Evaluation of spinal anesthesia blockade time with 0.5% hyperbaric bupivacaine, with or without sufentanil, in chronic opioid users: a randomized clinical trial

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Abstract

Objective: The primary outcome of this study was to evaluate the effect of adding sufentanil to hyperbaric bupivacaine on duration of sensory blockade of spinal anesthesia in chronic opioid users in comparison with non-addicts.

Methods: Sixty patients scheduled for orthopedic surgery under spinal anesthesia were allocated into four groups: group 1 (no history of opium use who received intrathecal hyperbaric bupivacaine along with 1 mL saline as placebo); group 2 (no history of opium use who received intrathecal bupivacaine along with 1 mL sufentanil [5 µg]); group 3 (positive history of opium use who received intrathecal bupivacaine along with 1 mL saline as placebo) and group 4 (positive history of opium use who received intrathecal bupivacaine along with 1 mL sufentanil [5 µg]). The onset time and duration of sensory and motor blockade were measured.

Results: The duration of sensory blockade in group 3 was 120 ± 23.1 min which was significantly less than other groups (G1 = 148 ± 28.7, G2 = 144 ± 26.4, G4 = 139 ± 24.7, p = 0.007). The duration of motor blockade in group 3 was 145 ± 30.0 min which was significantly less than other groups (G1 = 164 ± 36.0, G2 = 174 ± 26.8, G4 = 174 ± 24.9, p = 0.03).

Conclusions: Addition of 5 µg intrathecal sufentanil to hyperbaric bupivacaine in chronic opioid users lengthened the sensory and motor duration of blockade to be equivalent to blockade measured in non-addicts.

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Introduction

Motor vehicle trauma may result in lower limb fractures requiring operative intervention, and may occur in the setting of opium abuse. Since spinal anesthesia is a popular anesthetic technique in lower limb surgeries, the characteristics of spinal anesthesia in this population are important.

In the studied geographical region, Iran, determining a definite estimate of prevalence and incidence of substance abuse is not possible due to social stigmatization along with legal restrictions. Between different substances, most commonly, opioids are abused and inhalation the most frequent route of abuse. Furthermore, many of the victims of motor vehicle accidents are chronic opioid users and the accidents are the result of driver’s drug abuse.

The sensory and motor blockade behavior of spinal anesthesia in long-term chronic opioid users has not been previously studied thoroughly.

In a study conducted by Dabbagh et al., duration of spinal anesthesia with hyperbaric bupivacaine in chronic opioid abusers undergoing lower extremity orthopedic surgery was studied. It was shown that the duration of sensory block was much shorter in chronic opioid abusers compared with non-abusers. The hypothesis of our study was that the duration of spinal anesthesia in chronic opioid users is shorter than non-addict patients and adding intrathecal sufentanil can increase spinal anesthesia blockade time in chronic opioid user.

The primary outcome of this study was to evaluate the effect of adding sufentanil to intrathecal bupivacaine on duration of sensory and motor blockade of spinal anesthesia chronic opioid users compared to non-addict patients. The onset of sensory and motor blockade was considered secondary outcomes.

Materials and methods

The study protocol was approved by the Institutional Ethics Committee of Tehran University of Medical Sciences, and after a thorough detailed explanation of the nature of the study to the participants, an informed, written consent was obtained from all the patients.

Sixty American Society of Anesthesiologist physical status (ASA) class I and II, male and current smoker patients, aged between 18 and 60, who were scheduled for elective lower limb orthopedic surgery under spinal anesthesia (lasting less than 2 h) were enrolled in this randomized, double-blinded clinical trial. Patients with any contraindications to spinal anesthesia, patients with addiction to any substance other than opium and cigarettes, and patients with history of cardiac, respiratory, or psychological disease were not entered in the study. It had been considered that in instances of failed spinal anesthesia or when surgery took longer than two hours new patients were replaced in the study.

Prior to spinal anesthesia all the required drugs were prepared by an anesthetist who was neither involved in the administration nor observation of the patient; thus, both
the anesthesiologist and the patients were blinded to group assignment. The anesthesiologist who performed the subarachnoid block and documented the sensory levels was blinded to the patient’s group. On arrival to the operating room, based on a previously generated computer randomization list, patients were assigned into groups. Group 1 (n = 15) had no history of chronic opium use and received intrathecal hyperbaric bupivacaine along with 1 mL saline as placebo. Group 2 (n = 15) had no history of opium use and received intrathecal hyperbaric bupivacaine along with 1 mL sufentanil (5 μg; n = 15). Group 3 (n = 15) had a positive history of chronic opium use and received intrathecal hyperbaric bupivacaine along with 1 mL sufentanil (5 μg). The bupivacaine ampoules (20 mg/4 mL) contained 320 mg glucose monohydrate.

Chronic opium use was defined as recurrent and continuous daily consumption of 1–2 g of opium via inhalation route for at least one year without a cessation until the day of surgery based on the histories that reported by the patients. Patients with poly substance abuse were not enrolled in the study. None of the patients had any intention to stop opium use before surgery and all the patients were advised to continue using their typical inhaled opium until the day of surgery in the preoperative visit. Patients were given their daily doses of inhaled opium on the day of surgery. In order to rule out opium use in the control groups and confirm opium use in the study group, in all patients, an opiate urine test was performed.

Pre-operative pain management protocol was the same for all the patients. The patients received intermittent (every 6 h) intravenous apotel (15 mg/kg) (intravenous Paracetamol 1000 mg/6.7 mL, UNI-PHARMA S.A.) if the VAS score for pain was higher than 3. Diclofenac suppository was administered to patients who had pain despite intravenous apotel administration.

Two hours before surgery, patients received 1 mg oral lorazepam premedication. On arrival in the operating room, standard monitoring was established (electrocardiography, noninvasive blood pressure, pulse oximetry and heart rate) and oxygen was delivered via a venturi facemask at a rate of 3 L/min. An 18-gauge cannula was inserted into a vein on the dorsum of the non-dominant hand and a bolus dose of lactated ringer solution 7 mL/kg was administered. Then, with the patient in the lateral decubitus position a ducing an aseptic technique, a 25-gauge pencil point needle was inserted intrathecal via a midline approach into the L3–L4 or L4–L5 interspaces.

Patients in groups 1 and 3 received intrathecally 3 mL of 0.5% hyperbaric bupivacaine along with 1 mL saline. Patients in groups 2 and 4 were administered 3 mL of 0.5% hyperbaric bupivacaine and 1 mL (5 μg) of sufentanil. All the solutions were administered at a rate of 2 mL/s. All patients were placed in supine position following drug injection. To record the onset time and duration of sensory and motor block, sensory level was assessed using a pinprick test every minute for 10 min and then every 10 min for 120 min after the end of injection (zero time). The motor blockade was assessed by the Bromage Scale (Grade I: free movement of the legs and feet, Grade II: just able to flex knees with free movement of feet, Grade III: unable to flex knees, but with free movement of feet, Grade IV: unable to move legs or feet). The onset time of sensory blockade was defined as the time from drug administration until bilateral T8 level of sensory blockade was achieved. The duration of sensory block was considered as the time from the highest level of sensory blockade until 4 segment regressions were observed. The onset time of motor blockade was defined as the time from drug injection until a grade IV Bromage score was achieved. The duration of motor block was considered as the time from full intensity motor blockade until a Bromage grade I score was documented.

If any of the patients complained of pain at any time during the operation, this was considered to be a failed spinal anesthesia, and general anesthesia was then induced immediately.

Hypotension was defined as a decrease in systolic blood pressure to less than 90 mmHg or 25% less than baseline. Hypotension was treated with bolus doses of 10 mg intravenous ephedrine. Bradycardia (HR < 50 beat/min) was treated by 0.5 mg IV atropine. In cases of nausea or vomiting without the presence of bradycardia, patients received 10 mg IV metoclopramide.

It was determined that a sample size of 15 participants in each group would be sufficient to detect a 30 min difference in sensory block time, estimating an SD of 28 min, a power of 80%, and a significance level of 5%.

Statistical analysis of the data was performed using SPSS for windows, release 17.5 (SPSS, Inc). The distribution of data was evaluated using the Kolmogorov–Smirnov test. Age, weight, height, and duration of surgery followed a normal distribution and were analyzed by using one-way analysis of variance (ANOVA) and Tukey post hoc tests. However, sensory and motor onset time and duration of blockades did not follow normal distribution. Their comparisons were performed using Mann–Whitney test. Two tailed p-values < 0.05 were considered statistically significant.

Results

Sixty male patients were randomized. There were no protocol violations and all patients were included in the analysis. The basic characteristics of the participants, including age, weight, height, the duration of the surgery and the duration of anesthesia were similar in groups and are presented in Table 1. Different types of orthopedic surgeries performed in each group are presented in Table 2. There were no statistical differences between the types of surgeries in groups. The highest level of sensory blockade in each group is presented in Table 3. Urinary opium test was positive in all the patients in groups 3 and 4 and was negative in all patients in groups 1 and 2.

There was no significant difference in the mean onset time of the sensory blockade (group 1 = 2.8 ± 1.7 min, group 2 = 2.4 ± 0.9 min, group 3 = 3.4 ± 1.1 min, group 4 = 2.3 ± 1.4 min, p = 0.12) or the motor blockade (duration of group 1 = 5.5 ± 3.0 min, group 2 = 4.1 ± 1.3 min, group 3 = 5.8 ± 2.3 min, group 4 = 5.3 ± 2.3 min, p = 0.19) in groups. The duration of sensory blockade in group 3 was 120 ± 23.1 min, which was significantly shorter than group 1 (148 ± 28.7 min), group 2 (147 ± 26.4 min) and group 4 (139 ± 24.7) (one-way analysis of variance test, p = 0.03).
The duration of sensory blockade was significantly different between groups. The duration of motor blockade in group 3 (145 ± 30.0 min) which was significantly less than group 1 (164 ± 36.0 min), group 2 (174 ± 26.8 min) and group 4 (174 ± 24.9 min) (one-way analysis of variance test, \( p = 0.007 \)). There was no statistical difference in duration of sensory and motor blockade between groups 1, 2 and 4 (Tukey post hoc test) (Table 4).

**Discussion**

The present study illustrated that the duration of sensory and motor blockade in spinal anesthesia with intrathecal hyperbaric bupivacaine is shorter in chronic opioid users. Interestingly, adding 5 \( \mu \)g of sufentanil to the local anesthetic solution increased the duration of sensory and motor blockade in chronic opioid users.

Adding 5 \( \mu \)g of sufentanil to the local anesthetic solution had no effect on the duration of sensory and motor blockade in non-addicts. No difference in sensory or motor blockade onset time was observed in any of the groups.

Few data are available in the literature regarding the behavior of regional anesthesia in chronic opioid users. When a thorough search of the known databases such as ISI and PubMed was done, no study regarding the effect of adding opioids to local anesthetics in spinal anesthesia in chronic opioid users was found.

As previously mentioned, in a study conducted by Dabagh et al., it was observed that a shorter duration of sensory and motor blockade occurred with intrathecally administration of bupivacaine in chronic opioid users when compared to non-addicts. It was proposed that a cross-tolerance may exist between local anesthetics and opioid compounds at the level of spinal neurons. However, the effect of adding an opioid compound to local anesthetics in spinal anesthesia in order to modify this shortened duration was not examined by either of these studies.

In a survey, it was concluded that intrathecal sufentanil produces a similar quality but shorter duration of analgesia in cocaine-abuser parturient. The mechanism of modification of opioid effect in chronic opioid users is not completely clear. This effect may be partially explained by the down-regulation of opioid receptors or a cross tolerance between opioids and local anesthetic receptors, yet it is so far off to clearly describe the pathways which are altered or modified in chronic opioid users.

**Table 1** Demographic data of the patients and duration of surgery.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 15)</th>
<th>Group 2 (n = 15)</th>
<th>Group 3 (n = 15)</th>
<th>Group 4 (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)(^a)</td>
<td>34.4 ± 10.8</td>
<td>35.7 ± 8.3</td>
<td>40.3 ± 9.3</td>
<td>36.8 ± 5.8</td>
</tr>
<tr>
<td>Weight (kg)(^b)</td>
<td>74.4 ± 13.2</td>
<td>70.0 ± 15.4</td>
<td>73.6 ± 8.4</td>
<td>73.6 ± 14.3</td>
</tr>
<tr>
<td>Height (cm)(^b)</td>
<td>174.4 ± 10.2</td>
<td>174.2 ± 8.5</td>
<td>172.6 ± 6.3</td>
<td>171.4 ± 8.9</td>
</tr>
<tr>
<td>Duration of surgery (min)(^a)</td>
<td>110 ± 28.9</td>
<td>99.3 ± 22.9</td>
<td>91.3 ± 30.3</td>
<td>97.3 ± 30.7</td>
</tr>
</tbody>
</table>

\(^a\) There was no significant difference in groups.

\(^b\) There was a significant difference in groups, \( p < 0.05 \).

**Table 2** Types of surgeries.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 15)</th>
<th>Group 2 (n = 15)</th>
<th>Group 3 (n = 15)</th>
<th>Group 4 (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral fracture</td>
<td>4</td>
<td>5</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>Ankle fracture</td>
<td>6</td>
<td>7</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Tibia/fibula fracture</td>
<td>5</td>
<td>3</td>
<td>6</td>
<td>3</td>
</tr>
</tbody>
</table>

**Table 3** Highest level of sensory block achieved in each group.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 15)</th>
<th>Group 2 (n = 15)</th>
<th>Group 3 (n = 15)</th>
<th>Group 4 (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6th thoracic level</td>
<td>5</td>
<td>4</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>7th thoracic level</td>
<td>6</td>
<td>7</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>8th thoracic level</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
</tbody>
</table>

**Table 4** Sensory and motor blockade time, sensory and motor duration.

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 15)</th>
<th>Group 2 (n = 15)</th>
<th>Group 3 (n = 15)</th>
<th>Group 4 (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensory blockade onset time(^a)</td>
<td>2.8 ± 1.7</td>
<td>2.4 ± 0.9</td>
<td>3.4 ± 1.1</td>
<td>2.3 ± 1.4</td>
</tr>
<tr>
<td>Motor blockade onset time(^a)</td>
<td>5.5 ± 3.0</td>
<td>4.1 ± 1.3</td>
<td>5.8 ± 2.3</td>
<td>5.3 ± 2.3</td>
</tr>
<tr>
<td>Duration of sensory blockade</td>
<td>148 ± 28.7</td>
<td>147 ± 26.4</td>
<td>120 ± 23.1(^b)</td>
<td>139 ± 24.7</td>
</tr>
<tr>
<td>Duration of motor blockade</td>
<td>164 ± 36.0</td>
<td>174 ± 26.8</td>
<td>145 ± 30(^b)</td>
<td>174 ± 24.9</td>
</tr>
</tbody>
</table>

\(^a\) There was no significant difference in groups.

\(^b\) There was a significant difference in groups, \( p < 0.05 \).
Considering this fact that the relation between pain perception and substance abuse is multi-factorial, further study is needed to understanding the underlying mechanisms.

The effects of intrathecal addition of different classes of opioids to local anesthetics have been previously studied in non-addicts. The addition of fentanyl and sufentanil to continuous spinal anesthesia produces effective analgesia with low adverse effects, and intrathecal meperidine or sufentanil gave good postoperative analgesia in cesarean section surgery. There are some limitations in this study. First, due to cultural issues in Iran, addict women rarely agree to take part in such studies due to the stigmatization that addiction has in Iranian culture. Consequently, only men participated in our study. Furthermore, there is a possible statistical concern in our study. The sample size of each group (n = 15) may be inadequate to detect any differences in spinal anesthesia duration in non-addicts and opioid users who underwent spinal anesthesia with sufentanil and bupivacaine. Additionally, knowing the exact daily dose of opioid consumption in each of the patients and the concentration of the effective alkaloids in the opioid used by the patients was impossible.

In conclusion, this study showed that the length of sensory and motor blockade is shorter in chronic opioid users. The addition of 5 μg of intrathecal sufentanil to hyperbaric bupivacaine in opioid addicts lengthened the sensory and motor duration of blockade to be equivalent to blockade measured in non-addicts.

**Conflicts of interest**

The authors declare no conflicts of interest.

**References**