Journal of Clinical Anesthesia (2016) **35**, 13–19

ELSEVIER

Journal of Clinical Anesthesia

Original Contribution

Anticholinergic premedication to prevent bradycardia in combined spinal anesthesia and dexmedetomidine sedation: a randomized, double-blind, placebo-controlled study☆,☆☆

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Received 22 April 2016; revised 28 June 2016; accepted 5 July 2016

Keywords:
Bradycardia;
Dexmedetomidine;
Spinal anesthesia

Abstract

Objective: When dexmedetomidine is used in patients undergoing spinal anesthesia, high incidence of bradycardia in response to parasympathetic activation is reported. Therefore, we aimed to evaluate the effectiveness of atropine premedication for preventing the incidence of bradycardia and the hemodynamic effect on patients undergoing spinal anesthesia with sedation by dexmedetomidine.

Design: Randomized, double-blind, placebo-controlled study.

Setting: Operating room.

Patients: One hundred fourteen patients (age range, 2-65 years; American Society of Anesthesiology class I-II) participated in this study, willing to be sedated and to undergo spinal anesthesia.

Intervention: The patients were divided into 2 groups: group A and group C. After performing spinal anesthesia, dexmedetomidine was infused at a loading dose of 0.6 μg/kg for 10 minutes, followed by an infusion at 0.25 μg/(kg h). Simultaneously with the loading dose of dexmedetomidine, patients in group A received an intravenous bolus of 0.5 mg atropine, whereas patients in group C received an intravenous normal saline bolus.

Measurement: Data on administration of atropine and ephedrine were collected. Hemodynamic data including heart rate, systolic blood pressure, diastolic blood pressure (DBP), and mean blood pressure (MBP) were also recorded.

Main results: The incidence of bradycardia requiring atropine treatment was significantly higher in group C than group A ($P = .035$). However, the incidence of hypotension needing ephedrine treatment showed no significant difference between the 2 groups ($P = .7$). Systolic blood pressure and heart rate showed no significant differences between the 2 groups ($P = .138$ and .464, respectively). However, group A showed significant increases in DBP and MBP, and group C did not ($P = .014$ and .008, respectively).

☆ Competing interest: All authors have no competing interests to declare.

☆☆ Funding: This research was supported by the ChinooMTech Company.

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http://dx.doi.org/10.1016/j.jclinane.2016.07.012

Conclusion: Prophylactic atropine reduces the incidence of bradycardia in patients undergoing spinal anesthesia with dexmedetomidine sedation. However, DBP and MBP showed significant increases in patients when prophylactic atropine was administrated. Therefore, atropine premedication should be administered cautiously.

1. Introduction

Sedation is frequently required for patients undergoing regional anesthesia. Propofol, midazolam, and dexmedetomidine are widely used for sedation [1,2]. Dexmedetomidine is a highly selective alpha-2 receptor agonist. Both clinically desired sedation and analgesia could be achieved by dexmedetomidine to the satisfaction of patients and surgeons [3]. As a sedative agent, dexmedetomidine causes only minimal or no respiratory depression [4], and dexmedetomidine has less hemodynamic instability compared with propofol or midazolam [5,6]. When compared with propofol, dexmedetomidine sedation reduces the incidence of postoperative delirium in elderly patients after cardiac surgery [7]. Also, during spinal anesthesia, dexmedetomidine prolongs the duration of sensory and motor block and the time to first request for postoperative analgesia [8].

In a number of studies, the use of dexmedetomidine during spinal anesthesia increased the risk of bradycardia, which needs atropine administration, but did not increase the incidence of hypotension [8,9]. The symptoms of bradycardia that may include acute altered mental status, ongoing chest pain, hypotension, or other signs of shock from decreasing cardiac output are difficult to detect in the sedated status. In addition, arterial dilation and venous pooling combined with bradycardia may lead to profound hypotension or even cardiac arrest [10,11]. Therefore, bradycardia during spinal anesthesia should be treated or prevented by administration of anticholinergics. However, there is no clinical evidence to indicate whether dexmedetomidine-sedated patients during spinal anesthesia should be pretreated with an anticholinergic to prevent bradycardia and hypotension.

We evaluated the effectiveness of atropine premedication for preventing the incidence of bradycardia and hemodynamic effect on patients undergoing spinal anesthesia with dexmedetomidine sedation.

2. Methods

This study protocol was approved by the Institutional Review Board from the College of Medicine, Inje University Seoul Paik Hospital (IIT-2015-101). This prospective, randomized, controlled clinical trial (NCT02522858) was conducted at the university hospital from August of 2015 to January of 2016 and according to the principles of the Declaration of Helsinki (2000). Written informed consent was obtained from all participants before their inclusion in the trial.

This study included 120 patients (age range, 20-65 years; American Society of Anesthesiology of class I-II) who were willing to be sedated and were scheduled to undergo orthopedic knee and ankle surgery with spinal anesthesia in the supine position. Exclusion criteria included patients who were not indicated for spinal anesthesia, had previous history of anticholinergic use before entering the operating room, and had hypersensitivity to dexmedetomidine administration. Also, patients were excluded if they failed spinal anesthesia or had a level higher than T6 because of its impact on the cardiac accelerator center.

This was a randomized, double-blind, placebo-controlled study. The patients were randomly divided into 2 groups. Group A received intravenous atropine and group C received normal saline as a placebo. The group assignments were kept in sealed envelopes, each bearing only the case number on the outside. After the recruitment, the patients were given a case number, and 1 hour before admitting the patient to the operating room, the numbered envelope was opened with the card inside determining the group and the patient belonged to. The appropriate medications were prepared in identical syringes by a nurse who was not involved in the study. All the patients and the investigators were blinded about the group allocation.

All patients received the same anesthetic protocol. For the premedication, they received an intramuscular injection of midazolam 1 mg/kg before entering the operating room. Before induction of spinal anesthesia, 5 mL/kg (based on ideal body weight) of crystalloid was administered and infused at a rate of 6-12 mL/(kg h) during the surgery. Spinal anesthesia was performed by a 25-gauge Quincke needle at the midline between L4 and 5 or L3 and4 in the lateral decubitus position. The amount of hyperbaric bupivacaine 0.5% from 10 to 12 mg was determined by the anesthesiologist who had more than 5 years of experience. The determination was according to height, weight, and age of the patient and in consideration of the target sensory level of anesthesia at T10. After administration of the intrathecal drug, the patient's position was immediately changed to supine. The sensory block level was assessed by the pinprick test using a 24-gauge hypodermic needle and recorded 10 minutes after placement in the supine position.

After recording the block level, dexmedetomidine was infused at a loading dose of 0.6 μg/kg for 10 minutes followed by an infusion at 0.25 μg/(kg h). Simultaneously with the starting of the loading dose of dexmedetomidine, patients in group A received an intravenous bolus of 0.5 mg atropine. Patients in group C received an intravenous normal saline bolus. The noninvasive blood pressure, electrocardiography, and