# Epidural meperidine analgesia after cardiac surgery

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*Epidural meperidine (1 mg·kg$^{-1}$) was administered for relief of sternal pain to ten patients, at a mean of 24.8 hours after infusion of high dose fentanyl for cardiac surgery.*

*Lung function, cough, pain score, somnolence, respiratory rate, $PaCO_2$, pulse and blood pressure were studied before and for six hours after analgesic administration. Following epidural meperidine, four of ten patients were pain-free, and three had only minimal pain. Duration of analgesia was 8.8 ± 4.9 hours. Cough score was significantly improved for five hours. Postoperatively vital capacity was approximately 40 per cent, and $FEV_1$ was approximately 55 per cent of the preoperative value. There was no significant change in $FEV_1$ or vital capacity, following analgesia with epidural meperidine.*

*The somnolence score increased in seven patients. In the first two hours after epidural meperidine, three patients exhibited a fall in their respiratory rate, one had a $PaCO_2$ greater than 45, and two of these patients had marked hypotension. These side effects are easily treated without mechanical or pharmacological support, and do not preclude the use of epidural meperidine after a high dose fentanyl anaesthetic.*

**Key words**
ANAESTHETIC TECHNIQUES: epidural, epidural narcotics; ANALGESICS: meperidine; PULMONARY FUNCTION: postoperative.

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A Professor of obstetrics, recovering from open heart surgery writes: As expected I came to my senses briefly in the Intensive Care Unit. I noted that it was already dark, and my wife and daughter were standing on my left side gripping my wrist, and my wife feverently repeating, "Darling, we have got you back." Somewhere there was **the most almighty pain**, and evidently I had not registered the anaesthetist's customary remark that it was "all over."[1]

It is our clinical experience that such "almighty" pain is not always registered, and that sternal incisional pain is often well tolerated by patients after cardiac surgery. Parenteral analgesics are, however, ineffective in some patients who, despite repeated doses of narcotic analgesic, show an unwillingness to cough or breath deeply.

After cardiopulmonary bypass, patients have an approximate halfing of preoperative lung volumes.[2] Pulmonary function postoperatively has been shown to correlate with the number of pulmonary complications, and the need for artificial ventilation.[3] Those patients in severe pain may have more pulmonary complications if they are unable to cough effectively after cardiac surgery.

In our surgical intensive care unit, lumbar epidural meperidine has proven very effective for the relief of incisional and traumatic thoracic pain. Epidural meperidine has been shown to provide good postoperative analgesia following Caesarian section and laparotomy.[4] Intrathecal morphine has been used during cardiac surgery,[5] but there are no reports in the literature reviewing the use of epidural meperidine after open heart surgery.

We studied changes in lung function, cough, quality and duration of analgesia after administration of epidural meperidine, following cardiac surgery. We investigated the potential for increased respiratory depression and somnolence, following its use after high dose fentanyl anaesthesia, and recorded any cimplications.

## Methods

Following institutional approval, informed consent was obtained preoperatively from 21 consecutive patients scheduled for aorto-coronary bypass surgery. Five of these patients were subsequently excluded from the study because of either previous spinal surgery, a low postoperative platelet count (<100,000), confusion, early discharge from the intensive care unit, or absence of postoperative pain. Six patients withdrew their consent postoperatively because of the low level of pain they experienced. Ten patients completed the study.

Preoperatively, with the patient in a 90-degree sitting position, vital capacity, and $FEV_1$, were measured, as the best of three traces recorded on the same spirometer. All patients were premedicated with intramuscular morphine 0.15 $mg \cdot kg^{-1}$ and hyoscine 0.3 mg to 0.6 mg, one hour prior to insertion of intravenous, arterial and Swan-Ganz catheters.

In all patients, anaesthesia was induced with intravenous lorazepam 50 $\mu g \cdot kg^{-1}$, fentanyl 50 $\mu g \cdot kg^{-1}$ given by infusion, and pancuronium 0.15 $mg \cdot kg^{-1}$. Patients were ventilated with 100 per cent oxygen; 5 cm $H_2O$ of positive expiratory pressure was applied to the lungs during bypass, and isoflurane was given as needed to control hypertension during disection of the aortic root, and in the post bypass period.

Postoperatively patients were ventilated in the Surgical Intensive Care Unit ($V_t$ 12 $ml \cdot kg^{-1}$, IMV 10/minute, 5 cm $H_2O$ PEEP, $FiO_2$ 0.40–0.50), and sedated with morphine as necessary. Patients were weaned from the respirator overnight, and extubated the following morning. Prothrombin time, partial thromboplastin time and platelet counts were measured. Any patient exhibiting abnormal values was excluded from the study. None of the patients required or received inotropes during the study period.

One half to one hour following extubation, a catheter was inserted into the $L_{2-3}$ or $L_{3-4}$ epidural space of each patient.

*When a patient complained of pain*

1 $FEV_1$ and vital capacity were measured using the best of three traces, recorded on the same spirometer and with the patient in the same 90 degree sitting position as used for the measurements preoperatively.

TABLE I Somnolence score

| |
|---|
| 1 Wide awake. |
| 2 Sleeping: awakes with command. |
| 3 Sleeping: awakes with shaking, then responds to commands. |
| 4 Aroused by shaking but then will not respond to commands. |
| 5 Unrouseable. |

2 The patient was asked to score his pain on a scale of 0 (no pain on maximal inspiration) to 5 (the worse pain he had ever felt).

3 Cough was assessed subjectively by agreement of the same two observers using a cough score 1–3 (poor-moderate-good). A cough score of 3 signified that the patient could inspire deeply and produce a loud, forceful cough. A cough score of 1 meant that the patient could only inspire minimally, and expiratory effort produced only a weak, feeble sounding cough.

4 Level of consciousness was assessed by the same two observers, using a somnolence scale (Table I).

5 Resting respiratory rate was recorded.

6 $PaCO_2$ was measured from an arterial line sample while the patient was resting quietly.

7 Pulse rate and blood pressure were recorded.

Twenty to 25 ml of a solution of preservative free meperidine 1 $mg \cdot kg^{-1}$, without epinephrine, diluted in normal saline, was given by slow injection into the epidural cannula over a five-minute period. Vital capacity and $FEV_1$ were measured half an hour after analgesia was given. The above variables (2–7) were measured half an hour after administration of meperidine, then hourly for six hours. The duration of analgesia was determined by the patient's nurse who noted the time of the patient's next request for analgesia, or complaint of pain. The patient was not instructed to tell his nurse when he had pain. The nurse either waited for him to spontaneously complain, or if the patient was looking distressed, she was allowed to ask him if he was in pain.

Non-parametric data (pain, cough, somnolence) were analysed using a directional Wilcoxon signed rank test. Significance was tested on the $T^+$ value and the number of subjects whose scores changed. Parametric data were analysed using a non-directional paired t-test. Differences in both parametric and non-parametric data were accepted as significant if p was $< 0.05$.

TABLE II Mean scores/values following epidural meperidine administration (± SD)

| *Time* | *Pain score (0–5)* | *Cough score (1–3)* | *Somnolence score (1–5)* | *$PaCO_2$* | *Respiratory rate* |
|---|---|---|---|---|---|
| Pre-analgesia | 3.9 ± 1.1 | 1.7 ± 0.6 | 1.2 ± 0.2 | 38 ± 3 | 20 ± 3 |
| Hours post epidural | | | | | |
| 0.5 | 1.0 ± 1.1* | 2.4 ± 0.8† | 1.7 ± 0.3 | 39 ± 3 | 18 ± 3 |
| 1 | 0.9 ± 0.6* | 2.5 ± 0.7† | 1.9 ± 0.4 | 39 ± 5 | 19 ± 3 |
| 2 | 1.3 ± 1.0* | 2.3 ± 0.8† | 1.4 ± 0.2 | 40 ± 4 | 19 ± 4 |
| 3 | 1.6 ± 1.1* | 2.2 ± 0.4† | 1.1 ± 0.1 | 38 ± 5 | 18 ± 3 |
| 4 | 2.0 ± 1.5† | 2.2 ± 0.7† | 1.0 ± 0.0 | 38 ± 4 | 19 ± 3 |
| 5 | 1.6 ± 1.1† | 1.9 ± 0.8 | 1.1 ± 0.1 | 37 ± 5 | 20 ± 3 |
| 6 | 2.2 ± 1.0† | 1.5 ± 0.5 | 1.1 ± 0.1 | 38 ± 4 | 20 ± 3 |

*Statistically significant compared to pre-analgesic value $p < 0.01$.
†Statistically significant compared to pre-analgesic value $p < 0.05$.

## Results

Epidural analgesia was administered to ten patients, nine males and one female. All patients were in low or moderate risk groups as determined by the scoring system used in our institution.[6] Results are expressed as mean values ± SD. The mean age of the patients was 58.4 ± 8.8 years. Epidural meperidine was given a mean of 24.8 ± 7.5 hours after an induction dose of 50 $\mu g \cdot kg^{-1}$ of fentanyl.

### *Pain score*

Mean pain scores are listed in Table II. The pre-analgesic pain score was 3.9 ± 1.0. Following epidural meperidine administration, maximal pain relief occured at one-half and one hour, with a reduction in pain score to 1.0 ± 1.1 and 0.9 ± 0.6 respectively. Pain scores were significantly reduced for six hours. One patient became too somnolent at one hour to grade his own pain. His pain scores were, therefore, excluded from the statistical analysis.

Four patients, who graded their pain at 3, 3, 4, and 5 prior to analgesic administration, had complete pain relief (no pain on maximal inspiration) half an hour after epidural meperidine. Three patients had pain scores of 1, thirty minutes after epidural meperidine (pre-analgesic pain scores were 4, 3 and 4). The duration of analgesia was 8.8 ± 4.9 hours.

### *Cough score*

Mean cough scores are listed in Table II. Maximum improvement in cough score (from 1.7 pre-analgesia to 2.5) occurred at one hour. There was a statistically significant improvement in the cough score for five hours, following administration of epidural meperidine.

### *Lung volumes*

The values for the ten patients are shown in Table III. There was no significant improvement in $FEV_1$ or vital capacity following analgesia with epidural meperidine.

Postoperatively, before and after epidural meperidine, there was a significant improvement in the $FEV_1/VC$ ratio, compared to the preoperative value.

None of the patients had a preoperative history of chronic lung disease; however, six had preoperative $FEV_1/VC$ ratios less than .70 and seven patients had a history of cigarette smoking.

### *Somnolence*

Somnolence scores are shown in Table II. Although there were no significant increases in mean somnolence scores after epidural meperidine, three patients exhibited somnolence scores of 3, 3 and 4 in the first hour after epidural meperidine: the patient

TABLE III Mean lung volumes (± SD) before and one half an hour after administration of epidural meperidine. n = 10.

| | *$FEV_1$** | *VC** | *$FEV_1/VC$ %* |
|---|---|---|---|
| Pre-op | 100 | 100 | 57.2 ± 18.1 |
| Pre-epidural | 57.7 ± 32.0 | 42.2 ± 14.3 | 72.6 ± 14.6† |
| Post-epidural | 55.3 ± 22.2 | 43.8 ± 16.6 | 72.0 ± 11.7† |

*Percentage of pre-operative value.
†Statistically significant compared to pre-operative value ($p < 0.01$).

with a score of 4 had a pre-analgesic somnolence score of 3. Medical intervention was not needed and all three patients could be awakened by physical shaking.

*Resting respiratory rate and $PaCO_2$ (Table II)*
There was no significant decrease in mean resting respiratory rate in the six hours after epidural meperidine. The three patients mentioned above exhibiting increased somnolence, also had a fall in their respiratory rates one-half to one hour after epidural meperidine (from 20 to 14, from 20 to 16 and from 18 to 16). One hour after epidural meperidine only two of the ten patients had resting respiratory rates less than 20 (16 and 18). At three hours, three patients had respiratory rates of 16, 16 and 18, and at three hours, three patients had resting respiratory rates of 16.

There was no significant change in mean $PaCO_2$ following epidural meperidine. Two patients had resting $PaCO_2$ greater than 45 after epidural meperidine. One patient had $PaCO_2$ values of 48, 46, 47 at one-half, one and two hours respectivley, and one patient had a $PaCO_2$ of 46 at four hours.

*Heart rate and mean arterial blood pressure*
There were no statistically significant changes in heart rate at any sampling period after epidural meperidine administration. Mean arterial blood pressure showed a statistically significant fall from $92 \pm 29$ to $79 \pm 23$, to $79 \pm 19$, and to $80 \pm 12$ at half, one and two hours respectively.

Two patients who exhibited somnolence and mild respiratory depression as described above, showed a marked fall in blood pressure from 130/60 to 84/42 and from 140/90 to 85/60 within fifteen minutes of injection of epidural meperidine. In both patients pulmonary capillary wedge pressures before meperidine (9, 12 mmHg) were low compared to preoperative values (17, 16 mmHg). With the onset of hypotension, wedge pressures were unchanged (11 and 12 mmHg).

Hypotension was well tolerated (no chest pain or arrythmias). Blood pressure rose when the two patients were physically disturbed, and hypotension was corrected by infusion of crystaloid. Six patients studied later were pre-hydrated to their normal wedge pressures prior to epidural meperidine administration, and marked hypotension was not observed.

*Other complications*
Nausea and vomiting occurred in two patients within 15 minutes of epidural meperidine, lasted less than one hour, and was effectivley treated with intravenous dimenhydrate: one of these patients was nauseated prior to the epidural. None of the patients complained of itching.

## Discussion

When injected into the epidural space, meperidine is rapidly absorbed into the CSF. CSF levels are maximal after 15 minutes and coincide with the early onset of analgesia.[7] Blood concentrations after administration of 100 mg can reach the range $0.2–0.7\ \mu g \cdot ml^{-1}$ within twenty minutes, levels which are associated with analgesia after intravenous administration.[8] Doses of 30 mg, providing good analgesia, result in much lower non-analgesic blood levels.[7] Meperidine is rapidly cleared from the plasma, and at two hours serum meperidine is approximately one third of peak concentrations after administration.[7]

Seven of ten patients in our study had complete analgesia or minimal pain after administration of epidural meperidine; its effectiveness in relieving pain is probably a reflection of its good lipid solubility. Mean duration of analgesia (8.8 hours) was slightly longer than that reported by others,[8,9] and was longer than the duration of pain relief when used after flail chest injury in our institution (effective for three to four hours).

Relief of pain resulted in a statistically significant improvement in cough score. There was a wide variation in the standard deviation of the cough scores. This may reflect the subjective nature of the test, or may reflect the inconsistency of improvement of cough, after analgesia for sternal pain.

A more objective evaluation of maximal expiratory effort was reflected by the $FEV_1$, before and after the administration of analgesic. There was no improvement in $FEV_1$ after pain relief with epidural meperidine. This contrasts with the use of epidural narcotic analgesia, to improve the $FEV_1$ after abdominal and thoracic surgery.

Bromage *et al.* showed that following upper abdominal surgery, there were 67 and 45 per cent increases in $FEV_1$ with the use of epidural morphine and intravenous morphine respectively.[10] Shulman *et al.* showed significant improvement in $FEV_1$ in patients post-thoracotomy, after epidural mor-

phine.[11] A painful abdominal wound may be expected to reduce cough and $FEV_1$ significantly, as contraction of the abdominal muscles is needed to generate a maximal expiratory effort. Thoracotomy pain may be expected to limit $FEV_1$ and cough, by splinting the lateral bucket handle excursion of the chest cage, preventing maximal inspiration prior to a forced expiration. On the other hand the sternum moves little, even during maximal respiration. Relief of sternal pain should not be expected to result in much improvement of forced expiration, when a patient is encouraged to inspire maximally and cough.

Vital capacity was reduced to approximately 40 per cent and $FEV_1$ to approximately 55 per cent of preoperative levels, results which correlate well with results of other studies.[2] The greater reduction in the vital capacity compared to the $FEV_1$ probably is a reflection of the restrictive change in pulmonary function that occurs after cardiopulmonary bypass.

In our study, somnolence in three patients, nausea in two patients and mild respiratory depression in three patients occurred within the first two hours following epidural meperidine, and may have resulted from systemic absorption of the drug. We were especially interested in observing patients for central side effects, as our patients had received a high-dose fentanyl anaesthetic a mean of 24.8 hours prior to epidural meperidine.

This is the first study reporting the use of epidural meperidine after high-dose fentanyl anaesthesia. Fentanyl is rapidly absorbed into the CSF; concentrations attain 46 per cent of plasma levels, after intravenous injection.[12] There is a close correlation between the concentration of fentanyl in plasma and CSF, and intense respiratory depression.[12] Boyik and Steel[13] showed in five patients with a mean age of 65 years, that there was a mean blood fentanyl concentration greater than 1 $\mu g \cdot ml^{-1}$, 14 hours after injection of 60 $\mu g \cdot kg^{-1}$ for cardiac surgery. Two patients had fentanyl concentrations greater than 1 $\mu g \cdot ml^{-1}$ at 24 hours. A concentration of 1 $\mu g \cdot ml^{-1}$ has been suggested at the threshold for respiratory depression in dogs anaesthetized with enflurane,[14] the potential for respiratory depression and somnolence therefore exists, if epidural narcotic analgesics are given within 24 hours of cardiac surgery.

A decrease in mean arterial blood pressure in the first two hours after epidural meperidine administration, was most marked in two patients who were unintentionally given epidural meperidine while they were hypovolemic. The hypotension probably reflected a reduction of sympathetic tone with relief of pain, and sedation. Further studies are needed on the cardiovascular effects of epidural meperidine.

It has been shown that meperidine in equianalgesic doses is 100–200 times more potent a depressant of isolated ventricular myocardium than morphine.[15] There was no increase in pulmonary wedge pressures in the two patients exhibiting marked hypotension, and myocardial depression is therefore unlikely to be the cause. A central cause of hypotension may exist, as there are opiate receptors in the central cardiovascular control centres. Injection of beta endorphin into the brain ventricular system in animals has been shown to result in hypotension.[16]

In conclusion, epidural meperidine provides effective and consistent analgesia in patients who are distressed by sternal pain following cardiac surgery. There is an improvement in cough, but no immediate improvement in the $FEV_1$ or vital capacity after epipdural meperidine analgesia. Despite prior use of a high dose fentanyl anaesthetic, somnolence and respiratory depression when noted, were easily managed without therapeutic intervention. Patients who are hypovolemic should not recieve epidural meperidine as marked hypotension may occur.

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## Résumé

*De la mépéridine en injection épidurale (1 mg·kg$^{-1}$) a été administrée afin de soulager la douleur sternale chez dix patients après 24.8 heures en moyenne d'une perfusion de hautes doses de fentanyl pour chirurgie cardiaque.*

*Avant l'administration de mépéridine et pour six heures après administration de l'analgésique, la fonction pulmonaire, la toux, le degré de douleur, la somnolence, la fréquence respiratoire, la $PaCO_2$, le pouls et la tension artérielle ont été étudiés. Suite à l'administration épidurale de morphine, quatre des dix patients étaient libres de toute douleur et trois patients ont accusé une douleur minime. La durée de l'analgésie était de 8.8 ± 4.9 heures. Le degré de toux a été significativement atténué pour cinq heures. La capacité vitale post-opératoire était approximativement de 40 pour cent et la $FEV_1$ était approximativement de 55 pour cent de la valeur préopératoire. Il n'y avait aucun changement significatif dans la $FEV_1$ ou la capacité vitale après analgésie avec la mépéridine épidurale.*

*Le degré de somnolence a augmenté chez sept patients. Dans les deux premières heures après injection de mépéridine épidurale, trois patients ont démontré une diminution de leur fréquence respiratoire, un seul avait une $PaCO_2$ supérieure à 45 mmHg et deux de ceux-là ont démontré une hypotension marquée. Ces effets sont facilement traités sans support mécanique ou pharmacologique et n'empêchent pas l'utilisation de la mépéridine en injection épidurale après une anesthésie à haute dose de fentanyl.*