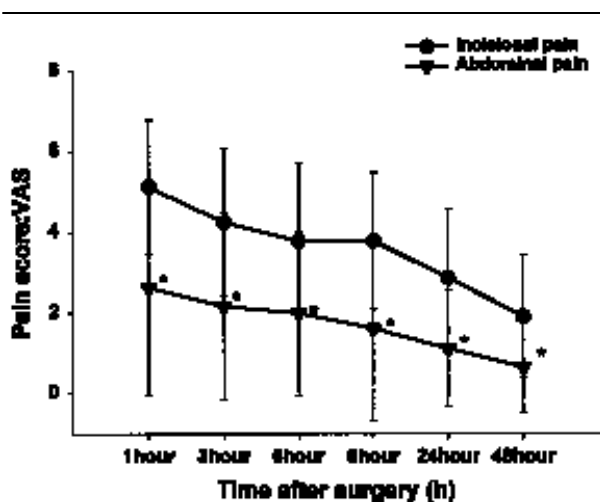


FIGURE 1 Intensity and localization of pain during the first 48 hr after elective laparoscopic cholecystectomy (LC). Pain was recorded by a visual analog scale (VAS) in the control group. Values are mean \pm SD; * $P < 0.05$.

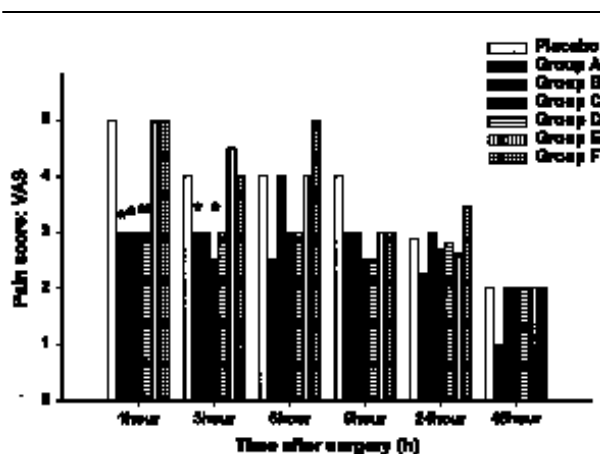


FIGURE 2 Intensity of incisional pain during the first 48 hr after elective laparoscopic cholecystectomy (LC). Pain was recorded by a visual analog scale (VAS). Values are median. * $P < 0.05$.

the study: one patient had an intraabdominal abscess postoperatively, three patients had intraoperative complications and had to be converted to open cholecystectomy, one developed an infection in the troca site, one had intraoperative drainage of the subhepatic space, and three patients’ data were not fully recorded.

Incisional pain dominated over intraabdominal pain in the control group at every interval ($P < 0.05$; Figure 1). The incisional pain of groups A, B, C and D was

TABLE I Patient's characteristics and clinical variables

	<i>Control</i>	<i>PRE-SV</i>	<i>POST-SV</i>	<i>PRE-S</i>	<i>POST-S</i>	<i>PRE-V</i>	<i>POST-V</i>
<i>n</i>	25	20	19	22	21	20	21
Male	13	11	12	13	10	11	9
Female	12	9	7	9	11	9	12
Age (yr)	45.3 ± 14.8	41.2 ± 10.3	49.5 ± 12.7	50.1 ± 12.8	46.5 ± 10.7	44.4 ± 15.9	51.7 ± 16.1
Weight (kg)	65.4 ± 4.7	64.1 ± 11.5	69.3 ± 11.6	70.3 ± 10.8	65.2 ± 14.3	68.2 ± 9.7	60.9 ± 11.8
D of surgery (min)	58.4 ± 20.9	70.6 ± 29	55.2 ± 14.8	65.1 ± 14.4	55.5 ± 10.3	60.4 ± 4.2	55.4 ± 18.1
ASA (I/II)	13/12	14/6	15/4	14/8	15/6	15/5	13/8

Values are number of patients or mean ± SD.

PRE-SV=preoperative somato-visceral group; POST-SV=postoperative somato-visceral group; PRE-S=preoperative-somatic; POST-S=postoperative-somatic; PRE-V=preoperative-visceral; POST-V=postoperative-visceral.

TABLE II Postoperative complications

Group	<i>Control</i> (<i>n</i> =25)	<i>PRE-SV</i> (<i>n</i> =20)	<i>POST-SV</i> (<i>n</i> =19)	<i>PRE-S</i> (<i>n</i> =22)	<i>POST-S</i> (<i>n</i> =21)	<i>PRE-V</i> (<i>n</i> =20)	<i>POST-V</i> (<i>n</i> =21)
Nausea	11	2	6	2	5	5	7
Shoulder pain	9	3	5	2	5	2	3
Epigastric pain	4	0	3	1	3	2	2
Headache	3	1	0	1	0	0	0
Rt flank pain	2	0	1	1	1	1	1
Back pain	1	0	2	0	2	1	1
Sore throat	1	1	3	1	3	2	3
Shivering	1	0	1	0	0	0	0

Values are number of patients. There were no significant differences among groups in the overall incidence of side effects.

PRE-SV=preoperative somato-visceral group; POST-SV=postoperative somato-visceral group; PRE-S=preoperative-somatic; POST-S=postoperative-somatic; PRE-V=preoperative-visceral; POST-V=postoperative-visceral.

significantly lower than that of the control group at one and two hours ($P < 0.05$). The incisional pain of groups A and C was significantly lower than that of the control group at three hours ($P < 0.05$). The incisional pain of group C declined significantly when compared to group E at three hours ($P < 0.05$). There was no significant difference in intraabdominal pain among groups at any time (Figures 2, 3).

Additional ketorolac requirements for the postoperative 48 hr were lower in groups A (median 0, [0-30]) and C (median 0, [0-30]) than in the control group (median 30, [0-60]) ($P < 0.05$). None of the patients required a more potent analgesic than ketorolac.

A total of 38 patients experienced nausea. Of these, two experienced vomiting. Most (35 patients) experienced nausea within 24 hr of the operation. All required metoclopramide (Table II). Five patients in the control group, four in groups B and F respectively, two in groups D and E respectively, required metoclopramide twice.

Nine patients in the control group experienced shoulder pain: five in groups B and D respectively, three

in groups A and F respectively, and two in groups C and E respectively. About half of them experienced shoulder pain within 24 hr after the operation, while incisional pain rapidly decreased. No significant differences in shoulder pain or other pain were seen (Table II).

Epigastric pain, headache, right flank pain, back pain, sore throat, and shivering were observed infrequently (Table II).

Discussion

The results of this study support the use of somatic blockade to reduce surgical incisional pain but fail to show the combined preemptive effects of somato-visceral blockade on deep intraabdominal pain, nausea or shoulder pain. Preoperative combined somato-visceral or somatic bupivacaine blockade reduced overall incisional pain during the first three postoperative hours but had no significant effect on deep abdominal pain. Analgesic requirements for the first 48 hr after LC in the preoperative somato-visceral or somatic bupivacaine groups was reduced. We chose the time of arrival in the recovery room as 'time 0' because the elapsed

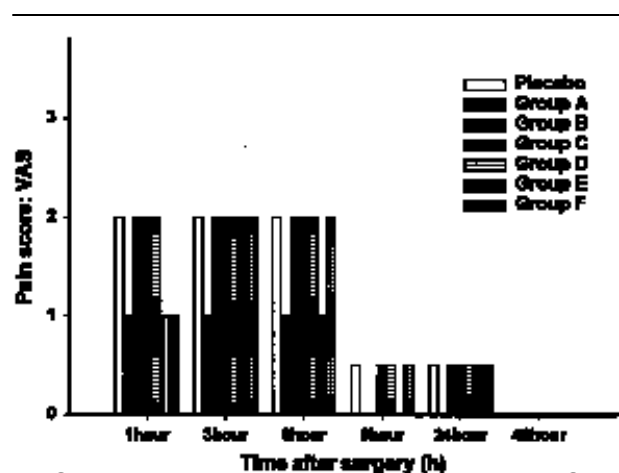


FIGURE 3 Intensity of abdominal pain during the first 48 hr after elective laparoscopic cholecystectomy (LC). Pain was recorded by a visual analog scale (VAS). Values are median.

time after preoperative or postoperative injection was not constant and the duration of surgery or emergence were not same. Even if analgesia began just after injection of the local anesthetic solution, we chose 'time 0' as the time of arrival in the recovery room because the purpose of preemption was to inhibit not only surgical pain but also inflammatory pain after operation.

Indeed, some authors have shown that topical peritoneal local anesthesia is effective in controlling postoperative pain.^{2,7,8,10,16} Others have shown that topical peritoneal local anesthesia is not effective in controlling postoperative pain.^{9,11-14} The latter asserted that postoperative pain induced by LC had a considerable visceral component and that a lesser component was somatic in origin.⁹ To evaluate the nature of pain after LC, the control group, using no local anesthetics, was assessed. Although the median VAS pain scores were low in our study, incisional pain still dominated over visceral pain. These findings were confirmed by Ure *et al.*,² but opposed by Joris *et al.*,⁹ who found that intraabdominal pain dominated. Interestingly, we found that the median visceral VAS pain scores of these studies^{2,9} and our results were similar. The median visceral VAS scores of these studies were usually below 3. We thought these pain scores were within the tolerable range. Our low visceral VAS scores may, in part, explain the lack of demonstrable effects of the combined somato-visceral or visceral regimen on the visceral pain.

While pain after LC is often dynamic and exacerbated by coughing or movement (supine to sitting), movement can also exacerbate nausea, vomiting or

other pain. Usually, pain at rest and at movement is correlated after LC^{9,17} and we expected movement would not exacerbate pain significantly. Even if dynamic pain can be a better measurement than static pain, we chose static pain because the purpose of this study was to investigate the nature of pain and other complications.

Our findings are also in contradiction with those of Pasqualucci *et al.*⁷ who found that an intraabdominal regimen (0.5% bupivacaine 20 mL) reduced postoperative pain and analgesic requirement if the treatment was administered before surgery. These authors did not evaluate the differences in the nature of the pain, incisional or deep intraabdominal. Moreover, they gave all patients 5 $\mu\text{g}\cdot\text{kg}^{-1}$ *iv* fentanyl before surgery. It has been reported that systemic opioids administered preoperatively reduce postoperative pain and wound hyperalgesia beyond the period when these effects can be explained by the direct analgesic action of these drugs.¹⁷ We assumed that preoperative fentanyl could reduce somatic pain after surgery, so we chose not to use opioids before surgery.

Another explanation for the lack of efficacy may be that our dosage of intraperitoneal bupivacaine (0.25% 40 mL) was too small for coverage of the intraabdominal organ surface. However, Scheinin *et al.*¹¹ used a large-dose of 150 mg bupivacaine in the right subdiaphragmatic space and was unable to demonstrate any analgesic effect. Moreover, Bisgaard *et al.*¹⁸ used a direct multiple visceral infiltration with a spray of ropivacaine and was unable to show analgesic effects. Given our negative results with regard to intraabdominal pain, we do not recommend routine use of intraabdominal local anesthetics.

Usually the nausea occurred within 24 hr of the operation, while half of the shoulder-tip pain was distributed after 24 hr. The incidence of nausea and shoulder-tip pain in groups A and C tended to be lower than in the control group although these were not statistically significant. Visceral blockade had no effect on the incidence of nausea, shoulder-tip pain, or other pain. Our results contradict those of Bisgaard *et al.*,¹⁸ who used a total nausea score (severity of nausea) to evaluate effectiveness. We used the incidence of nausea to compare effectiveness; this might explain the lack of demonstrable effects. Another explanation may be that our technique of blockade did not last long enough, with the exception of the initial period (three hours after operation).

Although our findings seem promising for the use of preemptive bupivacaine, we must acknowledge various limitations regarding the design of this investigation. Although the anesthesia team involved in intraoperative

care was aware of the bupivacaine analgesic technique, this team did not participate in data collection. The patients and data collectors were not informed of the treatment regimen and had no access to the anesthesia record. Second, we did not adopt a saline-control design, which may have raised more questions than a placebo-controlled study. Intraperitoneal saline treatment in itself can reduce postoperative pain.

In summary, incisional pain dominated during the first postoperative 48 hr after LC. A combination of incisional and intraabdominal local anesthetic treatment reduced incisional pain but had no effect on intraabdominal pain, nausea, or shoulder-tip pain in patients receiving preemptive analgesia. The effect of combined incisional and intraabdominal treatment was transient and no more favourable than the incisional treatment alone. Preoperative incisional infiltration of local anesthetics is recommended in LC.

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