

# Interpleural Bupivacaine Or Im Meperidine: Analgesia And Pulmonary Function Following Open Cholecystectomy

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## Citation

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## Abstract

Background: Interpleural analgesia has been effective following cholecystectomy.

Methods: Following open cholecystectomy 50 patients received interpleural bupivacaine (IB) or intramuscular meperidine (M). Boluses were repeated each 4 hours. Pain scores were recorded 15 minutes in the PACU (baseline), 1, 2, 4, 8, 12, 16, 20, 24 and 48 hours postoperatively. Respiratory rate (RR), maximal breathing capacity (MBC) and tidal volume (TV) were measured before anesthesia (baseline) 6, 24, 48 hours postoperatively.

Results: In both groups RR was higher ( $p < 0.001$ ) TV ( $p < 0.001$ ) and MBC ( $p < 0.001$ ) were lower at 6 hours. RR was lower ( $p < 0.001$ ) and MBC higher ( $p < 0.03$ ) with IB. Pain scores were lower ( $p < 0.001$ ) in both groups at 1, 2, 4, 8, 12, and 16 hours and lower in IB ( $p < 0.001$ ), 20 hours ( $2.8 \pm 0.3$  vs  $5.2 \pm 0.5$ ) and 24 hours ( $2.8 \pm 1$  vs  $4.8 \pm 2$ ) postoperatively.

Conclusion: IB was more effective than M for analgesia and preservation of lung function following open cholecystectomy.

## INTRODUCTION

Interpleural analgesia has been effective for postoperative analgesia following open and laparoscopic cholecystectomy (1,2,3). However, the method of administration of the local anesthetics into the interpleural space is not uniform (4,5,6).

We compared the effect of intermittent boluses of interpleural bupivacaine (IB) versus im meperidine (M) on the severity of pain and pulmonary function following open cholecystectomy.

## METHODS

After approval from the Hospital Ethics Committee all patients signed a full written consent. The study was undertaken in a 700-bed community hospital in Israel. Fifty patients, age 18-65 yr, who underwent open cholecystectomy, were enrolled in this prospective, randomized, double-blind and controlled study. All patients suffering from either chronic obstructive lung disease or coagulopathy were excluded from the study. No preoperative medication was administered. Anesthesia was standardized for both groups and consisted of thiopental, rocuronium and fentanyl ( $2 \mu\text{g} \cdot \text{Kg}^{-1}$ ) for induction of anesthesia, and  $\text{N}_2\text{O}$  in

$\text{O}_2$ , isoflurane and aliquots of  $50 \mu\text{g}$  of fentanyl (when deemed necessary) for maintenance of anesthesia. Thirty minutes before the end of surgery, all the patients received 75 mg of im diclofenac sodium.

Following the administration of iv boluses of meperidine 20 mg each bolus, up to  $0.5 \text{ mg} \cdot \text{Kg}^{-1}$  over 15 minutes, patients were randomly allocated (with the closed envelope technique) to two equal groups with regard to the postoperative pain management method. One group of 25 patients received  $1 \text{ mg} \cdot \text{Kg}^{-1}$  im meperidine – group M and the other group - IB, was managed with 40 ml of 0.125% bupivacaine (50 mg) with epinephrine (1:200,000), administered into the interpleural space, through an epidural catheter (SIMS Portex Ltd. Hythe, Kent, UK). The catheter was inserted at the end of surgery, into the interpleural space at the 4th intercostal space (midaxillary line) on the side of surgery. The interpleural space was detected with the “loss of resistance” technique and the epidural catheter was threaded through an 18G, Tuohy needle and was directed toward the posterior pleural space. The first bolus of either drug was administered 15 min after the patient's arrival in the PACU, after having confirmed the right position of the

catheter and after recording baseline pain scores.

Pain scores were assessed 15 min after arrival in the PACU (before the administration of iv meperidine, IB and im M), 1, 2, and 4 hours after surgery before discharge from the PACU and then, 8, 12, 16, 20, 24 and 48 hours postoperatively on the surgical floor. The bolus of im meperidine or interpleural bolus of bupivacaine was repeated every 4 hours, if the pain score (assessed on a Visual Analog Scale - VAS) was equal to or higher than 4 on a scale from 0 = no pain to 10 = unbearable pain, or after a longer interval if at the predetermined times the pain scores were <4. Pain scores were assessed again, 30 minutes after the administration of either drug. If, after a bolus, the patient was still complaining of pain, but the time elapsed since the last bolus was less than 4 hours, 75 mg of diclofenac were administered im. Pulmonary variables evaluated included respiratory rate (RR), maximal breathing capacity (MBC) & tidal volume (TV), measured with a bedside spirometer (Flow screen type B, Erich Jäger GMBH & Co, Germany).

Baseline values were recorded 15 min before induction of anesthesia. Subsequent measurements were performed 6, 24 and 48 hours postoperatively. Lung function measurements and assessments of pain scores were performed by a "blinded" anesthesiologist involved with the study, unaware of the method of analgesia employed. Meperidine was given im by a nurse, while interpleural bupivacaine was administered only by an anesthesiologist, after negative aspiration for blood. All the patients received oxygen through nasal prongs for the first 24 hours following surgery. Oxyhemoglobin saturation was measured at the same time frames as the pain scores. Also, patients were continuously monitored with ECG. Blood pressure and heart rate were recorded noninvasively (oscillometry) every 5 minutes up to 30 minutes after the bolus in both groups. Hypotension was defined as a decrease of 30% from baseline or episodes of systolic blood pressures <100mmHg. Hypertension was considered a systolic blood pressure elevation of >30% from baseline (considered as the first value measured 15 min after arrival in the PACU).

All episodes of hypotension/hypertension and bradycardia (heart rate<50 beats/minute) were recorded. Hypotension was managed with boluses of 200 ml of crystalloids and bradycardia with iv atropine, 0.5mg. The IB group was monitored for signs of CNS toxicity (tremor, muscle twitches, perioral numbness, metallic taste, tinnitus, convulsions, etc) and the chest X-ray was repeated 24 hours

after surgery to exclude inadvertent pneumothorax. The study was stopped after 48 hours because of concerns of the interpleural catheter displacement following mobilization of the patient and fear of catheter-related infection.

## STATISTICAL ANALYSIS

A multivariate repeated measure general linear model analysis with respiratory rate, tidal volume and maximal breathing capacity as outcome variables, and repeated measure linear model with the pain score as the outcome variable were employed. The p-values were adjusted for multiple comparisons by the Bonferonni method.

## RESULTS

Demographic data were similar in both groups. There were 60% females in both groups. Age was 56±8yr in IB and 53±8yr in M. No episodes of hypotension or bradycardia were recorded. Neither pneumothorax nor CNS toxic reactions, or severe bradypnea (RR<10) were encountered. Changes in pulmonary variables (maximal breathing capacity, tidal volume and respiratory rate) for both groups over the full time range are presented in Fig. 1-3. Prior to the induction of anesthesia (starting point-baseline), pulmonary variables were similar in both groups. In both groups, RR was higher (p<0.001) and TV (p<0.001) and MBC (p<0.001) were lower upon 6 hours after surgery as compared to baseline. Respiratory rates were significantly lower (p<0.001) and MBC higher (p<0.03) in IB vs M, while TV was not significantly different (p=0.18). The pulmonary measurements' values reached the baseline values 48 hours after surgery. At this point, no significant differences were recorded between the 2 groups.

Oxyhemoglobin saturation was not significantly different between the groups (97±3 in IB vs 96±2 in M). In both groups, pain scores (Table 1) were lower (p<0.001) compared to baseline (which was similar in both groups), 1, 2, 4, 8, 12, 16, 20, 24 and 48 hours after surgery and lower in IB compared to M (p<0.001), 20 and 24 hours after surgery.

Pain scores were similar within and between the groups at 1, 2, 4, 8, 12, and 16 hours after surgery. Pain scores were not significantly different between the groups 48 hours after surgery and decreased below the level which required analgesic treatment. As shown in table 1, there was a progressive decrease over time in the pain scores of the IB group. Upon the measurements at 1, 2, 4, 8, 12, and 16 hours, all the pain scores were =4. Therefore, all the patients received their 4 hours' doses of both drugs.

**Figure 1**

Table 1: Pain Scores

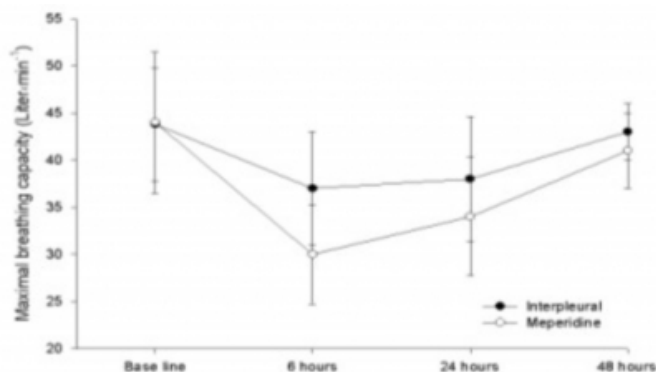
Time	Interpleural Pain score	Pethidine Pain score	p-value
Baseline	7.3±3	7.5±2	0.8
1 Hour	4.6±0.2	4.7±0.3	0.8
2 Hours	4.4±0.2	4.6±0.3	0.4
4 Hours	5.3±1.3	5.5±1	0.2
8 Hours	5.2±1.1	5.3±1	0.8
12 Hours	5.0±1	5.5±1.5	0.4
16 Hours	5.0±1	5.5±2	0.4
20 Hours	2.8±0.3	5.2±0.5	<0.001**
24 Hours	2.8±1	4.8±2	<0.001**
48 Hours	2.5±0.8	3±1.3	0.8
p-value	<0.001*	<0.001*	

\*Compares the baseline pain scores within each group with the scores recorded 1, 2, 4, 8, 12, 16, 20, 24 and 48 hours after surgery. \*\*Compares pain scores between the groups, 20 and 24 hours after surgery.

All the pain scores were <4 when measured 30 minutes after the administration of either drug (data not presented). Patients from M required twice much diclofenac during the first 24 postoperative hours (300 mg vs 150 mg). The mean dose of bupivacaine was 250 mg, while that of meperidine was 450±30 mg.

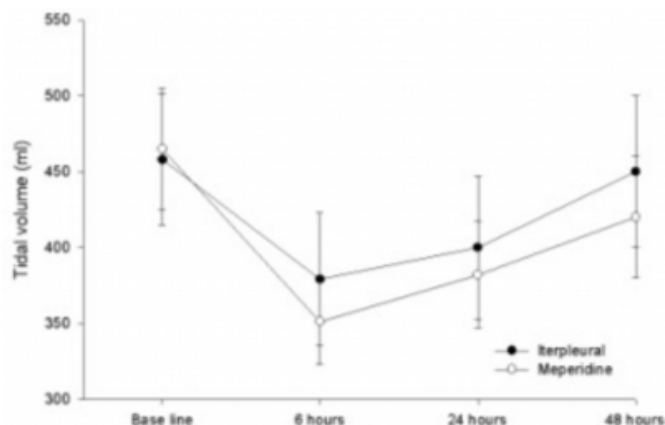
**Figure 2**

Fig 1: Maximal Breathing Capacity



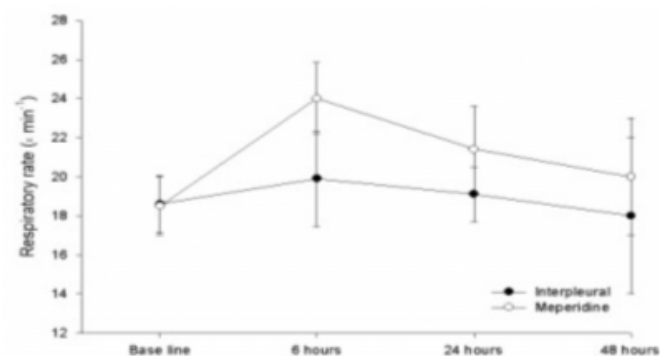
**Figure 3**

Fig 2: Tidal Volume



**Figure 4**

Fig 3: Respiratory Rate



**DISCUSSION**

Interpleural analgesia with local anesthetics following open cholecystectomy has been extensively used either intermittently (2,3) or as a continuous infusion (5,6).

In this prospective study, we evaluated the efficacy of intermittent boluses of low dose intrapleural bupivacaine compared to im meperidine, with regard to postoperative pain relief and preservation of pulmonary function following open cholecystectomy. Open cholecystectomy is more painful than laparoscopically performed cholecystectomy (7) and therefore it requires more aggressive postoperative pain management. We administered boluses of interpleural bupivacaine every 4 hours. With the addition of epinephrine to a diluted (0.125%) bupivacaine solution, the risk of systemic toxicity was reduced.

We used meperidine for comparison with interpleural bupivacaine because it has less of propensity for causing spasm of the Oddi sphincter compared to morphine (8). The

im rather than iv route of meperidine administration was chosen because of the simplicity of administration by nurses on the surgical floor. Finally, the 4 hours interval of meperidine administration was set according to the drug's clinical effect (9). When compared to meperidine, interpleural bupivacaine (intermittent or continuous infusion) was more effective for pain management after cholecystectomy (10,11). Although the pain scores decreased with both techniques 1, 2, 4, 8, 12, and 16 hours after surgery compared to the baseline, IB was more effective 20 and 24 hours after surgery (see Table 1). Pain scores almost equalized between the 2 groups 48 hours after surgery and reached a level which did not require analgesic treatment. The study was stopped after 48 hours because of concerns of the interpleural catheter displacement following mobilization of the patient and fear of catheter-related infection. Also, there was a decrease in the pain scores of the IB group 20 and 24 hours after surgery.

This delay in advantage of interpleural analgesia might be explained by time-related increasing local anesthetic levels. Moreover, the patients who had interpleural analgesia required less rescue analgesic medication (diclofenac). Compared to systemic opioids, the interpleurally administered local anesthetics have the potential advantage of less central respiratory depression and are less prone to cause spasm of the sphincter of Oddi (12).

Nevertheless, the use of interpleural local anesthetics is not devoid of side effects that include pneumothorax (the most frequently registered complication), systemic toxicity of local anesthetics, pleural effusion, Horner's syndrome, pleural infections, catheter rupture, and temporary phrenic nerve palsy (13,14). No such complications were recorded in our patients. Pneumothorax and phrenic nerve palsy were excluded in our patients by serial chest X-rays. Furthermore, the use of a diluted local anesthetic solution decreased the propensity for phrenic nerve palsy and toxic reactions.

Open cholecystectomy causes a considerable impairment of pulmonary function, leading to increased incidence of atelectasis and pneumonia. Laparoscopic cholecystectomy was associated with less postoperative pain, better pulmonary function, better arterial oxygenation, and shorter hospital stay (15,16).

Although a beneficial effect was equivocal in some studies (11), others (10) indicated that interpleural analgesia may lessen the post-cholecystectomy deterioration of pulmonary

function. Indeed, we found that maximal breathing capacity, a dynamic lung test, was better preserved in the IB group as compared to those receiving meperidine. Also, in IB, respiratory rate was lower, suggesting a lower work of breathing and/or better pain relief with interpleural analgesia. Possible explanation for the beneficial effect of interpleural analgesia may be less central respiratory depression, and better lung mechanics owing to more effective analgesia.

We believe that this method of provided good postoperative analgesia following open cholecystectomy. However, in our view, the local anesthetic should be administered only by a member of the anesthesia team and patients should be closely monitored for at least 30 minutes after each bolus, for possible hemodynamic and respiratory deterioration or systemic toxic effects of local anesthetics.

We conclude that intermittent interpleural analgesia with bupivacaine was more effective than intermittent intramuscular administration of meperidine, in reducing the severity of pain after open cholecystectomy 20 and 24 hours postoperatively. Lung function was better preserved in the interpleural group. We propose that further studies should be undertaken to compare the efficacy and drawbacks of intermittent versus continuous administration of interpleural analgesia.

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