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Original Contribution

A comparison of prophylactic use of meperidine, meperidine plus dexamethasone, and ketamine plus midazolam for preventing of shivering during spinal anesthesia: a randomized, double-blind, placebo-controlled study☆

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Abstract

Study objectives: The aim of this study is to compare the efficacy of combination of meperidine and dexamethasone with that of placebo, meperidine alone, and the combination of ketamine and midazolam in preventing shivering during spinal anesthesia.

Design: This is a prospective, placebo-controlled study.

Setting: The setting is at an operating room of a university-based teaching hospital.

Patients: Two hundred American Society of Anesthesiologists I and II patients undergoing orthopedic and urologic surgery under spinal anesthesia were included.

Interventions: Subarachnoid anesthesia was performed by using 15 mg of 0.5% hyperbaric bupivacaine. Patients were randomly allocated to receive saline (placebo, group C), meperidine 0.4 mg/kg (group Me), ketamine 0.25 mg/kg plus midazolam 37.5 μg/kg (group KMi), and meperidine 0.2 mg/kg plus dexamethasone 0.1 mg/kg (group MeD). All drugs were given as an intravenous bolus immediately after intrathecal injection.

Measurements: During surgery and stay in the recovery room, shivering score, blood pressure, and some other adverse effects were recorded at 5-minute intervals. Axillary and tympanic temperatures were recorded at 15-minute intervals during the perioperative period.

☆ This manuscript has not been published and is not under consideration for publication elsewhere. We have no conflict of interest to disclose.

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Main results: The incidence of shivering after 30 minutes of spinal anesthesia in groups C, Me, KMi, and MeD was 64%, 20%, 20%, and 4%, respectively, which was significantly higher in group C compared with other groups ($P < .0001$). Regarding adverse effects, there was no significant difference between groups ($P \geq .2$). Axillary temperature significantly increased in the 15th-120th–minute interval in groups Me, KMi, and MeD ($P < .0001$) and in group MeD was higher than that in other groups. Core temperature decreased in the 15th-120th–minute interval in group MeD, lower than that in other groups ($P < .0001$).
Conclusions: Prophylactic use of meperidine 0.2 mg/kg plus dexamethasone 0.1 mg/kg was more effective than meperidine 0.4 mg/kg as a sole agent or the combination of ketamine 0.25 mg/kg and midazolam 37.5 μg/kg in preventing shivering resulting from spinal anesthesia.
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1. Introduction

Shivering-like tremor is a distressing experience and was reported in 5%-65% of patients who recover from general anesthesia and 60% of those with regional anesthesia [1,2]. It leads to complications of sympathetic stimulation such as tachycardia and high blood pressure exacerbating ischemic heart disease [3,4]. It also increases cardiac output and both carbon dioxide consumption and production as well as intraocular and intracranial pressure. Intraoperative changes play a pivotal role in the mechanism of shivering in those undergoing surgery. These include pain, increased sympathetic tone, and inflammatory response due to systemic release of cytokines [5]. Inhibition of tonic vasoconstriction caused by spinal anesthesia results in thermoregulation system impairment [6]. The core heat from the trunk, just below the block level, can be easily redistributed during spinal anesthesia [7].

Although multiple strategies for shivering have been used, there is no preferred method of treatment or prevention globally accepted so far. Ketamine acts as a competitive *N*-methyl-D-aspartic acid receptor antagonist and can control postoperative shivering over regional anesthesia [8–11]. Ketamine in combination with midazolam has been shown to be more effective than ketamine alone [2]. On the other hand, the fear of hallucination, nausea, and vomiting limited the use of ketamine as a first pharmacological agent for shivering [14,17].

Meperidine has been known to be one of the most effective drugs [12–18]. Although its mechanism of action is not fully known, meperidine probably acts directly on the thermoregulatory center or via opioid receptors. However, it has been shown that about 0.4 mg/kg of meperidine is the optimal dose in preventing shivering, but this dose has been associated with significant incidence of dizziness, sedation, postoperative nausea, and vomiting.

Certain medications such as dexamethasone decrease the gradient between core and skin temperature and modifies the inflammatory response [5,19]. During the last decade, certain studies have reported the positive effects of dexamethasone to decrease the incidence of shivering after general and cardiac surgeries by regulating immune responses [5,19]. General anesthesia facilitates redistribution of the temperature from the central tissues to the peripheral tissues [19]. In general anesthesia, core temperature regulation responses like the vasoconstriction threshold are controlled, and most anesthetic drugs cause peripheral vasodilation [20].

This mechanism of shivering in general anesthesia is somewhat similar to that causing shivering during spinal anesthesia, and dexamethasone has been shown to be able to prevent this event after general anesthesia. Thus, we propose the hypothesis that dexamethasone may have the potency to reduce the postspinal shivering in combination with other medications such as meperidine. In this regard, the optimal dose of meperidine may decrease, and consequently, its adverse effects may be attenuated.

To our knowledge, there is no study to assess the combination of meperidine and dexamethasone with other drugs identified as effective agents to prevent shivering during spinal anesthesia. The aim of this study was to determine whether the addition of intravenous (IV) dexamethasone to meperidine resulted in reduction of postspinal shivering more than meperidine alone or the combination of ketamine and midazolam.

2. Methods

This study was a prospective, randomized, double-blind, placebo-controlled trial including 200 American Society of Anesthesiologists (ASA) I and II patients between the ages of 20 and 60 years who were candidates to undergo elective orthopedic and urologic surgery under spinal anesthesia. This study was approved by our institutional review board and ethics committee. The day before surgery, our anesthesiologist explained the purpose of this study to the patients and requested their participation. The patients were informed that participation was not compulsory. Written informed consent for enrolment was obtained, and patient anonymity was preserved. The exclusion criteria included those with hypo- or hyperthyroidism, an initial body temperature more than 38°C or less than 36°C, psychological disorders, cardiopulmonary disease, a known history of alcohol or substance abuse, a need for transfusion during surgery, or receiving vasodilators that may alter thermoregulation. Those patients with failed spinal anesthesia on the first try were also excluded from this study.

To maintain the integrity of results, none of the patients received preanesthetic medications. Upon arrival in the operating

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