Regional Anesthesia and Pain

Intrathecal fentanyl does not modify the duration of spinal procaine block

Carl Boucher MD,
Michel Girard MD MHPE FRCPC,
Pierre Drolet MD FRCPC,
Yvan Grenier MD FRCPC,
Lyne Bergeron MD,
Hong Hanh Le Truong MD

Purpose: To document the clinical characteristics of spinal procaine with or without the addition of fentanyl in light of the failure rate observed previously with procaine 10%.

Methods: In a randomized, prospective, double-blind study, 52 patients received spinal anesthesia with 100 mg procaine and either saline 0.9% (0.4 ml) (CONTROL group) or 20 µg fentanyl (0.4 ml) (FENTANYL group). Sensory anesthesia to needle prick was evaluated each minute for ten minutes, every three minutes for 33 minutes and every five minutes until regression to T10. Motor block was assessed with the Bromage scale. Patients were questioned by telephone for pain suggesting transient radicular irritation (TRI) 48 hr later.

Results: Mean time to reach highest sensory level, maximum number of segments blocked and mean time for regression of the sensory level to T10 showed no difference. Time to recuperate to full flexion of knees and feet (Bromage 4) showed no difference. Nine patients had nausea (five in CONTROL group and four in FENTANYL group) and nine had pruritus (three in CONTROL group and six in FENTANYL group). No patient reported pain suggesting TRI.

Conclusion: Spinal procaine is appropriate for short-duration surgery. Fentanyl does not change the characteristics of the block or the incidence of side effects associated with spinal procaine.

soit une solution salée à 0,9 % (0,4 ml) (groupe témoin), soit 20 mg de fentanyl (0,4 ml) (groupe fentanyl). L'anesthésie sensorielle à la piqure a été évaluée à chaque minute pendant dix minutes, toutes les trois minutes pendant 33 min et à toutes les cinq minutes jusqu'à une régression à T₁₀. L'anesthésie motrice a été évaluée avec l'échelle de Bromage. Les patients ont répondu par téléphone à des questions sur la douleur suggérant un transient radicular irritation (TRI) 48 h plus tard.

Résultats : Le temps moyen nécessaire pour atteindre le plus haut niveau sensoriel, le nombre maximal de segments bloqués et le temps moyen pour parvenir à une régression du niveau sensoriel à T₁₀ n'ont montré aucune différence. Le temps de retrouver la flexion totale du genou et du pied (4 à l'échelle de Bromage) n'a pas différé non plus. Neuf patients ont eu des nausées (cinq chez les témoins et quatre dans le groupe fentanyl) et neuf ont présenté du prurit (trois témoins et six du groupe fentanyl). Aucun patient n'a mentionné de douleur rappelant TRI.

Conclusion : La procaine en injection rachidienne est appropriée aux interventions chirurgicales de courte durée. Le fentanyl n'en change pas les caractéristiques anesthésiques ou l'incidence des effets secondaires.

Objectif : Documenter les caractéristiques cliniques de la procaine, en administration rachidienne avec ou sans addition de fentanyl, à la lumière du taux d'insuccès observé précédemment avec la procaine à 10 %.

Méthode : Lors d'une étude randomisée, prospective et à double insu, 52 patients ont reçu une rachianesthésie avec 100 mg de procaine et,

PROCAINE was developed in 1905, making it one of the oldest local anesthetics. In spite of its extensive clinical use, it remains one of the least studied. Although its short duration of action is an advantage in ambulatory anesthesia, means of prolonging its effect might be required for longer surgery. Fentanyl alters the quality of anes-

From the Département d'anesthésie-réanimation, Hôpital Maisonneuve-Rosemont and Université de Montréal, Montréal, Québec, Canada.

Address correspondence to: Dr. Michel Girard, Département d'anesthésie-réanimation, Hôpital Maisonneuve-Rosemont, 5415 boul. l'Assomption, Montréal, Québec, H1T 2M4, Canada. Phone: 514-252-3426; Fax: 514-252-3542; E-mail: girardmi@videotron.ca

Accepted for publication January 16, 2001.

thesia when administered intrathecally with other local anesthetics, improving the duration of sensory anesthesia without delaying recovery of motor function.¹⁻⁴ In a non-randomized pilot study, Axelrod *et al.*⁵ suggested that spinal fentanyl could extend procaine's motor block but the exact characteristics of a spinal procaine block, with and without fentanyl, have never been compared in a double-blind, randomized, prospective manner.

In this study, our primary goal was to define the influence of fentanyl on spinal procaine in light of the failure rate observed previously by our group with plain procaine and reported elsewhere in this issue of the Canadian Journal of Anesthesia. Our secondary goal was to assess the advent of side effects related to the use of these medications.

Methods

After institutional review board approval and written informed consent, 54 patients, ASA I and II, aged 18 to 65 yr, scheduled for short-duration surgery under spinal anesthesia, were studied. Exclusion criteria were allergy to local anesthetics or to p-amino benzoic acid (PABA), neurologic, coagulation or cholinesterase anomalies and a body mass index >28.

Patients were divided into two groups in a randomized, double-blind, prospective manner. Patients in the CONTROL group ($n=26$) received 100 mg procaine 10% (1 ml) plus saline 0.9% (0.4 ml); patients in the FENTANYL group ($n=26$) received 100 mg procaine 10% (1 ml) plus 20 µg (0.4 ml) of fentanyl. After arrival to the operating room, routine monitors were installed (Datex AS3, Helsinki, Finland). Patients received 1 or 2 mg midazolam *iv* and 10 ml·kg⁻¹ saline 0.9%, then a blood pressure (BP) measurement was taken and used as baseline value. With the patient sitting, a midline lumbar puncture was performed with a 27-G Whitacre needle at the L3-L4 space. One ml cerebrospinal fluid was drawn to dilute the procaine to 5%. The end of the injection was T0. Sensory anesthesia was evaluated with a 26-G needle on the left mid-axillary line, at one minute intervals for ten minutes, three-minute intervals for 33 min and then five minute intervals until regression to T10. Once in the post-anesthesia care unit (PACU), motor blockade was assessed with the Bromage scale.

The BP was measured simultaneously with sensory levels. Hypotension was defined as a decrease in systolic BP <90 mmHg or 20% <baseline value. It was treated with 5-10 mg ephedrine *iv*. Pain during surgery was treated with 50 µg fentanyl *iv* and nausea with 10 mg metoclopramide *iv*. Pain in the PACU was treated with 10 mg meperidine *iv*.

On the second post-operative day, patients were asked by telephone if they suffered from backache. If they answered yes, they were asked if it radiated into the buttocks or legs. Care was taken to differentiate pain suggesting transient radicular irritation (TRI) from pain related to spinal puncture or surgery proper. For this study, TRI was defined as a bilateral moderate or severe pain, which had to start at the back or buttocks and radiate to the thighs and calves. The pain had to begin within 24 hours of surgery and last more than 24 hr.⁶ Patients were also questioned regarding the onset, duration and treatment used for any symptom.

Demographic data, time to highest sensory level and regression to T10, fentanyl doses, incidence of nausea or pruritus and ephedrine administration were compared with Student's *t* test, chi square or Fisher's exact test. Blocked segments at each interval, were compared with Mann-Whitney U test with Bonferroni correction. Repeated BP measurements were analysed with two-way analysis of variance. Sensory and motor block regression were analysed with Kaplan-Meier curves and compared with a log-rank test. Results are expressed as mean ± SD unless stated otherwise. The sample size of the study allowed for detecting differences between groups of 19 min for sensory regression to T10 and 24 min for motor regression (Bromage 4) (alpha error=0.05, beta error=0.2).

TABLE I Demographic data and type of surgery

	Group CONTROL ($n=26$)	Group FENTANYL ($n=26$)
Age (yr)	41 ± 14	37 ± 14
Weight (kg)	71 ± 12	71 ± 12
Height (cm)	168 ± 8	167 ± 10
Sex (M/F)	18/8	14/12
Type of surgery (n)*	9/14/3	12/9/5

*Urology/orthopedic surgery/general surgery, NS.

TABLE II Characteristics of blocks

	Group CONTROL ($n=26$)	Group FENTANYL ($n=26$)
Time from injection to highest sensory level (min)	17.1 ± 11.4	12.0 ± 4.7
Maximum number of blocked segments above L4 (n)	11 (7-15)†	11 (8-14)†
Time for sensory regression to T10 (min)	66 ± 20	83 ± 23
Time for regression of motor block to Bromage 4 (min)	87 ± 31	79 ± 27

†Values are median (range), NS.

FIGURE 1 Recovery from motor block to Bromage 4, Kaplan-Meier curves, log-rank test. NS.

FIGURE 2 Sensory regression to T10 as a function of time, Kaplan-Meier curves, log-rank test. NS.

Results

There was no difference between groups with regard to demographic data, duration or type of surgery (Table I). One patient in each group had to be removed from the final analysis because the surgery outlasted the duration of spinal anesthesia. Time to highest sensory level, maximum number of segments blocked, time to sensory regression to T10 and for regression of the motor block to Bromage 4 were similar in both groups (Table II). Figure 1 shows that recovery from motor block was similar between

groups. Sensory levels showed no difference in their regression patterns (Figure 2). Doses of midazolam (CONTROL: 1.15 ± 0.81 mg, FENTANYL: 1.00 ± 0.84 mg) administered showed no difference. Systolic BP measurements were similar for each interval. Ephedrine doses were similar (CONTROL: 7.11 ± 9.0 mg, FENTANYL: 4.4 ± 6.9 mg). The incidence of nausea (CONTROL: five patients, FENTANYL: four patients) and pruritus (CONTROL: three patients, FENTANYL: six patients) did not differ between groups. One patient in each group received meperidine *iv* in the PACU. No patient reported pain suggesting TRI on follow-up.

Discussion

Our study suggests that adding fentanyl 20 µg does not influence the height or duration of the block resulting from 100 mg spinal procaine. However, this study did not address the issue of post-operative analgesia, therefore comparison with trials studying post-operative analgesia must be considered with caution.

Our results differ from those reported previously with other local anesthetics that demonstrated that the addition of fentanyl to lidocaine increased the depth of anesthesia, as evidenced by duration of tolerance to tourniquet by approximately 50%.¹ Similarly, fentanyl prolonged the time for regression to S2 of spinal bupivacaine (120 ± 25 m *vs* 146 ± 54 m).² Both of these studies showed no influence of fentanyl on the duration of motor block. Axelrod *et al.*⁵ reported, in the only other study measuring the influence of fentanyl on spinal procaine, that 20 µg fentanyl added to various doses of procaine had no effect on the sensory levels achieved, but prolonged duration of motor block from 72 to 97 min. Reasons for the apparent discrepancy between Axelrod *et al.*'s study and ours might be that they differed in design: non-randomized pilot study *vs* double-blind, randomized trial. Also the endpoints for evaluating motor block were not the same.

The lack of influence of fentanyl on the characteristics of spinal procaine in our study may tentatively be explained by the ester structure of procaine. Although post-operative analgesia (quality of block) and duration of sensory and motor block are not the same, a somewhat similar phenomenon has been described with epidural 2-chloroprocaine (2-CP), another ester type local anesthetic. Indeed, 2-CP antagonizes the effect of fentanyl in epidural use, shortening the duration of the opioid analgesia and decreasing the analgesic effectiveness of subsequently administered epidural narcotics.^{7,8} The exact mechanism responsible for this observation is still being debated; hypotheses are a direct action of local anesthetics on opioid

receptors, an action mediated by a metabolite (4-amino-2-chlorobenzoic acid) of 2-CP, presence of disodium ethylene diamine tetraacetic acid (EDTA) in the 2-CP solution and finally, a physiologic antagonism on the nociceptor pathway or at the single cell level.⁹ Some of these mechanisms may be present when fentanyl is added to procaine. Interestingly, Singh *et al.* showed that 10 µg fentanyl also had no effect on the onset time or the duration of spinal tetracaine, another ester type anesthetic.¹⁰ However, 0.5 mg morphine, when added to tetracaine, was associated with prolonged post-operative analgesia.¹¹ Therefore, the association between the use of ester type local anesthetics and their potential antagonism of spinal or epidural narcotics is not clearly established.

Conclusion

Spinal procaine is appropriate for short-duration surgery. Height of sensory and motor blocks was similar with or without the addition of fentanyl. The incidence of side effects was minimal. No TRI was encountered. Fentanyl is not an effective means of prolonging spinal procaine's anesthetic effect.

Acknowledgments

The authors wish to thank Mrs. Christiane Côté B.Sc. for her assistance in the data collection.

References

- 1 Liu S, Chiu AA, Carpenter RL, *et al.* Fentanyl prolongs lidocaine spinal anesthesia without prolonging recovery. *Anesth Analg* 1995; 80: 730-4.
- 2 Ben-David B, Solomon E, Levin H, Admoni H, Goldik Z. Intrathecal fentanyl with small-dose dilute bupivacaine: better anesthesia without prolonging recovery. *Anesth Analg* 1997; 85: 560-5.
- 3 Palmer CM, Voulgaropoulos D, Alves D. Subarachnoid fentanyl augments lidocaine spinal anesthesia for cesarean delivery. *Reg Anesth* 1995; 20: 389-94.
- 4 Belzarena SD. Clinical effects of intrathecally administered fentanyl in patients undergoing cesarean section. *Anesth Analg* 1992; 74: 653-7.
- 5 Axelrod EH, Alexander GD, Brown M, Schork MA. Procaine spinal anesthesia: a pilot study of the incidence of transient neurologic symptoms. *J Clin Anesth* 1998; 10: 404-9.
- 6 Pinczower GR, Chadwick HS, Woodland R, Lowmiller M. Bilateral leg pain following lidocaine spinal anaesthesia. *Can J Anaesth* 1995; 42: 217-20.
- 7 Grice SC, Eisenach JC, Dewan DM. Labor analgesia with epidural bupivacaine plus fentanyl: enhancement with epinephrine and inhibition with 2-chloroprocaine. *Anesthesiology* 1990; 72: 623-8.
- 8 Corke BC, Carlson CG, Dettbarn W-D. The influence of 2-chloroprocaine on the subsequent analgesic potency of bupivacaine. *Anesthesiology* 1984; 60: 25-7.
- 9 Coda B, Bausch S, Haas M, Chapkin C. The hypothesis that antagonism of fentanyl analgesia by 2-chloroprocaine is mediated by direct action on opioid receptors. *Reg Anesth* 1997; 22: 43-52.
- 10 Singh H, Liu J, Gaines GY, White PF. Effect of oral clonidine and intrathecal fentanyl on tetracaine spinal block. *Anesth Analg* 1994; 79: 1113-6.
- 11 Drakeford MK, Pettine KA, Brookshire L, Ebert F. Spinal narcotics for postoperative analgesia in total joint arthroplasty. A prospective study. *J Bone Joint Surg Am* 1991; 73: 424-8.