Original Article

Paravertebral block using bupivacaine with/without fentanyl on postoperative pain after laparoscopic cholecystectomy: A double-blind, randomized, control trial

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Abstract

Background: Postoperative pain is one of the most common complaints after elective laparoscopic cholecystectomy. The present study was aimed to evaluate the effect of paravertebral block using bupivacaine with/without fentanyl on postoperative pain and complications after laparoscopic cholecystectomy.

Materials and Methods: This study was done on 90 patients scheduled to undergo elective laparoscopic cholecystectomy. Patients were assessed in two groups: The case group received bupivacaine and fentanyl, and the control group received bupivacaine and normal saline. Primary outcomes were severity of postoperative pain at rest and during coughing. Secondary outcomes were postoperative cumulative morphine consumption and the incidence of side-effects.

Results: Pain score at rest before surgery, after recovery, hour-1 and hour-6 was not significantly different between the groups. But in hour-24 cases, the pain score during coughing was significantly higher than controls. Severity of pain at rest in time points was not different between groups. The frequencies (%) of moderate pain at mentioned times in case and control groups were 64, 31, 16, 9, 0 versus 67, 16, 7, 4, and 0, respectively. Pain score during coughing was lower in controls at hour-24 in comparison with cases, but in other time points was not significant. The control group significantly received more total dose of morphine in comparison with cases group. Nausea, vomiting and hypotension were similar in groups, but pruritus was significantly different between the groups.

Conclusion: Adding fentanyl to bupivacaine in paravertebral block did not significantly improve the postoperative pain and complications after laparoscopic cholecystectomy. However, further studies are needed to be done.

Key Words: Bupivacaine, fentanyl, laparoscopic cholecystectomy, paravertebral block, postoperative pain

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INTRODUCTION

In most of surgical procedures, pain is assumed to be ineffectively treated.[1] Pathophysiology of pain has suggested that it is possible to decrease or prevent the central neural hyperexcitability that contributes to greater postoperative pain.[2,3]

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Laparoscopic cholecystectomy is one of the most commonly performed minimally invasive surgical procedures and is the treatment of choice for symptomatic cholelithiasis.[4] Despite the clear benefits of laparoscopic cholecystectomy compared with open surgery, postoperative pain is still a common complaint after it, and patients undergoing laparoscopic cholecystectomy may suffer from severe postoperative pain if analgesia is not managed appropriately.[5] Postoperative pain after laparoscopic cholecystectomy can prolong hospital stay and lead to increased morbidity and this is the main reason for overnight hospital stay after day care surgery in 17-41% of the patients.[4,6,7]

To relieve postoperative laparoscopic cholecystectomy pain some methods have been suggested[8-10] and the paravertebral block technique has been studied as one of these methods that may offer comparable analgesic effectiveness and a better side-effect profile.[11] Paravertebral block is the technique of injecting local anesthetic adjacent to the thoracic vertebra close to where the spinal nerves emerge from the intervertebral foramina, resulting in ipsilateral somatic and sympathetic nerve blockade in multiple contiguous dermatomes above and below the site of injection.[12]

Bupivacaine is an amide-type local anesthetic that is capable of producing prolonged analgesia. This agent also provides high quality analgesia in the postoperative period.[13] It is shown that paravertebral block using bupivacaine significantly reduces pain score compared to controls.[14-18] Fentanyl is an adjuvant that improved the quality of blockade with an analgesic potency that is around 90 times stronger than that of morphine; this drug is often administered as an adjuvant after surgery, because comparable to the properties of opioid compounds, it has analgesic properties without opioid-related side-effects; however, this is associated with hypotension and nausea. One study demonstrated that spinal hyperbaric bupivacaine + fentanyl provided effective anesthesia for laparoscopic cholecystectomy.[19] In a systematic review by Joshi *et al*. showed that paravertebral block with bupivacaine significantly reduced the pain scores on day one, reduced the incidence of pulmonary complications compared with control and reduced the incidence of hypotension compared with thoracic epidural bupivacaine.[20]

The present study was designed to compare paravertebral block using bupivacaine + fentanyl versus bupivacaine + normal saline for laparoscopic cholecystectomy with respect to intraoperative parameters, postoperative pain, and complications. Nonsteriodal anti-inflammatory drugs (NSAIDs) have analgesic properties comparable to properties of opioid compounds without opioid-related side-effects.

MATERIALS AND METHODS

This randomized, parallel-group, double-blind study was investigated and approved by the ethics committee of Isfahan University of Medical Sciences. Ninety patients, of any gender, 16 to 65 years old, ASA physical status I-III, scheduled to undergo elective laparoscopic cholecystectomy, were assessed in this study. Patients with chronic pain diseases, use of opioids, patients with acute cholecystitis, allergy to corticosteroids, neuromuscular diseases and bleeding disorders did not enter the study. Additionally, patients with postoperative complications that increased postoperative pain and those whose pain evaluation was judged unreliable because of neurologic disease were excluded from the study. After the participating patients were explained about and informed of the purposes of the study, written informed consent was obtained from them all.

Eligible patients were randomly divided into two 45-member groups of case and control, using random-maker software "Random Allocation". Patients in the case group received regional injection of 20-mL bupivacaine 0.25% and 50 mcg fentanyl, and patients in the control group received regional injection of 20-mL bupivacaine 0.25% and 1 mL normal saline.

Anesthesia was conducted using a total intravenous technique consisting of a target-controlled infusion of fentanyl (2 mcg/kg), sodium thiopental (5 mg/kg) and atracurium (0.5 mg/kg). Endotracheal intubation was performed with a single-lumen tube. Balanced anesthesia was maintained using with inhalation of isoflurane (1-2%) and morphine (0.1 mg/kg). Patients' lungs were mechanically ventilated with the same setting during ventilation (VT, 10 mL/kg and RR, 10 min). Ventilation was controlled to maintain end-tidal CO_2 35 to 40 mmHg. The patients were monitored and observed using an electrocardiogram, non-invasive arterial blood pressure device and pulse oximeter.

To maintain blinding, patients were unaware of the treatment allocation; also, the research assistant was not allowed to enter the operating room when the study solutions were being prepared, the sealed white envelope containing patient allocation and instructions for the solution preparation given to a previously trained anesthesia nurse who was not involved in the study. The nurse was authorized to disclose the contents of the syringe to the anesthesiologist in charge

of the case who was not involved in the study and to the research assistant. Syringe solutions in the case group contained 20-mL bupivacaine 0.25% and 50 mcg fentanyl and also in the control group contained 20-mL bupivacaine 0.25% and 1 mL normal saline.

At the end of surgery, at the T5-6 level, paravertebral block was performed with the patient in the left-side lateral position, the area is disinfected with chlorhexidine and lidocaine 1%; the 22-gauge spinal needle was introduced 2.5 cm lateral from the top of the desired vertebral body in search of the transverse process. After the transverse process is contacted, at a 15° to 60° angle, the needle is then withdrawn to the skin and reintroduced 1 cm beyond the transverse process, allowing the positioning of the needle below the transverse process. The needle should be withdrawn to the skin and reoriented using a greater angle, if bone contact is established during the positioning of the needle.

Demographic and clinical parameters including age, sex, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), O_2Sat, ASA status, heart rate, respiratory rate were assessed in all patients. Abnormalities in SBP and DBP were defined as ≥140 and ≥90, respectively. Primary outcome was severity of postoperative pain at rest and during coughing. Secondary outcomes were postoperative cumulative morphine consumption and the incidence of side-effects such as postoperative nausea and vomiting, pruritus and hypotension if any. Additional morphine (5-10 mg) was administered if needed either intravenously. Both these outcomes were collected after arrival in the recovery room and 1, 6 and 24 hours after surgery by an independent nurse blinded to group allocation. Assessment of pain both at rest and during coughing was done by a 10-score visual analogue scale (VAS); 0, no pain; 10, worst imaginable pain. Also, severity of postoperative pain was assessed as follow; low pain (<4 on a 10-point scale), moderate pain (4-7 on a 10-point scale), and severe postoperative pain (>7 on a 10-point scale).

The sample size was calculated using the comparison of means formula with two-sided log-rank test, $\alpha = 0.05$, and 80% power. SPSS software for windows, version 20, was used for statistical analyses, and descriptive data are reported as mean ± SD, median [IQR] and number (percent). Independent sample *t*-test, Chi-square test and Mann-Whitney U test were used to compare all studied variables between groups as appropriate. The level of significance is considered to be less than 0.05.

RESULTS

Seven of 97 reviewed patients were not eligible and did not enter the study (2 patients did not meet inclusion criteria and 5 patients refused informed consent); finally, 90 patients completed the study and analyzed [Figure 1]. The mean age of the studied patients was 44.6 ± 16.7 years. Twenty-five

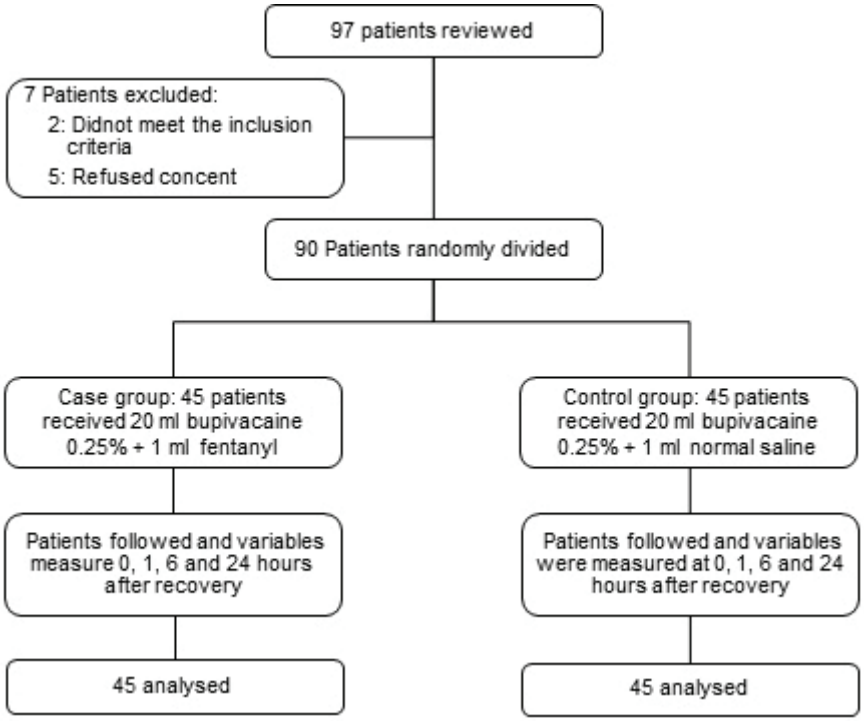

Figure 1: Patients who entered to the study, divided into the study groups and analyzed

patients (28%) were males and 65 patients (72%) were females. Comparisons of characteristics and clinical parameters in studied groups are shown in Table 1. Mean of age, sex combination, O_2Sat, HR ASA status, RR, SBP, DBP and pain before surgery were not significant between the studied groups ($P > 0.05$). Weight between the studied groups was statistically significant ($P < 0.05$).

Pain score at rest at time points were assessed using the Mann-Whitney U test and results showed that before surgery, after recovery, hour-1 and hour-6, median of pain score was similar in case and control groups and there were no significant differences ($P > 0.05$). But in hour-24 patients, the case group significantly reported higher pain score compared to patients in the control group [Figure 2].

Results to compare the frequency of severity of pain at rest between study groups are reported in Table 2.

Table I: Comparison of baseline characteristics and clinical parameters between study groups

Variables	Group (*n*=45)		*P* value
	Case	Control	
Age (year)	47.5±18.8	41.6±13.8	0.097*
Weight	71.4±7	75.3±8	0.014*
Sex			
Male	19 (42)	13 (29)	0.27†
Female	26 (58)	32 (71)	
O_2Sat	97.9±2.2	98.4±1.9	0.25*
ASA status			
I	32 (71)	31 (69)	0.8†
II, III	13 (29)	14 (31)	
HR	79.3±12.7	77.5±13	0.51*
RR	12.9±1.7	12.9±1.2	0.88*
SBP	125.7±21.3	120.8±21.3	0.29*
Abnormal SBP	12 (26)	6 (13)	0.11††
DBP	80.2±15.3	78.5±17.8	0.63*
Abnormal DBP	13 (29)	14 (31)	0.82†
Pain before surgery	7 (6-8)	7 (6-8)	0.9††

Data are mean±SD and number (%). Cases included patients who received I.V. injection bupivacaine 0.25% and fentanyl, controls included patients who received bupivacaine 0.25% and normal saline. HR; Heart Rate, RR; Respiratory Rate, SBP; Systolic Blood Pressure, DBP; Diastolic Blood Pressure. Abnormalities in SBP and DBP were defined as ≥140 and ≥90 respectively. *P*-values calculated by *Independent sample *t*-test, †Chi-square test and ††Mann-Whitney U test

As shown before surgery, most of the patients in both groups had severe pain but during 24 hours after surgery; most of the patients had low pain and in hour-24 all studied patients reported low pain. The differences between cases and controls were not statistically significant in assessed time points ($P > 0.05$).

Table 3 shows findings in comparison of pain score during coughing, total dose of morphine and the frequency of side-effects. Pain score during coughing was significantly lower in the control group at hour-24 in comparison with the case group but in other time points pain score during coughing was similar in both groups ($P > 0.05$). Patients in the control group significantly received more total dose of morphine in comparison with patients in the case group ($P = 0.0001$). Postoperative nausea and vomiting were reported in 29 of all patients; also, hypotension occurred in 19 of them, and the frequency of nausea and vomiting and hypotension were similar in both groups. Of 90 studied patients, 10 patients reported pruritus which was significantly different between groups (8 of cases versus 2 of controls, $P = 0.044$).

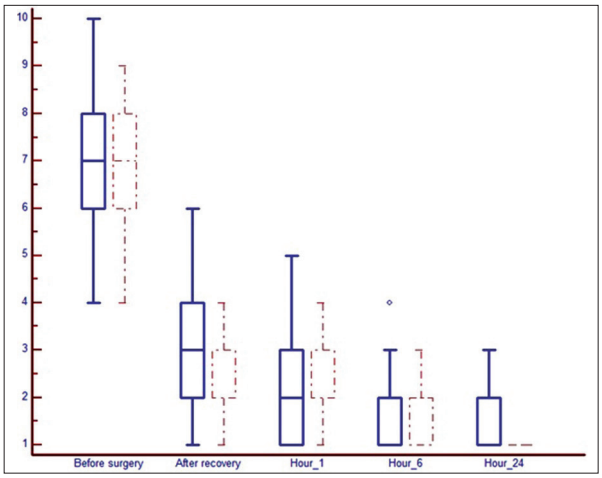

Figure 2: Comparison of pain at rest between study groups. Case group included patients who received I.V. injection bupivacaine 0.25% and fentanyl, control group included patients who received bupivacaine 0.25% and normal saline. Statistical significance was observed at hour_24 ($P = 0.003$)

Table 2: Frequency of severity of pain at rest between study groups

Variables	Case group (*n*=45)			Control group (*n*=45)			*P* value
	Low	Moderate	Severe	Low	Moderate	Severe	
Pain							
Before surgery	0	29 (64)	16 (36)	0	30 (67)	15 (33)	0.82
After recovery	31 (69)	14 (31)	0	38 (84)	7 (16)	0	0.081
Hour-1	38 (84)	7 (16)	0	42 (93)	3 (7)	0	0.18
Hour-6	41 (91)	4 (9)	0	43 (96)	2 (4)	0	0.39
Hour-24	45 (100)	0	0	45 (100)	0	0	-

Data are number (%), Cases included patients who received I.V. injection bupivacaine 0.25% and fentanyl, controls included patients who received bupivacaine 0.25% and normal saline. *P* values calculated by the Chi-square test

Table 3: Comparison of pain score on cough, morphine requirements and side effects between study groups

	Group (*n*=45)		*P* value
	Case	Control	
Pain on cough			
After recovery	4 (3-4)	4 (3-5)	0.46*
Houre-1	2 (1-3)	1 (1-3)	0.41*
Houre-6	1 (1-2)	2 (1-2)	0.81*
Houre-24	1 (1-1.5)	1 (1-1)	0.02*
Total dose of morphine	4.1±2.4	6.1±4.9	0.0001†
Nausea and vomiting	18 (40)	11 (24)	0.11†
Pruritus	8 (18)	2 (4)	0.044††
Hypotension	12 (27)	7 (16)	0.19††

Data are median (IQR), Cases included patients who received I.V. injection bupivacaine 0.25% and fentanyl, controls included patients who received bupivacaine 0.25% and normal saline., *P*-values calculated by *Mann-Whitney U test, †Independent sample *t*-test and ††Chi-square test

DISCUSSION

Laparoscopic cholecystectomy as a short-stay procedure is one of the most frequently performed elective surgeries. In these patients, immediately after surgery, postoperative pain is experiential in peaks and decreases after 24 hours.[21] In the present study, the effect of paravertebral block using bupivacaine plus fentanyl in postoperative pain and complications after laparoscopic cholecystectomy was assessed, and findings showed that pain score at rest before surgery, after recovery, hour-1 and hour-6, was not different between groups. But in hour-24, it was significantly higher than controls. Also, pain score during coughing was lower in controls at hour-24 in comparison with cases. The possible cause of these differences is that during the study, controls significantly requested and received more total dose of morphine in comparison with cases group. Nausea and vomiting and hypotension were similar in groups, but pruritus was significantly different between the groups. In totally, our findings showed that fentanyl plus bupivacaine in paravertebral block did not improved postoperative pain and complications after laparoscopic cholecystectomy.

Multimodal therapy may be necessary to optimize postoperative pain relief following laparoscopic cholecystectomy because this pain is multifactorial and complex, and the multimodal approach for pain management has been previously shown to be advantageous.[8-10]

Intraperitoneal local anesthetic instillation during laparoscopic surgery evaluated in previous studies and perhaps, because of differences in site of instillation, differences in timing of administration, differences in local anesthetic dose and concentration, and differences in perioperative analgesic regimens, had shown variable results.[5,22-24] Jabbour-Khoury *et al*.[25] concluded that a multimodal approach to pain management following elective laparoscopic cholecystectomy is best achieved whereas a combination of intraperitoneal bupivacaine and ketoprofen was effective in relieving postoperative abdominal pain at 0, 1, 2, and 6 hours in these patients. Also, Elhakim *et al*.[26] evaluated a combination of intraperitoneal lidocaine and tenoxicam and reported that this was more effective in reducing the pain scores and opioid consumption than either placebo.

In Navlet *et al*. study,[27] a continuous paravertebral infusion of ropivacaine/fentanyl, or bupivacaine/fentanyl, in 60 patients undergoing elective thoracotomy was done and authors concluded that both bupivacaine, 0.25%, and ropivacaine, 0.3%, with fentanyl are equally effective for post-thoracotomy pain control when used via continuous paravertebral blockade. In another study, Awwad *et al*.[28] assessed paravertebral block using bupivacaine 0.5% or normal saline in 44 patients undergoing renal surgery and reported that paravertebral blockade using bupivacaine is an effective and safe method for pain relief following renal surgery through loin incision. Also, Bhuvaneswari *et al*.[29] concluded that paravertebral block using bupivacaine and fentanyl in patients scheduled for surgery for breast cancer reduce analgesic consumption as well as cumulative pain scores at rest and on movement. Naja *et al*.[30] used as a complement to general anesthesia, bilateral nerve-stimulator guided paravertebral blockade with lidocaine, bupivacaine, fentanyl and clonidine, in laparoscopic cholecystectomy and show that mean pain scores visual analog scale were significantly less with active compared with control; also, they concluded that this regimen may improve postoperative pain relief.

The effect of paravertebral block using bupivacaine with fentanyl on pain after elective laparoscopic cholecystectomy has not been investigated, and the present study is the only one that investigates the use of bupivacaine with fentanyl, and results showed that adding fentanyl to bupivacaine did not improve postoperative pain and complications, which these finding can be confound by more total dose of morphine used in control group. Reported studies[25-30] shows different results on pain management and the difference in the results from our study could possibly be because of the difference in the nature of surgery, kind and dose of drugs, and the difference in the method of treatment.

Davies *et al*.[11] conducted a meta-analysis and found that paravertebral block was associated with fewer pulmonary complications, urinary retention, nausea

and vomiting and hypotension. Thus, they concluded that this provided equally effective analgesia to epidural but with a better side-effect profile. The analgesic effect of fentanyl may be done by acting on opioid receptors found in the dorsal root ganglia structures. Patients undergo breast surgery in Burlacu *et al*. study experienced side-effects like nausea and pruritus after using levobupivacaine with fentanyl infusion for postoperative analgesia paravertebrally.[31] Similar to Barlacu, *et al*. study,[31] in the present study pruritus was increased in patients who received paravertebral block using bupivacaine with fentanyl compared to bupivacaine alone, but nausea was not different between the groups. Thus, further works are suggested to determine the lowest effective dose of fentanyl.

One of the possible shortcomings of our study is that the low number of sample size. However, this was powered sufficiently for primary outcome measures such as pain score, but placed secondary outcome measures such as nausea and vomiting, hypotension and pruritus were at significant risk of type II errors. Therefore, future studies with appropriate sample size are necessary to specifically assess pain score and the incidence of nausea and vomiting, hypotension and pruritus in paravertebral block after laparoscopic cholecystectomy.

In summary, our findings revealed that infiltration of 20-mL bupivacaine 0.25% and 50 mcg fentanyl in paravertebral block after laparoscopic cholecystectomy did not improve postoperative pain and complications, whereas severity of pain at rest, during coughing and also complications such as nausea and vomiting and hypotension were similar between groups and pruritus in the case group was more than the control group.

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REFERENCES

1. Gottschalk A, Smith DS. New concepts in acute pain therapy: Preemptive analgesia. Am Fam Physician 2001;63:1979-84.
2. Woolf CJ. Evidence for a central component of post injury pain hypersensitivity. Nature 1983;306:686-8.
3. Wall PD. The prevention of postoperative pain. Pain 1988;33:289-90.
4. Agarwal A, Batra RK, Chhabra A, Subramaniam R, Misra MC. The evaluation of efficacy and safety of paravertebral block for perioperative analgesia in patients undergoing laparoscopic cholecystectomy. Saudi J Anaesth 2012;6:344-9.
5. Boddy AP, Mehta S, Rhodes M. The effect of intraperitoneal local anesthesia in laparoscopic cholecystectomy: A systematic review and meta-analysis. Anesth Analg 2006;103:682-8.
6. Lau H, Brooks DC. Predictive factors for unanticipated admissions after ambulatory laparoscopic cholecystectomy. Arch Surg 2001;136:1150-3.
7. Bisgaard T, Klarskov B, Rosenberg J, Kehlet H. Characteristics and prediction of early pain after laparoscopic cholecystectomy. Pain 2001;90:261-9.
8. Abdulla S, Eckhardt R, Netter U, Abdulla W. A randomized double-blind, controlled trial on non-opioid analgesics and opioid consumption for postoperative pain relief after laparoscopic cholecystectomy. Acta Anaesthesiol Belg 2012;63:43-50.
9. Salihoglu Z, Yildirim M, Demiroluk S, Kaya G, Karatas A, Ertem M, *et al*. Evaluation of intravenous paracetamol administration on postoperative pain and recovery characteristics in patients undergoing laparoscopic cholecystectomy. Surg Laparosc Endosc Percutan Tech 2009;19:321-3.
10. Akaraviputh T, Leelouhapong C, Lohsiriwat V, Aroonpruksakul S. Efficacy of perioperative parecoxib injection on postoperative pain relief after laparoscopic cholecystectomy: A prospective, randomized study. World J Gastroenterol 2009;15:2005-8.
11. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy: A systematic review and metaanalysis of randomized trials. Br J Anaesth 2006;96:418-26.
12. Cheema SP, Ilsley D, Richardson J, Sabanathan S. A thermographic study of paravertebral analgesia. Anaesthesia 1995;50:118-21.
13. Kopacz DJ, Allen HW, Thompson GE. A comparison of epidural levobupivacaine 0.75% with racemic bupivacaine for lower abdominal surgery. Anesth Analg 2000;90:642-8.
14. Bilgin M, Akcali Y, Oguzkaya F. Extrapleural regional versus systemic analgesia for relieving post-thoracotomy pain: A clinical study of bupivacaine compared with metamizol. J Thorac Cardiovasc Surg 2003;126:1580-3.
15. Carabine UA, Gilliland H, Johnston JR, McGuigan J. Pain relief for thoracotomy. Comparison of morphine requirements using an extrapleural infusion of bupivacaine. Reg Anesth 1995;20:412-7.
16. Carretta A, Zannini P, Chiesa G, Altese R, Melloni G, Grossi A. Efficacy of ketorolac tromethamine and extrapleural intercostal nerve block on post-thoracotomy pain. A prospective, randomized study. Int Surg 1996;81:224-8.
17. Deneuville M, Bisserier A, Regnard JF, Chevalier M, Levasseur P, Herve P. Continuous intercostal analgesia with 0.5% bupivacaine after thoracotomy: A randomized study. Ann Thorac Surg 1993;55:381-5.
18. Eng J, Sabanathan S. Continuous extrapleural intercostal nerve block and post-thoracotomy pulmonary complications. Scand J Thorac Cardiovasc Surg 1992;26:219-23.
19. Imbelloni LE, Fornasari M, Fialho JC, Sant'Anna R, Cordeiro JA. General anesthesia versus spinal block for laparoscopic cholecystectomy. Rev Bras Anestesiol 2010;60:264-73.
20. Joshi GP, Bonnet F, Shah R, Wilkinson RC, Camu F, Fischer B, *et al*. A systematic review of randomized trials evaluating regional techniques for postthoracotomy analgesia. Anesth Analg 2008;107:1026-40.
21. Castillo-Garza G, Díaz-Elizondo JA, Cuello-García CA, Villegas-Cabello O. Irrigation with bupivacaine at the surgical bed for postoperative pain relief after laparoscopic cholecystectomy. JSLS 2012;16:105-11.
22. Kehlet H, Gray AW, Bonnet F, Camu F, Fischer HB, McCloy RF, *et al*. A procedure-specific systematic review and consensus recommendations for postoperative analgesia following laparoscopic cholecystectomy. Surg Endosc 2005;19:1396-415.
23. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: A critical assessment of the evidence. Anesthesiology 2006;104:835-46.
24. Gupta A. Local anaesthesia for pain relief after laparoscopic cholecystectomy: A systematic review. Best Pract Res Anaesthesiol 2005;19:275-92.
25. Jabbour-Khoury SI, Dabbous AS, Gerges FJ, Azar MS, Ayoub CM, Khoury GS. Intraperitoneal and intravenous routes for pain relief in laparoscopic cholecystectomy. JSLS 2005;9:316-21.
26. Elhakim M, Amine S, Kamel S, Saad F. Effects of intraperitoneal lidocaine

combined with intravenous or intraperitoneal tenoxicam on pain relief and bowel recovery after laparoscopic cholecystectomy. Acta Anaesthesiol Scand 2000;44:929-33.
27. Navlet MG, Garutti I, Olmedilla L, Pérez-Peña JM, San Joaquin MT, Martinez-Ragues G, *et al*. Paravertebral ropivacaine, 0.3%, and bupivacaine, 0.25%, provide similar pain relief after thoracotomy.J Cardiothorac Vasc Anesth 2006;20:644-7.
28. Awwad ZM, Atiyat BA. Pain relief using continuous bupivacaine infusion in the paravertebral space after loin incision. Saudi Med J 2004;25:1369-73.
29. Bhuvaneswari V, Wig J, Mathew PJ, Singh G. Post-operative pain and analgesic requirements after paravertebral block for mastectomy: A randomized controlled trial of different concentrations of bupivacaine and fentanyl. Indian J Anaesth 2012;56:34-9.
30. Naja MZ, Ziade MF, Lönnqvist PA. General anaesthesia combined with bilateral paravertebral blockade (T5-6) vs. general anaesthesia for laparoscopic cholecystectomy: A prospective, randomized clinical trial. Eur J Anaesthesiol 2004;21:489-95.
31. Burlacu CL, Frizelle HP, Moriarty DC, Buggy DJ. Fentanyl and clonidine as adjunctive analgesics with levobupivacaine in paravertebral analgesia for breast surgery. Anaesthesia 2006;61:932-7.

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