

Epidural fentanyl plus bupivacaine 0.125 per cent for labour: analgesic effects

Danilo Celleno MD, Giorgio Capogna MD

Ninety-five healthy nulliparous women, ASA physical status I-II with an uncomplicated pregnancy and single fetus in vertex position were given lumbar epidural analgesia. Patients in Group A (n = 35) received bupivacaine 0.125 per cent with epinephrine 1:800,000; Groups B (n = 30) and C (n = 30) received the same agents as Group A but with the addition to the initial dose of 50 or 100 µg of fentanyl respectively. All patients were evaluated for duration and quality of analgesia, duration of labour, method of delivery and total dose of bupivacaine used. The addition of either 50 or 100 µg of fentanyl resulted in longer duration of analgesia (93 ± 9 min and 106 ± 8 min respectively vs 55 ± 7) and reduced bupivacaine total doses (64 ± 0.03 and 55 ± 1.5 respectively vs 109.5 ± 1.3). Only the addition of 100 µg of fentanyl improved significantly the quality of analgesia (43.3 per cent of excellent scores vs 6.6 per cent in Group B and 5.7 per cent in Group A). Addition of fentanyl did not affect the duration of labour, the method of delivery and the neonatal neurobehaviour scores.

The combination of epidural local anaesthetics and fentanyl has been demonstrated to have benefit in anaesthesia for labour and delivery.^{1,2} Because fentanyl has no effects on sympathetic or motor neurons,³ it provides certain advantages over local anaesthetics, but has been shown to be inadequate as the sole agent.⁴

Bupivacaine 0.125 per cent has been reported to produce satisfactory analgesia for labour.⁵ There is evidence that diluted solutions of local anaesthetics in a larger volume are more effective than concentrated solutions in a small volume.⁶ Moreover diluted concen-

trations of bupivacaine, having less motor effects, may be useful in reducing operative deliveries.⁷

On the other hand, when low concentrations of local anaesthetics are used alone, analgesia may be incomplete, especially in the second stage of labour.⁸ Indeed, limited dosages of diluted local anaesthetics are sufficient to block the non-myelinated C-fibres in the first stage of labour, but may be inadequate to block the myelinated A-delta fibres in the second stage.⁸ The combination of bupivacaine with fentanyl has been shown to result in longer and more effective analgesia.^{3,8} However, the studies performed to date have not documented the effect of varying the dosage of fentanyl added to 0.125 per cent bupivacaine as the sole local anaesthetic throughout labour.

The present double-blind study was designed to evaluate if the addition of fentanyl in two different doses to 0.125 per cent bupivacaine affects the duration and the quality of analgesia, the length of labour and the total dose of bupivacaine required.

Methods

Informed consent was obtained from each patient and the study was approved by the Hospital Human Investigation Committee. Ninety-five healthy nulliparous labouring women, each with an uncomplicated pregnancy and a single fetus in the vertex position, were assigned randomly to one of the following groups: Group A (n = 35) received epidural bupivacaine 0.125 per cent with epinephrine 1:800,000; Group B (n = 30) and Group C (n = 30) received bupivacaine 0.125 per cent with epinephrine 1:800,000 with the addition of 50 or 100 µg of fentanyl respectively, to a total volume, in all three groups, of 12 ml.

When cervical dilatation had reached 4 cm, and after the infusion of 500 ml of lactated Ringer's solution, the epidural block was established. The procedure was performed using a 16G Tuohy needle, with the parturient in left lateral decubitus position. A catheter was placed at L₂-L₃ interspace, using a loss of resistance technique and advancing the catheter 2 cm cephalad.

The patients were then placed in the supine position,

Key words

ANAESTHESIA: obstetric; ANAESTHESIA: regional, epidural; ANALGESICS, NARCOTIC: fentanyl.

From the Department of Anaesthesia, Ospedale Fatebenefratelli, Isola Tiberina, Rome, Italy.

Address correspondence to: Dr. Giorgio Capogna, v. Maria Saveria Sanzi, 21, 00151 Roma, Italy.

with left uterine displacement, and the solution was injected through the catheter, according to the randomization protocol.

After the initial dose, additional doses of 12 ml of bupivacaine 0.125 per cent with epinephrine 1:800,000 were injected when pain recurred, until the time of delivery. In the second stage of labour, the mother was placed in the semirecumbent position. All the patients received a dose of lidocaine one per cent for the episiotomy repair. The epidural catheter was not withdrawn until two hours after delivery, to allow for renewal of the block in the event that surgical treatment might be indicated.

Baseline pain intensity, defined as the intensity of the pain assessed just prior to the block, has been measured with a 10 cm visual analogue pain scale (visual analogue score). The quality of analgesia through the labour was assessed by the following scoring system:

EXCELLENT: when mother was completely painfree from the first or the second injection until the end of delivery.

GOOD: when the mother was satisfied but some pain was experienced for a short period during labour or delivery.

INCOMPLETE: when the mother had significant pain relief, but experienced some pain during most of the time of labour and delivery.

FAILURE: when, after the start of epidural analgesia, pain was experienced during most time of labour and delivery.

NOT POSSIBLE TO EVALUATE: delivery by Caesarean delivery.

The peak effect was defined as the first painless contraction. The duration of analgesia was assessed as the time of repeat injections. All patients were asked for the recurrence of pruritus. Evaluation of motor block was assessed with Bromage's criteria.⁹ Total dose of bupivacaine used, number of additional doses, duration and quality of analgesia, length of labour and mode of delivery were recorded.

Neonatal outcome was evaluated by Apgar scores, cord blood gas analysis and neurobehavioural testing, using the Neurologic and Adaptive Capacity Score (NACS)¹⁰ at the 2nd and 24th hour. Statistical analysis was performed by Kruskal-Wallis one-way analysis of variance, Student Newman-Keuls test and Chi-square test, when appropriate. A *p* value <0.05 was considered significant.

Results

The groups were similar with respect to age, weight and gestational age (Table I). Baseline pain intensity was six or more in all groups. There were no differences among the groups in the peak-effect of analgesia (13–18 min).

The analgesia was satisfactory in all groups. The addition of both doses of fentanyl reduced the incidence of incomplete analgesia (Group A 22.8 per cent; Group B 13.3 per cent; Group C 3.3 per cent). Moreover, the

TABLE I Population studied (Mean \pm SD)

Group	A	B	C
Maternal age (years)	26.4 \pm 2.4	25.1 \pm 2.7	24.0 \pm 3.5
Maternal weight (kg)	66.2 \pm 3.5	65.3 \pm 2.5	65.2 \pm 3.1
Gestational age (weeks)	39.6 \pm 1.4	38.0 \pm 1.7	39.5 \pm 1.2

No significant differences between groups.

TABLE II Quality of analgesia

Score (%)	Group A	Group B	Group C
Excellent	5.7	6.6	43.3*
Good	65.7	66.6	46.6
Incomplete	22.8	13.3†	3.3‡
Failure	—	—	—
Not possible to evaluate	5.7	10	6.6

**p* < 0.001 vs Groups A and B.

†*p* < 0.05 vs Group A.

‡*p* < 0.001 vs Group A.

addition of 100 μ g of fentanyl to bupivacaine increased significantly the quality of analgesia (*p* < 0.001) (Table II). As shown in Table III, in Groups B and C mean duration of analgesia was significantly prolonged (*p* < 0.001), number of supplementary doses was reduced (*p* < 0.01) and the mean total bupivacaine dose was decreased (*p* < 0.001) as compared with Group A.

There were no differences among the groups in respect to mean lidocaine dose employed for the episiotomy repair (Table III). No motor block was observed in any patients before the lidocaine dose.

There was no significant difference between groups in the mode of delivery, and the duration of labour was also comparable, as shown in Table IV. Itching was the only significant side effect in the fentanyl groups as compared with Group A, and was reported by six patients in Group B and 16 patients in Group C (*p* < 0.01).

Itching was not a spontaneous complaint and was mostly confined to the area of analgesia.

TABLE III Effects of the addition of fentanyl on duration of analgesia, number of refill-doses and total bupivacaine dose. Dose of lidocaine used for episiotomy repair (Mean \pm SD)

	Group A	Group B	Group C
Duration of analgesia (min)	55.0 \pm 7	93.0 \pm 9*	106 \pm 8*
Number of refill-doses	7.3 \pm 0.15	4.3 \pm 0.02*	3.7 \pm 0.15*
Total bupivacaine dose (mg)	109.5 \pm 1.3	64 \pm 0.03†	55 \pm 1.5†
Total lidocaine dose (mg)	130 \pm 28	128 \pm 25	132 \pm 21

**p* < 0.01; †*p* < 0.001 vs Group A.

TABLE IV Method of delivery (percentages)

%	Group A	Group B	Group C
Spontaneous	82.8	76.6	83.3
Low forceps	11.4	6.6	10
Vacuum	—	6.6	—
Caesarean delivery	5.7	10	6.6

No significant differences between groups.

Neonatal outcome was good and was similar in all groups (Table V). No neonatal neurobehavioural score differences between groups were observed.

Discussion

The dose of bupivacaine employed in this study (15 mg) is well below the central nervous system or cardiac toxic threshold.^{11,12} The mean dose of bupivacaine injected was only 0.25 mg·kg⁻¹ every 55 minutes in the bupivacaine group, and every 106 minutes in the fentanyl-bupivacaine groups (mean values).

In contrast to this, IV infusions of 1.87 mg·kg⁻¹ over 60 minutes¹³ and 2 mg·kg⁻¹ over 150 minutes¹⁴ produced only subtoxic reactions. The low bupivacaine dose used represents a negligible risk in the event of accidental intravascular administration, with a further decreased risk with the addition of fentanyl, due to the lower mean dose of bupivacaine employed.

Decreased local anaesthetic requirements also lessen the danger of maternal hypotension. In addition, this low dose of bupivacaine may reduce the likelihood of a serious complication due to an inadvertent subarachnoid injection.

Maternal or neonatal respiratory depression subsequent to epidural narcotics remains a serious consideration. No delayed respiratory depression has been reported with the doses of fentanyl given within this study.¹⁵ Moreover, the

addition of epinephrine slows vascular absorption of epidural narcotics,¹⁶ reducing furthermore the risk of respiratory depression. Indeed maternal respiratory depression was not assessed in this study, but no neonatal effects were noted.

Profound analgesia may sometimes be thought by the patients to be unpleasant. By employing epidural anaesthesia with low concentrations of bupivacaine (0.125 per cent), our patients were able to preserve some perineal sensation, at least the feeling of pressure.

These advantages may be important with respect to reducing the incidence of use of forceps. With this technique the influence of instrumental delivery was minimal, despite the fact that all the patients were primiparae. This also could be due to the semirecumbent position of the patient in the second stage, that allowed a good perineal analgesia although with a low dose of bupivacaine. It has been shown that the position of the patient is important for the relief of perineal pain when low concentrations of local anaesthetics are used.¹⁷

In this study, the addition of 100 µg of fentanyl increased significantly the quality of analgesia, preserving the benefit of a low dose of local anaesthetic. Previously 80–100 µg of fentanyl was demonstrated to be effective in producing good perineal analgesia in the presence of a persistent occipito-posterior position.^{3,18} The addition of either 50 or 100 µg of fentanyl to the bupivacaine resulted in a more prolonged duration of analgesia, with a reduced number of additional doses through the labour and of the total dose of bupivacaine employed. A shorter first stage of labour has been reported with the addition of 50 or 100 µg of fentanyl to 0.25 per cent bupivacaine:¹⁹ this finding was not observed in our study.

The addition of fentanyl did not affect the peak-effect of analgesia, the duration of labour, the mode of delivery or the neonatal outcome, when compared with the 0.125 per cent bupivacaine group.

The prolonged analgesia obtained with the addition of fentanyl is in accordance with the fentanyl clearance from the cerebrospinal fluid, and with the mean duration of fentanyl analgesia of four to five hours.²⁰

Finally, the main advantage of the addition of 100 µg of fentanyl to 0.125 per cent bupivacaine is to increase the quality of analgesia, including at the same time the increase of safety for the mother, without affecting the newborn.

References

- 1 Youngstrom P, Eastwood D, Patel H, Bhatia R, Cowan R, Sutteimeer C. Epidural fentanyl and bupivacaine in labor: double blind study. *Anesthesiology* 1984; 61: A414.

TABLE V Neonatal outcome

	Group A	Group B	Group C
Apgar score			
1st min > 7	97.1%	96.6%	96.6%
5th min > 7	100%	96.6%	100%
Umbilical vein pH (mean ± SD)	7.32 ± 0.07	7.30 ± 0.09	7.31 ± 0.05
Umbilical artery pH (mean ± SD)	7.17 ± 0.04	7.21 ± 0.05	7.22 ± 0.07
NACS score			
2nd hour > 35	91.4%	90%	93.3%
24th hour > 35	100%	96.6%	100%
Infant weight (g) (mean ± SD)	3204 ± 96.3	3196 ± 143.2	3213 ± 90.2

No significant differences between groups.

- 2 Desprats R, Mandry J, Granjean H, Amar B, Pontonnier G, Lareng L. Analgésie péridurale au cours du travail: étude comparative de l'association fentanyl-marcaïne et de la marcaïne seule. *J Gyn Obstet Biol Repr* 1983; 12: 901-5.
- 3 Justins DM, Francis D, Houlton PG, Reynolds F. A controlled trial of extradural fentanyl in labour. *Br J Anaesth* 1982; 54: 409-14.
- 4 Carrie IES, O'Sullivan GM, Leegobin R. Epidural fentanyl in labour. *Anaesthesia* 1981; 36: 965-9.
- 5 Bleyaert A, Soetens M, Vaes L, Van Steenberge A, Van der Donck A. Bupivacaine 0.125% in obstetric epidural analgesia: experience in three thousand cases. *Anesthesiology* 1979; 51: 435-8.
- 6 Knepp NB, Cheer TG, Gutshe BB. Bupivacaine: continuous infusion epidural analgesia for labor. *Anesthesiology* 1983; 59: A407.
- 7 Van Zundert A, Vanderaa PP, Van der Donck A, Meeuwis H, Vaes L. Motor blockade expulsion times and instrumental deliveries associated with epidural analgesia for vaginal delivery. *Obstet Anesth Digest* 1984; 4: 152-6.
- 8 Gauthier et Lafayer. *Precis d'anesthésie loco-régionale*. Masson (Ed.) Paris, 1985.
- 9 Bromage PR. *Epidural analgesia*. Philadelphia: WB Saunders, 1978 p. 144.
- 10 Amiel-Tison C, Barrier G, Shnyder M, Levinson G, Huges S, Stefani, S. A new neurologic and adaptive capacity scoring system for evaluating obstetric medications in full-term newborns. *Anesthesiology* 1982; 56: 340-50.
- 11 Reynolds F. A comparison of the potential toxicity of bupivacaine, lidocaine and mepivacaine during epidural blockade for surgery. *Br J Anaesth* 1971; 43: 567-70.
- 12 Wiklund L, Berlin-Wahlen A. Splanchnic elimination and systemic toxicity of bupivacaine and etidocaine in man. *Acta Anaesthesiol Scand* 1977; 21: 521-8.
- 13 Morishima HO, Pedersen H, Finster M et al. Bupivacaine toxicity in pregnant and nonpregnant ewes. *Anesthesiology* 1985; 63: 134-9.
- 14 Liu P, Feldman HS, Giasi R, Patterson MK, Covino BG. Comparative CNS toxicity of lidocaine, etidocaine, bupivacaine and tetracaine in awake dogs following rapid IV administration. *Anesth Analg* 1983; 62: 375-9.
- 15 Lam AM, Knill RL, Thompson JL, Clement GP, Varkey GP, Spoel WE. Epidural fentanyl does not cause delayed respiratory depression. *Can Anaesth Soc J* 1983; 30: S78-9.
- 16 Bromage PR, Camporesi EM, Durant PAC, Nielsen CH. Influence of epinephrine as an adjuvant to epidural morphine. *Anesthesiology* 1983; 58: 257-62.
- 17 Hanson AL, Hanson B. Continuous mini-infusion of bupivacaine into the epidural space during labor. *Regional Anesth* 1985; 10: 139-44.
- 18 Baraka A, Maktaby M, Noueihid R. Epidural meperidine-bupivacaine for obstetric analgesia. *Anesth Analg* 1982; 61: 652-6.
- 19 Cohen SE, Tan S, Albright GA, Halpern J. Epidural fentanyl/bupivacaine combinations for labor analgesia: effect of varying dosages. *Anesthesiology* 1986; 65: A368.
- 20 Muller H, Borner U, Stoianov M, Hempelmen G. The perioperative use of epidural opiate. In: Yaksh TL, Muller H, Henquist A. *Anesthesiology and Intensive Care Medicine: Spinal opiate analgesia*. Heidelberg, Springer Verlag, 1982; p. 67.

Résumé

Quatre-vingt-quinze femmes nullipares en bonne santé ASA classe I-II lors d'une grossesse non-complicquée ont reçu une analgésie épidurale lombaire. Les patientes du groupe A (n = 35) ont reçu de la bupivacaine 0.125 pour cent avec épinéphrine 1:800,000; les patientes du groupe B (n = 30) et C (n = 30) ont reçu les mêmes médicaments que celles du groupe A mais avec l'addition d'une dose initiale de 50 ou 100 µg de fentanyl respectivement. Les patientes furent évaluées pour la durée et la qualité de l'analgésie, la durée du travail, la méthode d'accouchement et la dose totale de bupivacaine utilisée. L'addition de 50 et 100 µg de fentanyl a prolongé la durée de l'analgésie (93 ± 9 minutes et 106 ± 8 minutes respectivement versus 55 ± 7) et a réduit les doses totales de bupivacaine (64 ± 0.003 et 55 ± 1.5 respectivement versus 109.5 ± 1.3). Seule l'addition de 100 µg de fentanyl a amélioré significativement la qualité de l'analgésie (43.3 pour cent des scores excellents versus 6.6 pour cent dans le groupe B et 5.7 pour cent dans le groupe A). L'addition de fentanyl n'a pas affecté la durée du travail, et la méthode de l'accouchement et le score néonatal.