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Efficacy of Pethidine and Buprenorphine for Prevention and Treatment of Postanesthetic Shivering

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ABSTRACT

Background: Postanesthetic shivering is a distressing postoperative complication. Pharmacological control is an effective method for treatment and prevention of postoperative shivering. Pethidine prevents or manages shivering far better than equianalgesic doses of other opioids. However, buprenorphine is an opioid with a similar structure to morphine but approximately 33 times more potent. This study aimed to assess and compare the effects of these two opioids in preventing post-anesthetic shivering.

Materials and Methods: This randomized double-blind clinical trial was designed to compare the efficacy of buprenorphine and pethidine in prevention of post anesthetic shivering. Sixty ASA grade I-II patients undergoing general anesthesia for elective Cesarean section entered the study. Patients received either buprenorphine 3 μ g/kg (n=30) or pethidine 0.5 mg/kg (n=30) intravenously 30 min before the end of surgery. Heart rate and blood pressure were measured 15 min after the injection. Occurrence of shivering was evaluated for one hour in the recovery room. Also, pain intensity was assessed by using a visual analog scale (VAS; 0-5).

Results: Shivering was significantly reduced in the pethidine group (5 of 30 versus 13 of 30, $p < 0.05$). Visual pain scores were similar in both groups. There was no difference between the two groups regarding hemodynamics.

Conclusion: Despite similar in pain control, pethidine is more effective than buprenorphine in prevention of post anesthetic shivering. (*Tanaffos* 2007; 6(3): 54-58)

Key words: Postanesthetic shivering, Buprenorphine, Pethidine, Cesarean section

INTRODUCTION

Shivering is an unpleasant post-anesthetic complication which continues for minutes to hours if not treated. Prevention or treatment of post-

anesthetic shivering not only results in relief but also decreases the associated complications such as increased oxygen use and increased cardiac output which can be problematic especially in patients with heart problems (1). Thus, treatment of shivering is as important as the pain relief (2,3). Opioids are widely used for anesthesia and pain control. They are also used for treatment of post-anesthetic shivering.

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Studies have indicated that the anti-shivering effect of opioids is due to the drug-induced inhibition of normal thermoregulatory control (4-6). Pethidine in 25-50 mg doses is the most effective opioid for prevention and treatment of shivering (4). Other opioids such as morphine, fentanyl and alfentanil are less effective for treatment of shivering (7,8). Buprenorphine is a μ receptor partial agonist that is 33 times more potent than morphine. But respiratory depression due to buprenorphine is less than morphine (4,9). We conducted a double-blind clinical study and compared the effects of these two opioids in preventing post-anesthetic shivering. The analgesic effects and hemodynamic changes of these drugs were also evaluated.

MATERIALS AND METHODS

This double-blind prospective randomized clinical trial was approved by the ethical committee of the hospital and a written consent was obtained from all patients before the operation. A total of 60 ASA class I-II female patients in the age range of 18-40 years who underwent elective Cesarean section with no complication under general anesthesia were entered in the study. Before the operation, these patients were randomly divided into two groups of pethidine (P) and buprenorphine (B) each comprising 30 patients. During the study period, mean temperature of the operating rooms was recorded by a wall thermometer.

Before the induction of anesthesia, standard monitoring was established for the patients.

Intravenous anesthesia induction was done with sodium thiopental 4 mg/kg and succinyl choline 1 mg/kg. Immediately afterwards, halothane 0.5% and fentanyl 2 μ g/kg and after delivery, atracurium were given. Intravenous fluids at room temperature were also administered. Heart rate and blood pressure of the patients were recorded 30 min before the termination of anesthesia. Then 0.5 mg/kg pethidine

and 3 μ g/kg buprenorphine were administered intravenously by the anesthesia assistant to group P and group B patients respectively.

HR and BP were recorded again 15 minutes after drug injection. HR and BP changes were categorized into 3 groups (1:<20%, 2:20-30%, 3:>30%).

Eventually, when the patient regained consciousness, the patient was extubated and taken to the recovery room. All patients were covered with a blanket after the operation. In the recovery room, the presence or absence of shivering was assessed and recorded in both groups based on the following four-point scale:

- 1: No shivering
- 2: Mild shivering, slight facial and cervical muscle contraction
- 3: Moderate shivering, obvious shivering in head and neck, shoulders and/ or extremities.
- 4: Severe shivering, obvious shaking all over the body.

The pain score for each patient was calculated from 0-5 by using visual analog scale (VAS) (0: no pain 5: severe pain). All measurements were performed by an anesthesiologist who was unaware of the type of understudy drug.

If the patient developed shivering or pain, the necessary managements were performed.

For data analysis, SPSS software version 11.5 was used. For comparison of the quantitative variables between the two groups the student t-test and for the qualitative variables the chi-square test was used. Data were expressed as mean \pm SD and $P < 0.05$ was considered statistically significant.

RESULTS

The mean age of patients was 26.55 yrs. (range 19-41 yrs). The mean age of patients in group B and group P was 26.2 \pm 5.1 yrs and 26.9 \pm 5.0 yrs respectively but this difference was not statistically significant ($P=0.592$). There was no significant

difference between the two groups in regard to the repetition of Cesarean section (first time or repeat section) and room temperature. Also, no significant difference was detected between the two groups regarding the dosage of fentanyl administered during the operation ($150 \pm 50 \mu\text{g}/\text{kg}$ in group B and $145 \pm 50 \mu\text{g}/\text{kg}$ in group P).

For the comparison of pain severity between the two groups, patients who had severe unbearable pain were placed in one group and the remaining were placed in another. No significant difference was detected between the two groups regarding the severity of pain as 19 patients in group B and 14 patients in group P expressed moderate, mild or no pain while in group B, 11 patients and in group P 16 patients expressed severe unbearable pain (Figure 1).

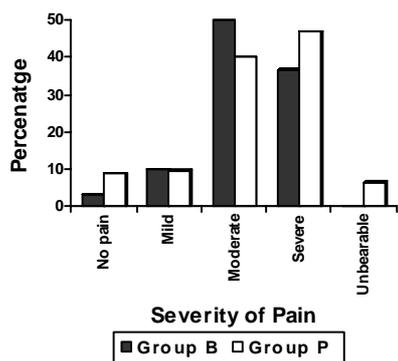


Figure 1. Comparison of the pain severity between the two groups post-operatively. The severity of pain was similar in both groups ($P > 0.05$).

Hemodynamic changes (HR and BP) were also similar in both groups ($p > 0.05$) (Figure 2 and 3).

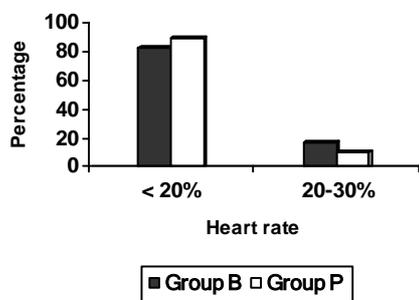


Figure 2. Comparison of heart rate alterations between the two groups. Heart rate alterations were similar in both groups ($P > 0.05$).

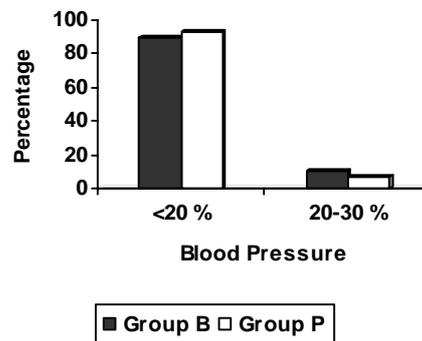


Figure 3. Comparison of the blood pressure alterations between the two groups. Blood pressure alterations were similar in both groups ($p > 0.05$).

Occurrence of shivering in group B was significantly higher than in group P. To compare the severity of shivering, patients without shivering were put in one group and the remaining patients were placed in another. Thirteen patients in group B (43.3%) and 5 patients in group P (16.6%) had shivering, this difference was statistically significant ($p = 0.047$) (Figure 4).

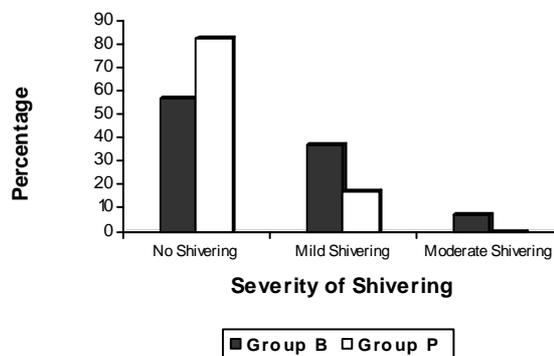


Figure 4. Comparison of the severity of post-anesthetic shivering between the two groups. Severity of shivering in pethidine group was significantly lower than buprenorphine group ($p < 0.051$).

DISCUSSION

Opioids are the most common and most effective drugs for prevention and treatment of post-anesthetic shivering among which pethidine is the most effective opioid drug of choice for treatment.

Several studies have been performed on the effects of opioids on treatment and prevention of post-anesthetic shivering (10,11). Opioids manage the shivering through reducing the vasoconstriction and shivering thresholds. Apparently, the anti-shivering effect of opioids is mostly due to the stimulation of κ receptors than μ receptors (6). Pethidine has specific anti-shivering effect and is a more effective medication for treatment of shivering than equianalgesic doses of other opioids (7, 8). Pethidine reduces the shivering threshold 2 folds greater than the vasoconstriction threshold and inhibits shivering. Pethidine stimulates μ and Kappa receptors and is mostly a Kappa receptor agonist while alfentanil, morphine and fentanyl are μ receptor agonists. Pethidine exerts its anti-shivering effect by activating the μ receptors in the hypothalamus and κ receptors in the spinal cord. It seems that the specific anti-shivering effect of pethidine is mostly due to its effect on Kappa receptors (8). Other Kappa receptor agonists like butorphanol probably have anti-shivering effect similar to pethidine. As demonstrated in previous studies, the anti-shivering effect of pethidine is not related to its analgesic effect.

It seems that the anti-shivering effect of pethidine is due 10% on opioid Kappa receptors. This hypothesis is supported by evidence indicating that a medium dose of naloxane inhibits the anti-shivering effect of pethidine only to some extent (8,12).

In spite of various studies and different hypotheses in this regard, the definite cause for specific anti-shivering effect of pethidine is under investigation. Buprenorphine is the μ receptor partial agonist and a Betaine derivative that is attached to Kappa and sigma receptors. This opioid is structurally similar to morphine but 33 times more potent; although respiratory depression due to its clinical doses is less reported than other opioids such as morphine (9). Therefore, it is indicated in those older than 65 years and cases of thoracic surgery

operations.

Our study results showed that the two groups were similar in regard to the severity of post-operative pain and hemodynamic responses. But, although pethidine was administered in one half the dose of buprenorphine, it reduced the occurrence of postanesthetic shivering more significantly than buprenorphine. In accordance with the previous studies, this study showed that pethidine is more effective for prevention of shivering and its preventive effect on post-anesthetic shivering is greater than buprenorphine. On the other hand, although pethidine is more effective in preventing postanesthetic shivering compared to buprenorphine, buprenorphine decreases the severity of shivering as well; as in buprenorphine group, no patient had severe post-anesthetic shivering and the severity of shivering was between 0 to 2. Since both drugs decreased the postoperative pain equally, it is concluded that the anti-shivering effect of these drugs is not related to their analgesic effects. Our results demonstrated that although the dosage of buprenorphine was twice that of pethidine, the latter is more effective in preventing post-anesthetic shivering. However, the analgesic effects and hemodynamic responses were similar in both groups. This study was in accordance with the previous studies indicating that pethidine 0.5mg/kg can control the post anesthetic shivering effectively (13,14).

CONCLUSION

Although buprenorphine is an effective analgesic drug with no hemodynamic complication, its anti-shivering effect even in higher doses is less than pethidine.

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