

## COMBINED SPINAL-EPIDURAL ANALGESIA IN LABOR

### - Comparison of Sufentanil vs Tramadol -

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#### Abstract

**Background:** Combined spinal-epidural (CSE) analgesia is becoming increasingly used to provide pain relief during labor. It combines both the rapid onset of the spinal analgesia and the flexibility of the epidural catheter.

Intrathecal sufentanil provides rapid-onset and profound analgesia during the first stage of labor. The dose required to produce this effect can be associated with maternal respiratory depression, hypotension, nausea, or pruritus. The major concern of the anesthesiologist is to limit these side effects sources of discomfort to a parturient, by choosing the optimal dose of sufentanil or searching for an alternative. The purpose of this study is to compare tramadol and sufentanil used in CSE analgesia in terms of duration of analgesia and frequency of adverse maternal or fetal effects.

**Methods:** Forty parturients requesting labor analgesia were included in this prospective study. In a combined spinal- epidural technique, at 3 to 4 cm cervical dilation, patients were randomly assigned to receive either one of the following intrathecal solutions: 2.5 mg sufentanil (n = 20) and 2.5 mg bupivacaine, or 25 mg tramadol (n = 20) and 2.5 mg bupivacaine. Visual analog scores for pain, blood pressure, heart rate, sensory levels,

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incidence of nausea and pruritus, motor blockade, and maternal satisfaction, were recorded.

**Results:** Patients receiving 25 mg intrathecal tramadol with 2.5 mg bupivacaine had significantly longer-lasting analgesia ( $114 \pm 7$  min) than those receiving 2.5 mg intrathecal sufentanil and 2.5 mg bupivacaine ( $54 \pm 11$  min). No adverse maternal or fetal effects were noted in the group sufentanil. Five parturients of the tramadol group, presented vomiting 10 min after induction. There was no difference in the time from analgesia to delivery, incidence of operative or assisted delivery or cervical dilation. During labor, maternal satisfaction was good.

**Conclusions:** 2.5 micrograms of intrathecal sufentanil combined with 2.5 mg bupivacaine provides rapid-onset and profound analgesia during the first stage of labor without adverse maternal or fetal effects. 25 mg intrathecal tramadol with 2.5 mg bupivacaine had longer-lasting analgesia. The major side effect was vomiting.

**Key words:** Analgesia; combined spinal epidural anesthesia; obstetrics; regional anesthesia.

## Introduction

The combined spinal-epidural technique using the intrathecal administration of opioid to parturient, is becoming routine. The intrathecal administration of sufentanil provides rapid-onset, potent, and reliable analgesia, without motor blockade during the first stage of labor. The dose required to produce this effect may be associated with maternal respiratory depression, hypotension, nausea, or pruritus. The choice of the optimal dose of sufentanil or the search for an alternative, can limit these side effects, sources of discomfort to a parturient.

Tramadol is an opioid-like analgesic that induces its analgesic effects through both opioid and monoaminergic pathways. Tramadol is a weak  $\mu$ -agonist and it inhibits reuptake of the norepinephrine. The absence of the neuronal toxicity of tramadol allowed its use in neuroaxial analgesia.

The present study was designed to compare tramadol and sufentanil used in CSE analgesia in terms of duration of analgesia and frequency of adverse maternal or fetal effects.

### **Methods and Materials**

Written informed consent was obtained, and the study was approved by the Ethics Committee of the local Medical Faculty.

This was a randomized study comprising 40 (ASA I) parturients in established labor of at least one contraction every 5-min intervals and who were scheduled to receive a combined spinal-epidural analgesia (CSE).

Exclusion criteria consisted of cervical dilation  $> 5$  cm, medical diseases (diabetes mellitus, hypertension, and bleeding dyscrasias), obstetric complications (preeclampsia, multiple pregnancy, preterm labor, noncephalic presentation).

The parturients were randomized into two groups: Group S Sufentanil and Group T Tramadol.

An IV access was achieved in every parturient. Each parturient received an IV preload of 0.5 L of lactated Ringer's solution for hydration. Baseline pain scores (on a 100-point visual analog scale, 0 = no pain and 100 = worst pain imaginable), systolic blood pressure (measured noninvasively on the left arm), and fetal heart tracing, were obtained.

Every parturient received CSE in sitting position at the L2-3 or L3-4 level. The epidural space was accessed by using the loss of resistance technique, followed by dural puncture with a 27-gauge Whitacre spinal needle.

Each parturient in Group S received a combination of 2.5 mg of IT sufentanil and 2.5 mg of plain bupivacaine. Group T parturients received 25 mg of IT tramadol plus 2.5 mg of bupivacaine.

The anesthetic solutions were injected over 20 s for each case, with the orifices of the respective spinal needles facing the cephalad direction. The epidural catheter was inserted 3-4 cm into the epidural space. After a

negative aspiration test for blood, the epidural catheter was flushed with 1 ml of isotonic sodium chloride solution. No test dose was given epidurally.

During the first 30 min after CSE, the parturients were assessed on the following variables and categories:

1. Blood pressure every 5 min.
2. Pain scores 5, 15, 20, 25 and 30 min after CSE until delivery.
3. Highest sensory block to cold (ice) every 5 min after CSE.

4. Maximal degree of motor block in the lower limbs 5, 15, 20, 25 and 30 min after CSE based on the modified Bromage scale (0 = no impairment; 1 = unable to raise the extended leg but able to move knees and feet; 2 = unable to raise extended leg as well as flex knees, able to move foot; 3 = not able to flex ankle, feet, or knees [complete block]).

5. Shivering, pruritus, nausea, vomiting, and sedation. In this study, sedation was defined by a Ramsay score of 4, i.e., patient was asleep but had a brisk response to a light glabellar tap or loud auditory stimulus.

Any reduction of the systolic blood pressure  $> 20\%$  of the baseline value (i.e., the preblock value obtained just before CSE), was promptly treated with 3 mg boluses of ephedrine IV. Respiratory depression (shallow respiration  $< 8$  RR) and severe sedation (Ramsay score  $> 4$ ) would have provided justification to abandon the study and to administer 0.4 mg of IV naloxone. If the pain score was still  $> 30$ , 15 min after CSE, the parturient would be excluded from the study.

The duration from CSE to the time when the parturient began to experience the onset of pain again (time as determined by the request for further analgesia), was noted. At this time, continuous perfusion of 0.125% bupivacaine would be given at 8 ml/h via the epidural catheter.

The following data were also collected for each group: cervical dilation, the mode of delivery, the neonatal birthweight and Apgar scores (at 1 and 5 min of birth), overall satisfaction with analgesia (0 = very dissatisfied and 100 = extremely satisfied), postdural puncture headache before discharge from hospital (36 h after CSE), and fetal heart tracing

1 h before and 1 h after CSE.

The cardiotocogram was classified as normal (reactive) based on the following criteria: at least two accelerations (> 15 beats for > 15 s) in 20 min, baseline heart rate 110-150 bpm, baseline variability of 5-25 bpm, and early decelerations. Any deviation from the above would be classified as abnormal (nonreassuring), and the appropriate obstetric intervention would be effected. All the fetal cardiotocograms were confirmed to be normal (reactive) before the labor analgesia.

Statistics: Data are presented as mean  $\pm$  standard deviation (SD). Parametric data were analyzed using unpaired t tests. Nonparametric data were analyzed using chi-square. A value of  $p < 0.05$  was considered significant.

## Results

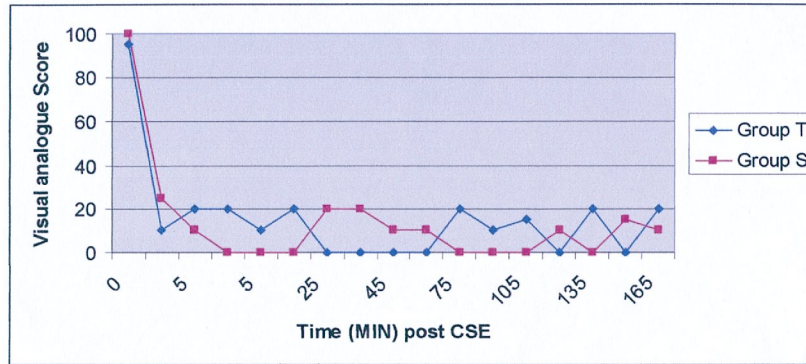
Both Groups S and T were similar in terms of weight, height, and age. Similarly, no significant difference was detected in their baseline values of systolic blood pressure, pain scores, cervical dilation and parity (Table 1).

*Table 1*  
*Parturient' Demographic Profile*

	Group S Sufentanil	Group T Tramadol	<i>P</i>
Age (years)	29 $\pm$ 3	29 $\pm$ 5	ns
Weight (Kg)	77 $\pm$ 12	72 $\pm$ 9	ns
Height (cm)	159 $\pm$ 10	162 $\pm$ 14	ns
Proportion of primiparas	11/20	14/20	
Pain scores (0-100 visual analog scale)	98 (90-100)	98 (90-100)	ns
Cervical dilation (cm)	3 (2-4)	3 (2-4)	
Systolic blood pressure (mmHg)	120 $\pm$ 9	116 $\pm$ 11	ns

Parturients were registered with low pain scores (highest score 20, lowest score 0) during the labor. This was probably a reflection of a rapid onset of analgesia (Figure 1).

Fig. 1  
Pain scores during labor



There was no significant difference in the duration of the second stage of the labor, the mode of delivery, the changes in the fetal heart rate, the Apgar scores, the neonatal birth weight, and the overall satisfaction scores (Table 2).

Table 2  
Parturient and Neonate Data

	Group S Sufentanil	Group T Tramadol	P
Time to first analgesia request after CSE (min)	54 ± 11	114 ± 7	0.05
Duration of second stage of labor (min)	145 ± 15	152 ± 5	ns
Intrapartum fetal heart tracing			
Normal	20	20	ns
Nonreassuring	0	0	ns
Apgar scores > 8			
1 min	20	20	ns
5 min	20	20	ns
Mode of delivery			
Normal	17	15	ns
Instrumental	2	1	ns
Abdominal	1	4	
Analgesia satisfaction score (0-100)	95 (90-100)	97 (97-100)	ns

The level of sensory dermatomal block to cold was similar in both groups (D10). The duration of analgesia as reflected by the time of the first request for analgesia was significantly longer in Group T ( $p < 0.01$ ).

In terms of side effects, 5 parturients in Group T had nausea and vomiting that occurred 10 min after CSE. Nausea and vomiting appeared in burst from 4 to 5 lasting episodes, then disappeared completely having left the sensation of fatigue and passing hypersweating. None of the parturients had hypotension, respiratory depression, sedation and motor blockade (Table 3).

*Table 3*  
*Incidence of side effects*

	Group S Sufentanil	Group T Tramadol
Hypotension	0	0
Motor block during CSE	0	0
Sedation	0	0
Pruritus	0	0
Nausea and vomiting	0	5
Respiratory depression	0	0
Post dural puncture headache	0	0

Three parturients in Group T and two in Group S have delivered vaginally before the epidural “Top-ups”.

## **Discussion**

The CSE technique has gained popularity as an alternative of the conventional epidural analgesia, because of its rapid onset of analgesia and minimal motor blockade<sup>1-2</sup>. Although it provides excellent labor analgesia, regional analgesia may affect the progress and outcome of labor. The rapid onset of pain relief with CSE analgesia may reduce the level of maternal catecholamine<sup>3</sup>. Maternal epinephrine may be tocolytic and its reduction therefore able to stimulate uterine contraction<sup>4</sup>. The spinal analgesia of a CSE technique allows, at least initially and potentially during the course of labor, for a reduction in local anesthetic exposure when compared with epidural analgesia<sup>5-6</sup>. In our study, for

instance, five parturients delivered with spinal analgesia alone. None of the parturients had any motor blockade allowing ambulation.

Intrathecal (IT) sufentanil provides effective analgesia in labor, although adding IT bupivacaine to sufentanil enhances the quality and duration of analgesia<sup>7-8-9</sup>. Lower doses of sufentanil were associated with a lower incidence of hypotension, nausea, vomiting, and severity of pruritus. It is likely that lower doses of sufentanil are associated with less respiratory depression<sup>10-11</sup>. Fetal heart rate changes not associated with hypotension have been described after regional labor analgesia. No one patient in our study had a nonreassuring FHR tracing after initiation of analgesia. This study has shown that 2.5mg sufentanil combined with 2.5mg bupivacaine provides satisfactory labor analgesia without any side effects. This finding may make the CSE analgesia technique safer.

Tramadol, a relatively new, centrally-acting analgesics drug has a low but preferential activity at opioid receptors, and also inhibits both noradrenaline and 5-hydroxytryptamine (5-HT) neuronal reuptake, and facilitates 5-HT release. Thus, it has been advocated as an analgesic, without respiratory depression<sup>12</sup>. Tramadol for patient-controlled analgesia (PCA) can produce effective postoperative analgesia in patients undergoing major abdominal surgery without any serious side effects<sup>13</sup>. Epidural tramadol provide adequate postoperative pain relief following Cesarean section<sup>14</sup>. Tramadol for patient-controlled analgesia (PCA) has been used also as an analgesic for labor pain with not affecting adversely a mother or a newborn<sup>15</sup>.

Our study is original because it is the first time that intrathecal (IT) administration of tramadol is used for labor analgesia. IT tramadol provides effective analgesia without motor blockade, sedation, hypotension and respiratory depression. Compared with sufentanil, IT tramadol prolongs duration of analgesia. The most frequently reported side-effect with tramadol is nausea and/or vomiting. This can be explained by the 5-HT action of the drug<sup>16-17</sup>. In our study five parturients had nausea and vomiting without decrease of patient satisfaction. Intravenous Drogéridol and Métoclopramide are particularly effective to prevent warn nausea and vomiting<sup>18</sup>.

In conclusion, our study has demonstrated that 2.5 micrograms of intrathecal sufentanil combined with 2.5 mg bupivacaine provides rapid-onset and profound analgesia without adverse maternal or fetal effects. On the other hand 25 mg intrathecal tramadol with 2.5 mg bupivacaine provides longer-lasting analgesia. The major side effect is vomiting.

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