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Effect of Induced Epidural Anesthesia before Surgical Incision on Acute Pain and Postoperative Pulmonary Events: Results from a Population with Lung Resection by Thoracotomy

De Wolf Julien*, Deblauwe Delphine, Labreuche Julien, Duhamel Alain, Desbordes Jacques, Wattier Jean-Michel and Porte Henri

Department of Thoracic Surgery, University Hospital of Lille, Boulevard du Professeur Jules Leclercq, 59000 Lille, France

***Corrseponding author:** De Wolf Julien, Department of Thoracic Surgery, University Hospital of Lille, Boulevard du Professeur Jules Leclercq, 59000 Lille, France, E-mail: juliendewolf@gmail.com

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Abstract

Introduction: Our study evaluated the effect on postoperative pain and pulmonary complications of a lidocaine injection in thoracic epidural anesthesia before surgical incision in patients with suspected lung cancer resected by thoracotomy.

Patients and methods: Between November 2012 and November 2013, we prospectively recruited patients requiring thoracotomy for suspected non-small cell lung cancer (NSCLC). All patients had a posterior lateral or lateral thoracotomy, and all had preoperative epidurals. Thoracic epidural catheter was removed 4 or 5 days after surgery. We studied NRS score on days 1 and 6 after surgery. Significant pain was defined as NRS>3. We recorded all pulmonary complications such as pneumonia, atelectasis requiring bronchoscopy, bronchopleural fistula, reintubation and tracheostomy.

Results: 128 patients were included; 91 patients were male and 37 were female (ratio M/F: 2.46). The median (IQR) NRS score at D1 and D6 post-surgery were 0 (0–3) and 2 (0–3) respectively. The prevalence of pain was 12.5% (95% CI 7.3–19.5) at D1, and 21.9% (95% CI 15.1–30.1) at D6. Postoperative pulmonary events arose in 24.2% of cases (n=31), including pneumonia in14.8% of cases (n=19), and atelectasis in 11.7% (n=15). No relationship was found between acute pain and pulmonary complications. There were no significant differences between groups of patients with and without pain related to the extent of lung resection or surgical technique. The D1 NRS score was correlated with the NRS score at D6 (r=0.24, *P*=0.006).

Conclusion: With our peroperative anesthetic management, postoperative acute pain is very low. Nevertheless, good care did not lead to a decrease in pulmonary complications. We conclude that thoracic epidural anesthesia should be induced before incision, to decrease acute post-thoracotomy pain.

Keywords: Thoracic epidural anesthesia; Acute pain; Pneumonia; Atelectasis

Abbreviations

ASA score: American Society of Anesthesiologists score; CI: Confidence Interval; D1: Day one after surgery; D6: Day six after surgery; IQR: Interquartile Range; NRS: Numerical Rating Scale; PCEA: Patient-Controlled Epidural Analgesia; TEA: Thoracic Epidural Anesthesia; VATS: Video-Assisted Thoracic Surgery

Introduction

Thoracotomy is one of the most painful surgical incisions, and post-thoracotomy pain syndrome occurs in 5% to 80% of patients [1,2]. Acute post-thoracotomy pain leads to pulmonary restriction and retention of secretions (deep breaths and effective coughs are impossible) [3].

Many surgical protocols have been trialed in attempts to decrease post-thoracotomy pain by minimizing intercostal nerve injury, such as harvesting an intercostal muscle flap, and closure of the thoracotomy through intracostal suture in the lower ribs. A systematic review suggested that these techniques could protect the intercostal nerve, and reduce postoperative pain and analgesic consumption [4]. Muscle-sparing incision, or axillary thoracotomy, has also been trialed, but did not show any differences in pain scores or complication rates [5].

Thoracic epidural analgesia remains the most effective anesthetic for thoracotomy but different options can be used to control post-thoracotomy pain, such as nerve block, paravertebral block or a paravertebral catheter [6,7].

Epidural analgesia reduces the intraoperative requirement of opioids [8,9]. Thoracic epidural anesthesia may contribute to better preservation of glucose period by reducing sympathetic activity, and thereby influences the perioperative function of vital organ systems. For instance, studies have demonstrated myocardial protective effects of epidural analgesia [10,11]. In our center, the thoracic epidural analgesia (TEA) is the usual technique for thoracotomy.

We conducted a prospective study on patients with suspected lung cancer who underwent thoracotomy with induced epidural anesthesia. The aim of our study was to evaluate the prevalence of acute post-thoracotomy pain syndrome and postoperative pulmonary

complications with our epidural anesthesia protocol. Our secondary objectives were to determine predictive factors for post-thoracotomy pain, the relationship between pain and pulmonary events, and to assess the complications of our analgesia strategy.

Materials and Methods

The study was approved by the ethics committee of the University Hospital of Lille. For all patients, written informed consent was obtained and signed the day before surgery. This prospective observational study was undertaken between November 2012 and November 2013 in the Department of Thoracic Surgery at the University Hospital of Lille. Procedures in the study followed our usual practice.

Inclusion criteria

All patients over 18 years requiring thoracotomy for suspected NSCLC were candidates for inclusion. All patients had a posterior lateral or lateral thoracotomy, and all had preoperative epidurals.

Exclusion criteria

We excluded patients with chronic pain syndrome, previous use of methadone, psychiatric illness, previous ipsilateral thoracotomy, or chest-wall resection. If preoperative epidurals did not function, these patients were also excluded from the trial. We did not include patients who refused consent.

Anesthesia protocol

An epidural catheter was inserted into all patients the day before surgery with a local anesthetic, and with the loss-of-resistance technique. The epidural space was identified with an 18-gauge Tuohy needle with the bevel directed cephalad via the midline approach between the T2–3 and the T5–6 vertebral interspace, and a catheter advanced 5 cm into the epidural space. The catheter was aspirated to exclude IV placement.

All the patients were pre-medicated the day before the intervention with hydroxyzine (1 mg/kg), and in the morning of the intervention with hydroxyzine (1 mg/kg) + alprazolam (0.5 mg).

For the surgery, all patients received an upper thoracic epidural anesthesia combined with total intravenous anesthesia. All patients had an epidural injection of lidocaïne 10 mg/ml before surgical incision (50 mg to 100 mg at least 5 minutes prior to the surgical incision, depending on the weight and patient's hemodynamic state). Induction and maintenance of anesthesia were done with propofol (10 mg/ml) and remifentanil (100 µg/ml) with the target controlled infusion technique (cerebral target). Remifentanil was stopped during surgery, because analgesia was totally taken by the thoracic epidural. Hypnosis was pursued by propofol according to the entropy monitoring, for an objective between 40 and 60. Neuromuscular blockade was obtained by administration of atracurium, cisatracurium, or rocuronium. The peripheral neuromuscular function was monitored using a train-of-four monitor in the adductor pollicis brevis. A double lumen tube was applied peroperatively for one-lung ventilation.

Postoperative analgesic treatment was with patient-controlled epidural analgesia (PCEA). PCEA was administered with an analgesic solution of levobupivacaine 1.25 mg/ml and sufentanil 0.5 µg/ml: basal infusion rate 4–10 mL/h, bolus dose 4 mL, and a 20-minute lock-out interval. Basal infusion was started after initial injection of lidocaïne, and boluses were administered by the anesthesiologist during surgery. Systematically, associated intravenous analgesia was started before the end of surgery with paracetamol (1000 mg) every 6 hours and tramadol (100 mg) every 8 hours for two days after surgery. Thoracic epidural catheter was removed four or five days after surgery, after chest tubes removal. The analgesia by paracetamol and tramadol was maintained.

Surgical protocol

The patient was placed in a lateral decubitus position, and chest cavity was accessed through a posterolateral thoracotomy with or without muscle-sparing, or through an axillary thoracotomy.

For posterolateral thoracotomy, a systematic rib section is performed in our department. This section is helpful to improve exposure and to avoid the risk of rib fracture. A Finochietto rib spreader is inserted. For axillary thoracotomy, there is no rib section. Inserting two tubes through a separate incision in the seventh interspace begins closure of the incision. Three systematic sutures are used to close the intercostal space.

Data collected

Before surgery we recorded demographic data, patient history, treatments, and ASA score, and we evaluated preoperative pain status with the Numerical Rating Scale (NRS). During surgery we recorded the side of the surgery, the surgical technique, cumulative doses of propofol, remifentanil, levobupivacaine, and lidocaine, number of chest tubes, and surgery duration. Postoperatively, we recorded analgesics administered, cumulative epidural dose of levobupivacaine, chest tube and TEA days, new chest drainage or surgical intervention, and the length of stay. We evaluated postoperative pain using the NRS at one (D1) and six days (D6) after surgery. We also recorded postoperative pulmonary events such as pneumonia, atelectasis requiring bronchoscopy, initial ventilatory support, reintubation, tracheostomy and bronchopleural fistula. We also evaluated the anatomopathology of the lung resection.

Endpoints

The primary endpoint was D6 postoperative pain at rest and on coughing, evaluated using the NRS. The score ranged from 0 (no pain) to 10 (worst pain imaginable). Significant pain was defined as NRS>3 on D6. The secondary endpoint was the prevalence of pulmonary complications.

Statistical analysis

Qualitative variables are expressed as numbers (percentages) and quantitative variables are expressed as means (standard deviation) or median (interquartile range) and range. 95% confidence intervals (CI) for the prevalence of pain at different evaluation times were calculated using the exact binomial distribution. Bivariate comparisons between patients with and without significant pain at D6 were made using the $\chi 2$ test (Fisher's exact test was used when the expected cell frequency was <5) for qualitative variables and Student's *t*-test for quantitative variables (or Mann–Whitney U test in the case of non-normal distribution checked graphically and using the Shapiro–Wilk test). Association between D1 and D6 NRS scores was assessed by

calculating the Spearman's rank correlation coefficient. No multivariate analysis was performed because of small sample sizes. Statistical testing was done at the two-tailed α level of 0.05. Data were analyzed using the SAS software package, release 9.3 (SAS Institute, Cary, NC).

Results

Patient characteristics

Between November 2012 and November 2013, 128 patients were included in our study, and had a thoracotomy for suspected primary lung cancer. Twenty-six patients were not included in the study because they had a secondary exclusion criterion (11 failures of epidural, 8 epidurals not induced before surgical incision and 7 surgeries unrealized). Baseline characteristics of patients are summarized in Table 1. Ninety-one patients were male and 37 were female (ratio M/F: 2.46), with a mean age of 61 (range 34–79) years. The mean weight was 74 kg (range 37–123 kg) and the mean body mass index was 25.6 kg/m^2 (range 15.4–39.2 kg/m^2).

	Values (%)
Patient characteristics	
Age, yrs, mean ± SD	60.6 ± 8.7
Men	91 (71.1)
Weight, kg, mean ± SD	74.2 ± 15.8
BMI, kg/m2, mean ± SD	25.6 ± 5.0
Smoking	102 (79.7)
Diabetes mellitus	27 (21.1)
Alcoholism	40 (31.3)
Cardiac disease	21 (16.4)
Vascular disease	29 (22.7)
Depressive syndrome	27 (21.1)
Neoadjuvant chemotherapy	7 (5.5)
Surgery characteristics	
Side	
Right	67 (52)
Left	61 (48)
Muscle sampling	59 (46)

Table 1: Characteristics of patients and surgical procedures.

Fifty-nine (46%) patients had a thoracotomy with muscle-sparing technique (52 mini-posterolateral thoracotomy and 7 lateral thoracotomy), and 69 patients (54%) had a classical posterolateral thoracotomy.

Twenty-six patients were classified with an ASA score of 1, 50 patients with an ASA score of 2, 50 patients with an ASA score of 3, and 2 patients with an ASA score of 4.

Peroperative data

Regarding the initial surgery, 59 (46%) patients had a lobectomy, 11 (9%) patients had a pneumonectomy, and 4 (3%) patients had a bi-lobectomy. Fifty-four (42%) patients had an infra-lobar resection. The median operative time was 211 min (IQR: 170–246). The median cumulative anesthetic dose was 1650 mg (0.12 mg/kg/min) for propofol and was 1.93 mg (0.14 µg/kg/min) for remifentanil. In 11 patients, remifentanil was stopped during surgery because it was unnecessary.

Postoperative data

Postoperatively, 19 (14.8%) patients suffered an atelectasis and 15 (11.7%) contracted pneumonia (Table 2). Seventeen (13.2%) patients required a new chest tube, and 7 (5.4%) patients required reintervention. Among the 128 patients in the study, no acute coronary syndrome or ischemic heart disease was observed preoperatively or postoperatively. There were no adverse effects from the epidurals and no neurological injuries were reported. The median of Levobupivacaïne cumulative daily dose was 170 mg (range 78-315). The median duration of postoperative hospitalization was nine days (range 5-86).

There was no peroperative mortality and only one death occurred at day 90 (due to pulmonary embolism).

Type of complication	Number (%)
Atelectasis	19 (14.8)
Postoperative pneumonia	15 (11.7)
Bronchopleural fistula	1 (0.78)
Adult respiratory distress syndrome	1 (0.78)
Reintubation	2 (1.56)
Tracheostomy	1 (0.78)
Total pulmonary complications	31 (24.2)

Table 2: Postoperative pulmonary events.

Pain evaluation, correlation and pain risk factors

The median (IQR) NRS score at D1 and D6 post-surgery were 0 (0–3), and 2 (0–3). Using a NRS cut-off of 3, the prevalence of significant pain was 12.5% (95% CI 7.3–19.5) on D1 and 21.9% (95% CI 15.1–30.1) at D6.

There was no relationship between positive pain score on D6 and any pulmonary event (p=0.69), either pneumonia (p=0.52) or atelectasis (p=0.56).

Patient characteristics, anesthetics data, surgical data, and postoperative outcomes were compared between patients with and without pain at D6 (Table 3). There was no significant difference between groups with and without pain in pre- and peroperative data in relation to lung resection or surgical technique. The only significant difference between groups was a higher D1 NRS score in patients with pain at D6 in comparison to patients without pain at D6. A significant correlation was found between D1 and D6 NRS scores (r=0.24, *P*=0.006).

	Significant pain at D6 post-surgery		
	No (n = 100)	**Yes (n = 28)**	*P*
Preoperative data			
Age, yrs, mean ± SD	60.6 ± 8.3	60.6 ± 10.1	0.99
BMI, kg/m^2, mean ± SD	25.8 ± 5.1	25.0 ± 4.6	0.44
Men	73 (73.0)	18 (64.3)	0.37
ASA score ≥ 3	45 (45.0)	7 (25.0)	0.06
Diabetes mellitus	21 (21.0)	6 (21.4)	0.96
Alcoholism	33 (33.0)	7 (25.0)	0.42
Smoking	78 (78.0)	24 (85.7)	0.37
Cardiac disease	19 (19.0)	2 (7.1)	0.16
Vascular disease	23 (23.0)	6 (21.4)	0.86
Depressive syndrome	20 (20.0)	7 (25.0)	0.57
Peroperative data			
Propofol dose, mg, median (IQR)	1560 (831–2180)	1750 (1300–2060)	0.35
Remifentanil, mg, median (IQR)	1.95 (1.51–2.65)	1.87 (1.52–2.32)	0.61
Lidocaine mg, median (IQR)	118 (100–200)	100 (50–175)	0.10
Levobupivacaine dose, mg, median (IQR)	42.1 (32.5–57.1)	45.4 (33.7–58.2)	0.64
Operative time, min, median (IQR)	211 (168–246)	214 (186–245)	0.68
Muscle-sparing technique	45 (46.9)	7 (26.9)	0.07
Supra-lobar surgery	57 (58.1)	17 (65.3)	0.50
Postoperative data			
Levobupivacaine daily dose, mg, median (IQR)	170 (120–98)	171 (125–218)	0.74
Numbers of days of TEA median (IQR)	6 (5–6)	6 (5–6)	0.25
Numbers of days of chest tube, median (IQR)	5 (5–6)	6 (5–6)	0.51
D1 NRS, median (IQR)	**0 (0–2)**	**2 (0–3)**	**0.02**
Total pulmonary complications	25 (25.0)	6 (21.4)	0.69
Atelectasis	14 (14.0)	5 (17.9)	0.56
Postoperative pneumonia	13 (13.0)	2 (7.1)	0.52

Table 3: Pain risk factors.

Discussion

In our study, incidence of postoperative pain was low (between 12.5 and 21.8%, depending on the time), and was lower than that reported in the literature, generally around 33% [12-16]. Prevalence of pain in our study increased after epidural ablation. The epidural was started before surgery and, in our study, the nonfunctional epidural rate was very low (7.1%). Hansdottir et al. reported a failure rate of 12% [17]. Epidural analgesia effective and started before surgery probably participated in the reduction of postoperative pain.

Our study suggested that patients with higher peroperative levobupivacaine doses would experience less postoperative pain. Helms et al. demonstrated a 5.2 pain score on day 2 with a daily ropivacaine dose of 920 mg for a mean patient weight of 75.85 kg [4]. These results are comparable to those demonstrated by Fibla et al. with a daily ropivacaine dose of 120 mg [18]. In our study, the median Levobupivacaïne daily dose was 170 mg, and epidural was left in place longer (five days on average). In our population, there was a significant correlation between NRS at D1 and NRS at D6. This suggests that the importance of postoperative pain can be screened very early.

We found incidence of pneumonia of 11.7% and of atelectasis of 14.8% in our population. These rates could be interpreted as high rate compared with the rates of 4.5% and 4.4% reported for the STS population described in 2012 by Ceppa [19]. However, our population consisted of high ASA score patients with advanced lung cancer and treated by induction chemotherapy.

We found no links between postoperative pain and pulmonary events. This is the first time that a study has clearly shown no relation between acute post-thoracotomy pain and pulmonary events. We explain our results by the fact that postoperative failure of the respiratory mechanism leading to pulmonary events is more due to the inflammatory reaction caused by surgery than by failure of diaphragm function.

In our series, 16% of the patients had a history of ischemic heart disorder, and were treated by anti-platelets. No patients presented a postoperative heart ischemia suggesting myocardial protection by the

epidural analgesia during surgery and also during the postoperative period. Myocardial ischemia arises in 20–69% of cases after non-cardiac surgery in high cardiovascular risk patients, and in 1.4–38% of cases with patients at lower cardiovascular risk [20]. More recently myocardial infarction has been described for only 0.2% of cases of postoperative lobectomy for NSCLC [21]. In our center, patients treated with anti-platelets (acetylsalicylic acid-like) benefits usually all of epidural analgesia, and no incidents were noted in our study.

We found no statistical differences in pain score or significant clinical outcomes that suggested the superiority of one incision type over another. However, because of small sample sizes, some differences may not be apparent due to the lack of adequate statistical power. In addition, in our study, no patients were operated using a minimally invasive approach, which could also improve postoperative pain control.

We didn't identify risk factor of acute post-thoracotomy pain in our population. No differences in postoperative pain or pulmonary complications were related to the extent of lung resection.

In conclusion, when using an epidural anesthesia, extent of surgery was not a predictor of post-operative pain in our series. We believe that epidural induction before starting surgery, as well as the dose of levobupivacaine used during surgery, are important to decrease acute post-thoracotomy pain. Even with high-efficacy pain management patients presented a high rate of pulmonary complications. We believe that the use of our anesthetic management to decrease pain and pulmonary complications should be evaluated on a larger population of patients undergoing thoracotomy.

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