Comparison of epidural and patient-controlled intravenous morphine following joint replacement surgery

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The authors conducted a randomized, prospective study comparing epidural morphine with patient-controlled intravenous (iv) morphine in 30 patients recovering from total hip or total knee arthroplasty. Six, 18, and 24 hr postoperatively, patients used a 10 cm visual-analogue scale to indicate both their current degree of discomfort and the maximum discomfort they had experienced since the previous evaluation. Pain at the time of evaluation did not differ between patients receiving epidural (2.6 ± 0.4 cm, mean $\pm$ SEM) and patient-controlled iv morphine (3.4 ± 0.3 cm). However, patients who received epidural morphine recalled less pain during the period preceding evaluation (4.2 ± 0.5 cm) than did those receiving patient-controlled analgesia (5.5 ± 0.4 cm, $P < 0.05$). Patients receiving epidural morphine were more likely to require treatment for pruritus (4 of 15) than patients who received patient-controlled iv morphine (none of 15, $P < 0.05$). Minimum respiratory rates were lower in patients receiving epidural morphine (15.0 ± 0.3) than in those receiving patient-controlled analgesia (16.5 ± 0.4 , $P < 0.05$), but no patients required treatment for respiratory depression. The authors conclude that epidural morphine may provide more consistent analgesia following joint replacement surgery than patient-controlled morphine; however, there is a higher incidence of side-effects with the epidural technique.

Les auteurs ont procédé à une étude prospective, randomisée, comparant la morphine épidurale avec l'administration intra-

veineuse (iv) de morphine contrôlée par le patient, chez 30 patients ayant subi une arthroplastie totale de la hanche ou du genoux. Les patients ont utilisé une échelle visuelle analogue de 10 cm à 6, 18 et 24 heures dans la période postopératoire pour indiquer le degré d'inconfort à ce moment et le degré d'inconfort maximal ressenti depuis l'évaluation précédente. La douleur, au moment de l'évaluation, n'était pas différente chez les patients sous morphine épidurale ($2,6 \pm 0,4$ cm, moyenne $\pm$ ET) comparativement à la morphine IV sous le contrôle du patient ($3,4 \pm 0,3$ cm). Cependant, les patients qui recevaient de la morphine épidurale étaient moins souffrants dans la période précédant l'évaluation ($4,2 \pm 0,5$ cm) que ceux qui recevaient de l'analgésie contrôlée par le patient ($5,5 \pm 0,4$ cm, $P < 0,05$). Quatre des 15 patients recevant de la morphine épidurale ont été traités pour un prurit, comparativement à aucun des 15 patients recevant de la morphine iv sous contrôle du patient ($P < 0,05$). Le rythme respiratoire minimum était plus lent chez les patients recevant de la morphine épidurale ($15,0 \pm 0,3$) que chez ceux recevant de l'analgésie contrôlée par le patient ($16,5 \pm 0,4$, $P < 0,05$), mais aucun patient n'a dû être traité pour dépression respiratoire. Les auteurs concluent que la morphine épidurale pourrait procurer une analgésie plus consistante que la morphine iv sous contrôle du patient suite à une chirurgie pour remplacement articulaire; cependant, il y a une incidence plus élevée d'effets secondaires avec la technique épidurale.

Key words

ANALGESIA: postoperative, epidural, PCA;
ANALGESICS: morphine;
ANAESTHETIC TECHNIQUES: epidural.

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Both epidural^{1,2} and patient-controlled iv narcotics^{3,4} provide better postoperative analgesia than on-demand intramuscular (im) narcotics. However, it has yet to be established which of these treatments is better suited to patients undergoing major orthopaedic surgery. The present randomized, prospective study was designed to compare the efficacy and side-effects of these two analgesic modalities following lower extremity joint replacement.

Methods

Thirty patients, ranging in age from 34 to 78 yr, scheduled to receive total hip or knee replacements with epidural anaesthesia consented to participate in this

Institutional Review Board (IRB)-approved study. On the day before surgery, each patient learned to use the patient-controlled analgesia pump and the visual-analogue pain scale⁵ (VAS). Although all patients were to receive epidural anaesthesia, they had the option of being awake (*iv* sedation) or asleep (general endotracheal anaesthesia) during surgery.

On the day of surgery, a lumbar epidural catheter was inserted and fractional doses of bupivacaine (0.5% or 0.75%) were administered for surgical anaesthesia. Most patients received an epidural test dose containing lidocaine with epinephrine prior to the bupivacaine. Once adequate epidural blockade was evident, patients received either *iv* sedation or supplemental general anaesthesia, as chosen the previous day. During surgery, patients received *iv* fentanyl as clinically indicated. One hour before the anticipated end of surgery, the patients were randomly assigned to receive either epidural morphine or patient-controlled *iv* morphine for postoperative analgesia. By delaying randomization until this time, the likelihood that intraoperative anaesthetic management would be modified based on the assigned method of postoperative analgesia was minimized (*vide infra*).

Immediately after randomization, patients in the epidural morphine group received 3 ml of 0.1% morphine followed by 2 ml of preservative-free saline via the epidural catheter. If they developed severe pain in the recovery room (VAS score >7) these patients received an additional 2 ml of 0.1% morphine via the epidural catheter. Twelve hours later, each patient received another dose of epidural morphine equal to the total dose which previously had been necessary to control his pain (either 3 or 5 mg).

Patient-controlled analgesia began in the recovery room; when patients assigned to this treatment complained of pain, they received *iv* morphine (2 mg every five minutes) until the pain was controlled (VAS ≤ 4). Following this "loading dose," we initiated patient-controlled morphine administration. Patients were able to self-administer 1.0 to 1.5 mg of morphine ($\approx 20 \mu\text{g} \cdot \text{kg}^{-1}$) as often as every ten minutes.

On return to the surgical ward, patients received no supplemental narcotics or sedatives. If patient-controlled or epidural morphine failed to provide adequate analgesia (VAS >7), or intolerable side-effects developed, the circumstances were recorded and appropriate treatment was administered. Data for these patients were analyzed until the time when such treatment was necessary. In addition to routine postoperative care, surgical nurses recorded patients' respiratory rates each hour. Beginning in the recovery room, patients undergoing total knee replacement received continuous passive motion (CPM) of the knee for at least 24 hr.

We evaluated patients 6, 18, and 24 hr after the end of

TABLE I Patient characteristics and intraoperative management (values for continuous variables are means $\pm$ SEM)

	Epidural morphine (n = 15)	Patient-controlled <i>iv</i> morphine (n = 15)
Age (yr)	66 $\pm$ 3	63 $\pm$ 3
Number of males	6	7
Total knee replacement	6	7
Supplemental general anaesthesia	11	5
Duration of surgery (hr)	4.7 $\pm$ 0.5	3.8 $\pm$ 0.2
Intraoperative fentanyl ($\mu\text{g} \cdot \text{hr}^{-1}$)	43 $\pm$ 1	42 $\pm$ 1
Loading dose of morphine (mg)	3.5 $\pm$ 0.2	8.3 $\pm$ 1.8*
Total 24 hr morphine dose (mg)	6.5 $\pm$ 0.5	50.5 $\pm$ 12.1*

* $P < 0.05$ compared with epidural morphine group.

surgery. From the nursing record, we determined the minimum respiratory rate and whether patients had been treated for pruritus, nausea, vomiting, or urinary retention since the last evaluation. An observer (freshman medical student) with limited knowledge of either analgesic technique assessed the level of sedation (alert, drowsy, or asleep). He used a standardized "script" to administer two visual-analogue-scale (VAS) pain determinations: one of these assessed pain at the time of evaluation (current pain), while the other assessed the maximum pain which the patient had experienced since the last evaluation (recalled pain). Patients recorded pain on a 10 cm scale with 0 representing no pain and 10 representing the "worst pain imaginable." To avoid awakening patients unnecessarily, the VAS was not administered to patients who were asleep at the time of evaluation, and these scores were not obtained later. Twenty-four and 48 hr postoperatively, we asked patients to "Characterize the method used for relieving your postoperative pain; overall was it poor, fair, good, or excellent?"

We used two-way analysis of variance (repeated measures) and the protected least significant difference (PSD) test⁶ to analyze continuous data. For contingency tables, we used chi-square (Yates' correction) or Fisher's exact test as appropriate. $P \leq 0.05$ indicated statistical significance.

Results

As shown in Table I, patients in the two study groups did not differ in age, sex, duration of surgery, intraoperative fentanyl dose, type of surgery (total hip vs total knee replacement), or method of supplementation of the epidural anaesthetic (general anaesthesia vs *iv* sedation). Both the loading dose and the 24-hr total dose of morphine were lower in patients receiving the drug via the epidural as opposed to the patient-controlled *iv* route ($P < 0.05$).

FIGURE 1 Pain at the time of assessment ("current pain") on a 10 cm visual-analogue scale. There is no significant difference between patients receiving epidural and PCA morphine.

FIGURE 2 Maximum pain experienced by patients in the period preceding each assessment ("recall pain") on a 10 cm visual-analogue scale. *Two-way ANOVA revealed that patients receiving epidural morphine recalled less pain than those receiving patient-controlled *iv* morphine (PCA) when all observations were considered ($P < 0.05$). However, *post hoc* testing (PSD test) could not attribute this difference to a specific observation time.

Two patients in the epidural morphine group withdrew from the study; one had inadequate analgesia while the other had severe pruritus which was not relieved by *iv* diphenhydramine.

Visual-analogue scale (VAS) pain assessment at the time of observation (current pain, *vide supra*) did not differ between patients receiving epidural (VAS = 2.6 ± 0.4 cm, mean $\pm$ SEM) and patient-controlled *iv* morphine (VAS = 3.4 ± 0.3 cm, Figure 1). However, patients in the epidural morphine group recalled having less pain (VAS = 4.2 ± 0.5 cm) between observations (recall pain, *vide supra*) than those in the patient-controlled morphine group (VAS = 5.5 ± 0.4 cm, $P < 0.05$, Figure 2).

Minimum respiratory rates were lower in patients who

FIGURE 3 Minimum respiratory rates in the period preceding each assessment. * $P < 0.05$ vs patient-controlled analgesia (PCA) by two-way ANOVA and PSD test.

received epidural morphine (15.0 ± 0.3 breaths $\cdot$ min $^{-1}$) than in those receiving patient-controlled morphine (16.5 ± 0.4 breaths $\cdot$ min $^{-1}$, $P < 0.05$, Figure 3). However, no patients developed clinically important respiratory depression: the lowest recorded respiratory rates in the epidural and patient-controlled *iv* morphine groups were ten and nine breaths $\cdot$ min $^{-1}$, respectively.

Patients who received epidural morphine were more likely to be treated for pruritus (4 of 15) than patients receiving patient-controlled *iv* morphine (0 of 15, $P = 0.05$). When mild pruritus not requiring treatment was included in the comparison, patients who received epidural morphine experienced more pruritus (8 of 15) than patients who received patient-controlled *iv* morphine (1 of 15, $P < 0.05$). The groups did not differ in the level of sedation or in the incidence of nausea, vomiting, or urinary retention requiring treatment (Table II). Patients' assessment of the quality of postoperative analgesia was also similar for the two treatment techniques (Table III).

Discussion

Although both epidural and patient-controlled *iv* narcotics (PCA) have been recommended for treatment of the severe pain which follows total joint replacement, the present study is the first to compare directly these modalities in this patient population. Loper and Ready performed a similar comparison in patients undergoing cruciate ligament repair. Unfortunately, their study was not randomized and the authors could not "be certain whether those patients who chose an epidural anaesthetic or an inhalational anaesthetic would have different responses to pain."⁷ The post-Caesarean section studies of Eisenach *et al.*⁸ and Harrison *et al.*⁹ were randomized and prospective, but postoperative pain may be less severe in these obstetric patients.^{10,11} Despite these

TABLE II Incidence of side-effects attributable to postoperative analgesic regimen. $N = 15$ except urinary retention, for which denominators are shown separately (patients with indwelling urinary catheters throughout the study period were excluded)

	<i>Epidural morphine</i>	<i>Patient-controlled iv morphine</i>
Pruritus	4	0*
Somnolent (drowsy or asleep)	8	12
Nausea or vomiting	5	5
Respiratory rate $\leq 10 \cdot \text{min}^{-1}$	1	1
Urinary retention	9/13	6/14

* $P = 0.05$ compared with epidural morphine patients.

TABLE III Patients' overall evaluation of the randomly assigned method of postoperative analgesia

	<i>Epidural morphine</i>	<i>Patient-controlled iv morphine</i>
Excellent	9	10
Good	3	4
Fair	2	0
Poor	1	1

There is no significant difference between the groups.

differences in design, our present findings are similar to those previously reported: epidural narcotics may provide somewhat better analgesia than patient-controlled *iv* narcotics, but with an increased incidence of side-effects. Our results with epidural morphine may have been improved had we used continuous infusion of epidural narcotic or added dilute local anesthetic to the narcotic.

Pain at the time of evaluation (current pain) did not differ between epidural and PCA morphine; however, patients who received epidural morphine recalled less pain during the hours since the last evaluation (recall pain). This discrepancy may have been related to pharmacokinetic and pharmacodynamic differences between the two techniques. Analgesia lasts 12–24 hr following single doses of epidural morphine;¹² patients in the epidural group received a repeat dose of morphine 12 hr postoperatively to maintain adequate spinal drug levels for the 24-hr observation period. In contrast, levels of analgesia are more likely to fluctuate in patients receiving PCA, because of morphine's shorter duration of action when administered *iv*. Following self-administration of sufficient morphine, patients may be comfortable enough to fall asleep. The administration of morphine then stops, and plasma levels gradually decrease until they are below the analgesic threshold. The return of pain may awaken the patient,¹³ who will remain in pain until he is able to self-administer enough morphine to re-establish analge-

sia. This may have taken 20 to 30 min because we required a minimum of ten minutes between morphine doses (i.e., ten-minute "lockout interval"). The time to peak effect of *iv* morphine might have contributed further to the delay in re-attaining analgesia. Such fluctuations in analgesia are more likely when, as in the present study, PCA patients are not receiving a "basal" infusion of narcotic, but the superiority of PCA with basal infusion over PCA alone has not been established.

Four patients in the epidural morphine group and one patient in the PCA morphine group were asleep at one of the times when the VAS was to be evaluated. Rather than assign a VAS of zero at these times,^{10,14} which would have increased the difference in VAS between groups, we eliminated these observations from the statistical analysis.

Total morphine doses were lower in patients who received the drug via the epidural route; therefore, one might expect that these patients would be less somnolent than those who received PCA *iv* morphine. A possible explanation for our observation that sedation did not differ between groups is that epidural morphine may spread rostrally via the neuraxis and produce sedation.¹⁵ In contrast, patient-controlled administration of *iv* morphine minimizes the likelihood of high "peak" plasma levels of morphine which may cause excessive sedation.¹⁶

Although pruritus may develop following both systemic and epidural narcotics, in the present study it was seen only in patients who received epidural morphine. In one case, pruritus was severe enough to require that a patient be withdrawn from the study so that we could administer a narcotic antagonist. In the remaining cases, *im* diphenhydramine provided adequate relief.

Epidural morphine may cause urinary retention; however, we found that patients receiving this treatment were no more likely to require catheterization than those receiving PCA morphine. This may be related to the already high incidence of urinary retention in patients undergoing joint replacement surgery¹⁷ (56% of our patients required postoperative bladder catheterization).

The anaesthetist caring for the patient was unaware of the assigned method of postoperative analgesia until one hour before the end of surgery (when epidural morphine was administered to patients in that group). This reduced the likelihood that knowledge of the assigned method of analgesia would influence intraoperative anaesthetic management. Despite the fact that we did not standardize the amount of fentanyl administered intraoperatively, patients in both groups received exactly the same dose of this drug (Table I). In addition, because of its short duration of action,¹⁸ fentanyl should not affect pain perception by the time of the six-hour postoperative evaluation.

Because a "placebo effect" may contribute to the analgesia associated with PCA *iv* narcotics,¹⁹ we felt that patient-controlled administration of an *iv* placebo might alter pain perception in patients who received epidural morphine. Therefore, patients were necessarily aware of the method of postoperative analgesia. For the same reason, the "observer" could not be blinded to the group assignment. To minimize bias, we selected observers (freshman medical students) who had only limited knowledge of any techniques of perioperative pain management.

Because of the clinical nature of the present study, we elected to use respiratory rate as an index of ventilatory depression; hourly determination of respiratory rate remains the most common clinical method for detecting narcotic-induced respiratory depression.²⁰ However, narcotics may cause ventilatory depression without reducing the resting respiratory rate.^{21,22} Had we used a more sensitive index of ventilatory control (e.g., CO₂ or hypoxic ventilatory response determinations) we might have detected a difference in the ventilatory effects of the two analgesic techniques.

We conclude that patients who receive epidural morphine following lower extremity total joint replacement surgery may recall less postoperative pain during the first 24 hr than patients treated with patient-controlled *iv* morphine. However, epidural morphine was associated with a greater incidence of pruritus which required treatment. Although respiratory rates were lower in patients receiving epidural morphine, the difference was not clinically important; no patients in either group required treatment for respiratory depression.

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