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A Randomized Comparison of Intravenous Versus *Lumbar and Thoracic Epidural Fentanyl for Analgesia after Thoracotomy*

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Administration of large doses of fentanyl is a popular method to provide postoperative analgesia after thoracotomy. It is however unclear whether epidural lumbar (L) or epidural thoracic (T) administration of fentanyl confers any major advantage over intravenous (iv) infusion. Using a randomized prospective study design, we compared the potential benefits of L, T, and iv fentanyl administration after thoracotomy in 50 patients. Epidural catheters were not injected during surgery. Postoperatively a fentanyl infusion (5 $\mu g/ml$) was started at 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$ after a bolus of 1 $\mu g/kg$ and adjusted to maintain a score $\leq$ 30/100 at rest using a visual analog scale (VAS) for pain. Data were prospectively collected before surgery, at fixed intervals during the 48 h of fentanyl infusions, and the day of discharge. There was no difference between the groups in overall quality of analgesia at rest and after coughing, quantity of fentanyl delivered (L = 1.15 ± 0.38, T = 1.22 ± 0.23, iv = 1.27 ± 0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$), incidence of pruritus needing treatment (L = 2, T = 1, iv = 0 patients), need to decrease fentanyl infusion rate because of side effects (L = 2, T = 2, iv = 4 patients), importance of pulmonary infiltrates, or arterial blood gas values. One patient (L group) needed naloxone (0.04 mg iv). Intravenous patients were more frequently nauseated (P = .009) and needed boluses of fentanyl more often (L = 3 ± 9, iv = 6 ± 12, T = 4 ± 8; P = .04). T fentanyl patients had a shorter hospital stay (L = 14.4 ± 5.6, T = 11.1 ± 2.5, iv = 15.6 ± 5.3 days; P = .02), and a shorter delay for first bowel movement (L = 5.2 ± 2.5, T = 3.6 ± 0.9, iv = 5.6 ± 2.6 days; P = .04). Patients receiving T fentanyl also had better pulmonary function than patients receiving iv fentanyl (FVC: P = .02; FEV_1: P = .04). We conclude that, after thoracotomy, T epidural administration of fentanyl confers only marginal benefit over L epidural administration; and that iv fentanyl provides equivalent analgesia to the epidural routes, though with slightly increased incidence of side effects. (Key words: Analgesia, postoperative. Analgesics, intravenous, epidural: fentanyl. Anesthetic technique: epidural.)

THORACIC SURGERY LEADS to severe pain that is associated with changes in respiratory mechanics, shallow breathing, and impaired ability to cough.[1] Although the best analgesic regimen is still undetermined for these patients, epidural opioids have been reported to produce good pain relief with minimal side effects.[2–4] Fentanyl is well suited for analgesia after thoracic (T) surgery because of its rapid onset of action and low potential for delayed respiratory depression.[5] However, reports of its efficacy *via* this route are inconclusive and controversial. Epidural administration of fentanyl has been reported to provide better pain relief and to result in improved pulmonary function in some studies,[3,6,7] but has shown no benefit over intravenous (iv) administration in others.[8] Similarly, when compared with placement of the epidural catheter at the lumbar (L) level, placement of the catheter at the T level has been reported to markedly improve analgesia,‖ or have no effect.[9]

To date, no single study has compared the efficacy of fentanyl administered iv, *versus* both T and L epidural routes. We therefore designed a prospective study to determine whether a route of fentanyl administration would confer any advantage, in terms of pain relief, drug dosage, side effects, and length of postoperative hospital stay.

Methods and Materials

Following Institutional Review Board approval and informed consent, we studied 50 consecutive patients scheduled for elective lung surgery *via* a lateral mid-thoracic incision. Patients with the following criteria were not included: age < 20 yr, ASA physical status > 3, forced vital capacity (FVC) and/or peak expiratory flow rate (PEFR) and/or forced expiratory volume in 1 s (FEV_1) < 60% of predicted value, active infectious pulmonary process, or abnormal coagulation tests.

On the day before surgery, patients received instructions in the use of a portable spirometer (Ohmeda 5410 Volume Monitor, Madison, WI) and a visual analog scale (VAS) for pain.[10] Spirometric data were obtained in triplicate while the patients were in the semirecumbent position, and the highest readings were utilized. Thereafter, patients were asked to complete the VAS score for pain at rest and after a strong cough.

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‖ Chamberlain DP, Bodily MN, Olssen GL, Ramsey DH: Comparison of lumbar versus thoracic epidural fentanyl for post-thoracotomy analgesia using patient-controlled dosage (abstract). Regional Anesthesia 14S:26, 1989.

On the day of operation, an iv infusion was begun and a 20-G catheter was inserted into a radial artery 90 min after oral premedication with midazolam. After assignment of treatment group according to a randomization table, the patients then had either an 18-G epidural catheter (Perifix®, Braun Melsungen AG, Germany) placed under local anesthesia at the T4–5 level (T group) or at L4–5 level (L group), or had no epidural catheter (iv group). Epidural catheters were not injected before tracheal extubation, except for a test dose of 3 ml 1% lidocaine with 15 μg epinephrine just after insertion. General anesthesia was induced in all patients with thiopental and maintained with pancuronium, iv fentanyl, and isoflurane in oxygen. All patients had a bladder catheter and a nasogastric tube inserted before incision. All operations were completed by the same surgical team, with similar technique. Two lateral chest tubes were inserted in each patient, except in case of pneumonectomy in which a single 7F catheter was inserted.

The trachea of each patient was extubated within 4 h after completion of surgery, after which oxygen was administered *via* a face mask with an initial FI_{O_2} of 0.5, and adapted to maintain $Sp_{O_2} > 90\%$. When the patients were awake enough to rate their pain intensity on the VAS and complete pulmonary function testing, a 1 μg/kg fentanyl bolus was administered (T, L, or iv according to group allocation). An infusion was then started with a volumetric pump (Perfusor® EDL 2, Braun Melsungen AG, Germany) at 1 $\mu g \cdot kg^{-1} \cdot h^{-1}$ at the same site. Fentanyl concentration (5 μg/ml) was kept identical for all the patients during the study. The analgesic infusion was adapted to obtain a pain score ≤ 30/100 on the VAS at rest. In the case of ineffective analgesia, supplementary fentanyl boluses equal to half of the hourly infusion dose were administered *via* the same site as the infusion, and the infusion rate was increased by 20%. In case of intractable pruritus or nausea, or excessive sedation (sedation score > 3/5) combined with either respiratory rate (RR) < 10 or $Pa_{CO_2} > 55$ mmHg, fentanyl infusion was stopped for 1 h, and then restarted at 66% of previous rate. Intravenous naloxone was administered if the preceding maneuvers were unsuccessful. Fentanyl infusion was maintained for 48 h while patients were in a surgical intensive care unit (ICU). The patients were then discharged for 2 days to an intermediary care facility, where they received as needed intramuscular morphine. After leaving the ICU, pain management was totally controlled by the surgical team. As a standard procedure, chest tubes were usually withdrawn on the sixth and eighth postoperative days, respectively. Time of home discharge was decided by the surgical team, based on usual clinical criteria in use in our hospital: good functional recuperation and absence of pleural effusion or signs of pulmonary infection at least 24 h after withdrawal of second chest tube.

The following data were collected during the preoperative visit, before starting the fentanyl infusion, and then after 1, 2, 6, 12, 24, 36, and 48 h, as well as on the day of discharge: FVC, FEV_1, PEFR, RR, sedation state, degree of nausea and pruritus, SBP, HR, hemoglobin, Sp_{O_2}, Pa_{CO_2}, and VAS at rest and after coughing. Degree of sedation (from 1 = fully awake, to 5 = responsive only to vigorous mechanical stimulus), nausea (from 1 = no nausea, to 4 = nausea or emesis unresponsive to treatment), and pruritus (from 1 = no pruritus, to 4 = itching unresponsive to treatment) were also recorded. A radiologic score (0–10) was calculated by a blinded observer by summing the radiologic infiltrates in each of the remaining lobes (0 = clear lobe, 1 = infiltrate, and 2 = atelectasis) at the same times.

All data were analyzed with one-way ANOVA for continuous data and Kruskal-Wallis for categorical data. Repetitive values (VAS, SBP, HR, RR, FVC, FEV_1, PEFR, radiologic score, sedation state, degree of nausea and pruritus, Sp_{O_2}, Pa_{CO_2}, and Hb) were analyzed with ANOVA for repeated measures for continuous data and Friedman test for categorical data. Intergroup differences were identified with Scheffé's test. Continuous data are reported as mean ± SD, and categorical data as median ± range. Significance level was accepted for $P < .05$.

Results

Two patients were excluded from the study: one (iv group) died of acute myocardial infarction 6 h after surgery, and in another (T group), the trachea could only be extubated on the third postoperative day because of acute postoperative respiratory insufficiency. Sixteen patients in each group (N = 48) completed the study.

Patients' characteristics, including type and duration of operation, mean peroperative fentanyl dose, and interval between the end of surgery and the beginning of the fentanyl infusion, were similar, except for a slight difference in weight (table 1). HR, MAP, rectal temperature, mean volume of blood transfused after the operation, Hb values, and time prior to discharge from the ICU were also similar.

Pain scores at rest and after coughing were similar in the three groups during the study. Significant decrease from baseline pain scores at rest occurred after 60 min in the T group and 120 min in others (intergroup difference $P = .07$; fig. 1). Decrease in pain scores after coughing was observed in all groups only after 12 h (fig. 2).

The mean hourly dose of fentanyl was significantly less from the first to the sixth hour in the T group when compared with the iv group ($P = .02$; fig. 3). This difference did not persist during the end of the study (L = 1.15 ± 0.38, T = 1.22 ± 0.23, iv = 1.27 ± 0.3 $\mu g \cdot kg^{-1} \cdot h^{-1}$). Patients in the iv group received larger (L = 104 ± 24,

TABLE 1. Demographic and Operation Data

	Lumbar	Thoracic	Intravenous
N	16	16	16
Age (yr)	57 ± 14	54 ± 18	59 ± 14
Weight (kg)*	74 ± 12	69 ± 12	62 ± 9
Sex (M/F)	14/2	15/1	10/6
ASA (1, 2, 3)	1/9/6	0/10/6	3/9/4
Type of surgery (1/2/3)†	2/10/4	2/11/3	0/13/3
Operation duration (min)	175 ± 66	151 ± 65	158 ± 64
Fentanyl ($\mu g \cdot kg^{-1} \cdot h^{-1}$)	3.1 ± 1.4	3.8 ± 2.0	3.2 ± 1.4
Study interval (min)‡	133 ± 108	107 ± 122	75 ± 53

* No significant differences between groups, except for weight (intravenous *vs.* lumbar: $P = .02$).

† Type of surgery: 1 = lobectomy; 2 = pneumonectomy; 3 = other (multiple metastatic resection, pleural surgery).

‡ Study interval = time from the end of surgery until the beginning of fentanyl infusion.

T = 93 ± 19, iv = 137 ± 71 μg) fentanyl boluses during the first 6 h ($P = .02$) and needed more frequent fentanyl boluses during the entire study (L = 3 ± 9, T = 4 ± 8, iv = 6 ± 12; $P = .04$).

Pa_{CO_2}, Sp_{O_2}, FI_{O_2}, and RR were clinically similar, despite slightly higher Sp_{O_2} in T patients ($P = .038$; table 2). We recorded no individual Sp_{O_2} value less than 90%, and no episode of apnea. The RR decreased to < 10 in only two patients (one iv and one L patient; least value 9/min). Pa_{CO_2} values between 55 and 60 mmHg were recorded once in one patient of each group. One L patient had five consecutive Pa_{CO_2} values > 55 mmHg, with a maximum of 70 mmHg at 36 h after the start of the infusion. An important decrease in all pulmonary function tests was observed in all patients during the study (figs. 4–6). However, absolute values of FVC, FEV_1, and PEFR were greater and percent of decrease was smaller in the T group when compared with the iv group ($P = .02$, $P = .04$, $P = .05$, respectively). The number of radiographic infiltrates and atelectatic lobes did not differ between groups. Four patients in the L group, two in the T group, and three in the iv group (NS) needed one or two bronchofibroscopic aspirations to treat atelectasis resistant to conservative treatment.

The incidence of pruritus needing treatment (rated >2/4) was low and similar in each group (L = 2, T = 1, iv = 0 patients). Intravenous patients were more frequently nauseated (L = 1, T = 2, iv = 8; $P = .009$) and needed larger doses of droperidol to relieve nausea ($P = .005$). The rate of the fentanyl infusion had to be reduced at one time in eight patients (L = 2, T = 2, iv = 4; NS), and only one patient in the L group received

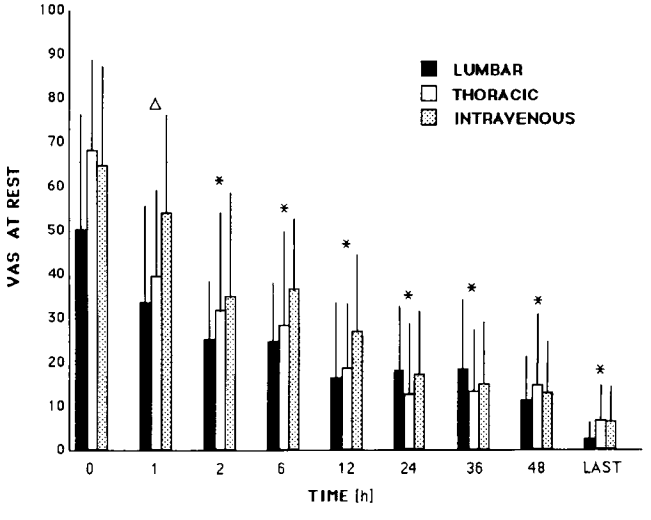

FIG. 1. Evolution of pain at rest (mean ± SD), as measured by a 10-cm visual analog scale (VAS), from the time just before starting the fentanyl infusion (0), until the day of discharge (last). Significant decrease in pain scores from baseline is observed after 1 h in patients receiving thoracic epidural fentanyl (△), and after 2 h in all groups (*).

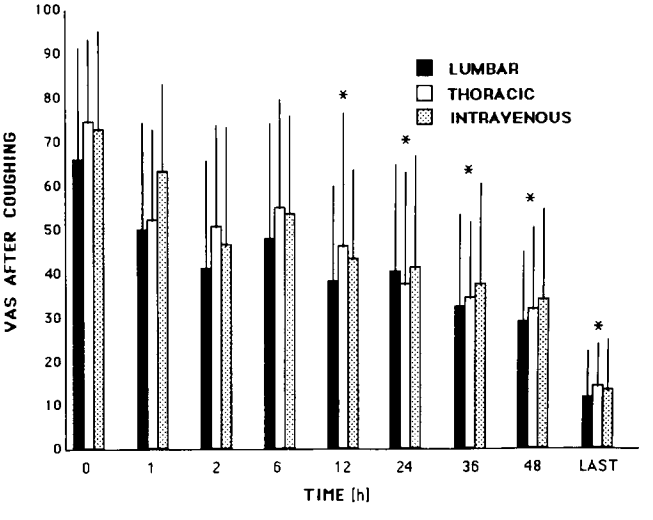

FIG. 2. Evolution of pain after coughing (mean ± SD), as measured by a 10-cm visual analog scale (VAS), from the time just before starting the fentanyl infusion (0), until the day of discharge (last). There is no difference between the groups receiving epidural lumbar, epidural thoracic or intravenous fentanyl: pain scores significantly decrease after 12 h (*).

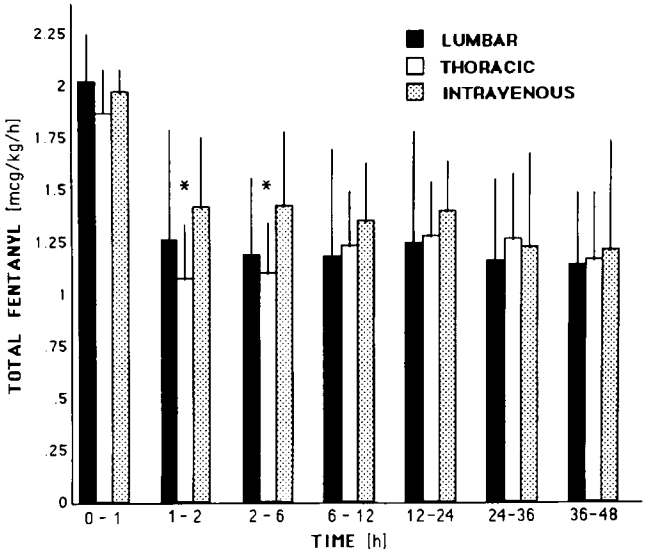

FIG. 3. Total fentanyl (constant infusion + bolus) administered to 48 patients during 48 h for pain relief after thoracotomy. Data are expressed as mean ± SD and represent averaged hourly values for the treatment period considered. Patients in the thoracic epidural group need significantly less fentanyl than patients in the intravenous group from the first to the sixth postoperative hours (*).

iv naloxone (0.04 mg) because of combination of hypercarbia (Pa_{CO_2} = 70 mmHg) and bradypnea (RR = 9).

Patients receiving T fentanyl had a shorter postoperative hospital stay (L = 14.4 ± 5.6, T = 11.1 ± 2.5, iv = 15.6 ± 5.3 days; P = .02), and a shorter delay for the time of passing of feces (L = 5.2 ± 2.5, T = 3.6 ± 0.9, iv = 5.6 ± 2.6 days; P = .04).

At the time of discharge, all investigated parameters were identical within the three groups.

Discussion

This prospective study is the first to compare three analgesic regimens containing fentanyl (iv and epidural T and L) after thoracotomy. Results from previous studies are controversial but suggest, at best, that marginal improvement may be observed with epidural fentanyl administration.[‖2-4,6-8,11] Moreover, recent data advised against placement of epidural catheters at the T level for pain relief after thoracotomy because similar analgesia and side effects were observed with L catheters.[9] However, no data on pulmonary function tests or length of hospital stay were provided. Our results show that: 1) similar adequate pain relief was obtained with similar doses of fentanyl in the three groups; 2) patients receiving iv fentanyl needed larger and more frequent initial boluses of fentanyl, and experienced more nausea; and 3) T and L fentanyl administration produced similar effects, except for a shorter postoperative hospital stay and shorter return of bowel function in the T group.

Analgesia

Efficient analgesia at rest was easily established in the three groups of patients, and most pain ratings decreased under 30/100 within 2 h. In contrast to pain relief at rest, pain resulting from coughing was poorly controlled by all three analgesic regimens. Most patients had ratings around 50/100 6 h postoperatively, which only decreased to 30/100 after 48 h. Similar differences between VAS at rest and after coughing have been reported previously.[11] They may be explained by the fact that our protocol was designed to offer the patients a high, though not complete, level of analgesia at rest (VAS ≤ 30/100). This level of analgesia is similar to that typically achieved when patients are allowed to self-administer opioids[12] and has been used used as endpoint by others.[7] Another reason we did not attempt to provide complete analgesia was that we were trying to limit the incidence and severity of opioid-induced side effects. In retrospect, the low incidence of side effects observed in this study suggests that larger doses of fentanyl could have been administered and that better analgesia could have been possible, especially during chest physiotherapy.

Fentanyl Dosage

Since this study was defined to attain a predetermined analgesic status, we expected to observe a difference in the doses of fentanyl. Despite large interpatient fluctuations and higher initial fentanyl needs in the iv group, we found, like others, that intrapatient analgesic requirements were fairly constant over time once a satisfactory pain-free state had been reached.[8,13] Consistent with previous results,[7-9,13] a mean dose of 1.2 $\mu g \cdot kg^{-1} \cdot h^{-1}$ of fentanyl was necessary in the three groups of patients. The widely different regimens used by others (0.38 to >2.0 $\mu g \cdot kg^{-1} \cdot h^{-1}$)[8,9] may be explained by different analgesic endpoints or by the use of constant flow *versus* PCA infusion devices, but not by the use of different fentanyl concentrations.[14] It may also be questioned if different patient populations, with different pain perceptions and analgesic requirements, were investigated.[13]

Respiratory Effects

Pulmonary function tests and Sp_{O_2} when breathing room air are markedly decreased after T surgery, with progressive return to preoperative values over weeks because of compensatory overinflation.[3,15] In our study, immediate postoperative flow rates and volumes were decreased to 30% of preoperative values in all groups, but had already returned to 75% of preoperative values by the time of discharge. The rate of improvement was fastest, however, in the T group, which had significantly better flow rates during the whole ICU stay. Our results confirm previous reports of improvement in pulmonary

TABLE 2. Respiratory Parameters

	Preoperative‡	0‡	1	2	6	12	24	36	48	Last Day‡
FI_{O_2} (%)										
L	21	55 ± 17	49 ± 3	46 ± 5	45 ± 6	44 ± 6	41 ± 9	40 ± 9	40 ± 19	21
T	21	49 ± 15	49 ± 15	43 ± 8	41 ± 8	39 ± 6	36 ± 7	34 ± 9	30 ± 8	21
iv	21	50	49 ± 2	48 ± 3	41 ± 7	42 ± 6	43 ± 14	36 ± 9	34 ± 9	21
Sa_{O_2} (%)*										
L	94.7 ± 3.2	96.8 ± 1.9	96 ± 5.3	96.0 ± 3.9	96.6 ± 1.8	96.5 ± 2.0	95.0 ± 2.8	94.1 ± 3.5	93.3 ± 2.2	94.9 ± 2.1
T	95.8 ± 2.0	96.6 ± 2.0	97.5 ± 2.2	97.8 ± 1.1	97.6 ± 1.3	97.7 ± 0.9	96.1 ± 1.7	96.0 ± 3.4	96.1 ± 1.5	95.4 ± 2.1
iv	95.2 ± 2.1	96.2 ± 2.4	97.6 ± 1.2	97.9 ± 1.0	97.3 ± 1.8	96.8 ± 1.9	95.9 ± 3.4	96.3 ± 1.8	94.5 ± 4.6	94.9 ± 1.8
Pa_{CO_2} (mmHg)										
L	36.2 ± 4.4	42.3 ± 5.6	43.7 ± 9.0	44.5 ± 5.8	44.2 ± 8.2	45.1 ± 6.5	43.3 ± 6.3	44.4 ± 6.8	44 ± 11.2	36.4 ± 4.6
T	36.5 ± 2.8	43.1 ± 4.3	42.3 ± 4.4	42.5 ± 4.6	42.0 ± 5.1	41.7 ± 3.7	43.0 ± 5.5	41.8 ± 5.9	38.6 ± 4.2	37.1 ± 2.6
iv	36.8 ± 3.7	44.8 ± 6.7	44.7 ± 5.7	45.8 ± 5.9	45.1 ± 6.2	45.3 ± 5.8	44.2 ± 6.1	45.5 ± 6.3	42.0 ± 6.6	36.9 ± 2.5
Respiratory rate										
L	16.5 ± 3.8	23.1 ± 4.7	20.6 ± 5.7	20.0 ± 5.3	19.6 ± 5.7	18.5 ± 4.0	18.3 ± 4.0	18.6 ± 3.4	18.3 ± 3.5	17.4 ± 2.8
T	15.3 ± 3.1	19.9 ± 4.0	19.3 ± 4.0	19.3 ± 3.7	18.1 ± 4.0	18.4 ± 3.7	18.1 ± 4.9	18.2 ± 4.6	17.0 ± 4.1	16.3 ± 3.2
iv	17.7 ± 3.6	20.8 ± 3.3	18.8 ± 4.0	18.8 ± 4.1	17.9 ± 3.2	18.4 ± 4.9	17.7 ± 2.6	17.8 ± 4.5	18.3 ± 4.3	17.6 ± 3.2
FVC (l)†										
L	3.2 ± 0.8	0.9 ± 0.6	1.1 ± 0.5	1.1 ± 0.3	1.3 ± 0.4	1.2 ± 0.5	1.2 ± 0.5	1.2 ± 0.5	1.2 ± 0.5	2.5 ± 0.8
T	3.3 ± 0.7	1.1 ± 0.5	1.5 ± 0.6	1.7 ± 0.5	1.6 ± 0.6	1.5 ± 0.5	1.6 ± 0.5	1.6 ± 0.5	1.6 ± 0.5	2.6 ± 0.7
iv	3.0 ± 0.8	0.6 ± 0.3	0.7 ± 0.4	0.8 ± 0.3	0.9 ± 0.3	1.0 ± 0.3	1.1 ± 0.2	1.2 ± 0.3	1.3 ± 0.3	2.4 ± 0.7
FEV_1 (l)†										
L	2.3 ± 0.7	0.6 ± 0.3	0.8 ± 0.4	0.9 ± 0.2	0.9 ± 0.3	0.9 ± 0.3	0.9 ± 0.3	0.8 ± 0.3	0.9 ± 0.3	1.7 ± 0.6
T	2.4 ± 0.8	0.7 ± 0.2	1.1 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	1.2 ± 0.4	1.9 ± 0.5
iv	2.2 ± 0.6	0.5 ± 0.2	0.5 ± 0.2	0.6 ± 0.2	0.7 ± 0.2	0.7 ± 0.2	0.8 ± 0.2	0.8 ± 0.2	0.9 ± 0.3	1.7 ± 0.4
PEFR (l/min)†										
L	398 ± 393	70 ± 38	90 ± 49	98 ± 39	112 ± 48	106 ± 41	119 ± 58	104 ± 50	113 ± 40	253 ± 92
T	316 ± 104	74 ± 31	123 ± 49	142 ± 60	140 ± 66	154 ± 69	162 ± 61	164 ± 86	161 ± 81	235 ± 91
iv	289 ± 63	45 ± 24	50 ± 20	66 ± 25	84 ± 32	88 ± 38	99 ± 26	94 ± 30	115 ± 34	211 ± 54

Data are expressed as mean ± SD, for the day before operation (preoperative), during the 48 h of the adminstration of fentanyl (0–48), and for the day of home discharge (last day).

* Significant difference between L *versus* T from 1 to 48 h by ANOVA for repeated measures.

† Significant difference between iv *versus* T from 1 to 48 h by ANOVA for repeated measures.

‡ No difference between fentanyl groups (L, T, iv), except CVF and PEFR at time 0: T *versus* iv by one-way ANOVA.

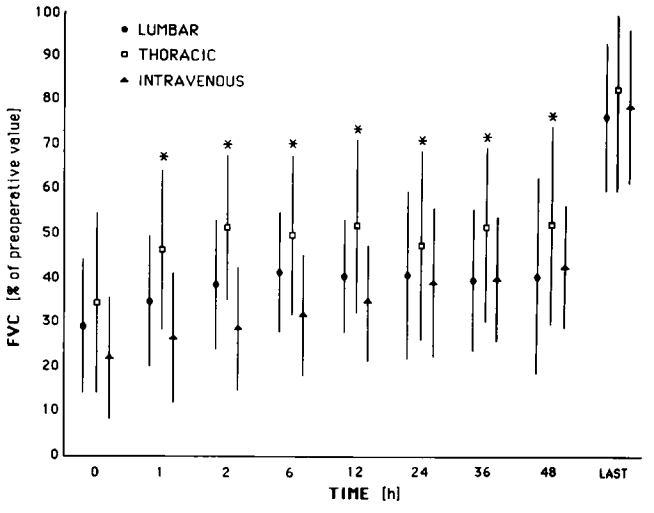

FIG. 4. Evolution of postoperative forced vital capacity (FVC), expressed as a percentage of preoperative value, in 48 patients receiving either intravenous, epidural lumbar or epidural thoracic fentanyl. Data are expressed as mean ± SD, from the time just before the administration of fentanyl (0), until the day of discharge (last). Patients receiving intravenous fentanyl had a significantly greater decrease in FVC compared with the thoracic route from the first to the 48th postoperative hour (P = .02).

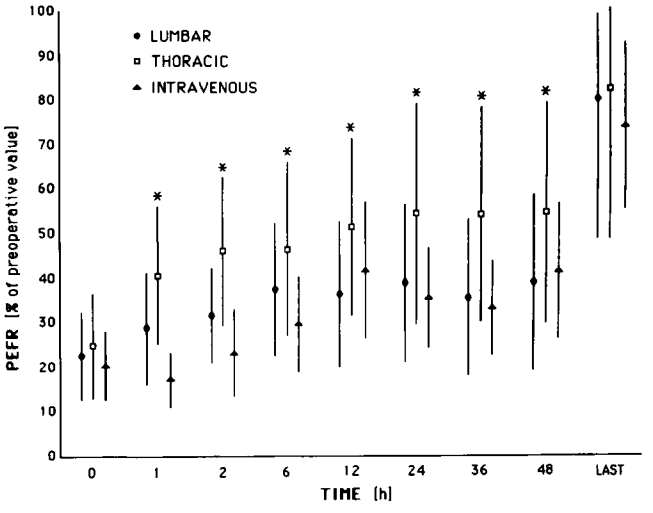

FIG. 6. Evolution of postoperative peak expiratory flow rate (PEFR), expressed as a percentage of preoperative value, in 48 patients receiving either intravenous, or epidural lumbar or epidural thoracic fentanyl. Data are expressed as mean ± SD, from the time just before the administration of fentanyl (0), until the day of discharge (last). Intravenous fentanyl administration results in marginally greater decrease in PEFR compared with the thoracic route from the first to the 48th postoperative hour (P = .05).

function tests with epidural opioids after major surgery.[2,3,6,7]

Respiratory depression and somnolence are major problems associated with systemic and epidural opioids especially when these drugs are coadministered.[5,16–18] As previously reported, we found greater sedation in the iv group, yet no difference in Pa_{CO_2} or RR.[6,7] Only one patient received naloxone, because of combined moderate bradypnea and hypercarbia. The absence of severe respiratory depression in our study may be due the close surveillance by nurses, leading to reduction in the infusion rate in eight patients, and to the avoidance of combined systemic and epidural administration of fentanyl in the same patients. Our data confirm that vital signs are to be regularly monitored in patients receiving epidural and systemic opioid infusions, though not necessarily in an ICU.[17,18]

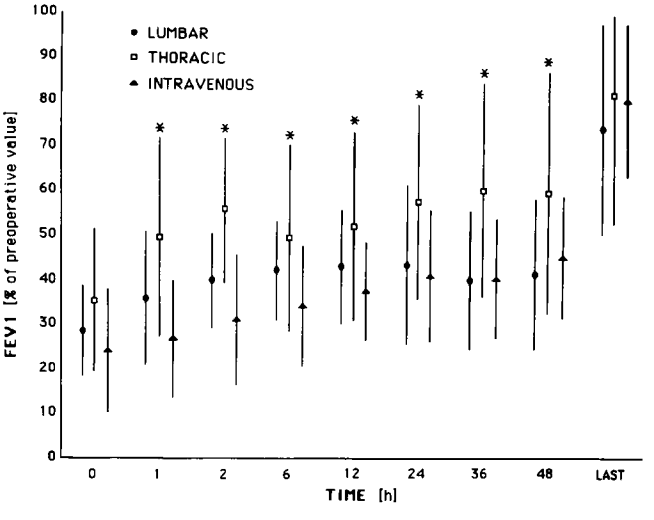

FIG. 5. Evolution of postoperative forced expiratory volume in 1 s (FEV_1), expressed as a percentage of preoperative value, in 48 patients receiving either intravenous, or epidural lumbar or epidural thoracic fentanyl. Data are expressed as mean ± SD, from the time just before the administration of fentanyl (0), until the day of discharge (last). Intravenous fentanyl administration results in significantly greater decrease in FEV_1 compared with the thoracic route from the first to the 48th postoperative hour (P = .04).

OTHER SIDE EFFECTS

The overall incidence of other side effects was low, confirming the good tolerance of epidural fentanyl infusions.[7–9] The increased incidence of nausea in the iv group, and the similar incidence of pruritus in the three groups had previously been reported;[7,9] but the shorter time until the first bowel movement in the T group was unexpected. The incidence of urinary retention could not be evaluated since all patients had urinary catheters.

HOSPITAL STAY

One major finding of that study was that epidural T fentanyl was associated with a statistically and clinically shorter (3.5 days between T and iv fentanyl) postoperative

hospital stay. Similar conclusions were previously reached in a retrospective study[19] and in a prospective investigation in grossly obese patients undergoing gastroplasty.[20] A trend toward shorter hospital stay also has been reported by Yeager *et al.* when using combined opioids and local anesthetics solutions after major surgery.[21] This study is however the first to show that a specific technique of postoperative analgesia (T epidural fentanyl) may be associated with a reduction in postoperative stay. Prospective cost utilizations were not performed; but it may be postulated that hospital savings occurred, as previously reported with postoperative epidural analgesia.[21,22]

The reasons why T fentanyl epidural administration was associated with improved pulmonary function tests, low incidence of nausea or sedation, shorter time for first bowel movement, and earlier discharge remain unclear. These findings may appear paradoxical in view of the nearly similar analgesia in the three groups and of the systemic levels of fentanyl, which probably developed after a few hours of epidural administration.[23,24] However, studies on analgesia after thoracotomy and during the first stage of labor could not find any relationship between plasma fentanyl levels and its analgesic potency after epidural administration.[11,25] Moreover, plasma opioid concentrations might not reflect the degree of binding of highly soluble compounds such as fentanyl to opiate receptors at a given level in the spinal cord. Because of the limited cephalad migration of fentanyl after epidural administration,[26] higher concentration of fentanyl should then be expected to reach opiate receptors at the T level after T epidural administration, even though we did not observe any clinical evidence of "suspended analgesia."‖[2,6,27] It is possible that the low incidence of nausea and low sedation state in the T group may have influenced the pulmonary function tests and Sp_{O_2}, since the number of pulmonary infiltrates and need for bronchofibroscopies were similar within the three groups. It may also be speculated that VAS as measured did not effectively reflect the potential for movement of patients, or that improved release of T muscle tension may have been obtained for equivalent level of analgesia with T fentanyl. Earlier mobilization, earlier oral alimentation, and bowel transit also may have contributed to faster recovery and earlier discharge.[20] It must however be appreciated that only part of these data were available for analysis, and that different findings have been reported by others.[3] A population effect appears also unlikely to explain our results, in view of the homogeneity of study groups, including the time of postoperative hospital stay.

Study Limitations

There are several limitations to our results, however. First, only 50 patients were studied. This number nevertheless compares favorably with other prospective studies on postoperative regimen.[2–4,6–9,14,20,21]

Second, this study was not double-blinded because we did not insert two epidural catheters, including one high T, in patients receiving only iv fentanyl. This decision was based on ethical reasons and was in accord with our Ethical Committee and Institutional Review Board. Despite frequent insertion of epidural catheter in most institutions, including ours, this remains an invasive and potentially risky procedure, especially at the T level. Preoperatively, no patient asked for a particular type of postoperative analgesia after adequate explanations and informed consent. Postoperatively, most of the patients and surgeons were not aware of the route of fentanyl administration. We thus are confident that no significant bias occurred because of our protocol. Bias from residents evaluating the pain scores and the pulmonary function testings, as well as from the surgeons deciding for the discharge delay, cannot be excluded because they were not blinded. This nevertheless seems unlikely as none of them directly participated in the study, and none expressed particular inclination for a certain type of postoperative pain treatment. Moreover, it seems improbable that a certain type of analgesia could have been consistently favored by resident anesthetists in the ICU and staff surgeons on the ward during the whole study period. Previous studies on postoperative pain management have frequently utilized the patient care team to provide analgesic drugs or assess pain scales.[4,17,21,22]

Third, our protocol did not include clear-cut, strictly pre-established criteria for home discharge, but rather relied on clinical judgment of surgeons, independent of the study. A bias in this decision cannot be excluded; however, it seems unlikely.

Last, it may be unfair to the patients not to use an epidural catheter before the end of the operation to ensure a relative pain-free state by the time of extubation. We used this particular design in our protocol to be able to compare equivalent baseline values of postoperative pain in all groups of patients. It is also likely that the administration of epidural fentanyl before extubation would have enhanced the difference between the groups, rather than reduced it.

In summary, the current study showed that, during the first 48 h after thoracotomy, the route of fentanyl administration (L, T, or iv) did not influence the overall quality of analgesia, nor the quantity of opioids delivered. The higher incidence of nausea and increased need for boluses with iv fentanyl may have favored the epidural administration. However, the advantage of shorter hospital stay and improved pulmonary function tests with T epidural fentanyl are to be balanced with the increased invasiveness and risks when compared with the L route.

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