

# Analgesic Effects of Intrathecal Sufentanil Added to Lidocaine 5% in Elective Cesarean Section

Mohammad Hosein Bakhshaei<sup>1</sup>, Nahid Manuchehrian<sup>2\*</sup>, Ebrahim Khoshraftar<sup>1</sup>, Hassan Mohamadipour-Anvary<sup>1</sup>, and Mehdy Sanatkarfar<sup>1</sup>

<sup>1</sup> Department of Anesthesiology, Beasat Hospital, Hamadan University of Medical Sciences, Hamadan, Iran

<sup>2</sup> Department of Anesthesiology, Fatemy Hospital, Hamadan University of Medical Sciences, Hamadan, Iran

Received: 12 May 2010; Received in revised form: 16 Sep. 2010; Accepted: 5 Oct. 2010

**Abstract-** The quality of subarachnoid block can be improved by adding opioids to the local anesthetics. We compared the analgesic effects of different doses of intrathecal sufentanil added to lidocaine 5% for elective cesarean section. This study was a prospective, randomized, double-blind, controlled trial. 90 pregnant women with ASA class I-II, scheduled for elective cesarean section under spinal anesthesia were enrolled in this study. Three groups were made of them by random; Group 1 (control group) was given lidocaine 5% (75 mg) and 2 ml of normal saline. Patients in Group 2 received lidocaine 5% (75 mg) and 5 micrograms sufentanil plus 1ml normal saline. Group 3 patients received lidocaine 5% (75 mg) and 10 micrograms sufentanil. Duration of sensory block and effective analgesia (need to analgesic) were measured. Opioid related side effects were recorded. Duration of sensory block and effective analgesia were prolonged in sufentanil groups in comparison of control group (50.3±4) that was significantly more in group 3 (128 ± 4) versus group 2 (58.3 ± 10) ( $P < 0.001$ ). There was mild to moderate respiratory depression in sufentanil groups which was more noted in group 3 ( $P < 0.001$ ). No differences were detected in other side effects such as hypotension, nausea & vomiting. The addition of sufentanil 10 versus 5 micrograms to lidocaine 5% provided more duration of analgesia for cesarean delivery. So, the adding of 10 micrograms sufentanil to lidocaine 5% for cesarean section has more effective analgesia with minimum side effects.

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*Acta Medica Iranica* 2010; 48(6): 380-384.

**Key words:** Sufentanil; cesarean section; pain; anesthesia spinal

## Introduction

Subarachnoid block is a widely used technique for cesarean section. Its quality can be improved by adding opioids to the local anesthetics. One of the important disadvantages of spinal anesthesia with lidocaine alone is a relatively short duration of action, which leads to early analgesic intervention that usually causes the intraoperative nausea especially during manipulation of the uterus and at the time of peritoneal closure and postoperative period. Several reports have shown beneficial effects of adding various opioids to the local anesthetic solution administered intrathecally. The addition of fentanyl 10 µg to local anesthetic increases the intraoperative and early postoperative quality of subarachnoid block (1, 2). More recently, sufentanil in intrathecal doses of 10, 15, or 20 µg added to hyperbaric bupivacaine 10.5 mg was equally effective in the

preoperative period (3). In analgesia for cesarean section, it is particularly important to use the optimal effective opioids doses to minimize potentially adverse maternal and neonatal risks (4). The aim of this study is to introduce a dose of sufentanil as an adjuvant to receive an effective and reliable sensory block and analgesia in single-shot technique spinal anesthesia with minimum side-effects.

## Patients and Methods

This is a randomized, double-blind study and processes were approved by the Local Ethics Committee (University of Hamedan Medical Sciences). Ninety patients scheduled for elective cesarean section under spinal anesthesia were selected in this study. Healthy patients with ASA class 1 and 2, who oriented given oral information, at the beginning explicated the protocols to

\*Corresponding Author: Nahid. Manuchehrian

Department of anesthesiology, Fatemy Hospital, Hamadan University of Medical Sciences, Hamadan, Iran  
Tel: +98 918 1110366, Fax: +98 811 8269835, E-mail: nmanuchehrian@yahoo.com

them and obtained knowledgeable participation. Exclusion criteria included uncooperative patients, coagulopathy disorders, unstable angina, recent myocardial infarction, significant aortic stenosis, or other established contraindications due to spinal anesthesia.

The patients were fasted overnight and received no medication preoperatively. Acetated Ringer's solution (20 mL/kg) was used for intravenous (IV) hydration. Preservative-free normal saline was used to dilute the study drugs. With the patient in the left lateral or sitting position, a 25-gauge needle was inserted in the subarachnoid space at the third or fourth lumbar interspace. The test solutions were prepared and marked with a code by an anesthetic nurse who was not otherwise involved in the study or care of the patients. Neither the anesthesiologist nor the patient herself was aware of the dose administered. Randomization was done according to systemic random sampling and the patients divided to three groups (30 in each group) and injected doses and volumes for groups was as follows: Group 1 (control group) was given of hyperbaric lidocaine 5% (75 mg) and 2 ml of normal saline. Patients in Group 2 received of hyperbaric lidocaine 5% (75 mg) and 5 micrograms sufentanil plus 1ml normal saline. Group 3 patients received of hyperbaric lidocaine 5% (75 mg) and 10 micrograms sufentanil. After the intrathecal injection, the patient was returned to the supine position with a left lateral tilt to accomplish a left uterine displacement. IV boluses of 5-10 mg ephedrine and additional IV fluids were given to treat hypotension, which was defined as a systolic blood pressure below 90 mm Hg or a decrease in systolic pressure of more than 20% of the baseline value. Oxygen 2-4 L/min was administered through a nasal cannula. Heart rate and noninvasive arterial blood pressure were recorded every minute for 5 min and then after every 2 minute for 10 min, at 15-min intervals for 45 min, and then at 30-min intervals for another 5 h. Respiratory rate, oxygen saturation, sensory level to pinprick, and the degree of motor block, as assessed according to the criteria of Bromage score (5), were recorded every 3 min for 15 min, after which recordings were made at the same intervals as above. Pain, nausea, pruritus, somnolence, tightness in the chest, and other possible side effects, as well their treatments, were recorded. The surgical technique was uniform in all patients and included exteriorization of the uterus. At delivery, blood samples were collected from the umbilical artery or vein for blood gas analysis. Apgar score was recorded at 1, 5, and 10 minutes. All parameters enrolled by a nurse that was totally blinded

about the groups according to check list that only marked with the code of patients.

In the recovery room, the visual analog scale (VAS) for pain was used. Duration of complete analgesia was defined as the time from the intrathecal injection to VAS score  $>0$ , and duration of effective analgesia was defined as the time to VAS score  $\geq 4$  (1), at which point the patient received 100 mg Diclofenac as a suppository, and morphine (3-5 mg, IV) was administered by the nurse to achieve a VAS score  $<4$ . Analgesic requirements and side effects were recorded for 24 h after block. The presence of headache, backache, urinary retention, and other neurological symptoms were also recorded. Continuously distributed variables were analyzed using two-tailed analysis of variance (ANOVA) followed by Schaffer's test for intergroup comparisons. Frequency data were analyzed with the 2 test and Fisher's exact test with a Yates' continuity correction, as appropriate. A P value 0.05 was considered statistically significant. Duration of sensory block and effective analgesia (need to analgesic) were measured. Opioid related side effects such as hemodynamic parameters, respiratory depression, nausea, vomiting and pruritus were recorded. Sensory and motor blockade were evaluated by using a pinprick technique. Criteria for return to the ward were: no nausea, VAS pain scores less than 3 and Bromage 0-1.

## Results

There were no significant differences in patients' height, weight and parity among the groups. Age, intrathecal injection and, skin incision to delivery time, uterine incision to delivery time, and duration of surgery did not differ among the groups (Table 1). Duration of sensory block and complete analgesia were prolonged in sufentanil groups in comparison with control group (Figure 1). That was  $50.3 \pm 4$  min in control group and was significantly more in group 3 ( $128 \pm 2$  min) versus group 2 ( $58.3 \pm 10$  min) ( $P < 0.001$ ). No differences were detected in time of sensory block to T4-T6 level, time to highest sensory block, time to regression of sensory and time to resolution of motor blockade between three groups. Addition of sufentanil was associated with some side effects. There was mild to moderate respiratory depression in sufentanil groups which was more noted in group 3 (Table 2) ( $P < 0.001$ ). No difference was detected in other side effects such as hypotension, nausea and vomiting (Figure 2). At 24 h, urinary bladder function was normal in all patients. None of the patients had neurological deficits.

Table 1. Patients' variables

Patients variables	Group 1	Group 2	Group 3	P value
Weight	54.4 ± 24	56.8 ± 18	55.4 ± 14	0.87
Height	158.2 ± 8.4	160 ± 8.6	159.6 ± 6.4	0.64
Parity	1.2	1.5	1.4	0.32
Age	24.2 ± 6.3	26.4 ± 8.4	22.8 ± 6.8	0.22
Intrathecal injection to delivery time (min)	20.1 ± 4.6	19.1 ± 4.3	18.8 ± 3.8	0.54
Skin incision to delivery time (min)	7.6 ± 3.3	6.5 ± 2.4	6.7 ± 2.5	0.23
Uterine incision to delivery time (min)	3.5 ± 14	3.3 ± 22	4.2 ± 18	0.18
Duration of surgery	58.4 ± 24	50.6 ± 32.4	59.8 ± 28.4	0.22
Duration of sensory block (min)	50.3	58.3	128	<0.001
Time of sensory block to T <sub>4</sub> level (min)	3.4 ± 3.4	3.0 ± 2.8	3.2 ± 2.3	0.09
Regression time to T <sub>10</sub> (min)	50.4 ± 18.6	48.6 ± 24	55.8 ± 14.4	0.32
Time to resolution of motor blockade	44.2 ± 8.6	48.2 ± 6.8	42.8 ± 10	0.14

The newborn infants had a gestational age of 38 ± 1 wk and a birth weight of 3390 ± 450 g, without statistical differences among the groups. Umbilical arterial or venous blood gases showed no significant differences among the treatment groups. No infant had a 5-min Apgar score <7. One infant in control group was transferred to the neonatal intensive care unit due to respiratory disturbances and had a favorable outcome.

**Discussion**

In an earlier study (1), it was shown that the addition of fentanyl 6.25-50 µg to 10.5 mg (on average) hyperbaric 0.75% bupivacaine for spinal anesthesia reduced the intraoperative need for supplemental IV analgesics from 67% to 0% during cesarean section. In another study (3), sufentanil 10-20 µg added to 10.5 mg hyperbaric 0.75% bupivacaine similarly reduced the need for supplemental analgesics from 70% to 0%.

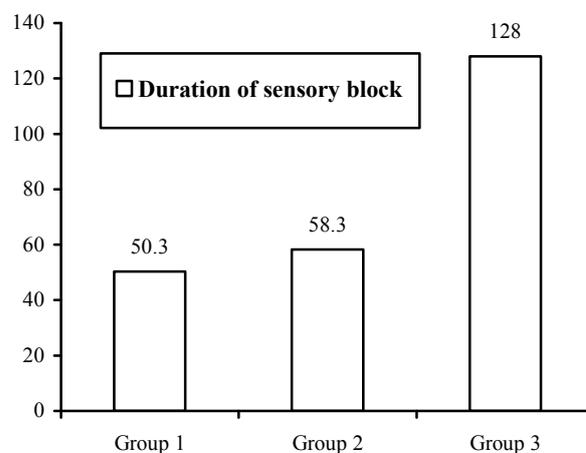


Figure 1. Duration of sensory block and complete analgesi

Table 2. Comparison of side effects between three groups.

Patients variables	Group 1	Group 2	Group 3	P value
Respiratory depression	Zero	Zero	46.7%	<0.001
Hypotension	66.7%	73.3%	93.3%	0.188
Nausea and vomiting	60%	66.7%	46.7%	0.529
Arrhythmia	26.7%	20%	46.7%	0.26
Umbilical arterial blood gases (PH)	7.28 ± 0.05	7.27 ± 0.03	7.25 ± 0.04	0.24
Apgar score (5 min)	9-10	7-10	8-10	0.32

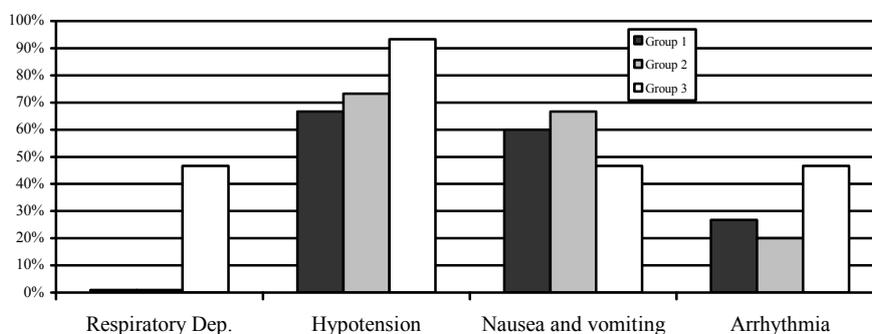


Figure 2. Comparison of side effects between three groups

In the present study, in which 75 mg lidocaine 5% was used, intraoperative IV analgesics were used in only 2 of the 90 subjects studied. These results are in accordance with another study (2).

The increased duration of complete analgesia in the patients receiving intrathecal opioids, from approximately  $50.3 \pm 10$  min in the placebo group to  $128 \pm 2$  min in the treatment groups, is in line with earlier studies using lipophilic opioids (1-3). We chose sufentanil (which is more lipophilic than fentanyl and morphine) because it rapidly penetrates the spinal cord and produces excellent segmental analgesia for short surgical procedures (13-15). The use of a combination of a local anesthetic and intrathecal morphine has been shown to produce a longer duration of postoperative analgesia (8-10).

Morphine, however, has a slow onset of action (11) and has the potential for late side effects, such as respiratory depression. In our study combination of lidocaine 5% with sufentanil given as a single shot induced an acceptable block with adequate duration with a high quality during the surgical procedures. The addition of high lipid solubility opioid such as sufentanil with high affinity to opioid receptors (13-22) will potentially allow manage of surgical pain.

The moderate increase in duration of analgesia in the present study was certainly clinically significant. The positive effects of the addition of intrathecal fentanyl or sufentanil were confined to the intraoperative and early postoperative phase. The equipotent dose for sufentanil when administered intrathecally in conjunction with local anesthetic has not yet been established. Previous study concluded that the 50% effective dose for intrathecal sufentanil was 2.5  $\mu\text{g}$  or smaller and that the 95% effective dose was between 5 and 10  $\mu\text{g}$  (13). In the present study, sufentanil 10  $\mu\text{g}$  prolonged the duration of intraoperative analgesia compared with control. The mechanism for the longer duration of the sensory block in the sufentanil groups compared with control may be an example of synergism between sufentanil and the local anesthetic (14). Maternal side effects from the use of intrathecal opioids in this study were restricted to the respiratory depression effects of sufentanil, however, this complication in opioid groups could very easily managed. Umbilical blood gas analyses, neonatal Apgar scores did not differ among the study groups. From these data, it seems unlikely that there were any neonatal adverse effects related to the use of intrathecal opioids. In our study no differences were detected in other side effects such as hypotension, nausea and vomiting. We concluded that the addition of sufentanil 10  $\mu\text{g}$  versus 5

$\mu\text{g}$  to lidocaine 5% provided more duration of analgesia for cesarean delivery. In addition, respiratory depression in sufentanil groups very easily managed. Therefore, the addition of 10  $\mu\text{g}$  sufentanil to lidocaine 5% for cesarean section provided more effective analgesia with minimum and not important side effects.

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