Epidural opioid analgesia after Caesarean section: a comparison of patient-controlled analgesia with meperidine and single bolus injection of morphine

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The quality of analgesia, patient satisfaction and incidence of side effects following a single bolus of epidural morphine were compared with patient-controlled epidural analgesia (PCEA) with meperidine during the first 24 hr after elective Caesarean section. Seventy-five women were randomly assigned to three equal groups. Group 1 received 30 mg epidural meperidine after delivery and PCEA with meperidine; Group 2 received 3 mg epidural morphine after delivery and PCEA with saline in a double-blind fashion. Group 3 received 3 mg epidural morphine after delivery without saline PCEA. Visual analogue pain scores (VAS) were higher with PCEA meperidine from 8–16 hr post-operatively ($P < 0.05$) than in both epidural morphine groups. Two patients in Group 1 and one in Group 3 required supplemental parenteral analgesia. The incidence of nausea was 16% in Group 1, compared with 52% in Group 2 and 56% in Group 3 ($P < 0.01$). Pruritus occurred in 24% of Group 1 patients, 84% of patients in Group 2 and 68% of patients in Group 3 ($P < 0.001$). Forty-six percent of patients in Group 1 were very satisfied with pain management, compared with 77% in Group 2 and 79% in Group 3. Nurse workload was higher in the PCEA study groups than in Group 3 ($P < 0.05$).

A single bolus of epidural morphine provides superior analgesia and satisfaction at low cost, but with a higher incidence of nausea and pruritus than PCEA with meperidine.

La qualité de l'analgésie, la satisfaction de la patiente et l'incidence des effets secondaires consécutifs à une dose unique de morphine épidurale sont comparées au cours de l'anesthésie épidurale auto-contrôlée (AEAC) à la mépéridine pendant les premières vingt-quatre heures qui suivent la césarienne. Soixante-quinze accouchées sont assignées au hasard à un de trois groupes égaux. Le groupe 1 reçoit mépéridine épidurale 30 mg après l'accouchement et l'AEAC à la mépéridine par la suite; le groupe 2 reçoit morphine épidurale 3 mg après l'accouchement et l'AEAC au soluté physiologique en double aveugle. Le groupe 3 reçoit morphine épidurale 3 mg après l'accouchement sans l'AEAC au soluté physiologique. Sur l'échelle visuelle analogue (EVA), les scores sont plus élevés avec la mépéridine en AEAC de 8 à 16 h en postopératoire ($P < 0,05$) que dans les deux groupes de morphine épidurale. Deux patientes du groupe 1 et une du groupe 3 ont besoin d'analgésie parentérale supplémentaire. L'incidence de la nausée est de 16% dans le groupe 1, comparativement à 52% dans le groupe 2 et 56% dans le groupe 3 ($P < 0,01$). Vingt-quatre pour cent des patientes du groupe 1, 84% des patientes du groupe 2 et 68% des patientes du groupe 3 ($P < 0,001$) se plaignent de prurit. Quarante-six pour cent des patientes du groupe 1 se déclarent très satisfaites de la façon dont leur douleur a été traitée, comparativement à 77% du groupe 2 et 79% du groupe 3. Pour le personnel infirmier, les groupes d'étude de l'AEAC ont occasionné plus de travail que le groupe 3 ($P < 0,05$). Le bolus unique de morphine épidurale procure une anesthésie de qualité supérieure associée à une satisfaction à meilleur coût, mais provoque aussi une incidence plus élevée de nausées et de prurit que l'AEAC à la mépéridine.

Key words
ANAESTHESIA: epidural, obstetric;
ANALGESICS: meperidine, morphine;
PAIN: postoperative.

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Epidural bolus administration of morphine is a popular mode of pain management after Caesarean delivery.[1-4] The mean duration of effective pain relief following 3 mg epidural morphine has been estimated to be 19.6 hr ± 10.3 (SD).[4] However, incomplete analgesia cannot be treated by a supplemental dose of neuraxial morphine, unless the epidural catheter has been left *in situ* after surgery. Patient-controlled analgesia (PCA) may provide a sense of control of postoperative pain management resulting in decreased anxiety and improved patient satisfaction.[5] Patient-controlled epidural analgesia with the lipid soluble opioids fentanyl[6] and sufentanil[7] (combined with low concentration of bupivacaine) as well as hydromorphone[8] and meperidine[9] have been used to provide pain relief after Caesarean delivery. There are no studies comparing single bolus epidural morphine with PCEA opioid analgesia. We designed this prospective, randomized, double-blind study to compare the analgesic efficacy of a single injection of epidural morphine with PCEA meperidine during the 24 hr post-partum period. We also recorded the frequency of side effects, and nurse and patient satisfaction with each treatment modality. An open study group receiving epidural morphine bolus injection without PCEA was included to detect any placebo effect from the use of a PCA device.

Methods

After approval from the Research Ethics Committee at the Ottawa Civic Hospital, informed written consent was obtained from 75 healthy women at full term, scheduled for elective Caesarean section with epidural anaesthesia. Patients taking tranquilizers, or with a history of substance abuse, allergy to morphine or meperidine or body weight in excess of 90 kg were excluded.

All patients received 30 ml 0.3 M sodium citrate and an infusion of 1.0–1.5 L Ringer's lactate *iv.* The epidural catheter was inserted at the L_{2-3} or L_{3-4} interspace and surgical anaesthesia was achieved with incremental injections of lidocaine CO_2 with 1:200 000 epinephrine via the epidural catheter. The patients were randomly assigned to three equal study groups; Groups 1 and 2 in a double-blind fashion. Patients assigned to Group 1 received 30 mg epidural meperidine (10 mg · ml^{-1}) following delivery of the infant and a PCEA infusion for 24 hr. The PCA device (Abbott Lifecare 4100, Chicago, Illinois, USA) was programmed to deliver 10 mg doses of meperidine on demand with a ten minute lock-out interval. The basal infusion was 10 mg · hr^{-1} with a four hour maximum delivered dose of 120 mg. Patients in Group 2 received 3 mg epidural morphine (1 mg · ml^{-1}) after delivery of the infant and a PCEA saline infusion for 24 hr at the same settings and volume as patients in Group 1. Women in Group 3 received 3 mg of epidural morphine (1 mg · ml^{-1}) immediately after delivery of the infant and the epidural catheter was removed at the completion of the surgical procedure. If any patient experienced inadequate pain relief during the study, the patient was assessed by an anaesthetist who ensured that the epidural catheter remained *in situ* and that there was no disconnection in the tubing from the PCA device and that the patient had used the device optimally. Meperidine injection, *im* were given for inadequate pain relief to all patients, and the PCEA infusion was discontinued (Groups 1 and 2).

TABLE I Sedation scale

0	Alert
1	Occasionally drowsy
2	Frequently drowsy, easy to arouse
3	Somnolent, difficult to arouse
4	Unresponsive

The quality of analgesia during the study period was assessed using a ten point visual analogue pain scale at two-hour intervals; 0 = no pain and 10 = most severe pain. The hourly and total consumption of PCEA solution and the record of unsatisfied PCA demands during the study period was retrieved from the PCA computer using a text printer. The level of sedation (Table I), and incidence of nausea and pruritus during the study period were recorded at two-hour intervals by the ward nurse. In addition, the respiratory rate was measured every hour. The use of dimenhydrinate for the treatment of nausea and diphenhydramine for pruritus was also noted. The patients completed a questionnaire at the end of the study period detailing whether they would opt for the same method of postoperative pain control if they had the same operation in the future. They were also questioned whether the PCA device itself interfered with ambulation and care of the newborn. The nurse questionnaire assessed the workload for the nurses associated with pain management in each study group, compared with prn *im* meperidine injections during the first 24 hr after Caesarean section.

Parametric data were analyzed using repeated measures ANOVA with Tukey's post-hoc testing, and Student's t test where appropriate. Non-parametric data were analyzed with Mann-Whitney U-test and Fisher's exact test. $P < 0.05$ was considered significant.

Results

There was no difference between study groups in age, gravity, parity, weight, height, and gestational age (Table II). The incidence of intraoperative nausea, vomiting and discomfort was similar in all groups. There were no differences in postoperative pain scores between Group 2 and Group 3 except at 24 hr when the mean pain score

TABLE II Demographic data

	Group 1 (n = 25)	*Group 2 (n = 25)*	*Group 3 (n = 25)*
Age (yr)	29.5 ± 5.0	30.4 ± 5.1	30.0 ± 4.1
Weight (kg)	77.3 ± 13.5	79.9 ± 12.7	80.5 ± 9.6
Height (cm)	158.7 ± 6.5	160.4 ± 7.1	162.6 ± 7.5
Incidence of previous CS	15/25	16/25	16/25

(Mean ± SD).

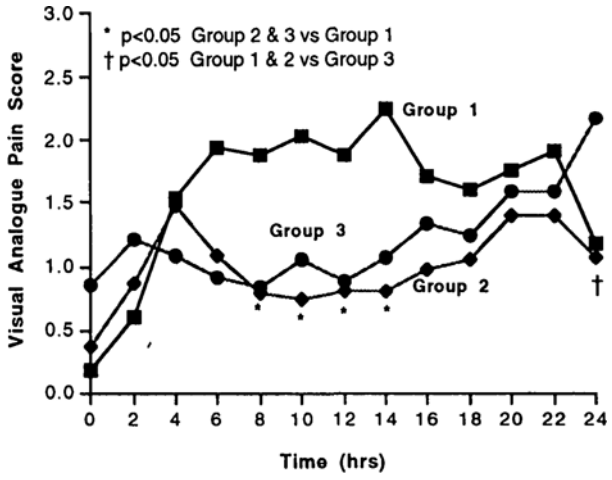

FIGURE 1 Visual analogue pain scores (mean) measured during first 24 hr after Caesarean section.

was higher in Group 3 ($P < 0.05$). The pain scores in Group 1 were higher than both epidural morphine groups between 8 and 16 hr after Caesarean section ($P < 0.05$) (Figure 1). The volume of meperidine administered by the PCEA device per hour (ml/hr) was higher than the amount of saline administered per hour in Group 2 (Figure 2), ($P < 0.05$). There were no differences between PCEA groups in the number of unsatisfied demands. Supplemental *im* meperidine was required for two of the patients in Group 1 and one patient in Group 3. Postoperative nausea and pruritus occurred more frequently in patients who received epidural morphine ($P < 0.01$) (Figures 3 and 4). Vomiting occurred in 8% of patients in Group 1, 40% of patients in Group 2 and 32% of patients in Group 3 ($P < 0.05$, Group 1 vs both epidural morphine groups). Recrudescence of herpes simplex labialis occurred in two of the patients in Group 3, both of whom experienced pruritus. There was no difference between groups in the degree of sedation, which was mild (sedation score 0–1) in all study groups throughout the study period. Respiratory rate was not less than 10 min^{-1} at any time in any of the patients.

Ninety percent of women in all study groups would

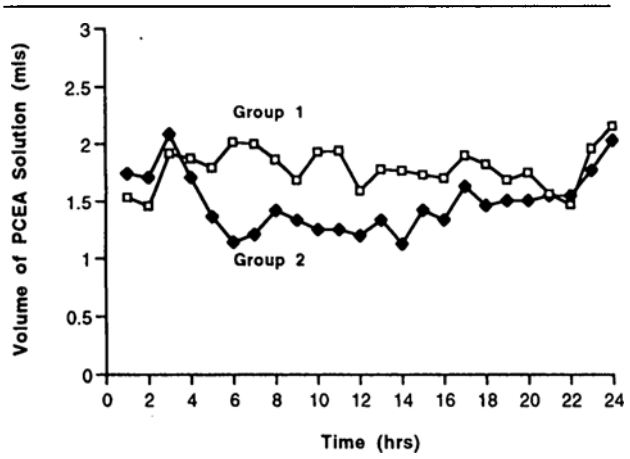

FIGURE 2 Hourly consumption of PCEA solution measured during 24 hours after Caesarean delivery.

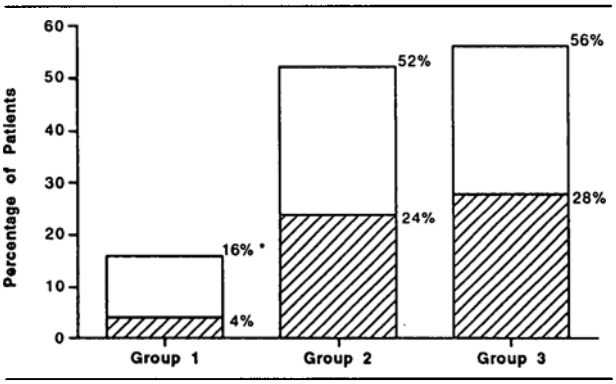

FIGURE 3 Percentage of patients in each group reporting nausea. Cross-hatched bars indicate the percentage of patients requiring treatment for nausea. *$P < 0.05$ Group 1 vs Group 2 and Group 3.

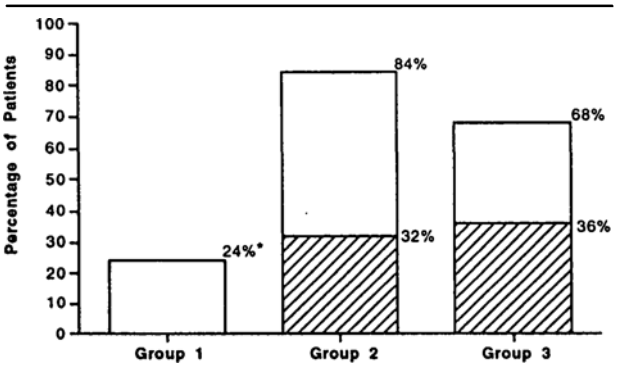

FIGURE 4 Percentage of patients in each group reporting pruritus. Cross-hatched bars indicate percentage of patients requiring treatment for pruritus. *$P < 0.001$ Group 1 vs Group 2 and Group 3.

use the same pain control therapy following future Caesarean section. However, the proportion of women who were very satisfied with their pain therapy was higher

in the epidural morphine groups (Table III). The workload for the nurses associated with the pain management modality was less in Group 3 ($P < 0.05$) (Table IV). There was no difference between groups in the time to hold or breastfeed the baby or time to first ambulation. However, patients in Group 1 experienced more pain when moving to the sitting position and when walking than those who received epidural morphine ($P < 0.05$) (Table V). Thirteen percent of the women in the PCEA groups felt that the pump per se (rather than pain) limited their ability to ambulate.

TABLE III Satisfaction with pain treatment

	Group 1 (n = 25)	*Group 2 (n = 25)*	*Group 3 (n = 25)*
Very satisfied	46%*	77%	79%
Satisfied	46%	23%	17%
Unsatisfied	8%	0%	4%

*$P < 0.05$ Group 1 vs Group 2 and Group 3.

TABLE IV Nurse workload associated with pain management

	Group 1	*Group 2*	*Group 3*
More than average	12%	12%	0%
Average	76%	76%	56%
Less than average	12%	12%	44%*

*$P < 0.05$ Group 3 vs Group 1 and Group 2.

TABLE V Pain associated with activity

	Group 1	*Group 2*	*Group 3*
Sitting	56%*	10%	18%
Walking	75%*	36%	30%
Coughing	60%	36%	36%

*$P < 0.05$ Group 1 vs Group 2 and Group 3.

Discussion

The administration of epidural morphine provides pain relief of longer duration than an equivalent dose of morphine *im* after Caesarean delivery.[10] It is common practice to inject the drug after delivery of the infant and remove the epidural catheter at the completion of the operation. However, some women may require supplemental parenteral analgesia during the first postoperative day. Lipophilic opioids have been investigated as an alternative to epidural morphine because neuraxial morphine is associated with a high incidence of pruritus, nausea and vomiting. A single bolus of epidural fentanyl after Caesarean section has not been shown to provide improved postoperative analgesia.[11] Furthermore, an epidural infusion of fentanyl provides similar pain relief with similar incidence of side effects compared to an *iv* fentanyl infusion after Caesarean delivery.[12] Sufentanil, a highly lipid-soluble opioid, provides two to three hrs of analgesia following epidural injection after Caesarean section.[13] Meperidine is less lipophilic than fentanyl and sufentanil and provides three to five hours of pain relief after epidural bolus administration following Caesarean delivery.[14,15]

The efficacy of an *iv* PCA regimen after Caesarean section has been compared with epidural morphine.[16,17] Epidural morphine was found to provide superior analgesia, but with a higher incidence of pruritus. However, patient satisfaction was similar in both groups. Parker and White[8] recently demonstrated that although pain scores were similar following *iv* PCA and PCEA with hydromorphone after Caesarean section, the total dose of hydromorphone administered was lower in the PCEA study group. Epidural meperidine administered by a PCA device resulted in improved pain relief and lower drug consumption than prn *im* meperidine injections following Caesarean delivery.[9] Our results indicate that the quality of analgesia following PCEA with meperidine is inferior to a single dose of 3 mg epidural morphine. The pain scores were higher in the PCEA meperidine group than the two epidural morphine groups during the middle third of the 24 hr study period. Also, pain associated with movement (sitting, walking) occurred less frequently in the women who received epidural morphine (Table V). There were no differences in pain scores between women in Groups 2 and 3, indicating that the opportunity to press a button did not contribute to postoperative analgesia. The use of epidural morphine provided a considerable dose-sparing effect since 3 mg epidural morphine resulted in superior analgesia compared with the women who received PCEA with meperidine and consumed 398 ± 106 mg (mean ± SD) of meperidine. The total dose of epidural meperidine in our study was similar to the consumption of meperidine (449 ± 247 mg) reported with *iv* PCA administration during the first 24 hr after Caesarean delivery.[18] Intravascular absorption occurs following epidural administration of meperidine and morphine.[19] Epidural meperidine bolus injection during labour results in higher plasma meperidine levels than those measured following *im* injection of an equivalent dose,[20] thus making less meperidine available for transfer via cerebrospinal fluid to opioid receptors in the spinal cord. In addition, the pharmacodynamic drug-receptor interaction of the two drugs may be different, thus explaining the difference in analgesic potency between epidural morphine and PCEA with meperidine.

Patient satisfaction with *iv* PCA has been found to be comparable to that after epidural morphine, despite

higher pain scores associated with *iv* PCA therapy.[16] Our results indicate that epidural morphine provided superior analgesia and patient satisfaction than PCEA meperidine after Caesarean section. Higher satisfaction scores associated with epidural morphine were seen despite an increased incidence of nausea, vomiting and pruritus. The fact that 13% of women using PCEA felt that the use of the PCA apparatus per se impeded their mobility may also have influenced the satisfaction score. The 4% incidence of recrudescence of herpes simplex labilalis in our patients who received epidural morphine is similar to the 3.5% incidence reported by Fuller,[4] although Crone *et al.*[21] found the incidence to be as high as 9%. The risk of delayed respiratory depression following epidural morphine administration is well documented, and has been estimated at 0.25%.[4] However, the possibility of subarachnoid catheter migration exists when the epidural catheter is left *in situ* for PCEA therapy.[22] Inadvertent subarachnoid administration of 50 mg meperidine has resulted in respiratory arrest requiring resuscitation and *iv* naloxone.[23] There is also a small risk of erroneous or inappropriate programming of the PCA device resulting in the administration of an overdose.[24,25] The relative risk of respiratory depression following bolus epidural morphine compared with a PCEA regimen with a lipophilic opioid remains to be defined.

In summary, PCEA meperidine administration provided adequate pain relief for most women after Caesarean section. However, the quality of analgesia was inferior to that of a single 3 mg bolus of epidural morphine. The incidence of nausea, vomiting and pruritus was higher in women who received epidural morphine. Nevertheless, patient satisfaction was higher among women who received epidural morphine. A PCEA regimen after Caesarean delivery is associated with an increased workload for ward nurses compared to a single bolus of epidural morphine administration. Epidural bolus administration with morphine at Caesarean delivery provides superior pain relief, improved patient satisfaction and less cost than PCEA with meperidine. Patient-controlled analgesia with meperidine is an alternative pain treatment for women with drug allergy to morphine, pruritic dermatological conditions or recurrent herpes simplex labialis.

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