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Research Article

Role of intrathecal nalbuphine on prevention of postspinal shivering after knee arthroscopy

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Abstract *Background:* Shivering associated with spinal anesthesia is a common and uncomfortable problem and may interfere with monitoring, oxygen consumption and carbon dioxide production. The aim of the study was to evaluate the effect of intrathecal nalbuphine on the prevention of shivering during spinal anesthesia in patients undergoing knee arthroscopy.
Methods: 60 patients (ASA physical status I or II) scheduled for knee arthroscopy under spinal anesthesia were randomly assigned to one of two equal groups: Group C (control group, $n = 30$) receiving 2.5 ml of 0.5% bupivacaine during spinal anesthesia; and Group N patients (nalbuphine group, $n = 30$) receiving 2.5 ml of a mixture of 400 μg nalbuphine plus 0.5% bupivacaine during spinal anesthesia. Before commencing regional anesthesia, standard monitoring was established and patients were given intravenous 15 ml/kg/h of crystalloid solution (at room temperature 23–25 °C). All operations were performed in the same operating room which maintained at a constant temperature of 23–25 °C and no means of active warming were used. Mean arterial blood pressure (MAP), heart rate (HR), arterial oxygen saturation (SPO2), core (tympanic) temperature, the incidence and severity of shivering were all determined and recorded at baseline and every 10 min after anesthesia till end of surgery.
Results: Shivering was observed in 19 patients (63.3%) in control group and 7 patients in nalbuphine group (23.3%) with significant difference between the two groups ($P = 0.004$) and significant difference in intensity of shivering and core temperature ($P < 0.001$). No significant statistical difference was observed as regards hemodynamic parameters and oxygen saturation between the two groups.
Conclusion: Intrathecal nalbuphine is an effective and safe method to prevent shivering during spinal anesthesia in patients undergoing knee arthroscopy.

1. Introduction

Shivering is a common post-operative event, defined as an involuntary, repetitive activity of one or more skeletal muscles. The incidence of shivering has been found to be high, approximately 40–50% in different studies [1]. Postanesthetic

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shivering leads to feelings of discomfort in the patient as well as an increase in oxygen consumption, carbon dioxide production, catecholamine release, cardiac output, intraocular pressure and complications such as tachycardia and hypertension. In addition to this, shivering may inhibit accurate monitoring by causing artifacts in the monitor [2–5]. Shivering also increases intracranial pressure, and may contribute to increased wound pain, delayed wound healing, and delayed discharge from post-anesthetic care [6,7].

The treatment of shivering includes both pharmacological and non-pharmacological methods. The non-pharmacological management is by external heating like the use of forced air warming, warming blankets, and warmed fluids. According to the results of a meta-analysis, the most frequently reported pharmacological interventions include clonidine, pethidine, tramadol, nefopam and ketamine [8]. Unfortunately, no gold standard treatment is known for shivering as the administration of all the available drugs is associated with various adverse effects.

Nalbuphine is a lipophilic semi-synthetic opioid related to both oxymorphone and naloxone, and it has relatively potent μ-antagonist and κ-agonist activities. Because of its κ-antagonist properties, nalbuphine should produce fewer μ-mediated side effects such as respiratory depression, pruritus, nausea and vomiting [9]. It has a high affinity for κ-opioid receptors in the central nervous system. Theoretically, nalbuphine may have a significant effect on postanesthetic shivering [9]. Intrathecal nalbuphine was widely used for postoperative analgesia in many studies [9,10].

The present study designed to study the effect of intrathecal nalbuphine on prevention of postspinal shivering in patients undergoing knee arthroscopy.

2. Materials and methods

This study was performed between January 2013 and August 2013 after approval of ethical committee of Faculty of Medicine, Menoufiya University and Pan African Clinical Trial Registry (www.pactr.org) PACTR 201505001091143. In a prospective, controlled, randomized clinical trial, after receiving written consent from patients, 60 patients, 20–60 years of both sex and American Society of Anesthesia (ASA) physical status I or II scheduled for knee arthroscopy under spinal anesthesia were enrolled. Patients with contraindications to regional anesthesia, allergy to the study medication, and obese with body mass index (BMI) >30 were excluded. Patients were randomly assigned to one of two groups through closed envelop technique. Group C (control group, $n = 30$). Group N (nalbuphine group, $n = 30$). Before commencing regional anesthesia, standard monitoring was established and patients were given intravenous 15 ml/kg/h of crystalloid solution (at room temperature 23–25 °C) through an 18-gauge peripheral venous catheter. Oxygen 5 L/min was administered through a mask during anesthesia and patients were covered with drapes but not actively warmed. Spinal anesthesia was performed in the setting position at the L3–4 or L4–L5 levels, midline approach by 25-gauge Quinkle needle using 2.5 ml hyperbaric bupivacaine, 5 mg/ml in group C and 2.5 ml of a mixture of 400 μg nalbuphine plus hyperbaric bupivacaine, 5 mg/ml. After the procedure, patients were positioned supine. Sensory levels were determined by pinprick and the motor blockade was evaluated using Bromage's criteria. All operations were performed in the same operating room which maintained at a constant temperature of 23–25 °C and no means of active warming were used. The mean arterial pressure (MAP), heart rate (HR), arterial oxygen saturation (Spo2), and core (tympanic) temperature were measured and recorded preoperative then every 10 min till the end of surgery. The incidence and severity of shivering were recorded during the operation and in the recovery room. Shivering was graded with a scale described by Bedside Shivering Assessment Score (BSAS) as follows [11]:

1. None: no shivering noted on palpation of the masseter, neck, or chest wall.
2. Mild: shivering localized to the neck and/or thorax only.
3. Moderate: shivering involves gross movement of the upper extremities (in addition to neck and thorax).
4. Severe: shivering involves gross movements of the trunk and upper and lower extremities.

Also any complications were recorded for example hypotension was defined as a decrease in the (MBP) to less 20% than the baseline value, which was treated with increments 5–10 mg of intravenous ephedrine. Bradycardia was defined as a decrease in HR less than 50 b/min which was treated with 0.5 mg IV atropine.

2.1. Statistical analysis

A power analysis was performed using a power of 90% and an α value 0.05. From previous clinical studies, we assumed that the incidence of shivering would be 20% in the nalbuphine group after premedication and 60% in the placebo group after premedication with a standard deviation 40. The sample size was calculated to be 29 patients so we decided to include 30 patients in each group in the study. We used Power and Sample size statistics program (PS version 3.0.43) for power analysis.

The collected data were analyzed by Statistical Package for Social Science (SPSS) version 16. Parametric data were expressed as mean ± SD. The comparison of the mean ± SD of two groups was done using the paired and unpaired Student's t test. Nonparametric data were expressed as number and percentage of the total number of patients. Determining the extent of a single observed series of proportions, difference from a theoretical or expected distribution was done using the Chi square test. P-value <0.05 was considered statistically significant.

3. Results

The demographic data including age, sex, weight, height and the duration of surgery (Table 1) were comparable between both groups. The mean arterial blood pressure decreased in both groups from the baseline measurements with insignificant difference between the two groups (Table 2). As well as the heart rate decreased from the baseline with insignificant difference between the studied groups (Table 3). The number of patients receiving vasoactive agents was comparable between the two groups (6 vs 5). Three of eight patients in group C received ephedrine, two received atropine and one received both atropine and ephedrine. Three of the five patients in group N received ephedrine and two received atropine.

Table 1 Demographic data and duration of surgery.

	Group C (n = 30)	Group N (n = 30)	P-value
Age (Years)	47.67 ± 7.68	45.47 ± 7.35	0.262
Sex (F/M)	12/18	9/21	0.588
Height (Cm)	165.63 ± 9.07	167.83 ± 9.12	0.353
Weight (kg)	89.17 ± 10.79	88.27 ± 10.67	0.746
Duration of surgery (Min)	43.76 ± 6.75	45.72 ± 7.38	0.288

Group C: control group, Group N: nalbuphine group. Data were presented as Mean ± SD, number of patients.

Table 2 Mean arterial blood pressure.

	Group C (n = 30)	Group N (n = 30)	P-value
Baseline	95.92 ± 8.11	94.88 ± 10.42	0.668
10 min	93 ± 6.89	91.08 ± 6.93	0.286
20 min	92.4 ± 7.97	90.56 ± 5.32	0.297
30 min	88.96 ± 8	89.87 ± 6.54	0.631
40 min	90.27 ± 4.26	90.23 ± 4.36	0.971
50 min	92.27 ± 6.82	91.76 ± 6.57	0.769

Group C: control group, Group N: nalbuphine group. Data were presented as Mean ± SD.
* $P < 0.05$ significant between the two groups.

Table 3 Heart rate.

	Group C (n = 30)	Group N (n = 30)	P-value
Baseline	82.1 ± 8.53	81.23 ± 8.21	0.689
10 min	79.97 ± 9.24	79.33 ± 8.32	0.779
20 min	77.53 ± 10.08	77.6 ± 8.43	0.977
30 min	76.67 ± 9.26	75.82 ± 9.23	0.723
40 min	76.37 ± 6.16	75.48 ± 8.14	0.635
50 min	77.87 ± 8.15	76.83 ± 7.74	0.614

Group C: control group, Group N: nalbuphine group. Data were presented as Mean ± SD.
* $P < 0.05$ significant between the two groups.

Table 4 Core temperature.

	Group C (n = 30)	Group N (n = 30)	P-value
Baseline	37.03 ± 0.16	37.13 ± 0.15	0.015
10 min	36.9 ± 0.12	37.05 ± 0.17*	<0.001
20 min	35.94 ± 0.17	36.8 ± 0.12*	<0.001
30 min	35.33 ± 0.23	36.73 ± 0.11*	<0.001
40 min	35.51 ± 0.18	36.72 ± 0.11*	<0.001
50 min	35.69 ± 0.24	36.73 ± 0.12*	<0.001

Group C: control group, Group N: nalbuphine group. Data were presented as Mean ± SD.
* $P < 0.05$ significant between the two groups.

Both groups showed a decrease in body core temperature with significant lower values ($P < 0.001$) in nalbuphine group when compared to control group (Table 4). As regards the incidence of shivering (Table 5) was significantly less in nalbuphine group (7 of 30) versus 19 of 30 in control group ($P = 0.019$). SPO_2 exceeded 95% in all patients at all the study times with insignificant difference between the two groups.

Table 5 Postanesthetic shivering.

	Group C (n = 30)	Group N (n = 30)	P-value
Shivering score			
0	11(36.7%)	23(76.7%)*	0.019
1	9(30%)	3(10%)	0.107
2	7(23.3%)	4(13.3%)	0.505
3	3(10%)	0(0%)	0.237
Incidence of shivering	19(63.3%)	7(23.3)*	0.004

Group C: control group, Group N: nalbuphine group. Data were presented as number of patients (%), Mean ± SD.
* $P < 0.05$ significant between the two groups.

4. Discussion

The present study showed that adding a small dose (400 μg) of nalbuphine to the intrathecal bupivacaine during anesthesia for knee arthroscopy reduces the incidence and severity of shivering without hemodynamic effects.

Shivering associated with neuraxial anesthesia is a common and uncomfortable side effect. It develops in up to 60% of patients. The mechanism of shivering during regional anesthesia has not been fully understood. Postanesthesia shivering is probably due to redistribution of heat from core to periphery, loss of thermoregulatory vasoconstriction below the level of blockade resulting in an increased heat loss from body surfaces [12,13], and altered thermoregulation characterized by a decrease in vasoconstriction threshold [14]. Shivering causes patient distress and also leads to other adverse effects, including increased oxygen consumption, carbon dioxide, lactic acid production and increased left ventricular systolic work index [15,16]. Prevention seems essential especially in vulnerable patients and should be effective, simple, and cheap. IV drugs are the "gold standard" for the treatment of postoperative shivering [17]. Although IV nalbuphine has long been used for the treatment of postanesthetic shivering [16–18], it is generally administered to treat shivering that has already begun. As compared with its use in treatment, its use in prevention of shivering has not been well investigated especially its intrathecal route of administration. Nalbuphine, a semisynthetic opioid related to both naloxone and oxymorphone, has the characteristics of μ-antagonist and κ-agonist activities [9,18]. It has a high affinity for κ-opioid receptors in the central nervous system [18], through which, it exerts its possible antishivering mechanisms. As suggested by many studies, κ-opioid receptors may play a more important role than μ-opioid receptors in the treatment of postspinal shivering [18,19].

In this study, the significant reduced incidence of shivering with intrathecal nalbuphine versus placebo ($p < 0.05$) is similar to that reported by Roy and colleagues who found similar effects of intrathecal meperidine [20], and by Tiwari et al. [10]. Also, this is comparable with the studies used nalbuphine intravenously to control postoperative shivering [18,21]. The core temperature was also, significantly decreased in

nalbuphine group more than control group as noticed in many studies [20–23]. The insignificant change in the mean arterial blood pressure documented in the study is in accordance with other studies that used intrathecal nalbuphine as Roy and colleagues [20], Fournier and co-workers [9], Tiwari et al. [10], and Chaney [24].

5. Conclusion

In conclusion, intrathecal nalbuphine, a κ-receptor agonist, provides a safe and effective prevention of postspinal shivering in patients undergoing knee arthroscopy.

Conflict of interest

The authors declare that there are no conflict of interests.

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