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ORIGINAL ARTICLE

Effects of adding 5 mg meperidine to 10 mg bupivacaine for spinal anesthesia on postoperative pain in cesarean section surgery

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Abstract

Introduction: Meperidine has the advantages of being widely available and inexpensive. It would be highly cost-benefit if it is used at doses that are without any side-effect. Thus, this study aimed to assess the effect of meperidine 5 mg as an additive to bupivacaine for spinal anesthesia on postoperative pain in cesarean section surgery.

Methods: This double-blind randomized clinical trial was performed on 40 patients aged 20-40 yr. They were in classes 1 or 2 according to the American Society of Anesthesiologists (ASA) physical status classification system and were scheduled for elective cesarean surgery under spinal anesthesia. Patients were randomly allocated into two groups according to whether meperidine or normal saline was used as an additive to bupivacaine for spinal anesthesia. All patients with pre-existing or pregnancy-induced hypertension, known fetal abnormality or allergy to bupivacaine or meperidine were excluded. Postoperative analgesia was compared between the two groups immediately and 2, 12, 24 hours after surgery. Also, the need for antiemetic was compared between the groups. The collected data was analyzed in SPSS software (version 16) using independent t-test, Mann-Whitney, and Chi-square. The significance level for all tests was considered less than 0.05.

Results: The severity of postoperative pain 12 and 24 hours after surgery was significantly higher in normal saline group. There was no significant difference in incidence of pruritus, nausea and vomiting between the two groups.

Conclusions: Addition of meperidine 5 mg to intrathecal bupivacaine is associated with increased duration and quality of postoperative analgesia but has no significant effect on severity and incidence of pruritus, nausea and vomiting.

Key Words: Anesthesia, Spinal; Analgesia; Meperidine; Bupivacaine

Introduction

Addition of opioids to intrathecal injection of local anesthetics usually increases the duration and quality of early postoperative analgesia (1-3). When fentanyl and sufentanil were added to local anesthetics, the early postoperative analgesia lasts for 4 to 13 h (4). Addition of hydrophilic opioids to intrathecal local anesthetics is associated with prolonged duration of postoperative analgesia in comparison with addition of lipophilic opioids. However, hydrophilic opioids increase the risk of delayed apnea (5). Meperidine is an opioid with intermediate lipid solubility and local anesthetic properties. Spinal anesthesia with meperidine as a sole agent is associated with prolonged postoperative analgesia lasting to

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even seven days. Nevertheless, its use has been limited by side-effects such as nausea and vomiting, hypotension, pruritus and urinary retention (6-9). According to the study conducted by yu et al, upon adding meperidine 10 mg to bupivacaine, the mean duration of effective analgesia was prolonged significantly in comparison with the control group (P<0.001) although the risk of nausea and vomiting was not reduced (10). Since meperidine has the advantage of being widely available and inexpensive, if it is used with doses that could be without any side-effects, it would be very cost-benefit. Thus, the aim of this study was to compare between postoperative analgesic effect of meperidine and normal saline in combination with bupivacaine 10 mg.

Methods

This randomized double-blind clinical trial was approved by the Ethics Committee of Birjand University of Medical Sciences and registered in the Iranian Registry of Clinical Trials (IRCT) with an identified registry number of IRCT2015052821383N2. The study was performed on 40 patients aged 20 to 40 years. They were in classes 1 or 2 according to the American Society of Anesthesiologists (ASA) physical status classification system and scheduled for elective cesarean section under spinal anesthesia in Valiasr Hospital affiliated with Birjand University of Medical Sciences. All the patients with a history of addiction to opiates, drug or substance abuse, use of analgesic or antiemetic drug during the last 24 hours, pre-existing hemodynamic abnormality, skin infection in the lumbar site, dissatisfaction for spinal anesthesia, and any history of allergy to bupivacaine or meperidine were excluded.

For randomization, the name of each group was written on 20 pieces of paper and placed in closed envelopes. The envelopes were mixed and dialed from 1 to 40. When a patient entered the operating room, a number from 1 to 40 was generated by a computerized program. The selected envelope was given to the anesthetic technicians who were responsible for drug preparation but were not directly involved in data collection and analysis. The drugs were prepared in the same shaped syringe, a combination of bupivacaine 10 mg with either meperidine 5 mg (0.5 ml) in meperidine group or with normal saline (0.5 ml) in the saline group. The statistical investigator and data collector were blinded. After prape and drape, spinal anesthesia was performed by a 25 G quince needle at the L4-L5 or L5-S1 intervertebral spaces in sitting position, immediately after which the patients were placed in supine position. Standard monitoring including continuous pulse oximetry and ECG was applied. Blood pressure was measured every 3 minutes from intrathecal injection to the end of the operation. Hypotension, defined as a decrease in systolic blood pressure to less than 90 mm Hg or a decrease of 25% from baseline, was treated with ephedrine 10 mg intravenously as required.

Intraoperative pruritus, nausea, and vomiting were recorded and the prevalence of each of them was compared between the two groups. The patients with any degree of pruritus received ondansetron 4 mg intravenously. The vomiting cases were treated with metoclopramide 10 mg after the first excluding hypotension.

The severity of postoperative pain was measured by the Visual Analog Scale (VAS). The time from intrathecal injection to the first time at which the patient reported any score of pain (VAS greater than zero) was considered as the effective analgesic period. Postoperative pain was measured immediately, 2, 12, and 24 hours after surgery. Patients with VAS score ≥4 at any time was considered as severe pain whereby morphine 2 mg was administered intravenously and the participant was excluded. At the end of the study, the time of the analgesic period and pain scores using the VAS at the aforementioned times were compared between the two groups. Statistical calculations were performed using SPSS 16. We used Student's *t*-test to analyze continuous data and Mann–Whitney *U*-test for non-continuous data. Dichotomous data were analyzed with the Chi-square test.

Results

This study was conducted on 40 patients scheduled for elective cesarean section under spinal anesthesia. Five patients in the saline group and only 1 patient in the meperidine group had VAS score ≥ 4 at 12 hours after surgery so they received morphine 2 mg intravenously and were removed from the study. There was no significant difference between the two groups in terms of age, weight, and duration of surgery (Table 1). Mean duration of effective analgesia in the meperidine group was significantly higher than the saline group, i.e., 2.32±0.76 versus 1.46±0.50 respectively (p=0.0001).

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Table 1: Comparison of age, weight, and duration of surgery between the two groups (mean±SD)

Effect Modifiers	Meperidine group (n=20)	Saline group (n=20)	P-value
Age	30.7±4.68	30.6±5.61	0.951
Weight	73.4±10.48	76.1±8.21	0.392
Duration of surgery (min)	70.3±14.34	69.8±13.08	0.908

Table 2: Comparison of the mean of the pain severity immediately, 2, 12, and 24 hours after surgery between the two groups

Severity of pain	Meperidine group	Saline group	P-value
Immediately after surgery	0.0±0.00	0.05±0.43	0.601
2 hours	0.2±0.89	0.0±0.11	0.271
12 hours	2.3±0.71	3.3±0.22	<0.0001
24 hours	2.5±0.23	3.0±0.043	<0.0001

Sixteen patients in each group had nausea or vomiting after correction of hypotension. The prevalence of nausea and vomiting was not significantly different between the two groups, (80% versus 76.2%, respectively) (p=0.494). Also, the prevalence of pruritus was not significantly different in the two groups.

The pain did not show any significant difference between the two groups immediately and 2 hours after surgery. However, 12 and 24 hours after surgery, there was significant increase in the normal saline group (Table 2).

Discussion

In this study, we found that the analgesia duration increased when meperidine 5 mg was added into intrathecal bupivacaine. While similar studies report increased duration of analgesia with admixture of intrathecal meperidine and bupivacaine in comparison with placebo and bupivacaine, there was no study to show the effect of intrathecal meperidine combined with a dosage lower than 10 mg and bupivacaine for cesarean (10, 11).

The risk of intraoperative nausea and vomiting may be increased in the cesarean section because of peritoneal manipulation. Also, the application of opioids for intrathecal injection solely or in combination with local anesthetics may lead to increased risks (12). Moreover, in some studies, intrathecal fentanyl has been shown to be more effective than intravenous ondansetron in the prevention of nausea and vomiting during spinal anesthesia for cesarean section (13). According to a similar study, the incidence of nausea and vomiting increases as meperidine 10 mg is added to bupivacaine for spinal anesthesia in cesarean in comparison with the placebo group (10). In our study, addition of meperidine 5 mg to hyperbaric intrathecal bupivacaine for cesarean had a comparable effect on the incidence of intraoperative nausea and vomiting versus normal saline group. Probably, the decrease in dosage of intrathecal meperidine had a significant role in reducing the risk of nausea and vomiting.

Intrathecal opioids can induce systemic pruritus. Pruritus begins shortly after analgesia. The onset depends on the route, type, and dosage of opioid used. The onset and duration of pruritus depend respectively on the time needed to achieve effective concentration for pruritus and the time required to reduce concentration below it. The use of the minimum effective dose and addition of local anesthetics seem to decrease the prevalence and the severity of itching (14). Therefore, the more lipid soluble an opioid is, the longer the onset and the shorter the duration of pruritus. Thus, the pruritus induced by morphine is substantially longer and more difficult to treat (15). Accordingly, it seems that it can be used for spinal anesthesia with much lower complications than morphine (16). In our study, there was no report of pruritus during operation. A previous study with a combination of intrathecal meperidine 10 mg to bupivacaine was compatible with the results of our study (10). Thus, it seems that intrathecal meperidine with a dosage of 10 mg and lower, especially in combination with local anesthetics, can reduce the risk of itching.

We assessed the VAS scores of pain in this study at the following times: immediately, 2, 12, and 24 hours after surgery. Patients with VAS score ≥4 at any times after surgery received morphine and

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were excluded from the study. The results showed no differences in pain scores between meperidine and saline group although the VAS score was significantly higher in the last 12 hours after surgery in the saline group. In contrast to our study, morphine consumption in patient-controlled analgesia was used to assess pain in the study of Yu et al. They found that intrathecal meperidine 10 mg added to bupivacaine in comparison with the saline group was accompanied by less morphine consumption during the first 6 hours after surgery. Surprisingly, the need for morphine consumption increased in the remaining time to 24 hours. The difference between our result and that of Yu et al's study is probably due to acute spinal tolerance or hyperalgesia with meperidine 10 mg in comparison with 5 mg.

Conclusions

In summary, the addition of intrathecal meperidine 5 mg to hyperbaric bupivacaine prolonged analgesia about 2 to 3 hours after elective caesarean section compared with placebo. Meperidine has the advantage of being widely available and inexpensive. An important limitation of its use, i.e., increased intraoperative nausea and vomiting, will be avoided by using meperidine 5 mg. In this study, we did not assess the anti-shivering effect of intrathecal meperidine. Thus, other studies are recommended to assess the anti-shivering effect of adding intrathecal meperidine 5 mg to bupivacaine.

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Conflict of interests

None

Authors' Contribution

All colleagues have had the same contribution in the study.

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