Intravenous meperidine for control of shivering during Caesarean section under epidural anaesthesia

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To determine the efficacy of meperidine in controlling shivering during epidural anaesthesia for Caesarean section, forty-six parturients were studied. After delivery of the infant, shivering patients received either a single dose of intravenous meperidine 50 mg, or saline in a randomized double-blind fashion. Shivering was classified on a scale of 0 to 3 (grade 0 = none, grade 3 = severe shivering that was distressing to the patient and interfered with monitoring). Shivering and other variables were recorded at epidural placement, skin incision, delivery, and 2, 5, 15, 30 and 60 minutes following injection. Administration of meperidine resulted in a significant decrease in both the overall incidence of shivering (87 to 35 per cent, $p < 0.01$) and severity of shivering (grade 3: 57 to 0 per cent, $p < 0.01$), compared with saline (incidence: 87 to 83 per cent, grade 3: 57 per cent, no change). This effect was apparent within two minutes of drug injection and persisted throughout the study period. There were no differences in vital signs, oxygen saturation or temperature between groups. The incidence of nausea was similar, although patients receiving meperidine were more drowsy at two and five minutes following injection ($p < 0.01$) compared with patients in the saline group. There were no differences in level of consciousness at the later intervals. The mechanism of action of meperidine on shivering remains to be elucidated.

Key words

ANAESTHESIA: obstetrics; ANAESTHESIA TECHNIQUES: epidural; COMPLICATIONS: shivering; ANALGESICS, NARCOTIC: intravenous meperidine.

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Shivering is a well recognized side effect of epidural anaesthesia.[1-3] It is distressing to the patient, interferes with monitoring devices and increases oxygen consumption and cardiac output.[4,5] Intravenous meperidine has been employed successfully to treat shivering following general anaesthesia,[7] amphotericin chemotherapy,[8] and cardiac surgery.[9] The study was designed to evaluate the efficacy and safety of intravenous meperidine in controlling shivering during epidural anaesthesia for Caesarean section.

Methods

The protocol was approved by the Hospital Ethics Committee. Informed consent was obtained from each patient. Forty-six patients (ASA physical status I) undergoing Caesarean section with epidural anaesthesia were studied. Patients with known sensitivity to meperidine, or with any obstetrical or anaesthetic condition that might dictate against the use of regional anaesthesia, were excluded.

The epidural catheter was inserted at the L_{2-3} or L_{3-4} interspace at the time of Caesarean section (12 patients), unless previously placed for analgesia during labor (34 patients). After fluid loading with 1–2 L of 0.9 per cent saline, carbonated two per cent lidocaine with 1:200,000 epinephrine was given in 4 ml increments via the epidural catheter to achieve an adequate block. Arterial pressure, electrocardiograph, oxygen saturation, respiratory rate and tympanic membrane temperature were monitored continuously. Oxygen, 6 $L \cdot min^{-1}$, was administered via a plastic face mask.

After delivery of the infant, patients received a single dose of intravenous meperidine 50 mg or 0.9 per cent saline in a randomized double-blind fashion. If not shivering at the time of delivery, the patient did not receive intravenous treatment, and no further measurements were recorded. Shivering was classified as 0 = none, 1 = mild, but not distressing to the patient, 2 = moderate and distressing, 3 = severe, distressing, and interfering with monitoring. Potential side effects of meperidine such

as nausea, vomiting or diminished respirations were carefully noted. Level of consciousness was classified as 0 = asleep, 0.5 = drowsy but arousable, and 1 = awake. Shivering and other variables were recorded at epidural placement, skin incision, delivery, and 2, 5, 15, 30 and 60 minutes following injection of meperidine or saline. All patients received an infusion of syntocinon (20 units·L^{-1}) following clamping of the umbilical cord, and a single dose of epidural fentanyl (50 μg diluted in 10 ml 0.9 per cent saline) 30 minutes after delivery.

Data were analyzed by Chi Square with Yates' correction for continuity, Wilcoxon's rank sum test, analysis of variance, and Student's t test where applicable.[10–12] The results are expressed as mean values (± SEM). A p value < 0.05 was considered significant.

Results

Forty patients received meperidine or saline for shivering (n = 20 in each group). The remaining six patients did not receive intravenous treatment as they were not shivering at the time of delivery. The groups were similar with respect to age (meperidine: 29.2 ± 1.1 years, vs saline: 27.9 ± 1.4 years) and height (meperidine: 158.7 ± 1.3 cm, vs saline: 157.7 ± 1.0 cm), although the mean weight of the saline group was less than that of the meperidine group (69.2 ± 2.3 vs 78.6 ± 2.6 kg, $p < 0.05$). The majority of patients in both groups were primigravidas (16 meperidine, 12 saline) undergoing emergency Caesarean section. The indication for Caesarean section was usually cephalopelvic disproportion and failure to progress (28 patients) or malpresentation (seven patients). The duration of labour prior to Caesarean section was similar between groups, being 12.3 ± 2.2 hours for meperidine and 8.4 ± 2.2 hours for the saline group ($p > 0.1$). The dose of epidural lidocaine (17.4 ± 1.6 ml meperidine group vs 19.3 ± 0.7 ml saline) and level of block achieved were similar between groups. There were no differences in time of skin or uterine incision to time of delivery, or total duration of surgery between the meperidine and saline groups (7.3 ± 0.9 vs 6.4 ± 0.6 min, 1.6 ± 0.2 vs 1.7 ± 0.1 min, and 46.3 ± 5.3 vs 48.2 ± 2.7 min, respectively).

TABLE I Number of patients experiencing varying degrees of shivering prior to epidural lidocaine (Epid), at skin incision (Inc), delivery (Del), and following administration of intravenous meperidine or saline.† (See text for classification of shivering).

				Minutes post delivery				
	Epid	*Inc*	*Del*	*2*	*5*	*15*	*30*	*60*
Meperidine								
None	13	4	3	15	18	20	17	18
Mild	4	1	0	4	1	2	5	4
Moderate	2	5	7	4	4	1	1	1
Severe	4	13	13	0	0	0	0	0
Saline								
None	8	3	3	4	6	6	5	9
Mild	1	2	1	1	1	4	3	5
Moderate	6	5	6	7	5	6	6	6
Severe	8	13	13	11	11	7	9	3

$p < 0.01$ between groups for all observation periods following delivery (Wilcoxon's rank sum).
†3 patients in each group did not receive intravenous treatment as they were not shivering at the time of delivery.

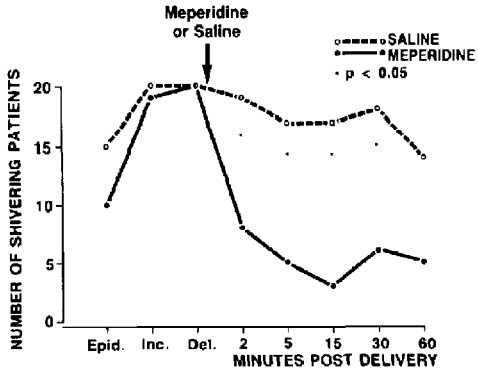

FIGURE 1 Number of patients shivering during Caesarean section prior to epidural lidocaine (Epid), at skin incision (Inc), delivery (Del), and following intravenous administration of meperidine or saline.

The incidence of shivering before administration of epidural lidocaine was 43 per cent in the meperidine group and 65 per cent in the saline group (Table I). By delivery, nearly all patients in both groups were shivering (40 of 46 parturients), the majority experiencing severe grade 3 shivering (57 per cent). Administration of intravenous meperidine resulted in a significant decrease in the incidence ($p < 0.01$, Chi Square) and severity ($p < 0.01$, Wilcoxon's rank sum) of shivering compared with saline (Figures 1 and 2, Table I). This effect was apparent within 2 min, and persisted throughout the study period.

There were no significant differences in blood pressure, heart rate, oxygen saturation, respiratory rate or temperature between the two groups before or after administration of meperidine or saline (Table II). The incidence of nausea was similar between groups (meperidine nine patients, saline eight patients). Supplemental drug requirements (diazepam and droperidol) were similar between the meperidine (four and nine patients) and saline groups (seven and eight patients), respectively. Patients receiving meperidine were significantly more drowsy at 2 and 5 min following injection ($p < 0.01$,

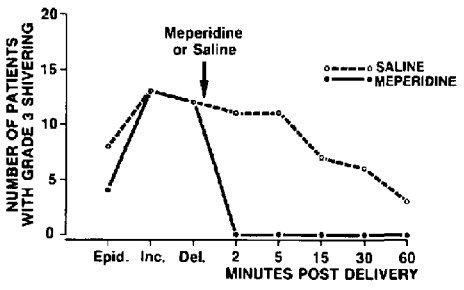

FIGURE 2 Number of patients experiencing grade 3 shivering (severe, distressing shivering that interfered with monitoring). Time intervals as in Figure 1. $P < 0.01$ between groups at all time intervals following the administration of the study drug (Wilcoxon's rank sum test).

Wilcoxon's rank sum) although there were no differences in levels of consciousness between groups at the later intervals (Table III).

TABLE III Level of consciousness following injection of meperidine or saline (number of patients per group).* All patients were awake prior to the study drug

	Minutes				
	2	*5*	*15*	*30*	*60*
Meperidine					
Awake	11	7	10	9	10
Drowsy	6	9	4	5	4
Asleep	3	4	6	6	6
Saline					
Awake	19	17	15	12	10
Drowsy	1	3	2	3	6
Asleep	0	0	3	5	4

$p < 0.01$ between groups at 2- and 5-minute observation periods (Wilcoxon's rank sum).
Min refers to minutes after treatment drug.
*Data are only for patients receiving intravenous treatment for shivering (n = 20 in each group).

Discussion

The incidence of shivering in parturients receiving epidural analgesia varies between 20 and 50 per cent.[3,13,14] It is also recognized that shivering may occur during labour and delivery in the absence of epidural anaesthesia.[1,2] Intense and uncontrollable shivering in the obstetrical setting interferes with monitoring of the arterial pressure, electrocardiograph and oxygen saturation. In addition, studies of non-obstetrical shivering have documented the potential deleterious effect of this complication. Post-anaesthetic shivering may increase oxygen consumption up to 500 per cent, increase cardiac work, decrease mixed

TABLE II Systolic arterial pressure in mmHg (SAP), heart rate (HR) beats per min, temperature (T) °C, respiratory rate (RR) breaths per min, and oxygen saturation (SaO_2) per cent during the study period. M = Meperidine group, S = Saline. Mean ± SEM

				Minutes				
	Epid	*Inc*	*Del*	*2*	*5*	*15*	*30*	*60*
SAP								
M	126 ± 3	120 ± 4	117 ± 3	117 ± 4	118 ± 3	113 ± 3	113 ± 3	115 ± 4
S	121 ± 3	117 ± 2	116 ± 2	115 ± 3	116 ± 3	112 ± 3	113 ± 3	110 ± 4
HR								
M	101 ± 4	106 ± 3	114 ± 3	113 ± 3	109 ± 3	106 ± 3	104 ± 4	97 ± 3
S	102 ± 3	113 ± 4	117 ± 5	118 ± 5	116 ± 5	114 ± 5	116 ± 5	109 ± 5
T								
M	36.1 ± 0.2	36.0 ± 0.2	36.0 ± 0.2	36.0 ± 0.2	36.0 ± 0.2	35.9 ± 0.2	35.7 ± 0.2	35.8 ± 0.2
S	36.3 ± 0.2	36.3 ± 0.3	36.2 ± 0.3	36.2 ± 0.2	36.1 ± 0.3	36.2 ± 0.2	36.2 ± 0.2	36.2 ± 0.3
RR								
M	18 ± 1	18 ± 1	18 ± 1	17 ± 1	17 ± 1	16 ± 1	16 ± 1	16 ± 1
S	17 ± 1	19 ± 1	19 ± 1	19 ± 1	19 ± 1	17 ± 1	17 ± 1	16 ± 1
SaO_2								
M	98.1 ± 0.3	99.0 ± 0.2	98.8 ± 0.2	98.2 ± 0.3	97.8 ± 0.3	97.4 ± 0.3	96.2 ± 0.4	96.7 ± 0.4
S	98.5 ± 0.3	98.0 ± 0.3	98.8 ± 0.3	98.0 ± 0.3	97.3 ± 0.6	97.5 ± 0.3	97.2 ± 0.2	96.9 ± 0.3

There were no significant differences between groups. Epid = prior to epidural lidocaine, Inc = skin incision, Del = delivery; Min refers to number of minutes following administration of meperidine or saline. Data are only for patients receiving intravenous treatment for shivering (n = 20 in each group).

venous oxygen saturation, and increase demand on ventilation such that hypoxaemia and acidosis develop.[4,5,15–17] Thus, muscle activity involved in shivering may be both distressing and potentially hazardous to the parturient.

The incidence of shivering in the present study was very high, even before epidural anaesthesia was established (43 per cent in the meperidine group and 65 per cent in the saline group). By delivery, the majority of patients (87 per cent) were shivering, many (57 per cent), severely so. Various mechanisms have been invoked to explain the shivering observed during epidural anaesthesia including decreases in core temperature and misinformation from receptors. Decreases in core temperature may be due to sympathetic blockade which results in peripheral vasodilatation, increased cutaneous blood flow, and subsequent increased heat lost via skin.[14,18] A fall in core temperature may also be due to a cold operating room, or the rapid infusion of crystalloid solutions at room temperature.[19–21] Shivering with epidural anaesthesia may also result from the differential inhibition of afferent thermoreceptors fibres within the spinal cord[22] or direct effects of cold anaesthetic solutions upon thermosensitive structures within the spinal cord.[23] As well, local anaesthetics introduced into the epidural space might act to modify environmental thermal cues, with resultant inappropriate thermal responses to false information.[24]

Based on these mechanisms, various authors have attempted to reduce the incidence of shivering in their patients. Successful treatment modalities for non-obstetric patients have included covering the patient with blankets and/or warming the operating room suite.[14,19] Other modalities such as warming the local anaesthetic solution[3,20] or warming the intravenous fluids[21,25] have met with varying degrees of success. For example, Webb *et al.*[3] were unable to show any difference in incidence of shivering between epidural bupivicaine (0.25 per cent, 10 ml) at 15, 20 or 37° C, despite similar levels of analgesia in 48 labouring patients. Similarly, McCaroll *et al.*[25] were unable to document any benefit of administering warmed (34°C) intravenous fluids (0.9 per cent saline, 2 L) compared with fluids at room temperature in a randomized study of 40 patients undergoing elective Caesarean section with epidural lidocaine 2 per cent. In fact, the incidence of shivering was higher in patients receiving the warmed fluids (55 versus 35 per cent).

Meperidine has previously been shown to be effective in the non-obstetric treatment of postanaesthetic shivering following general anaesthesia with volatile or narcotic based techniques,[26] after cardiopulmonary bypass,[5] and during chemotherapy with amphotericin B infusions.[8] Burks *et al.*[8] observed that 25 to 60 mg of meperidine administered over 20 minutes was highly effective in treating the shaking chills and fever in 19 patients receiving amphotericin chemotherapy. Pauca *et al.*[7] administered meperidine (pethidine) in 5 mg increments to 27 patients shivering after general anesthesia. This was found to be effective only at the higher cumulative dose (> 20 mg). In constrast, morphine and fentanyl were not effective in decreasing shivering.[7] Similarly, Claybon and Hirsh[27] found a dose–response relationship for meperidine. Postoperative shivering ceased in 68 per cent of cases with 12.5 mg, in 75 per cent of cases with 25 mg and in 89 per cent of cases with 50 mg. Guffin *et al.*[9] found that meperidine 25 or 50 mg was effective in reducing the incidence of shivering and improving mixed venous oxygen saturation following cardiopulmonary bypass in 11 of 20 patients, whereas morphine 5 or 10 mg was ineffective. In contrast, Harris *et al.*[28] were unable to demonstrate any protective effects of 12.5 or 25 mg of meperidine in preventing shivering during extracorporeal shock wave lithotripsy under lidocaine epidural anaesthesia. They were also unable to show any benefit from the administration of small doses of meperidine (6.25, 12.5 or 25 mg) in the treatment of subsequent shivering.

The present study documents that a single dose of 50 mg meperidine reduces both the incidence and severity of shivering during Caesarean section under epidural anaesthesia. The drug was given in a randomized, double-blind fashion, and was especially effective in eliminating the severe grade 3 shivering. The administration of meperidine appeared to be safe in our patients, although there was an initial period of drowsiness (two and five minutes post drug injection). However, the levels of consciousness were similar between groups within 15 minutes of drug administration. Respiratory rate and oxygen saturation were both maintained within normal limits, as were arterial pressure and heart rate. As well, the incidence of nausea and the requirements for anti-emetics and anxiolytics were similar between groups.

The mechanism of action of meperidine on reducing shivering is uncertain. It may include a central action, perhaps related to that of taurine. Taurine is a sulfur containing neurotransmitter which inhibits central heat production and conservation pathways.[29,30] Murphy *et al.*[31] demonstrated that intracerebroventricular and intravenous administration of this putative inhibitory neurotransmitter stopped the shivering in unoperated squirrel monkeys anaesthetised with halothane and nitrous oxide. Another possible mechanism of action of meperidine could be via modulation of nociceptive and temperature information in the brain, spinal cord or rexed laminae, mediated through one or more of the recognized subpopulations of opioid receptors.[32] However, the failure of other opiates such as morphine or fentanyl in reducing the incidence of shivering following cardiopulmonary bypass or general anaesthesia[5,7,27] makes this theory less likely.

Recently, the application of radiant heat to the face and chest was shown to be highly effective in inhibiting postanaesthetic shivering in patients undergoing various surgical procedures (including elective Caesarean section) with spinal, epidural or general anaesthetic techniques.[33] This may be due to the activation of "warmth receptors" that are densely distributed in the blush region, which may alter the thermal signals reaching the nervous system and thus inhibit postanaesthetic shivering despite low core temperature.[33] One can therefore speculate that meperidine may exert some effect on these "warmth receptors."

In summary, shivering during epidural anaesthesia was a common complication in patients undergoing emergency Caesarean section. The high incidence of shivering may be due to decreases in core temperature secondary to peripheral vasodilation from sympathetic blockade and/or cold intravenous fluids. As well, effects of cold epidural solutions on thermoregulating structures and/or other mechanisms may also play a role. Shivering in these patients may be successfully and safely treated with intravenous meperidine after delivery of the infant. The mechanism of action of meperidine on shivering remains to be answered.

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Résumé

Afin de déterminer l'efficacité de la mépéridine dans le contrôle des frissons lors d'une anesthésie épidurale pour césarienne, 46 parturientes ont été étudiées. Après l'accouchement de l'enfant, les patientes ayant frissonné ont reçu à double insu soit une dose unique intraveineuse de mépéridine 50 mg ou du salin après randomisation. Les frissons ont été classifiés selon une échelle de 0 à 3 (grade 0 = aucun, grade 3 = frisson sévère qui était inconfortable pour la patiente et interférant avec la surveillance). Les frissons ainsi que d'autres variables ont été enregistrés lors de la mise en place de l'épidurale, l'incision, l'accouchement, et à 2, 5, 15, 30 et 60 minutes après l'injection. L'administration de mépéridine provoqua une diminution significative de l'incidence totale des frissons (87 à 35 pour cent, $p < 0.01$) ainsi que de la sévérité des frissons (grade 3: 57 à 0 pour cent, $p < 0.01$), comparativement au salin (incidence: 87 à 83 pour cent, grade 3: 57 pour cent, aucun changement). Cet effet était apparent en dedans de deux minutes après l'injection du médicament et persista tout le long de l'étude. Il n'y avait aucune différence dans les signes vitaux, la saturation d'oxygène ou la température entre les groupes. L'incidence des nausées était identique même si les patientes avant reçu la mépéridine étaient plus somnolentes à 2 et 5 minutes après l'injection ($p < 0.01$) comparativement au groupe salin. Il n'y avait aucune différence dans le niveau de conscience aux autres phases de l'étude. Le mécanisme d'action de la mépéridine sur les frissons demeure à être élucidé.