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Effects of Fentanyl and Morphine on Shivering During Spinal Anesthesia in Patients Undergoing Endovenous Ablation of Varicose Veins

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABE 1 Didem Onk
ACE 2 Tülin Akarsu Ayazoğlu
D 1 Ufuk Kuyrukluyıldız
B 3 Mehmet Aksüt
F 1 Zehra Bedir
F 1 İlke Küpeli
F 3 Oruç Alper Onk
E 1 Ayşin Alagöl

1 Departnent of Anesthesiology and Reanimation, Erzincan University, Erzincan, Turkey
2 Departnent of Anesthesiology, Göztepe Training and Research Hospital, Istanbul, Turkey
3 Departnent of Cardiovascular Surgery, Erzincan University, Erzincan, Turkey

Corresponding Author: Didem Onk, e-mail: d.hesapdar@gmail.com
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Background: We sought to investigate the effect of morphine and fentanyl on shivering when used adjunctively with bupivacaine during spinal anesthesia in patients undergoing varicose vein surgery on an outpatient basis.

Material/Methods: The study included a total of 90 patients, aged 25–45 years, ASA I–II, scheduled to undergo endovenous laser ablation under spinal anesthesia for lower extremity venous insufficiency/varicose vein disease. Patients were randomly allocated into 3 groups: Group M (morphine group) received 5 mg 0.5% hyperbaric bupivacaine + 0.1 mg morphine, Group F (fentanyl group) received 5 mg 0.5% hyperbaric bupivacaine + 25 µg fentanyl, and Group C (control group) received 5 mg 0.5% hyperbaric bupivacaine + physiologic saline. The level of sensory blockade was assessed with pin-prick test and the level of motor blockade was assessed with Bromage scale at 5-min intervals. Shivering grade and time to first postoperative analgesic requirement was recorded.

Results: Level and time of sensory block showed a slight but insignificant increase in the Morphine Group and Fentanyl Group. Time of postoperative analgesic requirement was significantly longer in patients who received morphine ($p<0.05$). Shivering was significantly less common in patients who received morphine and fentanyl than in patients who are in the Control Group ($p<0.02$).

Conclusions: Morphine or fentanyl may be used as adjunctives to spinal anesthesia to prevent shivering in patients undergoing venous surgery.

MeSH Keywords: Anesthesia, Spinal • Fentanyl • Morphine Dependence

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Background

Human core temperature ranges between 36.5ºC and 37.5ºC. Body temperature is regulated by the anterior hypothalamus when the peripheral temperature reaches a certain threshold. This regulation is mainly achieved by reflex activity when the temperature exceeds or falls below a certain level [1].

It is well known that both general and regional anesthesia affects the homeostatic system. In addition, regional anesthesia-related perioperative hypothermia may occur above the level of the anesthetized dermatome. Body temperature falls by 0.5ºC with regional anesthesia, leading to vasoconstriction and resultant shivering above the level of the blockade [2]. Shivering occurs in 40–60% of all regional anesthetizations [3]. Perioperative shivering is known to be associated with an increase in metabolic activity and also with a 2-fold increase in oxygen consumption. It is reported to cause arterial hypoxia and thus is associated with an increased risk for myocardial ischemia. Shivering triggers a variety of mechanisms, including increased cardiac output, elevated peripheral resistance, and increased CO_2 and lactic acid production. It also increases intracranial pressure and intraocular pressure [4]. Thus, shivering during spinal anesthesia should be quickly recognized and appropriately treated to make anesthesia safer.

Drugs used adjunctively with bupivacaine during spinal anesthesia enhance the effectiveness of anesthesia by prolonging the action of the regional anesthetics. These drugs are also useful because they may lower the dose needed to achieve adequate anesthesia and thus may reduce the risk of adverse effects. Moreover, these drugs help reduce analgesic consumption by prolonging the time until the first analgesic administration.

This study sought to determine the effects of morphine and fentanyl on shivering and patient comfort when used adjunctively with bupivacaine during spinal anesthesia in patients undergoing varicose vein surgery on an outpatient basis.

Material and Methods

A placebo-controlled, randomized, double-blinded (patients and the data collector were blinded to the group allocation) clinical study was conducted in a tertiary care university hospital. After receiving approval from the Institutional Review Board (19.02.2014/11-1040), a total of 90 patients, ages 25–45 years, ASA (American Society of Anesthesiologists) I–II were included into the study. Randomization was achieved using computer-based software. Patients were excluded if they had certain contraindications for spinal anesthesia. We also excluded patients with a previous history of allergic reaction to opioid drugs, surgery of the vertebra, neuromuscular or neuropsychiatric diseases, or who failed spinal anesthesia despite 2 consecutive attempts, patients who refused, patients who had sepsis at the site of injection, and those with hypovolemia, coagulopathy, or increased intracranial pressure. All patients were informed about the study protocol and signed the procedure-oriented informed consent forms. Premedication was not given.

Patients were randomly allocated into 3 groups: Group M (morphine group) received 5 mg 0.5% hyperbaric bupivacaine (Butesin 0.5%, Vem Pharma, Ankara, Turkey) + 0.1 mg morphine (Morfin HCL, Osel Pharma, Istanbul, Turkey); Group F (fentanyl group) received 5 mg 0.5% hyperbaric bupivacaine + 25 µg fentanyl (Fentanyl, Mercury Pharma, London, UK); and Group C (control group) received 5 mg 0.5% hyperbaric bupivacaine + physiologic saline.

In all patients, a 20-G peripheral venous line was introduced and 0.01 mg/kg of intravenous midazolam (Zolamid, Defarma, Istanbul, Turkey) was given. Standard monitoring included non-invasive blood pressure, electrocardiogram, and pulse oximetry. Nasal oxygen was given at a rate of 2 L/min. Spinal anesthetic was injected with a 25-G Quinke needle entering through the L3–4 or L4–L5 midline intervertebral space. The operating room temperature was maintained at 23–25°C with approximately 60% humidity.

Study data included the effect of morphine and fentanyl on shivering scoring (Table 1), peak sensory block level (pinprick test), peak time to motor blockade, time to 2-segment regression, maximal motor blockade (Bromage scale), time to complete regression of motor blockade, nausea, vomiting, sedation (Ramsey sedation scale), intraoperative need for analgesics, respiratory depression, time to postoperative need for analgesics, and patient/surgeon satisfaction.

The Bromage scale [5] has 4 grades:
Grade I – free movement of legs and feet;
Grade II – just able to flex knees with free movement of feet;
Grade III – unable to flex knees, but free movement of feet;
Grade IV – unable to move legs or feet.

Patients were kept in the recovery room until motor and sensory blockade had completely regressed. An independent observer, blinded to the group allocation, recorded the frequency of visible shivering during surgery and then in the recovery room. Shivering was graded on a scale described by Crossley and Mahajan [6]:

0 No shivering;
1 Piloerection or peripheral vasoconstriction, but no visible shivering;
2 Muscular activity in only 1 muscle group;
3 Muscular activity in more than 1 muscle group, but not generalized shivering;
4 Shivering involving the whole body.

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Table 1. Baseline characteristics and analgesia assessment data of the patients.

	Group I	Group II	Group III	P value
	n=30	n=30	n=30	
Age (years)	42.05±13.028	46.60±11.997	46.30± 12.541	0.183
Weight (kg)	77.45±16.713	79.05±11.105	76.75±11.589	0.191
Height (cm)	169.20±8.408	169.55±8.976	170.75±8.996	0.284
Time of operation (min)	50.15±12.394	45.90±11.411	45.45±9.208	0.134
Level of peak sensory block (T+)	10.80±1.152	8.50±3.873	9.15±3.746	0.212
Level of peak motor block (min)	5.250±1.7053	6.65±3.167	5.075±1.4444	0.107
2 segment regression time (hours)	2.375±0.6664	2.200±0.6366	2.275±0.5495	0.204
Maximum motor block time	2.15±.745	2.15±0.813	2.45±0.605	0.121
Time for complete regression of motor b blockade	5.725±0.9101	5.350±0.6091	5.400±0.6609	0.101
Surgeon's satisfaction (Perfect/Good/Moderate)	9/11/0	8/11/1	7/12/1	0.151
Patient's satisfaction (Perfect/Good/Moderate)	9/8/3	6/6/8	6/11/3	0.111
Nausea (Yes/No)	2/20	7/13	4/16	0.124
Vomiting (Yes/No)	0/20	2/18	0/20	0.191
Pain, intraoperative analgesic requirement (Yes/No)	0/20	4/16	3/17	0.213
Time to first postoperative analgesic requirement	15.27±3.4000	5.025±1.1059	3.525±0.8025	0.002

Statistical analysis

All statistical analyses were performed using the IBM Statistical Package for Social Sciences (SPSS) software. Continuous parameters are expressed as mean ± standard deviation. Normally distributed variables were compared using the independent samples *t* test and non-normally distributed variables were tested using Mann-Whitney test and Kruskal-Wallis test. A p value of less than 0.05 was considered to be statistically significant. To test whether there was a significant difference between the average of more than 2 groups, ANOVA (analysis of variance) was performed.

Results

Baseline characteristics of patients were given in Table 1. There were no significant differences among groups in regard to age, height, or weight. Groups were also similar in regard to the frequencies of nausea, vomiting, and intraoperative analgesic requirement (p>0.05) (Table 1).

Groups were similar in regard to level of sensorial and motor blockade, whereas time to first analgesic requirement was significantly higher in Group C (p<0.05) (Table 1). Level of shivering was significantly higher in Group C, but no significant difference was found between Groups M and F (p<0.01) (Table 2).

No significant difference was found among groups in regard to surgeon and patient satisfaction (p>0.05) (Table 1).

Discussion

Shivering under spinal anesthesia has been explained by several mechanisms, including internal redistribution of the core temperature, loss of thermoregulatory vasoconstriction below the level of the blockade, and decrease of vasoconstriction [7]. In this study we observed that core body temperature did not differ among groups.

Large parenteral doses of morphine, fentanyl, and pethidine can cause hypothermia in animals and may also occur with small doses of intracerebral morphine. Furthermore, low environmental temperatures may accentuate the hypothermic effect of these drugs [8,9]. Hong et al. [10] performed a prospective, randomized, double-blinded study to compare the effects of morphine and pethidine on shivering. They found that shivering was less frequent in patients receiving morphine and pethidine in addition to local anesthetic as compared to those only receiving local anesthetic. Moreover, shivering was less common in the pethidine group than in the morphine group. In our study, groups receiving morphine and fentanyl were similar in regard to the occurrence of shivering, whereas shivering was less common in these groups than in the group that received only normal saline. In the study of Hong et al., all of the patients were in cool environmental conditions (23–25°C) and they received small doses of morphine and pethidine. Patients receiving small doses of intrathecal morphine and pethidine did not have significant core body temperature changes. However, these results do not provide direct evidence for

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Table 2. Comparison of level of shivering among groups.

	Group I (n=30)	Group II (n=30)	Group III (n=30)	P
Grade 0	15	10	5	0.001
Grade 1	3	5	4	0.072
Grade 2	10	10	6	0.061
Grade 3	2	5	15	0.000
Grade 4	0	0	0	Nil

reduced incidence and intensity of shivering by use of these drugs during spinal anesthesia.

Lower doses of narcotics produce hyperthermia. Their hypothermic effects are lost at higher doses in thermoneutral or warm environments, but hyperthermia may occur in some species [11].

Chow et al. [12] reported that adding 12.5 micrograms of fentanyl significantly decreased shivering in patients undergoing transurethral prostate resection under spinal anesthesia. However, Chu et al. [13] reported that 7.5 micrograms of fentanyl added to bupivacaine had no analgesic effect and did not decrease shivering, whereas 12.5 micrograms or 15 micrograms of fentanyl provided adequate analgesia and also decreased shivering.

Sadegh et al. [14] compared effects of 12.5 mg of fentanyl (25 microgram) with normal saline in patients receiving spinal anesthesia with bupivacaine. They found that patients in the fentanyl group had significantly less nausea, vomiting, and shivering.

Techanivate et al. [15] reported that use of 20 micrograms of fentanyl added to bupivacaine was not associated with any significant increase in hypotension, nausea, or vomiting, but produced less shivering compared to normal saline. These findings are in line with ours; we found that patients receiving 25 microgram fentanyl had less shivering than those receiving normal saline.

There have been several studies demonstrating that opioid drugs used in spinal anesthesia accelerate the onset of spinal analgesia, enhance drug delivery, and increase the depth of blockade; however, they produce some adverse effects, including nausea, vomiting, itching, and respiratory depression [16,17]. Intrathecal morphine and fentanyl have been used for achieving postoperative pain relief following spinal anesthesia. In our study, we observed no significant adverse effects during or after the operation, which may be attributable to the low doses of the drugs used. Abaulesh et al. [18] reported that a 0.2-mg morphine and bupivacaine combination is effective and safe. None of our patients had respiratory depression during or after the operation. Although groups showed no significant difference in levels of sensory or motor blockade, the time to first analgesic requirement was significantly longer in the physiologic serum group. Moreover, no significant difference was found among groups in surgeon or patient satisfaction. We think that these results may also be attributable to the low doses of drugs. More prospective studies, consisting of patients who undergo spinal anesthesia during operations, are needed [19–21].

Conclusions

Our study demonstrated that 25 micrograms of fentanyl or 0.1 mg of morphine added to bupivacaine may prevent shivering during spinal anesthesia without causing significant hypotension, nausea, or vomiting.

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