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## Mood during Epidural Patient-controlled Analgesia with Morphine or Fentanyl

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**Background:** Mood states during epidural opioids are not known. The authors studied the change in mood during the 48-h period of epidural morphine and epidural fentanyl in 47 patients after elective hip or knee joint arthroplasty.

**Methods:** An epidural catheter was inserted at the L2-L3 or L3-L4 interspace. Anesthesia was induced with thiopental and maintained with isoflurane and nitrous oxide. One hour before the conclusion of the operation, patients received an epidural bolus injection of 2 mg morphine ( $n = 23$ ) or 100  $\mu$ g fentanyl ( $n = 24$ ), followed by the same opiate (125  $\mu$ g/ml morphine or 25  $\mu$ g/ml fentanyl) epidurally delivered by a patient-controlled analgesia (PCA) pump in the postoperative period for 48 h. Mood was assessed using the bipolar form of the Profile of Mood States before operation and 24 h, 48 h, and 72 h after operation.

**Results:** There was no significant difference in pain intensity between the groups during epidural PCA. Mood states became more positive over time in the patients who received morphine ( $P < 0.01$  at 48 h) and negative in those who were given fentanyl ( $P < 0.01$  at 24 and 48 h, respectively) compared with those before the operation, and they were more positive in the morphine than in the fentanyl group at 24 h, 48 h ( $P < 0.05$ ), and 72 h ( $P < 0.01$ ). Patients in the morphine group were more composed, agreeable, elated, confident, energetic, and clearheaded than were those in the fentanyl group ( $P < 0.05$ ). There was no correlation between mood scores and pain scores in either group. There was an inverse correlation at 48 h between mood scores and plasma fentanyl concentrations ( $r = -0.58$ ,  $P < 0.05$ ).

**Conclusion:** Mood states are significantly more positive during epidural morphine PCA than they are during epidural fen-

tanyl PCA. (Key words: Analgesic technique; epidural;  $\mu$  opioids; mood.)

EPIDURAL opioids, such as morphine and fentanyl, provide profound pain relief and have been used widely in patients after surgery. The cerebrospinal fluid (CSF) concentration of morphine injected in the epidural space far exceeds, in the second order, that in plasma.<sup>1</sup> Epidural morphine, because of its hydrophilicity, tends to spread rostrally *via* CSF and can be detected as long as 24 h later.<sup>1</sup> Lanz *et al.*<sup>2</sup> found a sense of well-being in a significantly higher proportion of patients receiving epidural morphine than in those receiving intramuscular morphine in the postoperative period. On the other hand, fentanyl injected in the lumbar epidural space is detected briefly in the CSF at the level of the cervical spine in concentrations approximately one tenth of that in the lumbar CSF.<sup>3</sup> The fentanyl concentration in the CSF, however, declines rapidly due to its lipophilic property, and that in plasma increases<sup>3</sup> to levels comparable to those obtained during intravenous infusions of the same dose. The CSF pharmacokinetics of morphine and fentanyl appear to suggest the possibility that the difference in the magnitude of CSF concentrations of morphine and fentanyl may affect psychological processes differently after injection in the epidural space. We studied, therefore, changes in mood during patient-controlled epidural morphine or fentanyl analgesia in patients who underwent elective hip or knee joint arthroplasty.

## Materials and Methods

Fifty-two patients of both sexes who were classified as American Society of Anesthesiologists physical status I or II, who were aged 20-65 yr and scheduled for elective hip or knee joint arthroplasty during general anesthesia were recruited for this randomized, double-blind, two-group, parallel study. The primary endpoints were mood changes and pain intensity in the postopera-

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tive period. Institutionally approved written informed consent was obtained from each patient. Inclusion criteria were willingness to participate in the study and an understanding of the purpose of the measures to be used in the study. Exclusion criteria included a known allergy to morphine or fentanyl, abnormal coagulation profile, psychiatric diseases, mental confusion, alcohol or drug abuse, psychotropic medications, morbid obesity, and chronic pain with evidence of central sensitization, such as severe pain that was out of proportion to the lesion or the sustained injury and the presence of disease-related pain such as dysesthesia or allodynia.

#### *Randomization and Blinding Procedure*

Patients were randomly assigned to one of two groups according to a computer-generated randomization schedule: (1) those receiving epidural morphine and (2) those receiving epidural fentanyl for postoperative pain. A sealed envelope containing the group assignment was prepared for each patient. One of the investigators, who did not help assess the patients, opened the envelopes on the morning of and before operation and prepared a syringe containing 10 ml of either 0.1% morphine or 0.005% fentanyl for an epidural bolus injection and a bag of 200 ml normal saline solution containing 0.0125% morphine or 0.0025% fentanyl for epidural patient-controlled analgesia (PCA) according to the group assignment, respectively. Patients, investigators who assessed patients, and personnel who managed anesthesia and postoperative pain were unaware of the group assignment.

#### *Measures and Study Procedure*

Mood was assessed using the bipolar form of the Profile of Mood States.<sup>4-7</sup> Each of the six mood states in this profile (*i.e.*, composed-anxious, agreeable-hostile, elated-depressed, confident-unsure, energetic-tired, and clearheaded-confused) consisted of 12 adjectives scales, of which one pole represents the positive aspects of the dimension and the other pole refers to the negative aspects. Each adjective was rated on a four-point intensity rating scale: 0 = much unlike this, 1 = slightly unlike this, 2 = slightly like this, and 3 = much like this. The total score (a Likert scale with a range of 0-36) was the sum of positive items and negative items plus a constant of 18 for each of the mood states, which was transformed to T scaling that normalizes distributions with the mean value of  $50 \pm 10$  (SD) with an approximate range of 20-80. Pain intensity at rest was assessed by a 10-cm visual analog scale (VAS)

with a range of 0-100, anchored by "no pain" at one end and by "worst possible pain" at the opposite end. Respiratory effect of epidural PCA opioids was assessed by respiratory rate and arterial oxygenation monitored by a pulse oximeter. Arterial blood gas was analyzed when respiratory rate was 10 breath/min or less. Somnolence and pruritus were assessed by subjective VAS scores.<sup>8,9</sup> The worst somnolence was defined as present when patients could hardly keep their eyes open and the worst pruritus was defined as present when pruritus is unbearable to the point that patients prefer pain. Nausea was assessed by subjective VAS scores anchored by retching, vomiting, or both at one end.<sup>8,9</sup> The presence or absence of hallucination and ileus was recorded.

Plasma concentration of morphine was measured as the 3,6-dipentafluoropropionyl-morphine derivative with stable isotope dilution mass spectrometry, using an adaptation of the method of Bowie and Kirkpatrick.<sup>10</sup> The limit of sensitivity and quantification was 0.5 mg/ml and 1 ng/ml, respectively. Fentanyl was measured using gas chromatography with nitrogen-selective detection, adapting the method published by Watts and Caplan.<sup>11</sup> The limit of sensitivity and quantification was 0.05 mg/ml and 0.1 ng/ml, respectively.

The purpose of the study and VAS and questionnaires were explained at an interview a few days before operation at the last visit to the clinic. Patients were introduced to the PCA pump and instructed in its use. The VAS scores for pain, side effects, and mood were obtained on the morning of surgery before the operation (baseline). The VAS scores for pain and side effects were assessed 3, 6, 12, 24, 48, and 72 h after operation. Consumption of PCA morphine was recorded using an Abbott TRW printer model TP 40 (Abbott Life Care Infuser, Chicago, IL) 3, 6, 12, 24, 36, and 48 h after operation. Mood was assessed 24, 48, and 72 h after operation. Blood samples were drawn in the first 30 patients before operation and 24, 48, and 72 h after operation for plasma concentrations of morphine or fentanyl.

#### *Management of Anesthesia and Postoperative Pain*

Premedication was omitted. A lumbar epidural catheter was inserted at the L2-L3 or L3-L4 interspace and was advanced 3 cm cephalad. Catheter placement was judged to be correct when the patient felt warm or lost the sensation to cold in both lower extremities after a 3-5 ml injection of 1.5% lidocaine with epinephrine.



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Anesthesia was induced with 3–5 mg/kg thiopental, and tracheal intubation was facilitated by administration of succinylcholine. Anesthesia was maintained with isoflurane and 50% nitrous oxide. No opiate was used during the operation. Muscle relaxation was achieved with vecuronium. Approximately 1 h before the completion of the operation, 2 ml of the study solution, either 2,000  $\mu$ g morphine (Duramorph; Elkins-Sinn, Cherry Hill, NJ) or 100  $\mu$ g fentanyl, were injected epidurally. The bolus injection was followed by epidural infusion at the rate of 2 ml/h of the solution, either 250  $\mu$ g/h morphine or 50  $\mu$ g/h fentanyl, using a Pain Management Provider (Abbott Laboratories, North Chicago, IL). Neuromuscular blockade was reversed, and the trachea was extubated at the end of operation.

Patients were asked on arrival to the postanesthesia care unit and every 10–15 min thereafter whether they needed pain medication until they were alert enough to use the PCA pump. Each affirmative response was followed by a 1-ml epidural injection of the study drug from the syringe prepared for bolus injection (1,000  $\mu$ g morphine or 50  $\mu$ g fentanyl) administered by the investigator who assessed the patient. The pump was set to deliver an epidural background infusion of 2 ml/h of the study solution and a 1-ml bolus of the same on demand with a lockout time of 15 min and a maximum dose of 30 ml in any 4-h period. Patients were instructed to maintain VAS pain score  $<30$  but  $>0$ . When the pain (score  $>30$ ) persisted, the infusion rate was increased by 50%. When the VAS score was 0, the infusion rate was reduced by 50% every 3 h. The PCA was discontinued 48 h after operation, and the catheter was removed. Patients received Vicodin (5 mg hydrocodone and 500 mg acetaminophen; Knoll Laboratories, Mount Olive, NJ) for pain.

Patients with a respiratory rate  $<10$ /min and a partial pressure of carbon dioxide in arterial blood approaching 50 mmHg were observed closely. Further increases in this parameter with progression of somnolence was considered respiratory failure and an indication for treatment with an intravenous infusion of 100–200  $\mu$ g/h naloxone. Nausea and pruritus were to be treated with naloxone only when the patient requested treatment and VAS scores were  $>80$ . Somnolence with VAS scores  $>80$  was to be followed closely for possible treatment with naloxone. Those who were treated were to be excluded from the study.

#### Data Analysis

Differences during epidural PCA between the groups and changes over time in the T scores for each mood

Table 1. Demographic Data

	Epidural Morphine (n = 23)	Epidural Fentanyl (n = 24)
Age (yr)	48.4 $\pm$ 16.0	51.7 $\pm$ 15.5
Weight (kg)	85.7 $\pm$ 15.8	89.5 $\pm$ 20.1
Height (cm)	170.0 $\pm$ 7.8	166.0 $\pm$ 13.5
Male/female	13/10	13/11
Replacement of hip/knee	14/9	13/11
Duration of anesthesia (h)	3.6 $\pm$ 1.2	4.0 $\pm$ 1.5

Values are mean  $\pm$  SD.

state and VAS scores for pain and for each side effect were tested by analysis of variance for repeated-measures design. These data were further tested for differences and changes, where appropriate, by Bonferroni simultaneous confidence intervals. Individual relations between mood scores and VAS scores for pain, nausea, pruritus, or somnolence and those between mood score and the sum of VAS scores for pain, nausea, pruritus, or somnolence were assessed using the Pearson correlation coefficient and linear regression analysis. A side effect was considered present when the VAS score was  $>30$ . The 72-h data were analyzed using unpaired Student's *t* tests.

## Results

The epidural space could not be identified in five patients because of severe arthritis and scoliosis of the lumbar vertebrae. There were no significant differences between the groups in sex distribution, age, weight, height, or the type of operation performed in the remaining 47 patients (table 1). Morphine consumption was  $4.2 \pm 3.3$  (SD) mg for bolus injection and  $22.6 \pm 5.3$  mg for the subsequent 48-h infusion. The first 24-h morphine consumption was  $16.9 \pm 6.6$  mg, and the second 24-h consumption was  $9.9 \pm 4.7$  mg. Fentanyl consumption was  $190 \pm 163$   $\mu$ g for bolus injection and  $4,282 \pm 748$   $\mu$ g for the 48-h infusion. The first 24-h fentanyl consumption was  $2,529 \pm 885$   $\mu$ g, and the second 24-h consumption was  $1,944 \pm 730$   $\mu$ g. No patient required naloxone treatment for side effects in this study.

Table 2 summarizes VAS scores for pain and side effects. There was no significant drug main effect in VAS pain score during epidural PCA. There were significant time main effects in VAS scores for side effects (somnolence,  $P < 0.001$ ; pruritus,  $P < 0.001$ ; nausea,  $P <$



**Table 2. VAS Scores for Pain Intensity at Rest, Somnolence, Pruritus, and Nausea during 48-h Epidural Morphine (n = 23) and Epidural Fentanyl (n = 24)**

			After Operation		
		Baseline	24 h	48 h	72 h*
Pain at rest	Morphine	16 ± 4	22 ± 3	20 ± 4	26 ± 4
	Fentanyl	24 ± 6	32 ± 3	28 ± 4	32 ± 4
Somnolence	Morphine	4 ± 1 (0)	44 ± 6 (14)	30 ± 5 (8)	17 ± 5 (3)
	Fentanyl	8 ± 4 (2)	50 ± 6 (17)	28 ± 5 (10)	29 ± 4 (8)
Pruritus	Morphine	0 (0)	35 ± 6 (9)	24 ± 5 (4)	3 ± 1 (0)
	Fentanyl	0 (0)	25 ± 5 (9)	15 ± 4 (4)	3 ± 1 (0)
Nausea	Morphine	0 (0)	7 ± 4 (2)	4 ± 3 (1)	3 ± 2 (0)
	Fentanyl	3 ± 3 (1)	11 ± 4 (2)	13 ± 5 (2)	16 ± 6† (5)

Data are mean ± SE. Values in parentheses are the number of patients with VAS scores above 30.

\* Twenty-four hours after cessation of epidural morphine or fentanyl.

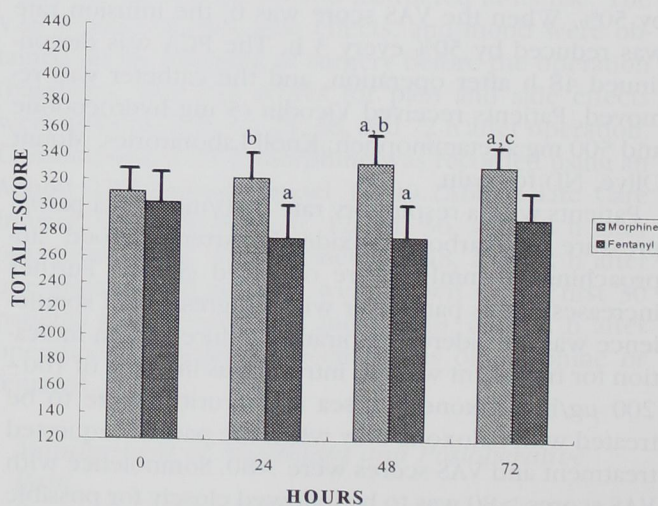
†  $P < 0.05$  versus the fentanyl group using Student's  $t$  test.

0.05), but there were no drug main effects in VAS scores for side effects. At the 72-h assessment (24 h after cessation of epidural PCA), the mean VAS nausea score in the fentanyl group was significantly higher than that in the morphine group ( $P < 0.05$  using Student's  $t$  test). There was no difference in respiratory rate between the groups (morphine group,  $17.6 \pm 2.7$  [SD] breath/min at 24 h and  $17.8 \pm 2.8$  breath/min at 48 h; fentanyl group,  $18.8 \pm 2.7$  breath/min at 24 h and  $18.6 \pm 2.4$  breath/min at 48 h). There were no differences in the incidence of side effects (VAS >30) between the groups.

There was a significant drug-time interaction in the analysis of total T scores ( $P < 0.004$ ). The mean total T score increased over time during the epidural morphine PCA ( $P < 0.01$  at 48 h), whereas the score decreased during the epidural fentanyl PCA ( $P < 0.01$  at 24 and 48 h, respectively; fig. 1). The mean scores were significantly higher in the morphine group than in the fentanyl group at 24 and 48 h ( $P < 0.05$ , respectively). At 72 h, the mean score was also higher in the morphine group ( $P < 0.01$ ).

Further analysis of six subsets of the bipolar form of the Profile of Mood States showed that the mean T score increased with the progression of time in the morphine group in three subsets of mood states (*i.e.*, composed-anxious, elated-depressed, and clearheaded-confused) during epidural PCA. The mean T score decreased in the fentanyl group in five subsets of mood states (*i.e.*, agreeable-hostile, elated-depressed, confident-unsure, energetic-tired, and clearheaded-confused). The mean T scores thus were significantly higher in the epidural morphine group than in the epi-

dural fentanyl group in five subsets of mood states (*i.e.*, composed-anxious, elated-depressed, confident-unsure, energetic-tired, and clearheaded-confused) during the 48-h period of epidural PCA ( $P < 0.05$ , respectively). At the 72-h measurement (24 h after cessation of PCA), the mood scores were significantly higher in patients who received epidural morphine than in those in the fentanyl group in four subsets of mood states (*i.e.*, agreeable-hostile, elated-depressed, confident-unsure, and clearheaded-confused) ( $P < 0.05$ , respectively; table 3).



**Fig. 1.** Total T scores (means with 95% confidence limits; range, 121–438) during 48-h epidural morphine (n = 23) and epidural fentanyl (n = 24). (A)  $P < 0.01$  compared with baseline values. (B)  $P < 0.05$  compared with the fentanyl group. (C)  $P < 0.01$  compared with the fentanyl group 24 h after cessation of epidural patient-controlled analgesia (Student's  $t$  test).



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**Table 3. T Scores for Bipolar Profile of Mood States during 48-h Epidural Morphine (n = 23) and Epidural Fentanyl (n = 24)**

		After Operation			
		Baseline	24 h	48 h	72 h*
Composed-anxious	Morphine	49.4 ± 1.7	55.7 ± 1.7†	55.4 ± 2.2†	57.8 ± 2.0
	Fentanyl	47.0 ± 2.0	48.0 ± 2.8	47.9 ± 2.5	52.4 ± 2.5
Agreeable-hostile	Morphine	56.0 ± 1.7	56.6 ± 2.3	58.6 ± 2.4	60.0 ± 2.2‡
	Fentanyl	53.3 ± 2.6	51.7 ± 3.3	49.3 ± 2.6	51.1 ± 2.8
Elated-depressed	Morphine	51.3 ± 1.5	54.6 ± 2.3†	55.3 ± 2.4†	55.6 ± 2.0§
	Fentanyl	50.4 ± 2.8	45.7 ± 3.0	44.9 ± 2.2	46.5 ± 2.2
Confident-unsure	Morphine	51.0 ± 1.9	50.7 ± 1.9†	54.5 ± 2.2†	52.6 ± 1.8‡
	Fentanyl	49.0 ± 2.2	43.3 ± 2.8	45.3 ± 2.1	46.2 ± 2.3
Energetic-tired	Morphine	50.7 ± 1.7	48.8 ± 1.8†	50.2 ± 1.7†	48.0 ± 1.5
	Fentanyl	47.2 ± 2.0	41.0 ± 2.1	41.5 ± 1.7	44.3 ± 1.7
Clearheaded-confused	Morphine	52.6 ± 2.3	54.3 ± 1.7†	57.0 ± 1.9†	57.6 ± 1.2‡
	Fentanyl	54.5 ± 1.8	47.5 ± 3.2	48.3 ± 2.7	50.8 ± 2.3

\* Twenty-four hours after cessation of epidural morphine or fentanyl.

†  $P < 0.05$  versus the fentanyl group.‡  $P < 0.05$ , §  $P < 0.01$  versus the fentanyl group using Student's *t* test.

There was no correlation between T scores and VAS pain scores at any time period in either group during the 72-h study period (table 4). There were some sporadic inverse correlations during epidural morphine PCA between the total T scores and VAS scores for somnolence, pruritus, and the sums of unpleasant experiences; that is, VAS scores of pain and all side effects. There were no correlations in the fentanyl group between total T scores and any of the side effects, or the sum of unpleasant experiences during epidural fentanyl

PCA. At 72 h, however, there were some inverse correlations in the fentanyl group between the total T scores and VAS scores for somnolence and the sums of VAS scores for unpleasant experiences.

Plasma concentrations of morphine (n = 16) were  $3.1 \pm 1.5$  ng/ml,  $1.8 \pm 1.5$  ng/ml, and  $1.8 \pm 1.5$  ng/ml, 24 h, 48 h, and 72 h after operation, respectively. Plasma concentrations of fentanyl were  $1.5 \pm 0.7$  ng/ml,  $1.8 \pm 0.8$  ng/ml, and  $0.2 \pm 0.1$  ng/ml, 24 h, 48 h, and 72 h after operation, respectively. There was an inverse correlation between total T scores and plasma concentrations of fentanyl at 48 h ( $r = -0.58$ ,  $n = 14$ ;  $P < 0.05$ ; fig. 2). There was no correlation between total T scores and plasma concentrations of morphine.

Hypotension developed in two small, elderly women approximately 15 min after the initial bolus epidural injections of fentanyl. The background infusion of fentanyl was discontinued. The hypotension lasted 3–4 h and responded to infusion of epinephrine but not to ephedrine or phenylephrine. The patients did not report pain in the recovery room. The subsequent hospital course was uncomplicated in both patients. Bowel sounds were present in all patients by the first postoperative day. Hallucinations were not observed in this study. Most patients walked on the first postoperative day, and all did so by the second postoperative day.

## Discussion

Injections in humans of therapeutic doses of  $\mu$  receptor agonists (*i.e.*, morphine, heroine, codeine, and dipi-

**Table 4. Correlations (r) of Mood State (Total T Score) to Pain at Rest and Side Effects (VAS Score) during 48-h Epidural Morphine (n = 23) and Epidural Fentanyl (n = 24)**

		After Operation		
		24 h	48 h	72 h*
Morphine	Pain at rest	-0.45	-0.11	-0.10
	Somnolence	-0.51†	-0.23	-0.01
	Pruritus	-0.28	-0.51†	-0.14
	Nausea	-0.28	+0.03	+0.15
	Total VAS score	-0.50†	-0.38	-0.07
Fentanyl	Pain at rest	-0.30	+0.12	-0.22
	Somnolence	-0.25	-0.31	-0.49‡
	Pruritus	-0.11	+0.11	-0.16
	Nausea	-0.41	-0.35	-0.34
	Total VAS score	-0.37	-0.22	-0.53‡

\* Twenty-four hours after cessation of epidural morphine or fentanyl.

†  $P < 0.02$ .‡  $P < 0.05$ .



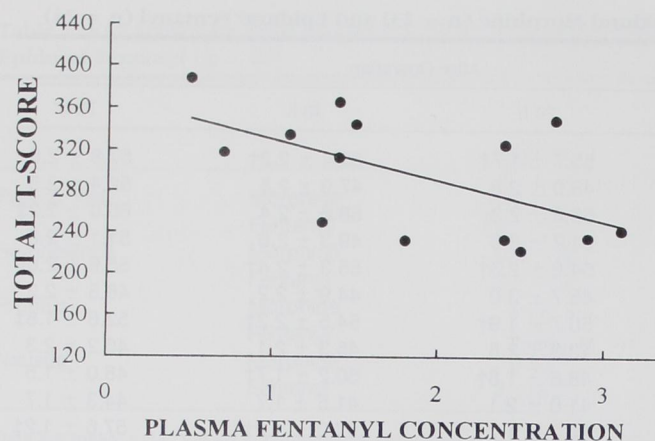


Fig. 2. Relations of total T scores to plasma fentanyl concentrations (nanograms per milliliter) at 48 h (total T =  $-40.2 \times [\text{plasma fentanyl concentration}] + 369.5$ ;  $r = -0.58$ ;  $n = 16$ ;  $P < 0.05$ ).

panone) have been reported in earlier studies<sup>12-15</sup> to induce negative or aversive subjective effects, such as muzziness, confusion, sedation, and mental slowness. More recently, studies of the subjective effects of intravenously injected fentanyl in the dose range of 100–250  $\mu\text{g}$  have reported divergent results in humans.<sup>16-20</sup> The studies, in which subjective effects were measured within 15 min of the injection, generally had positive results,<sup>16-18</sup> but those in which measurements were made 30 min after the injection had negative results.<sup>19,20</sup> Subsequently, Zacney *et al.*<sup>21</sup> found an early and transient euphoric effect after a bolus intravenous injection of fentanyl that was followed by negative feelings in 7 of 13 persons they studied, suggesting that low plasma concentration of fentanyl may be associated with negative emotional states. Vasselis *et al.*<sup>22</sup> showed further in volunteers that impairment of memory, impairment of psychomotor function, and an increase in negative feelings may be dose related at low plasma fentanyl concentrations such as 1, 1.5, and 2.5 ng/ml.

In our patients, the mean mood scores decreased significantly during epidural fentanyl PCA. Plasma fentanyl concentrations were 1.2 and 1.8 ng/ml at 24-h and 48-h assessments of mood state, which were within the range of fentanyl concentrations previously reported<sup>23-26</sup> during continuous epidural infusion or epidural PCA. The rapid decline in CSF fentanyl concentration and the increase in plasma fentanyl concentration suggest that the concentration of fentanyl in the brain during epidural fentanyl PCA may correlate with the plasma concentration to a large extent. Although there were

no significant differences in pain scores between the groups, the mean pain scores during epidural fentanyl PCA were higher than those during epidural morphine PCA, raising the possibility that mood may have been inversely affected by pain intensity. Pain, however, was generally mild in both groups, with mean scores approximately 30 or less, during epidural PCA, and all patients rated their pain relief as satisfactory. Further, there was no correlation in our patients between mood states and pain or other side effects during epidural fentanyl PCA, suggesting that the observed decrease in mood scores may have been independent of pain or other unpleasant experiences. As previously reported,<sup>22</sup> there also was some inverse correlation between mood scores and plasma fentanyl concentrations in our patients. Thus the subjective effects that we observed in our patients appear to be consistent with those demonstrated in the lower range of plasma concentrations often found during intravenous fentanyl used for post-operative pain relief.

The mood scores of our patients increased during epidural morphine PCA, and the scores were significantly higher at 48-h assessments than before the operation. Nordberg *et al.*<sup>1</sup> showed that CSF morphine attains concentrations in the range of 300–1,000 ng/ml or more within 1 h after epidural injection of 2–6 mg morphine, and that the extrapolated mean CSF concentration 24 h after a bolus epidural injection was approximately 16 ng/ml, the minimum effective analgesic plasma morphine concentration previously measured<sup>26</sup> after abdominal surgery. Thus the CSF morphine concentrations during epidural morphine PCA may be expected to far exceed those during intravenous morphine PCA. Plasma concentrations of morphine were low in our patients, ranging from 1.8–3.1 ng/ml during epidural PCA yet providing adequate pain relief. There was no correlation between mood scores and plasma morphine concentrations. Although the mean pain scores were lower during epidural morphine than epidural fentanyl PCA, again there was no correlation between mood scores and pain scores. The CSF pharmacokinetic behavior of epidural morphine and the conflicting but generally negative observations of the changes in mood state after parenteral intake of opiates in humans appear to support the possibility that the positive changes in mood states observed in our patients may have been related to the higher morphine concentrations that were maintained in the CSF during epidural morphine than during parenteral use of morphine.

Our results suggest that mood states may be more



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positive during epidural morphine PCA and more negative during epidural fentanyl PCA than they are before operation and that mood states are more positive during epidural morphine PCA than they are during epidural fentanyl PCA. The mood changes that we observed in our patients may be explained by the differences in lipid solubility and pharmacokinetic behavior in the CSF of epidurally injected morphine and fentanyl.

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