Patient-controlled epidural analgesia after Caesarean section using meperidine

Warwick D. Ngan Kee FANZCA,
Kim S. Khaw FRCA,
Marlene L. Ma RN

Purpose: To determine the effects of the addition of a background infusion to patient-controlled epidural analgesia (PCEA) using meperidine for analgesia after Caesarean section.

Methods: In a randomized, double-blind study, we assigned 40 patients having elective Caesarean section to receive postoperative analgesia by patient-controlled epidural analgesia (PCEA) using meperidine 5 mg·ml^{-1} with (group Pi) or without (group Po) a background infusion of 10 mg·hr^{-1}. The PCEA settings (20 mg bolus , 10 min lockout interval, four-hour maximum dose 150 mg) were otherwise identical. We compared pain at rest, pain on coughing, side effects, number of PCEA demands, drug consumption and patient satisfaction between groups in the first 24 hr after surgery.

Results: Total consumption of meperidine was greater in group Pi (median 390 mg) than in group Po (median 240 mg; $P = 0.017$) and the number of PCEA demands was greater in group Po (median 12) than in group Pi (median 7.5; $P = 0.012$). Analgesia, side effects and patient satisfaction was similar between groups.

Conclusion: Addition of a background infusion to PCEA using meperidine after Caesarean section has no clinical benefit.

Objectif : Déterminer après la césarienne les effets de la perfusion continue pour l'analgésie épidurale auto-contrôlée (PCEA) à la mépéridine.

Méthodes : Au cours d'une étude aléatoire, en double aveugle, nous avons désigné 40 parturientes programmées pour une césarienne non urgente pour une analgésie épidurale auto-contrôlée avec mépéridine 5 mg·ml^{-1} avec (groupe Pi) ou sans (groupe Po) une perfusion continue de 10 mg·h^{-1}. Le réglage de la PCEA (dose de charge 20 mg, intervalle réfractaire 10 min, dose maximale 150 mg aux quatre heures) étaient les mêmes. Nous avons comparé entre les groupes, la douleur au repos, à la toux, les effets secondaires, le nombre de demandes de PCEA, l'utilisation du morphinique et la satisfaction de la patiente pendant les premières 23 h.

Résultats : L'utilisation totale de mépéridine était plus importante dans le groupe Pi (médiane 390 mg) que dans le groupe Po (médiane 240 mg ; $P = 0,017$) et le nombre de demandes de PCEA était plus important dans le groupe Po (médiane 12) que dans le groupe Pi (médiane 7,5 ; $P = 0,012$). L'analgésie, les effets secondaires et la satisfaction de la patiente étaient identiques entre les groupes.

Conclusion : Après la césarienne, l'ajout d'une perfusion continue à la PCEA à la mépéridine ne procure pas d'avantages cliniques.

From the Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, New Territories, Hong Kong.

Address correspondence to: Dr. W. D. Ngan Kee, Phone: +852 2632 2735; Fax: +852 2637 2422; E-mail:warwick@cuhk.edu.hk

Accepted for publication April 13, 1997.

PATIENT-CONTROLLED epidural analgesia (PCEA) using meperidine is effective for pain relief after Caesarean section.[1–4] It has been found to be superior to patient-controlled intravenous analgesia (PCIA) using meperidine,[2,4] preferred to PCEA using fentanyl,[3,4] and has fewer side effects than epidural morphine.[5] However, the optimum regimen for PCEA meperidine is unknown. In early reports of PCEA using meperidine after Caesarean section a background infusion of 10 $mg \cdot hr^{-1}$ was used[1,5] but in subsequent reports a bolus-only technique was used.[2–4] When PCEA with a background infusion was compared with PCEA alone using the lipophilic opioids fentanyl and sufentanil, drug consumption was greater but analgesia was not better in the groups receiving an infusion.[6,7] However, there have been no similar studies using meperidine, an opioid with intermediate lipophilicity. Therefore, we performed a randomized double blind study to compare PCEA plus background infusion, with PCEA alone using meperidine for analgesia after elective Caesarean section.

Methods

After obtaining approval from the local Clinical Research Ethics Committee, we studied 40 ASA physical status 1 or 2 women undergoing elective Caesarean section under epidural anaesthesia. Using data from previous studies where we used PCEA meperidine after Caesarean section, we calculated that a sample size of 20 would be sufficient to detect a 50% difference in 24 hr meperidine consumption (levels of significance $\alpha = 0.05$, $ß = 0.2$). All patients gave written informed consent and were instructed in the use of a 100-mm visual analogue scale (VAS) for the measurement of pain and side effects, and a patient-controlled analgesia device (Abbott Pain Management Provider, Abbott Laboratories, North Chicago, IL, USA). Patients received 150 mg ranitidine *po* the night before and the morning of surgery and 30 ml 0.3 M sodium citrate on arrival in the operating room. After intravenous preload, the epidural space was located at the L_{2-3} or L_{3-4} vertebral interspace with a 16 gauge Tuohy needle using a loss of resistance technique with the patient lateral. An epidural catheter was then threaded 3–4 cm into the epidural space and the patient was turned supine with 15° left lateral tilt. Sensory anaesthesia to the T4 dermatome was achieved using lidocaine 2% with adrenaline 1:200,000. All patients received 25–50 mg epidural meperidine, at the anaesthetist's discretion, after the block was established, with further intraoperative analgesia provided, if required, using nitrous oxide *via* facemask or 10 mg increments of ketamine *iv*. Hypotension was treated with fluid and boluses of ephedrine *iv* according to our standard practice.

On arrival in the postanaesthesia care unit, patients were randomly assigned, by drawing of shuffled coded envelopes, to receive either PCEA using meperidine 5 $mg \cdot ml^{-1}$ with a background infusion of 10 $mg \cdot hr^{-1}$ (group Pi) or PCEA alone (group Po). The PCEA settings were otherwise identical between the two groups (20 mg bolus, 10 min lockout interval, 150 mg four-hour maximum). The PCEA solutions were prepared and the device was programmed by an investigator who was not involved with subsequent patient assessment. For the purposes of blinding, the liquid crystal display of the PCEA device was covered with an opaque adhesive label that remained in place for the duration of the study, but could be removed in the event of alarms or emergencies.

After transfer to the postnatal ward, patients were observed by the nursing staff according to our usual protocol for PCEA, which includes hourly recording of level of consciousness and respiratory rate. Metoclopramide 10 mg *im* was prescribed as required for nausea. One of the investigators or the on-call anaesthetic resident was available to attend at all times. Patients were visited by one of the investigators at 2, 6, and 24 hr after surgery. At each of these visits, patients were asked to grade their pain at rest, pain on coughing, nausea and sleepiness using the VAS. In addition, at 24 hr, patients were asked to grade their satisfaction with the method of analgesia according to an 11-point numerical scale (0 = completely satisfied, 10 = completely unsatisfied). The time of first PCEA demand, total number of PCEA demands, number of boluses delivered, total meperidine dose, and the number of occlusion alarms that occurred were obtained from the electronic memory of the PCEA device. The number of doses of metoclopramide given were obtained from the drug chart.

Patient characteristics were compared using the unpaired Student's t test. Analgesia was assessed by comparing VAS pain scores at each assessment time and the aggregated total of the three pain scores for each patient, at rest and on coughing, using the Mann-Whitney *U* test. Parity, intraoperative drug doses, time to first PCEA demand, total number of PCEA demands and boluses received, and total dose of meperidine received were compared using the Mann-Whitney *U* test. Side effects during the study period were compared by adding the VAS scores for the three assessment periods and comparing the aggregated totals using the Mann-Whitney *U* test. The number of doses of antiemetic and the number of occlusions were com-

pared using Fisher's Exact test. A value of $P < 0.05$ was considered statistically significant.

Results

Thirty-nine patients completed the study. One patient in group Po was rejected from the study shortly after arrival in the postnatal ward because of technical problems with the PCEA device. Inadvertent dural puncture occurred during insertion of the Tuohy needle in one patient; repeat insertion was successful but the patient was rejected from the study before randomization and a further patient was recruited as a replacement. Patient characteristics were similar between groups (Table I).

There was no difference in VAS pain scores at rest (Figure 1) or on coughing (Figure 2) at any of the assessment times and no difference in the aggregated scores ($P = 0.14$ for pain at rest and $P = 0.15$ for pain on coughing). Details of PCEA usage and patient satisfaction are shown in Table II. No patient exceeded the programmed four-hour limit. Total consumption of meperidine in 24 hr was greater in group Pi than in group Po. The number of PCEA demands and PCEA boluses received was greater in group Po than in group Pi. The ratio of demands to boluses received and the time to first PCEA demand were similar in each group. Patient satisfaction scores were high but similar and the incidence of side effects was low and similar in each group (Table III). No patient required metoclopramide for nausea and there was only one instance of an occlusion alarm which occurred in a patient in group Pi (differences between groups not significant). No patient required treatment for respiratory depression or excessive sedation.

TABLE I Patient Characteristics

	Group Pi (n = 20)	*Group Po (n = 19)*	*P*
Age (yr)	31.9 ± 5.9	31.8 ± 4.8	0.97
Height (cm)	152 ± 6.8	155 ± 5.5	0.10
Weight (kg)	65.2 ± 10.2	67.2 ± 7.9	0.50
Parity	1 (1–1.5)	1 (1–1)	0.83
Lidocaine 2% dose (ml)	17.5 (15–20)	20 (17–23.8)	0.07
Intraoperative meperidine (mg)	25 (25–37.5)	25 (25–25)	0.63

Values are mean ± standard deviation or median (interquartile range).

TABLE II PCEA Usage and Patient Satisfaction

	Group Pi (n = 20)	*Group Po (n = 19)*	*P*
Total consumption of meperidine in 24 hr (mg)	390 (310–480)	240 (185–395)	0.017
Number of PCEA boluses received	7.5 (3.5–12)	12 (9.3–19.8)	0.019
Number of PCEA demands	8 (5–13.5)	15 (9.3–27.5)	0.012
Demands: Boluses received ratio	1.0 (1.0–1.2)	1.1 (1.0–1.4)	0.32
Time to first PCEA demand (min)	108 (50–220)	119 (93–186)	0.63
Patient satisfaction score	8 (6.75–9.3)	8 (7.0–9.0)	0.89

Values are median (interquartile range).

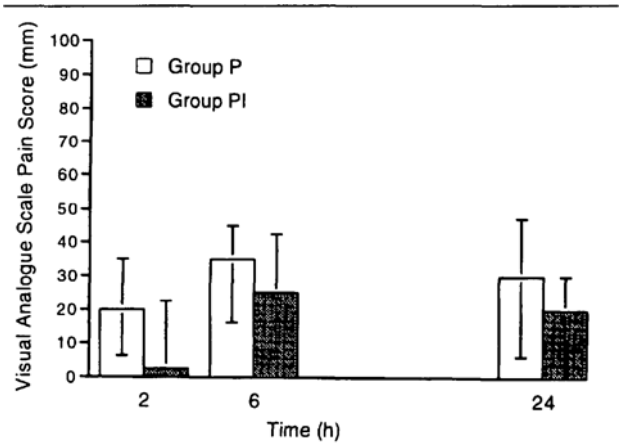

FIGURE 1 Visual analogue scale pain scores at rest (median and interquartile range).

There were no differences between groups.

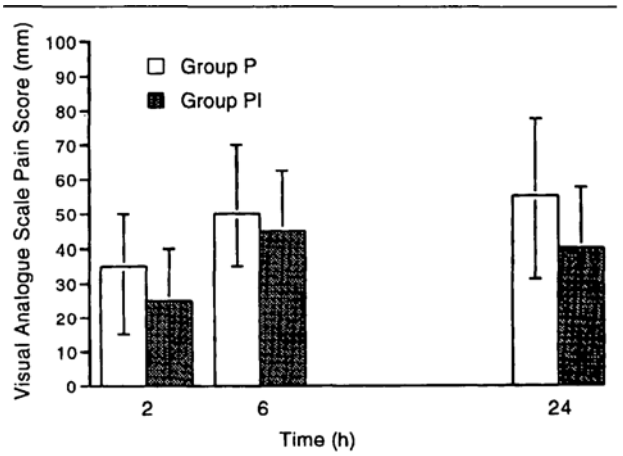

FIGURE 2 Visual analogue scale pain scores on coughing (median and interquartile range).

There were no differences between groups.

TABLE III Side Effect Scores

	Group Pi	*Group Po*	*P*
Nausea (mm)	0 (0–0)	0 (0–0)	0.57
Sedation (mm)	105 (58–158)	60 (16–144)	0.08

Values are aggregated totals of three scores (median (interquartile range)).

Discussion

A number of studies have evaluated the addition of a background infusion to patient-controlled analgesia (PCA). For patient-controlled intravenous analgesia (PCIA), these have had conflicting results; some studies showed that a background infusion increased drug consumption without improving analgesia,[8,9] whereas others showed improved analgesia with similar or increased drug consumption.[10–12] Thus, the optimum regimen for PCIA is undetermined.

Evaluations of the addition of a background infusion to PCEA are more limited because PCEA is a relatively new modality. Vercauteren *et al.*[6] compared PCEA with a background infusion *versus* PCEA alone using sufentanil after Caesarean section and found drug consumption and sedation were greater in patients receiving a background infusion. Analgesia was better in patients receiving an infusion at six hours after surgery but was similar at other times. Side effects, the quality of sleep, and the number of PCEA demands were similar between groups. Owen *et al.*[7] gave epidural fentanyl after abdominal surgery by continuous infusion with nurse-administered boluses as required, PCEA, or PCEA plus infusion and found that patients in the continuous infusion group had a greater proportion of time with low oxyhaemoglobin saturation and patients using PCEA-only used less drug than other groups; pain scores and sedation were similar between groups. In our study of epidural meperidine, we also found that drug consumption was increased in patients receiving a background infusion, with no difference in analgesia. However, in contrast to the findings of Vercauteren *et al.*, we found that patients receiving PCEA-only made more PCEA demands than in patients receiving a background infusion. This might reflect our use of an hourly infusion rate that was a smaller proportion (50%) of the bolus dose than in the previous study where the hourly rate was 80% of the bolus dose. We found no difference in patient sedation between groups which was similar to the findings of Owen *et al.*

We attempted to achieve double-blinding by not telling patients the group to which they were assigned and by covering the liquid crystal display of the PCEA device. However, although the PCEA device has a quiet mechanism, some patients may have been aware of the infusion running. Vercauteren *et al.* achieved blinding by using a separate infusion device to deliver saline or drug. However, this effectively increased the dilution of drug for patients receiving saline which influences the efficacy of epidural sufentanil.[13] In addition, epidural saline itself may have segmental sensory effects in non-pregnant patients.[14] We have also noted this in our own study of pregnant patients (unpublished data).

Meperidine is a suitable opioid for PCEA. A single bolus of epidural meperidine has a relatively short duration of action, unlike epidural morphine.[15] When PCEA meperidine was compared with a single dose of 3 mg epidural morphine after Caesarean section, side effects were lower with meperidine. In that study, analgesia from epidural morphine was superior to that of PCEA meperidine. However, a relatively high concentration of meperidine (10 $mg \cdot ml^{-1}$) was used which is less effective than more dilute solutions.[16] Unlike epidural morphine, epidural meperidine has not been associated with delayed respiratory depression. Meperidine has intermediate lipophilicity (octanol:buffer partition coefficient 38.8 compared with morphine 1.42, fentanyl 813, and sufentanil 1778).[17] Previous studies of epidural meperidine have consistently shown better analgesia with lower drug consumption and lower plasma concentrations of meperidine compared with intramuscular or intravenous meperidine.[2,18,19] In contrast, there is controversy whether epidural administration of more lipophilic opioids has advantages over intravenous administration.[20–22] In addition, comparative studies showed that meperidine had advantages over fentanyl for PCEA after Caesarean section.[3,4]

Meperidine, in common with other phenylpiperidine derivatives has local anaesthetic properties. Unlike fentanyl, this is seen at concentrations in which meperidine is given for analgesia.[23] Although meperidine has been used as the sole agent for spinal anaesthesia for Caesarean section,[24] it is unclear whether its local anaesthetic properties contribute to analgesia when it is given epidurally.

We reported previously the use of a disposable device for PCEA using meperidine after Caesarean section.[25] Because the device used delivered boluses of small volume, occlusion of the epidural catheter was an occasional problem. In the present study, we expected that occlusions might be less common with the use of a background infusion but found a similar low incidence in both groups. However, we used catheters with a relatively large diameter and it is possible that occlusions might more frequent with finer catheters.

In summary, we found that the addition of a background infusion to PCEA using meperidine after Caesarean section was of no clinical benefit. A background infusion increased drug consumption without improving analgesia. Side effects and patient satisfaction were similar.

References

1 *Yarnell RW, Polis T, Reid GN, Murphy IL, Penning JP.* Patient-controlled analgesia with epidural meperidine after elective cesarean section. Reg Anesth 1992; 17: 329–33.

2 *Paech MJ, Moore JS, Evans SF.* Meperidine for patient-controlled analgesia after cesarean section. Intravenous *versus* epidural administration. Anesthesiology 1994; 80: 1268–76.
3 *Goh JL, Evans SF, Pavy TJG.* Patient-controlled epidural analgesia following Caesarean delivery: a comparison of pethidine and fentanyl. Anaesth Intensive Care 1996; 24: 45–50.
4 *Ngan Kee WD, Lam KK, Chen PP, Gin T.* Comparison of patient-controlled epidural analgesia with patient-controlled intravenous analgesia using pethidine or fentanyl. Anaesth Intensive Care 1997; 25:126–32.
5 *Rosaeg OP, Lindsay MP.* Epidural opioid analgesia after Caesarean section: a comparison of patient-controlled analgesia with meperidine and single bolus injection of morphine. Can J Anaesth 1994; 41: 1063–8.
6 *Vercauteren MP, Coppejans HC, ten Broecke PW, Van Steenberge AL, Adriaensen HA.* Epidural sufentanil for postoperative patient-controlled analgesia (PCA) with or without background infusion: a double-blind comparison. Anesth Analg 1995; 80: 76–80.
7 *Owen H, Kluger MT, Ilsley AH, Baldwin AM, Fronsko RRL, Plummer JL.* The effect of fentanyl administered epidurally by patient-controlled analgesia, continuous infusion, or a combined technique of oxyhaemoglobin saturation after abdominal surgery. Anaesthesia 1993; 48: 20–5.
8 *Owen H, Szekely SM, Plummer JL, Cushnie JM, Mather LE.* Variables of patient-controlled analgesia 2. concurrent infusion. Anaesthesia 1989; 44: 11–3.
9 *Doyle E, Robinson D, Morton NS.* Comparison of patient-controlled analgesia with and without a background infusion after lower abdominal surgery in children. Br J Anaesth 1993; 71: 670–3.
10 *Sinatra R, Chung KS, Silverman DG, et al.* An evaluation of morphine and oxymorphone administered *via* patient-controlled analgesia (PCA) or PCA plus basal infusion in postcesarean-delivery patients. Anesthesiology 1989; 71: 502–7.
11 *McCoy EP, Furness G, Wright PMC.* Patient-controlled analgesia with and without background infusion. Analgesia assessed using the demand:delivery ratio. Anaesthesia 1993; 48: 256–65.
12 *Dawson PJ, Libreri FC, Jones DJ, Libreri G, Bjorkstein AR, Royse CF.* The efficacy of adding a continuous intravenous morphine infusion to patient-controlled analgesia (PCA) in abdominal surgery. Anaesth Intensive Care 1995; 23: 453–8.
13 *Vercauteren M, Meert T, D'Hooghe R, Boersma F, Melis W.* Spinal sufentanil in rats: part III: effect of diluent volume on epidural sufentanil. Acta Anaesthesiol Scand 1992; 36: 305–8.
14 *Hore PJ, Silbert BS, Cook RJ, Beilby DSN.* A double-blind assessment of segmental sensory changes with epidural fentanyl *versus* epidural saline in patients undergoing extracorporeal shock-wave lithotripsy. Anesthesiology 1990; 72: 603–6.
15 *Ngan Kee WD, Lam KK, Chen PP, Gin T.* Epidural meperidine after cesarean section. A dose-response study. Anesthesiology 1996; 85: 289–94.
16 *Ngan Kee WD, Lam KK, Chen PP, Gin T.* Epidural meperidine for postoperative analgesia: the effect of diluent volume. Anesthesiology 1996; 85: A744.
17 *Cousins MJ, Mather LE.* Intrathecal and epidural administration of opioids. Anesthesiology 1984; 61: 276–310.
18 *Brownridge P, Frewin DB.* A comparative study of techniques of postoperative analgesia following Caesarean section and lower abdominal surgery. Anaesth Intensive Care 1985; 13: 123–30.
19 *Perriss BW, Latham BV, Wilson IH.* Analgesia following extradural and I.M. pethidine in post-Caesarean section patients. Br J Anaesth 1990; 64: 355–7.
20 *Glass PSA, Estok P, Ginsberg B, Goldberg JS, Sladen RN.* Use of patient-controlled analgesia to compare the efficacy of epidural to intravenous fentanyl administration. Anesth Analg 1992; 74: 345–51.
21 *Miguel R, Barlow I, Morrell M, Scharf J, Sanusi D, Fu E.* A prospective, randomized, double-blind comparison of epidural and intravenous sufentanil infusions. Anesthesiology 1994; 81: 346–52.
22 *van den Nieuwenhuyzen MCO, Burm AGL, Vletter AA, Stienstra R, van Kleef JW.* Epidural vs. intravenous infusion of alfentanil in the management of postoperative pain following laparotomies. Acta Anaesthesiol Scand 1996; 40: 1112–8.
23 *Power I, Brown DT, Wildsmith JAW.* The effect of fentanyl, meperidine and diamorphine on nerve conduction in vitro. Reg Anesth 1991; 16: 204–8.
24 *Kafle SK.* Intrathecal meperidine for elective Caesarean section: a comparison with lidocaine. Can J Anaesth 1993; 40: 718–21.
25 *Ngan Kee WD, Lam KK, Twyford CJ, Gin T.* Evaluation of a disposable device for patient-controlled epidural analgesia after Caesarean section. Anaesth Intensive Care 1996; 24: 51–5.