

The Effect of Adding a Minidose of Clonidine to Intrathecal Sufentanil for Labor Analgesia

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Background: Preliminary studies have suggested that the addition of clonidine to intrathecal sufentanil prolongs analgesia without producing motor blockade.

Methods: Fifty-three nulliparous women in painful labor were included in this prospective, randomized, double-blinded study. Parturients at 2- to 5-cm cervical dilation received either 5 μ g sufentanil plus 30 μ g clonidine or 5 μ g sufentanil intrathecally, followed by 5 mg bupivacaine epidurally. The primary outcome was time until first request for additional analgesia. Visual analog pain scores, sensory changes, blood pressure, heart rate, ephedrine requirements, motor blockade, sedation, pruritus, and nausea were also recorded.

Results: All parturients but one had effective analgesia in both groups, with similar sensory levels never exceeding T2. The duration (mean \pm SD) of analgesia was longer in the sufentanil-clonidine group: 125 ± 46 versus 97 ± 30 min ($P = 0.007$). The incidence of hypotension and the ephedrine requirements (median with range) were higher in the sufentanil-clonidine group: 63% versus 12% ($P < 0.001$) and 7.5 mg [range, 0–25.5 mg] versus 0 mg [range, 0–6 mg] ($P < 0.0001$). The incidence of

fetal heart rate abnormalities during the first 30 min after intrathecal injection was similar in both groups (17% vs. 19%). No parturient had motor blockade.

Conclusions: The addition of 30 μ g clonidine to 5 μ g intrathecal sufentanil extended the duration of labor analgesia without producing motor blockade. However, as previously reported with 100–200 μ g clonidine, the incidence of hypotension and the ephedrine requirements were also increased, even when 30 μ g clonidine only was added. (Key words: α_2 -Adrenergic agonists; combined spinal epidural anesthesia; obstetrics; pain relief; regional anesthesia.)

INTRATHECAL sufentanil (5–10 μ g) has been shown to reduce pain without producing motor blockade during the latent phase of the first stage of labor.^{1–5} The combination of intrathecal sufentanil with other drugs has been investigated primarily in an attempt to prolong this relatively short-lasting labor analgesia (90–120 min mean duration). The addition of 250 μ g intrathecal morphine or 200 μ g intrathecal epinephrine has been disappointing; the former slightly prolonged the duration of action of 10 μ g intrathecal sufentanil at the expense of a high incidence of side effects,² and the latter had little² or no effect at all.⁴ In contrast, it has been shown that the addition of 2.5 mg intrathecal bupivacaine significantly prolongs the duration of 10 μ g intrathecal sufentanil.⁶ However, the addition of 2.5 mg intrathecal bupivacaine sometimes produces motor blockade^{7–9} and hypotension that can be severe.¹⁰ When 200 μ g intrathecal epinephrine is added to this combination, the duration of analgesia is further prolonged, but motor blockade appears less rare.¹¹

The α_2 -adrenergic agonist clonidine produces analgesia by a primarily spinal mechanism when administered intrathecally and potentiates intrathecal-epidural opioids but does not produce motor blockade.¹² In preliminary results published by Chiari *et al.*,^{||} the addition of 100–200 μ g clonidine prolonged the duration of action of intrathecal sufentanil during labor. However, the incidence of hypotension increased when these doses of clonidine were used. The combination of 30 μ g

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clonidine and 5 μ g sufentanil was assessed recently in a small, open-label, nonrandomized study conducted at our institution.¹³ This dose of clonidine also significantly increased the duration of action of intrathecal sufentanil during labor and the incidence of hypotension was not increased. However, it was impossible to draw any definite conclusions because of the study design. Thus we designed a prospective, randomized, double-blinded study to assess the effect of adding 30 μ g clonidine to 5 μ g intrathecal sufentanil during labor.

Materials and Methods

After we received institutional review board approval at both centers and written informed patient consent, we enrolled 53 parturients who requested epidural analgesia. Inclusion criteria included age ≥ 18 yr, weight ≤ 100 kg, height between 150 and 190 cm, American Society of Anesthesiologists physical status 1 or 2, nulliparity, uncomplicated full-term pregnancy, singleton pregnancy in vertex presentation, regular and painful uterine contractions, cervical dilation between 2 and 5 cm, normal fetal heart rate tracings, and initial systolic blood pressure (SBP) ≥ 115 mmHg.

After a preload of 250–500 ml lactated Ringer's solution, a "needle through needle" combined spinal epidural technique was performed with the parturient in the sitting position. A 8-cm (overall, 10.5 cm) 18-gauge Tuohy needle (Portex, Hythe, UK) was inserted into the epidural space at either the L2–L3 or the L3–L4 interspace using a loss-of-resistance-to-saline technique. A 12-cm, 27-gauge Whitacre spinal needle (Vigon, Ecouen, France) was passed through the epidural needle into the subarachnoid space. After a clear, free flow of cerebrospinal fluid was obtained, the study solution was injected through the spinal needle. The spinal needle was removed, and a 20-gauge epidural catheter (Portex) was inserted 3–5 cm into the epidural space. Aspiration was immediately attempted; if no fluid was obtained, a test dose of 5 mg bupivacaine (without epinephrine) was injected to check for intrathecal misplacement of the catheter.¹⁴ Patients were then placed in the recumbent position with left uterine displacement and head elevation.

Patients received intrathecally either 5 μ g sufentanil plus 30 μ g clonidine (SUF-CLO) or 5 μ g sufentanil alone (SUF) in a total volume of 2 ml preservative-free saline. Both the patient and the investigator were blinded to the study solution, which was prepared by

an anesthesiologist not involved in the patients' care, according to the group indicated in numbered sealed opaque envelopes. These envelopes had been prepared using a block-of-four random table with stratification to allocate the same number of patients in the two groups within each center.

The primary outcome variable was the duration of spinal analgesia defined as the time elapsed from intrathecal injection to the patient's first request for additional analgesia. Pain was assessed using a visual analog pain score (VAPS) (0 = no pain, 100 = worst imaginable pain) immediately before study drug injection; 5, 10, 15, 20, 30 min after injection; and every 15 min thereafter. On patient request, additional analgesia was provided *via* the epidural catheter using 12 ml 0.125% bupivacaine.

The upper level of sensory changes was determined in the mid-clavicular line using an alcohol swab. Blood pressure and heart rate were measured using an automated device (Dinamap; Critikon, Tampa, FL) every 5 min throughout the period of intrathecal analgesia, and additional measurements were made if abnormal fetal or maternal symptoms or signs were observed. For each parturient, the minimal SBP observed during the entire period of spinal analgesia (*i.e.*, before any supplemental analgesia *via* the epidural catheter) was noted specifically. Hypotension defined as an SBP < 95 mmHg or a decrease $> 25\%$ in SBP was documented and systematically treated by an intravenous injection of ephedrine (3–9 mg) that was repeated as needed. Motor blockade was assessed using the Bromage's scale modified by Phillips.¹⁵ Oxyhemoglobin saturation was monitored continuously by pulse oximetry (Nellcor 200, Hayward, CA). Sedation, pruritus, and nausea were rated subjectively as none, mild, moderate, or severe. All of these parameters were recorded at the same intervals as VAPS, except sensory changes and motor blockade, which were recorded 10, 20, and 30 min after intrathecal injection and every 15 min thereafter until the end of intrathecal analgesia.

Fetal heart rate and uterine activity were monitored throughout labor using external cardiotocodynamometry. During the period of intrathecal analgesia, any fetal heart rate abnormality was recorded by the anesthesiologist in accordance with the obstetric team (both blinded to the study drug). The following classification was used: absent or decreased variability, early decelerations, late decelerations, variable decelerations, and bradycardia. The duration of the first and second stages of labor, mode of delivery, total intravenous ephedrine and

local anesthetic requirements (excluding supplemental dosing for instrumental or cesarean delivery), and neonatal Apgar scores with arterial umbilical pH were also recorded.

Data are expressed as mean \pm SD unless stated otherwise. Groups were compared for single parametric, ordinal, and nominal variables by Student's unpaired *t* test, the Mann-Whitney U test, and Fisher's exact test or chi-squared analysis, respectively. The duration of analgesia was determined by Kaplan-Meier survival analysis followed by the log-rank test. The VAPS and hemodynamic data are presented using 95% confidence intervals¹⁶ and were compared using analysis of variance for repeated measures, followed by Student's unpaired *t* tests with Bonferroni corrections to assess differences between groups at each time point.¹⁷ Upper levels of sensory changes are presented as medians with the interquartile range in box plots and were compared using Mann-Whitney U tests with Bonferroni corrections to assess differences between groups at each time point. $P < 0.05$ was considered significant.

Results

Fifty-three patients were enrolled in the study. No technical difficulty was encountered during the combined spinal epidural procedure, and cerebrospinal fluid was identified in all patients. However, one patient had no analgesia at all within 15 min of the injection (SUF-

Table 2. Labor Analgesia Data and Maternal Side Effects during Intrathecal Analgesia

	SUF-CLO (n = 24)	SUF (n = 26)
Baseline VAPS (mm)	70 \pm 21	76 \pm 16
VAPS at reinjection	46 \pm 13	49 \pm 14
Duration of intrathecal analgesia (min)	125 \pm 46†	97 \pm 30
Total bupivacaine in labor* (mg)	74 \pm 38	63 \pm 22
Hypotension: incidence (%)	63‡	12
Minimal SBP recorded (mmHg)	94 \pm 12 [69]§	108 \pm 9 [84]
Motor blockade: incidence > 0 (%)	0	0
Sedation: incidence (%)	46	23
Score = 0, 1, 2, 3	13, 11, 0, 0	20, 6, 0, 0
Pruritus: incidence (%)	84	88
Score = 0, 1, 2, 3	4, 18, 2, 0	3, 23, 0, 0
Nausea: incidence (%)	8	0
Score = 0, 1, 2, 3	22, 0, 1, 1	26, 0, 0, 0

Values are mean \pm SD, if not stated otherwise [lower range in brackets].

SUF = sufentanil; CLO = clonidine; VAPS = visual analog pain score; SBP = systolic blood pressure.

* Bupivacaine used epidurally after intrathecal analgesia has vanned.

† $P = 0.007$ between the two groups.

‡ $P = 0.0003$ between the two groups.

§ $P < 0.0001$ between the two groups.

CLO group). Another patient had an emergency cesarean delivery (SUF-CLO group) 35 min after the intrathecal injection. A third patient (SUF-CLO group) had rapid cervical dilatation and an instrument-assisted vaginal delivery 110 min after the intrathecal injection without requesting additional analgesia. These three patients were excluded, so data from 50 patients were available. Patient characteristics, gestational age, baseline cervical dilatation, rate of spontaneous or augmented or induced labor, weight of the neonate (table 1), and baseline VAPS (table 2) were comparable for the two groups.

Figure 1 illustrates the duration of intrathecal analgesia as the percentage of patients not requesting additional analgesia *versus* time after the intrathecal injection. The duration of analgesia was longer in the SUF-CLO group than in the SUF group: 125 \pm 46 min *versus* 97 \pm 30 min ($P = 0.007$, table 2).

Figure 2 illustrates the onset of intrathecal analgesia during the first 45 min. The VAPS decreased dramatically and significantly in both groups after intrathecal injection, and no statistical differences were detected between the groups. All parturients had effective analgesia (VAPS \leq 25 mm) at 15 min.

The spread of the upper level of sensory changes

Table 1. Demographic and Obstetric Data

	SUF-CLO (n = 24)	SUF (n = 26)
Age (yr)	28 \pm 4	28 \pm 3
Weight (kg)	70 \pm 8	71 \pm 7
Height (cm)	166 \pm 6	166 \pm 5
Gestational age (wk)	40 \pm 0.9	40.1 \pm 1.1
Baseline cervical dilation (cm)	2.8 \pm 1.1	2.9 \pm 1.2
Cervical dilation at reinjection (cm)	5.5 \pm 2.0	5.7 \pm 2.4
Augmented labors	16/24	17/26
Induced labors	5/24	7/26
Intrathecal injection to delivery (min)	347 \pm 160	280 \pm 111
Stage 1 labor (min)	467 \pm 140	389 \pm 143
Stage 2 labor (min)	79 \pm 57	64 \pm 44
Instrumental delivery	9/24	8/26
Cesarean delivery	4/24	2/26
Weight of neonate (g)	3,501 \pm 485	3,433 \pm 346

Values are mean \pm SD.

SUF = sufentanil; CLO = clonidine.

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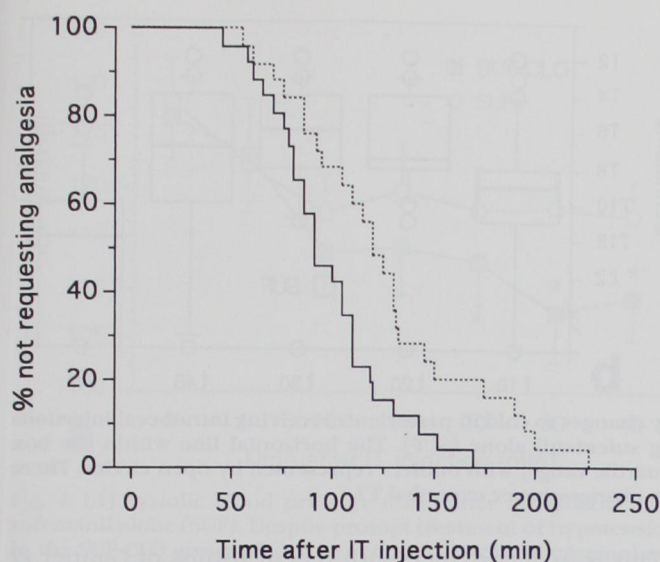


Fig. 1. The duration of spinal analgesia, as the percentage of parturients not requesting additional analgesia, after intrathecal injection of 5 µg sufentanil plus 30 µg clonidine (dotted line) or 5 µg sufentanil alone (solid line). The two groups differ according to Kaplan-Meier survival analysis followed by the log-rank test.

during intrathecal analgesia and at the time of epidural injection is shown in figure 3A (SUF-CLO group) and figure 3B (SUF group). There were no significant differences between the groups. No patient in any group had sensory changes above T2.

The incidence of hypotension during intrathecal analgesia was increased five times (63%) in the SUF-CLO group when compared with the SUF group (12%; $P = 0.0003$), and the minimal SBP observed was significantly lower in the SUF-CLO group (table 2). Ephedrine requirements (median \pm interquartile [range]) were also greater: 7.5 ± 16.5 [0–25.5] versus 0 ± 0 [0–6] mg ($P < 0.0001$). Despite prompt treatment of hypotension with intravenous ephedrine, the SBP remained significantly lower in the SUF-CLO group ($P = 0.02$; fig. 4A). In addition, administration of ephedrine was still required 65–120 min after intrathecal injection on four occasions in the SUF-CLO group, whereas no patient had hypotension beyond 45 min in the SUF group (fig. 4B). The incidence of abnormal fetal heart rate patterns during the first 30 min after intrathecal injection, Apgar scores, and umbilical arterial pH were similar in both groups (table 3). Hypotension during the 30-min period after redosing with 12 ml 0.125% bupivacaine in the epidural catheter was less pronounced (SUF-CLO vs. SUF group: 5 cases vs. 2 cases, and 0 ± 0.75 [0–15] vs. 0 ± 0 [0–6] mg for ephedrine requirements; difference not significant).

Maternal heart rates during intrathecal analgesia were significantly higher in the SUF-CLO group ($P < 0.0001$; fig. 5); more precisely, it did not decrease in this group when compared with baseline values ($P = 0.19$ by one-way analysis of variance for repeated measures), whereas it did in the SUF group ($P < 0.0001$).

No parturient had any motor blockade. Oxyhemoglobin saturation never decreased to $<93\%$ while parturients were breathing ambient air. There were no other significant differences in maternal side effects during intrathecal analgesia, although the incidence of mild sedation was twice as high in the SUF-CLO group (46 vs. 23%; $P = 0.14$; table 2).

The progress of labor (cervical dilation at reinjection, intrathecal injection to delivery, stage 1 and stage 2 duration) and the mode of delivery were not significantly different between the two groups (table 1). The total dose of bupivacaine administered epidurally during labor after the period of intrathecal analgesia was similar in both groups (table 2).

Discussion

Little information is available in the literature regarding the use of intrathecal clonidine for labor pain relief,¹² yet reports have been published in abstracted form^{18,19} or as a preliminary report.¹³ This prospective, randomized, double-blinded study shows that the addition of 30 µg

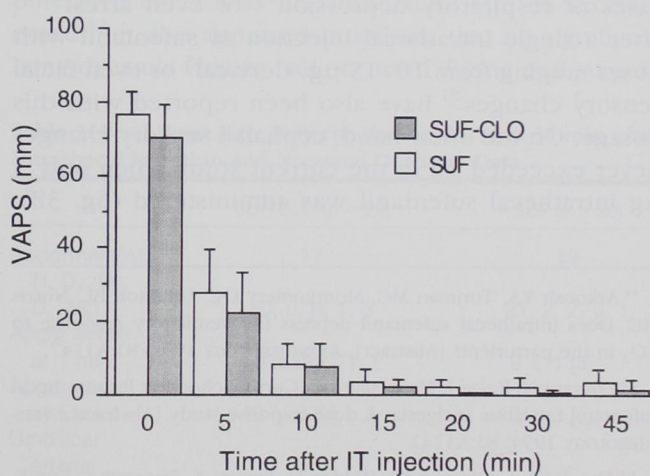


Fig. 2. The onset of spinal analgesia assessed by visual analog pain score (VAPS), after intrathecal injection of 5 µg sufentanil plus 30 µg clonidine (SUF-CLO) or 5 µg sufentanil alone (SUF). Each point represents the mean \pm 95% confidence interval. All VAPSs beyond baseline differ from their respective baseline values, but there was no significant difference between the two groups.

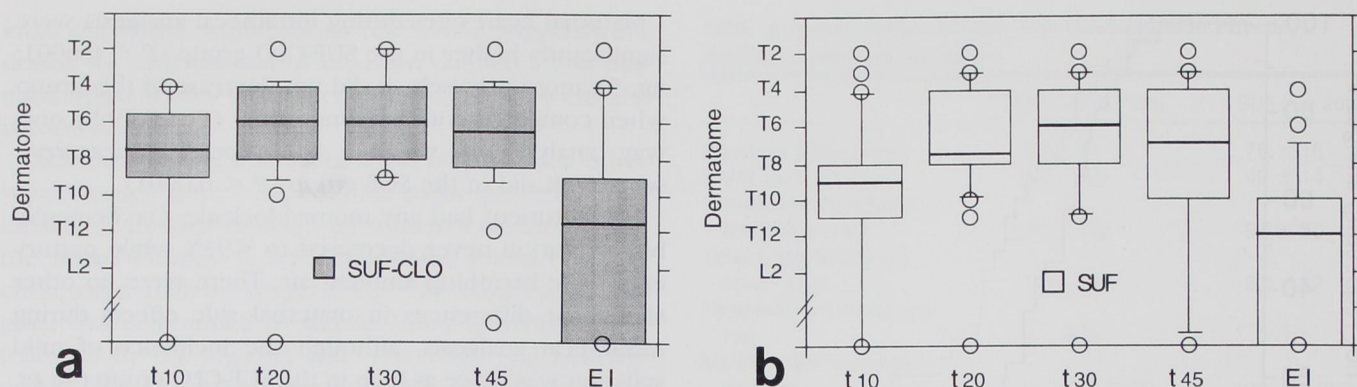


Fig. 3. Box plots representing the spread of the upper level of sensory changes to cold in parturients receiving intrathecal injections of (A) 5 μ g sufentanil plus 30 μ g clonidine (SUF-CLO) or (B) 5 μ g sufentanil alone (SUF). The horizontal line within the box represents the median, whereas the box itself represents the interquartile range, with outliers represented by open circles. There was no significant difference between groups, and cephalad sensory changes never exceeded T2.

clonidine to 5 μ g intrathecal sufentanil extends the duration of labor analgesia but also increases the incidence of hypotension.

Analgesia and Choice of Doses

The dose of intrathecal sufentanil used most often during labor is 10 μ g. However, this dose may depress the ventilatory response to carbon dioxide in the parturient.^{**} In addition, 10 μ g sufentanil has a significantly greater effect than 5 μ g on maternal end-tidal carbon dioxide level.¹⁹ Furthermore, there are several cases of transient difficulties in breathing and/or an inability to swallow using 10 μ g,^{3,20} and at least three cases of respiratory depression²¹ or even arrest^{22,23} after a single intrathecal injection of sufentanil with doses ranging from 10–15 μ g. Cervical⁵ or even facial sensory changes²⁰ have also been reported with this dosage. On the other hand, cephalad sensory changes never exceeded T2 in the current study when only 5 μ g intrathecal sufentanil was administered (fig. 3B).

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‡‡ Abouleish A, Camann W, Holden D, Emami A, Eisenach J, Yun E, Datta S: Antinociceptive interaction between intrathecal sufentanil and epidural bupivacaine: Additivity or synergism? [Abstract]. *ANESTHESIOLOGY* 1994; 81:A1144

§§ Gaiser R, Adams H, Cheek TG, Gutsche BB: Comparison of three different doses of intrathecal fentanyl and sufentanil for labor analgesia [Abstract]. *Reg Anesth* 1995; 20(suppl 2S):75

This is in accordance with recent results of Gautier *et al.*²⁴ In addition, 5 μ g intrathecal sufentanil¹ or even less has been reported to provide adequate analgesia during early labor.^{††‡‡} This was confirmed in the current study (fig. 2). Finally, the mean duration of analgesia ranged from 90–123 min with 10 μ g intrathecal sufentanil,^{2–6,25} 90–104 min with 7–5 μ g,^{1,13,‡} and still 97 min with 5 μ g in the current study. The similar duration of analgesia using either 5 or 10 μ g was confirmed in two randomized preliminary studies,^{††§§} although another randomized study suggests that a dose-response relationship might exist.²⁶

Of note, a 5-mg bupivacaine test dose was administered epidurally in the current study soon after the intrathecal injection, for safety considerations described in another publication.¹⁴ This epidural test dose did not seem to prolong the duration of spinal analgesia when compared with durations reported using a similar dose of intrathecal sufentanil without a concurrent test dose.^{1,13,§§} Although this was not a bias because it was used in both groups, this epidural test dose may have interacted with intrathecal sufentanil (\pm clonidine) to strengthen the intensity of analgesia,^{‡‡} and thus may have increased hemodynamic effects (see below).

We chose to investigate a low dose (30 μ g) of intrathecal clonidine based on the following considerations. First, clonidine has higher efficacy after intrathecal rather than after epidural or systemic administration¹² and acts synergistically with opioids.^{27,28} Second, a study performed in rats suggests that low-dose systemic clonidine enhances pregnancy-induced analgesia to visceral but not to somatic stimuli.²⁹ This corresponds well with the situation of our study done during early labor.¹

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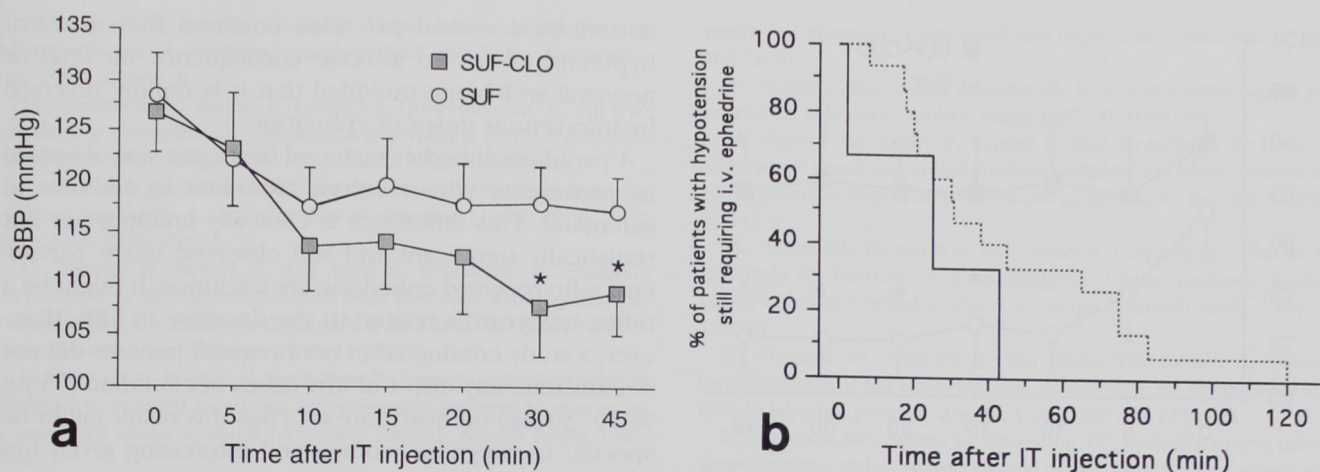


Fig. 4. (A) Systolic blood pressure (SBP) after intrathecal injection of 5 μ g sufentanil plus 30 μ g clonidine (SUF-CLO) or 5 μ g sufentanil alone (SUF). Despite prompt treatment of hypotension with intravenous ephedrine, the SBP remained significantly lower in the SUF-CLO group ($P = 0.02$). * $P < 0.05$ with Bonferroni corrections compared with the SUF group. (B) Kaplan-Meier survival analysis representing the time course of intravenous ephedrine administration after intrathecal injection of 5 μ g sufentanil plus 30 μ g clonidine (dotted line) or 5 μ g sufentanil alone (solid line). Administration of ephedrine was still required 65–120 min after intrathecal injection on four occasions in the SUF-CLO group, whereas no patient had hypotension beyond 45 min in the SUF group.

Third, nonobstetrical preliminary studies have shown that small doses of intrathecal clonidine (from 75 μ g to 30–25 μ g) significantly increase the duration of postoperative analgesia.^{30,|||###} Our results confirm this rationale. The mean duration of additional analgesia obtained in the current study with the addition of 30 μ g intrathecal clonidine averages 30 min and therefore is nearly comparable to the ≈ 40 min prolongation afforded by the addition of 100–200 μ g intrathecal clonidine to 2–7 μ g intrathecal sufentanil.^{12,||#} It is also comparable to the 35-min prolongation obtained with the addition of 2.5 mg intrathecal bupivacaine to intrathecal sufentanil.⁶

Hemodynamic Effects

The potential for hypotension after neuraxial administration of clonidine is well established.¹² However, we did not expect the important increase in both the incidence and intensity of hypotension that we observed with the addition of a dose as low as 30 μ g intrathecal

clonidine. The dose response for epidural or intrathecal clonidine is generally considered to be U shaped.^{12,31,32} Filos *et al.*³³ found that 150 μ g intrathecal clonidine decreased blood pressure by 21% when administered 45 min after cesarean section delivery, whereas larger doses (300 or 450 μ g) were not associated with this side-effect. When smaller doses (75 μ g to 30–25 μ g) of clonidine were associated with a local anesthetic to perform spinal anesthesia for nonobstetrical surgery, no additional hypotensive effect was first observed.^{##,***} As recently noted,¹² it also appeared promising that no significant hemodynamic change had occurred during anal surgery

Table 3. Fetal Heart Rate Patterns during the First 30 min after Intrathecal Injection and Neonatal Outcome Data

	SUF-CLO (n = 24)	SUF (n = 26)
Abnormal (%)	17	19
N, D ₁ , D ₂ , D _v , BC	20, 0, 0, 1, 3	21, 2, 2, 0, 1
Apgar score at 1 min*	9 \pm 0.5 [7]	9 \pm 1 [5]
Apgar score at 5 min*	10 \pm 0 [9]	10 \pm 0 [9]
Umbilical arterial pH*,†	7.22 \pm 0.10 [7.10]	7.20 \pm 0.10 [7.09]

SUF = sufentanil; CLO = clonidine; N = Normal; D₁ = early deceleration; D₂ = late deceleration; D_v = variable deceleration; BC = bradycardia.

* Median \pm interquartile range [lower range in brackets].

† Four missing values in SUF-CLO group and two missing values in SUF group.

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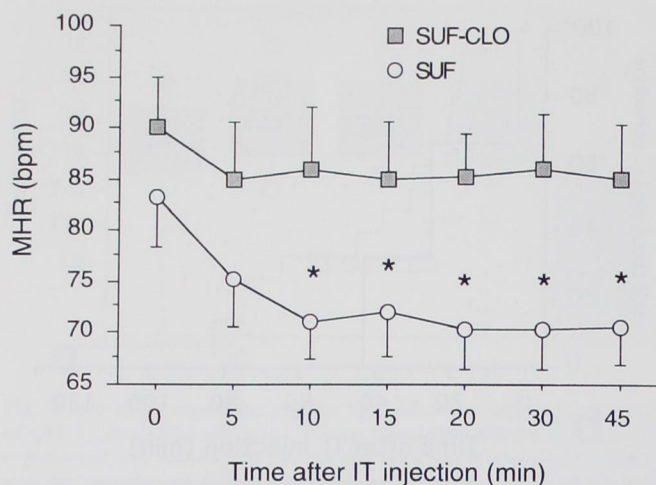


Fig. 5. The maternal heart rate (MHR) after intrathecal injection of 5 μ g sufentanil plus 30 μ g clonidine (SUF-CLO) or 5 μ g sufentanil alone (SUF). The MHR was significantly higher in the SUF-CLO group ($P < 0.0001$). * $P < 0.05$ with Bonferroni corrections compared with the SUF group.

when 60 μ g clonidine had been added to only 2.5 mg intrathecal bupivacaine.^{||||} Finally, because 200 μ g intrathecal clonidine alone^{||} or 100 μ g intrathecal clonidine in combination with intrathecal sufentanil[#] induced significant hypotensive effects in parturients, it was tempting to speculate that lower doses of intrathecal clonidine should be investigated.

Nonetheless, our results clearly show that even 30 μ g intrathecal clonidine added to intrathecal sufentanil still produces similar untoward hypotensive effects. This is not related to an increased cephalad spread (fig. 3A vs. 3B), but rather might have been promoted by the combined effects of the opioid with clonidine, as described for epidural procedures.³⁴ Alternatively, parturients might be particularly sensitive to intrathecal clonidine. However, significant hypotensive effects from low clonidine doses were also observed recently in nonpregnant patients.³⁰ These results do not necessarily conflict with those of Gautier *et al.*,¹⁸ who reported no significant exacerbation of maternal hypotension when 15 or 30 μ g clonidine was combined with various doses of intrathecal sufentanil during labor. A trend was noted in each small group that had received clonidine, and this might have become significant with more patients or fewer groups. On the other hand, the 5-mg bupivacaine test dose we administered epidurally soon after spinal analgesia may have interacted with intrathecal clonidine to enhance its hypotensive effect. Nevertheless, it is reassuring to note that it did not increase the incidence of abnormal fetal heart rate patterns or alter Apgar scores

or umbilical arterial pH. This confirms that maternal hypotension has no adverse consequence on fetal or neonatal well-being provided that it is rapidly reversed by intravenous doses of ephedrine.

A paradoxical higher maternal heart rate was observed in parturients who received clonidine in addition to sufentanil. This difference is clinically unimportant but statistically significant and still observed when parturients who received ephedrine are excluded. It might be a reflex tachycardia related to the decrease in SBP. However, a study conducted in nonpregnant patients did not demonstrate any effect of low doses of clonidine (75 μ g to 50–30 μ g) on heart rate.^{##} Thus this result might be specific to pregnant women and interesting given further physiopharmacologic investigations.

In conclusion, this double-blinded, randomized study shows that the addition of 30 μ g intrathecal clonidine to 5 μ g intrathecal sufentanil extends the duration of labor analgesia without producing any motor blockade. However, the incidence of hypotension and the ephedrine requirements were markedly increased. There were no obvious adverse effects of this hypotension in this group of healthy parturients, and there was a minor benefit.

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