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Epidural meperidine does not cause hemodynamic changes in the term parturient

K.S. Khaw MBBS FRCA,
W.D. Ngan Kee MD FANZCA,
L.A.H. Critchley MD FFARCSI

Purpose: Meperidine has local anesthetic properties and, therefore, when given epidurally it has the potential to cause hemodynamic changes. Our objective was to study the hemodynamic effects of an analgesic dose of epidural meperidine (50 mg) in 34 ASA I-2 term parturients scheduled for elective Cesarean section under epidural anesthesia.

Methods: A lumbar epidural catheter was inserted and patients lay in the supine left wedge position. Intravenous fluid preload was withheld, and hemodynamic measurements comprising of mean arterial pressure, cardiac output and heart rate were made using automatic oscillometry (Dinamap 1486SX) and transthoracic electrical bioimpedance (Bomed NCCOM3). Following baseline measurements, the hemodynamic effects of sequential epidural injection of first, 10 ml saline, and 20 min thereafter, 50 mg meperidine diluted to 10 ml with saline, were recorded. Sensory blockade was assessed following each injection using loss of temperature discrimination to ice. Paired Student t tests were used to compare changes in hemodynamic variables.

Results: Epidural meperidine produced a small increase from the saline values in the mean (SD) cardiac output of 5.81 ± 1.44 to $6.04 \pm 1.54 \text{ L}\cdot\text{min}^{-1}$ ($P < 0.05$), and mean arterial pressure of 77.1 ± 8.8 to $79.3 \pm 9.9 \text{ mmHg}$ ($P < 0.05$). Sensory changes, the upper level of which ranged from L1 to T1, were detected in 94% of patients given epidural meperidine. Epidural saline injection had no such hemodynamic effects, but produced a detectable sensory level in two patients.

Conclusion: Epidural meperidine, 50 mg, caused minimal hemodynamic changes in term parturients.

Objectif : La mépéridine présente les propriétés d'un anesthésique local et peut donc causer des changements hémodynamiques lorsqu'on en fait l'administration péridurale. Notre objectif était d'en étudier les effets hémodynamiques d'une dose analgésique de 50 mg chez 34 parturientes à terme, d'état physique ASA I-II, dont la césarienne était prévue sous anesthésie péridurale.

Méthode : Un cathéter péridural lombaire a été inséré et les patientes ont été placées en décubitus dorsal, le flanc gauche soulevé par un coussin. Une précharge de liquide intraveineux n'a pas eu lieu et les mesures hémodynamiques comprenant la tension artérielle moyenne, le débit cardiaque et la fréquence cardiaque ont été réalisées par oscillométrie automatique (Dinamap 1486SX) et bio-impédance électrique transthoracique (Bomed NCCOM3). Les mesures de départ étant faites, on a mesuré ensuite les effets hémodynamiques de l'injection péridurale séquentielle de 10 ml de solution salée et, 20 min plus tard, de 50 mg de mépéridine diluée dans 10 ml de solution salée. Le blocage sensitif a été évalué après chaque injection en utilisant la perte de discrimination de la température de la glace. Les tests t de Student pour paires appariées ont été utilisés pour comparer les changements des variables hémodynamiques.

Résultats : La mépéridine péridurale a produit une faible augmentation, à partir des valeurs provenant de la solution salée, de l'écart type du débit cardiaque de $5,81 \pm 1,44$ à $6,04 \pm 1,54 \text{ L}\cdot\text{min}^{-1}$ ($P < 0,05$) et de la tension artérielle moyenne de $77,1 \pm 8,8$ à $79,3 \pm 9,9 \text{ mmHg}$ ($P < 0,05$). Les changements sensitifs, dont les niveaux supérieurs s'étendaient de L1 à T1, ont été détectés chez 94 % des patientes qui avaient reçu la mépéridine péridurale. L'injection péridurale de solution salée n'a pas présenté d'effets hémodynamiques semblables, mais a produit un niveau sensitif détectable chez deux patientes.

Conclusion : La mépéridine péridurale, 50 mg, a produit de minimes changements hémodynamiques chez des parturientes à terme.

From the Department of Anaesthesia and Intensive Care, Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong, Peoples Republic of China.

Address correspondence to: Dr K.S. Khaw. Phone: +852-2632-2735; Fax: +852-2637-2422; E-mail: kimkhaw@cuhk.edu.hk

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MEPERIDINE is an opioid that has both structural and pharmacological similarities to the local anesthetics. Although most commonly used as an opioid, meperidine has been also been used as a local anesthetic in many studies. It has been used in place of, or in combination with conventional local anesthetics, for skin infiltration, spinal, and plexus anesthesia.¹⁻⁷ At clinical doses and concentrations, the local anesthetic properties of meperidine are comparable to those of lidocaine.¹⁻³ Therefore, intrathecal and epidural administration of meperidine may potentially block sympathetic outflow, with resultant hemodynamic effects such as hypotension.

We have previously shown that *intrathecal* meperidine caused hypotension and bradycardia that were equivalent to, or greater than, those seen with heavy bupivacaine 0.5%.⁵ Whether similar hemodynamic effects occur following *epidural* administration of meperidine has not been previously described. Thus, the purpose of this study was to determine whether an analgesic dose of epidural meperidine (50 mg) causes hemodynamic effects in non-labouring term parturients.

Methods

Local Ethics Committee approval and informed written consent from all patients were obtained. Forty ASA I-2 term parturients scheduled for elective Cesarean section under epidural anesthesia were recruited. Patients were premedicated with 150 mg ranitidine *po*, the night before, and on the morning of surgery. The study was conducted in a quiet room adjacent to the operating theatre. On arrival, intravenous access was secured but intravenous fluid was withheld for the duration of the study. An epidural catheter was sited at a lumbar (L₂₋₃ or L₃₋₄) vertebral interspace. The patient was then placed in the supine left wedged position using a standard wedge cushion tilted at 20° and blood pressure and impedance cardiography monitoring attached.

Mean arterial pressures (MAP) were measured at two-minute intervals using an automated oscillonometer (Dinamap 1846SX, Critikon, Florida, USA) and data were recorded on an integral printer. Cardiac output (CO) and heart rate (HR) were measured continuously using the BoMed NCCOM3-R7S (BoMed Manufacturing, Irvine, CA, USA) and these data were uploaded to a laptop computer, as described in previous studies.^{5,8,9} The BoMed NCCOM3 was connected to the patient using an eight electrode montage to the neck and lower thorax.¹⁰ Fetal well being was continuously monitored using a cardiotocograph, and regularly assessed by a midwife present for the duration of the study.

Following a 10 min stabilisation period, baseline

hemodynamic data were collected over 20 min. Ten millilitres of normal saline (placebo) were then injected epidurally over 30 sec and hemodynamic variables were recorded for a further 20 min. Following this, 50 mg meperidine (Antigen Pharmaceuticals Ltd., Roscrea, Ireland) diluted to 10 ml with normal saline was injected epidurally, and hemodynamic variables were measured for a further 20 min. Thus, three sets of hemodynamic monitoring data were obtained from each patient. The presence of sensory blockade was assessed at 20 min intervals following each epidural injection using loss of temperature discrimination to ice in the midline.

Our protocol for treatment of hypotension, defined as a decrease in MAP of > 25% from baseline, was a rapid infusion of 15 ml·kg⁻¹ Ringer's lactate solution and boluses of 6 mg ephedrine *iv*. Nausea and vomiting were treated with 10 mg metoclopramide *iv*, once hypotension had been excluded. After data collection was completed, the patient was prepared for Cesarean section by extending the epidural block to the appropriate level using lidocaine 2% with 1:200000 adrenaline.

Statistical analysis was performed using the programme Statview 4.5 (Abacus Concepts, Inc., Berkeley, CA, USA). Hemodynamic data were analysed using methods similar to those used in our previous studies of hemodynamic changes associated with spinal anesthesia.^{5,8,9} The BoMed produced a cardiac output and heart rate measurement every 16 heartbeats, and these were averaged to produce mean values for each two-minute time period. To allow time for the hemodynamic changes associated with epidural meperidine to become established, only data collected during the second half (10 min), following each epidural injection were analysed. In each patient, "typical" mean values for cardiac output, heart rate and mean arterial pressure were calculated by averaging data collected during each of the three 10-20 min time periods. Paired Students *t* tests (two tailed) were used to compare hemodynamic variables from each study period. *P* < 0.05 was considered significant.

Results

Data from 34 of the original 40 patients were included in the final analysis. Six patients were excluded, in one because of early onset of labour during the study and in five because of technical problems with data collection.

Hemodynamic variables recorded during the study are plotted in Figure. Results after analysis are presented as mean ± SD in the Table. The mean value of hemodynamic variables at baseline, and at 10-20 min following epidural injection with normal saline (placebo) and

TABLE Hemodynamic variables (mean $\pm$ SD) at baseline and after epidural injection of saline and of meperidine (n=34).* $P < 0.05$ compared with previous measure.

	Baseline	Saline	Meperidine
Cardiac output (L·min ⁻¹)	5.83 $\pm$ 1.32	5.81 $\pm$ 1.44	6.04 $\pm$ 1.54*
Mean arterial pressure (mmHg)	76.9 $\pm$ 8.4	77.1 $\pm$ 8.8	79.3 $\pm$ 9.9*
Heart rate (bpm)	86.0 $\pm$ 9.2	85.9 $\pm$ 9.4	85.3 $\pm$ 10.1

meperidine are shown. Cardiac output increased by $0.23 \pm 1\text{-min}^{-1}$ (3.9%), ($P < 0.05$) and MAP increased by $2.2 \pm \text{mmHg}$ (3.0%) ($P < 0.05$) after the injection of meperidine. All patients proceeded uneventfully to Cesarean section. No interventions were required for hypotension or nausea and vomiting, and no adverse maternal side effects, or fetal cardiotocograph changes were encountered during the study.

Loss of sensory discrimination to ice was detected in all but two patients (94%) following epidural meperidine. All blocks had a lower limit commencing from L₅, and the upper levels were (median (range)) T₈ (T₂-L₁). Two patients (6%) also developed sensory changes up to T₈ and L₁ following epidural normal saline.

Discussion

We found that epidural meperidine, given in a standard size analgesic dose, did not cause clinically important hemodynamic effects which required treatment interventions in term parturients. Cardiac output increased by $0.23 \text{ l}\cdot\text{min}^{-1}$ (3.9%) and MAP increased by 2.2 mmHg (3.0%), 10 min after injection of epidural meperidine but these increases were not accompanied by any changes in heart rate. Although the cardiac output and MAP increases were significant statistically, the magnitude of change was small and thus unlikely to be of clinical importance.

This is in agreement with a previous study in which we investigated epidural meperidine in doses up to 100 mg for analgesia after Cesarean section and found no clinically important changes in arterial pressure or heart rate.¹¹ However, in that study the patients were studied in the early postoperative phase, and the administration of peri-operative fluids and the persisting effects of epidural local anesthetic made it difficult to clearly exclude any hemodynamic effects of epidural meperidine. In this study, fluid administration was withheld, and no other drugs were administered epidurally other than the study drug, thus allowing more subtle changes in hemodynamic status to be detected.

We chose to investigate a dose of 50 mg epidural

FIGURE Heart rate, mean arterial pressure and cardiac output recorded during the study. At baseline, and after epidural injection of saline and meperidine.

meperidine as this dose has previously been described for intraoperative analgesia during Cesarean section under epidural anesthesia.¹² In our unit, we commonly use this dose intra-operatively to supplement local anesthesia, followed by a smaller dose (25 mg) for postoperative analgesia. For the purpose of this study, meperidine was given earlier, before giving the local anesthetic. When used for patient controlled epidural analgesia after Cesarean section and other surgery, meperidine has compared favourably with fentanyl^{13,14} and local anesthetic-opioid combinations.¹⁵ In our own previous study, we found that a dose of 25 mg was the optimum for postoperative analgesia use.¹¹

At higher doses ($2.6\text{-}3.8 \text{ mg}\cdot\text{kg}^{-1}$), surgical anesthesia can be obtained by using only epidural meperidine. However, at this dose, epidural meperidine can have clinically significant hemodynamic effects as well as causing drowsiness and hypoventilation.¹⁶ There are no published reports of such high doses used in obstetric anesthesia. Concern for systemic absorption, and transplacental transfer of meperidine may be a factor precluding the use of such high doses.

Several mechanisms can be postulated for our present hemodynamic findings. In most patients, there was evidence of sensory block, which would also have been associated with some degree of sympathetic block. This would result in vasodilatation and the accompanying reduction in afterload would account for the small increase in the stroke volume and hence cardiac out-

put.¹⁷ However, this mechanism does not account for the increase in arterial blood pressure, which would imply that the contractility of the heart had also increased. Although it is possible that systemic absorption of meperidine may have contributed to such hemodynamic changes either by acting centrally or by direct vasodilatation, we have previously found that plasma concentrations of meperidine were relatively low (median concentration 213 ng·ml⁻¹) 20 min after epidural injection of 50 mg meperidine.¹¹

Epidural meperidine resulted in sensory changes, with upper limits at T₈ (L₁-T₂) in most of the patients (94%). We measured our sensory changes commencing from L₅ but did not attempt to measure lower limits, as this would have interfered with the impedance cardiography monitoring. Saline was injected unknown to the patients, to exclude psychological factors, such as sensation of the epidural injection as a cause of the patient's hemodynamic changes. Interestingly, epidural saline also caused sensory blocks in two patients (up to T₈ and L₁), but without any accompanying hemodynamic changes. This unexpected finding has been previously reported by Hore *et al.*, although the exact mechanism is uncertain.¹⁸ Although we did not formally test for motor block, as this would have interfered with the monitoring of hemodynamic variables, none of our patients complained of leg weakness during or at the completion of the study.

Both the Dinamap and BoMed are well-established devices for determining changes in hemodynamic variables in healthy adult subjects.¹⁹⁻²² During pregnancy, the Dinamap reportedly overestimates systolic arterial pressure, though the repeatability of its measurements is well maintained with confidence limits of $\pm 10\%$.¹⁹ Milson *et al.* compared the stroke volume from transthoracic electrical bioimpedance devices against dye dilution in late pregnancy, and showed that the method is a reliable trend monitor in this setting.²¹ As a prelude to our current study, we validated our use of the Dinamap and the BoMed in a group of 20 parturients requiring Cesarean section who were given lidocaine 2% with adrenaline 1:200,000. The Dinamap and BoMed were consistently able to detect the changes in cardiac output and arterial pressure that occur after the epidural injection (unpublished data).

In summary, we found that epidural meperidine 50 mg given to non-labouring term parturients produced small increases in hemodynamic variables that are unlikely to be of clinical importance. Although meperidine produces marked hemodynamic changes when given intrathecally for anesthesia, similar hemodynamic changes were not seen when meperidine was used for epidural analgesia.

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