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ORIGINAL ARTICLE

The effects of intravenous dexmedetomidine on spinal hyperbaric ropivacaine anesthesia

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Abstract
Purpose In this study we investigated the effects of intravenously administered dexmedetomidine on the duration of hyperbaric ropivacaine in spinal anesthesia, and the side effects.
Methods In a prospective, double-blind study, sixty ASA I-II patients were randomized to two groups of 30 individuals. All patients were administered hyperbaric ropivacaine (22.5 mg) for spinal anesthesia. Intravenous dexmedetomidine was administered in group I for 60 min, physiological saline at the same amount and duration was infused in group II.
Results Measurements of mean blood pressure before and after the procedure revealed significant decreases in group I compared with group II after 20, 25, and 30 min. The times for two dermatomes regression of the blockade and complete resolution of motor blockade were significantly prolonged in group I. The sedation score in the dexmedetomidine group was significantly increased compared with controls. Atropine requirement was found to be significantly higher in group I than in group II.
Conclusion Our results show that intravenously administered dexmedetomidine prolonged the duration of spinal anesthesia, provided sufficient sedation, and had few side effects. Therefore, dexmedetomidine is appropriate during spinal anesthesia, if the anesthesiologist is alert for development of bradycardia.

Keywords Dexmedetomidine · Hyperbaric ropivacaine · Spinal anesthesia

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Introduction

Spinal anesthesia has several advantages, for example spared spontaneous respiration, low cost, reduced risk of pulmonary aspiration secondary to vomiting in patients with full stomach, facilitated surgery via provision of relaxation in the intestines and abdominal wall, elimination of the need for intubation, minimal disruption of blood chemistry, reduced surgical hemorrhage, and earlier return of intestinal motility [1]. Spinal anesthesia also has complications and contraindications, for example refusal by the patient, inability to estimate the duration of surgery, postdural puncture headache (PDPH), urinary retention, and waist and back pain [2].

To prolong the duration of spinal anesthesia, addition of sodium bicarbonate, carbon dioxide, or vasoconstrictor agents to the local anesthetic drug have been used, and use of intravenous clonidine, an α-2 agonistic agent [2, 3]. Although Kanazi et al. [4] demonstrated that intrathecal addition of a low dose of clonidine or dexmedetomidine results in significant prolongation of the duration of the sensory and motor blockade induced by hyperbaric bupivacaine, little information is available about the effect of alpha-2 agonists on the duration of spinal anesthesia with ropivacaine. We hypothesized that intravenous administration of an alpha-2 agonist could prolong the duration of spinal anesthesia with ropivacaine. This study was designed to investigate the effects of intravenous

dexmedetomidine on the duration of sensory and motor blockade induced by intrathecal administration of ropivacaine, and its associated adverse events.

Methods

After obtaining approval of the Ethics Committee, informed consent was obtained from 60 ASA I-II patients who were undergoing lower extremity surgery under spinal anesthesia, and they were included in this prospective, double blind study.

Patients with hypovolemia, coagulation disorders, local infection at the site of operation, history of headache, pregnancy, heart diseases, and history of allergy, chronic alcohol use or abuse, anemia, congenital heart diseases, bundle block, congestive heart failure or arrhythmias, and patients who had recently received sedative drugs or were under antidepressant treatment were not included in the study. Patients were randomized to either group I or group II. Randomization was performed by using a list of random numbers and a sealed envelope method. Before infusion a sealed randomization envelope was opened and the patient was allocated to group I or group II. A blinded investigator who did not know which solution had been injected observed the developing block. The patients and the other investigators who were responsible for administering the study solutions, perioperative patient care, and study follow-up were blind to the treatment groups. Patients in group I received dexmedetomidine infusion, whereas those in group II received physiological saline at the same dose and duration. One day before surgery each patient was visited, and their physical status and laboratory data were evaluated by the anesthesiologists. All patients were informed about spinal anesthesia and signed informed consent. None of the patients received premedication.

Each patient was admitted to the preoperative preparation unit and was hydrated with lactate ringer solution containing 5% dextrose (10 ml/kg) through a venous line on the dorsum of the hand. Following admission to the operation theater, ECG, blood pressure (BP), heart rate (HR), and SpO_2 monitoring were initiated (PETAŞ-KMA 800, Ankara, Turkey). Lumbar puncture was performed with aseptic techniques in the sitting position through the L4-L5 or L5-S1 space in the midline using a 25-G Quincke needle (Spinocan, B-Braun Melsungen, Germany), the tip of which was held in parallel with the dural fibers. Upon observing clear CSF flow, 4 ml (22.5 mg) prepared hyperbaric ropivacaine solution (ropivacaine 0.75%, 3 ml + dextrose 5%, 0.8 ml + physiological saline, 0.2 ml) was administered into the subarachnoidal space [5–8]. The patients then were brought to the supine position and their heads were elevated by 20°, followed by administration of O_2 3 l/min. Following spinal anesthesia, infusion of dexmedetomidine was started in group I at a loading dose of 1 μg/kg administered within 10 min, followed by maintenance at a dose of 0.4 μg/kg/h for 50 min. In group II, physiological saline was administered at the same loading and infusion rates as in group I. Spinal anesthesia was administered by the same doctor. The duration of surgery for the patients included in the study was estimated to last 60–90 min and considering the half-life of dexmedetomidine (~2 h), the duration of infusion was planned to be 60 min. Sensorial blockade was determined with the pin-prick test, whereas motor blockade was determined with the Bromage scale [9] as follows: 0, free movement of legs and feet; 1, just able to flex knees with free movement of feet; 2, unable to flex knees, but with free movement of feet; 3, unable to move legs or feet. The level of sedation was evaluated according to the Ramsay sedation scale [10, 11] as follows: 1, patient is anxious and agitated or restless, or both; 2, patient is cooperative, oriented, and tranquil; 3, patient responds to commands only; 4, patient exhibits brisk response to light glabellar tap or loud auditory stimulus; 5, patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus; 6, patient exhibits no response. During anesthesia, the BP, HR, and SpO_2 were recorded at 3-min intervals within the first 10 min, at 5-min intervals within the remaining part of the first hour, and at 15-min intervals during the rest of the recordings. The levels of sensorial and motor blockade were assessed at 2-min intervals until the maximum level of anesthesia was achieved and at 5-min intervals later on. Hypotension was defined as >30% decrease in mean BP compared with the initial preoperative value, and bradycardia was defined as HR < 50 beats per minute. The patients with hypotension were treated with fluid replacement and intravenous ephedrine at bolus doses of 5 mg, and the patients with bradycardia were treated with intravenous atropine 0.01 mg/kg. The time to achieve maximum sensorial blockade and the duration of motor blockade were recorded. The duration of persistence of sensorial anesthesia was defined and recorded as the time for maximum level of anesthesia to regress 2 dermatomes. The duration of motor blockade was defined as complete abolishment of the motor blockade (i.e., achievement of Bromage = 0). Complications, for example paresthesia, headache, allergy, hypotension, bradycardia, nausea, vomiting, shivering, waist and back pain, total spinal anesthesia, and voiding difficulty were also recorded.

The patients were observed for 4 h in a recovery room then discharged to their wards. The patients were observed at 4 h intervals for first 24 h, and at 8 h intervals for the next 96 h in their wards by same anesthesiologist.

The data obtained were statistically evaluated by use of Student's *t* test and analysis of variance for repeated

Table 1 Demographic data (mean ± SD)

	Group I (n = 30)	Group II (n = 30)
Age (year)	38 ± 14	38 ± 14
Height (cm)	172 ± 8	171 ± 8
Weight (kg)	70 ± 11	65 ± 11
Sex (M/F)	25/5	26/4

measurements (post-hoc Tukey test), side effects were evaluated with the chi-squared test. A power analysis indicated that 27 patients were needed in each group ($\alpha = 0.05$, $\beta = 0.81$); consequently, the study was designed with 30 patients in each group. $P < 0.05$ was considered as statistically significant.

Results

No statistically significant difference was found between groups regarding demographic data (Table 1). Group I received lactated Ringer solution 1950 ± 150 ml, group II received 1850 ± 100 ml ($P > 0.05$). Reduction in HR was found in group I to be significantly greater than that in group II at the 15th minute (Fig. 1, $P < 0.05$). Mean arterial pressure was significantly lower in group I than in group II at the 20th, 25th, and 30th minutes (Fig. 2, $P < 0.05$). In group I, SpO_2 (98%) was found higher than in group II (95%) at the 180th and 210th minutes (Fig. 3, $P < 0.05$).

Comparison of the groups regarding the time to achieve peak motor and sensorial blockade revealed no statistically significant difference. The time (mean ± SD) to reach peak sensory level (PSLT) was similar in the 2 groups (group I, 10 ± 2 vs. group II, 10 ± 1 min). The times to achieve peak motor blockade (PMBT) were 12 ± 2 in group I and 13 ± 1 in group II ($P < 0.05$) (Table 2). Median (range) peak sensory level was similar in the 2 groups according to the pin-prick test (group I, T10 (T4–T10); group II, T10 (T4–T11)). Median and range of sedation levels were 3 (2–4) in group I, and 2 (1–2) in group II ($P < 0.001$). The time for two dermatomes regression (TDRT) and the time for complete regression of motor blockade (MBRT) are also displayed in Table 2. TDRT in group I (249 ± 56 min) was significantly greater than that in group II (195 ± 53 min) ($P < 0.001$). MBRT in group I (284 ± 63 min) was significantly much longer than that in group II (225 ± 53 min) ($P < 0.001$). Interestingly, motor blockade did not develop in 5 patients in each group (i.e., the Bromage score remained 0). However, the level of sensorial blockade was T10 (T8–T12) in those patients. In group I, 5 patients received ephedrine, while this happened to 2 patients in group II. This difference

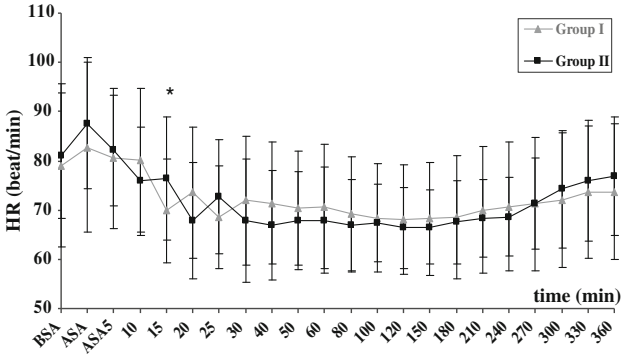

Fig. 1 Heart rate (mean ± SD). *BSA* before spinal anesthesia and infusion, *ASA* after spinal anesthesia and infusion, *$P < 0.05$

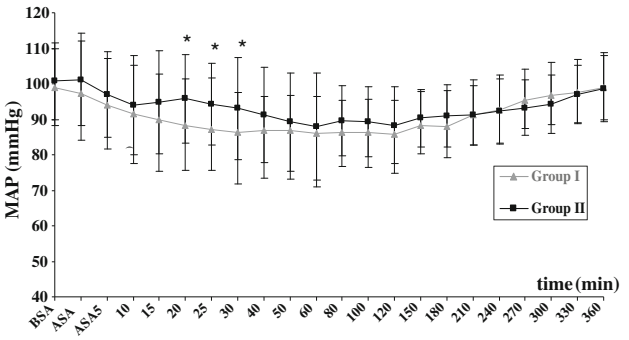

Fig. 2 Mean arterial pressure (mean ± SD). *BSA* before spinal anesthesia and infusion, *ASA* after spinal anesthesia and infusion, *$P < 0.05$

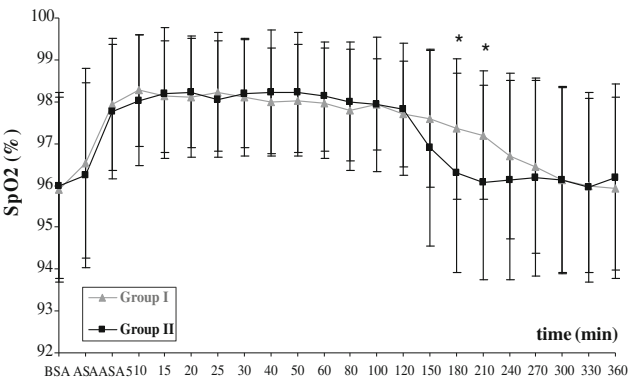

Fig. 3 Peripheral oxygen saturation (%; mean ± SD). *BSA* before spinal anesthesia and infusion, *ASA* after spinal anesthesia and infusion, *$P < 0.05$

between groups was not statistically significant ($P = 0.235$). Whereas 9 patients in group I received atropine, none of group II patients was administered atropine, which was statistically significant ($P < 0.001$).

Evaluation of the groups regarding complications revealed that paresthesia, PDPH, allergic reactions, total spinal anesthesia, voiding difficulty, and vomiting were absent in both groups, whereas waist and back pain was

Table 2 The time of sensory and motor blockade

	Group I	Group II
PSLT (min)	10 ± 2	10 ± 1
PMBT (min)	12 ± 2	13 ± 1
TDRT (min)	249 ± 56*	195 ± 53
MBRT (min)	284 ± 63*	225 ± 53

PSLT the time to reach peak sensory level, *PMBT* the times to achieve peak motor blockade, *TDRT* the times for two dermatomes regression, *MBRT* the times for complete regression of motor blockade, *SD* standard deviation

* $P < 0.001$

encountered in 1 patient in each group. Nausea was reported in 3 patients (10%) in group I, and in 2 patients (6.7%) in group II ($P > 0.05$).

Discussion

Despite the many advantages of spinal anesthesia, the relatively short duration of the local anesthetic during prolonged surgery can be a problem. Prolonging the duration of spinal anesthesia would allow longer surgical interventions. Various additives have been used in order to prolong the duration of spinal anesthesia, including vasoconstrictive agents such as epinephrine, phenylephrine, and clonidine. Agents such as opioids and neostigmine have also been used [2, 12, 13]. In this study, intravenous dexmedetomidine significantly prolonged both the TDRT of sensorial blockade, and the time for complete reversal of motor blockade. Clinically, α-2 agonists such as clonidine and dexmedetomidine are used as adjuvants in anesthesia [14, 15]. It has been reported that the α-2 agonists used in regional anesthesia alter the characteristics of anesthesia by inducing vasoconstriction, potentiating the blockade of C-fibers, or augmenting the effects of local anesthetics by positively affecting slow retrograde axonal transport along the nerve at the spinal cord level [16, 17].

Probably, subtype-specific α-2 agonists provide analgesia and anesthesia without causing hemodynamic effects by stimulating the intended receptor population only. It has also been reported that the α-2 adrenergic receptors in the nerve endings may contribute to the analgesic effect by preventing norepinephrine release [17–20].

Although ropivacaine can be safely used in spinal anesthesia [21], its hyperbaric form is not commercially available. In order to increase the density of ropivacaine and obtain its hyperbaric form, dextrose has been added at different concentrations and amounts. In previous studies, dextrose has been used at doses of 5, 10, 50, and 100 mg/ml [4–7], and this has been reported to increase the time of initiation of sensorial blockade and the duration of anesthetic effect. The combination that includes dextrose 10 mg/ml was preferred in our study. We found that intravenous dexmedetomidine significantly prolonged both the TDRT of sensorial blockade and the time for complete reversal of motor blockade compared with the control group. This condition may be because of its adjuvant effect. Intravenous dexmedetomidine did not effect the onset time of sensorial block.

When dexmedetomidine is administered intravenously, it induces strong hypotension and bradycardia until the central sympatholytic effect is established, after which it causes moderate drops in mean arterial pressure and HR. This limits the administration of dexmedetomidine in daily surgery patients because of the hypotension and bradycardia that may occur in the postoperative period [22–24]. The incidence of hypotension after spinal anesthesia has been reported to be 30–40%, and this has been attributed to sympathetic blockade [2, 25]. The incidence of reduced mean arterial pressure after dexmedetomidine infusion has been found to be 14, 17, 23, and 27% at infusion doses of 0.25, 0.5, 1.0, and 2.0 μg/kg, respectively [23]. In our study, the mean arterial pressures were found to be significantly lower in group I than group II at the 20th, 25th and 30th minutes. The incidence of ephedrine-requiring hypotension was found to be 16 and 10% in the dexmedetomidine and control groups, respectively. This has been attributed to the spinal anesthesia reaching maximum sensorial levels, and the hypotension secondary to this is augmented by addition of the hypotensive effects of dexmedetomidine. The low incidence of hypotension has been attributed to provision of sufficient preoperative hydration to the patients.

In the literature, the incidence of bradycardia after spinal anesthesia has been reported to be 10–15%. The incidence of reduced HR after dexmedetomidine infusion has been reported to be 25% [23]. In our study, we found significant reduction in HR in group I at the 15th minute, compared with group II. Besides, the incidence of bradycardia in group I was found to be 30%, whereas bradycardia was not observed in group II. This has been attributed to the bradycardia-inducing effect of dexmedetomidine.

Sedation is frequently required during regional anesthesia. Propofol, midazolam, clonidine, and dexmedetomidine are frequently used with this purpose [10, 11]. In studies performed with dexmedetomidine, the intended level of sedation has been reported to be achieved at doses of 0.2–0.7 μg/kg/h. Sedation has been also reported to be deepened with increasing doses [22, 24]. In our study, deeper sedation was induced in group I than in group II, from which we have concluded that dexmedetomidine has the advantage of eliminating the need for extra sedative agents. One of the main objectives in using sedative agents is that respiratory depression should not occur. In previous studies it has been

shown that the α-2 adrenergic agonists cause no or minimum respiratory depression [19]. In our study, respiratory depression was not observed in any of the patients.

The incidence of back pain secondary to spinal anesthesia has previously been shown to range between 2.5 and 54% [25–27]. In our study, the incidence of back and waist pain was 3.3%, in agreement with literature reports. The incidence of shivering after spinal anesthesia has been reported previously to range between 10 and 40% [28, 29]. Absence of shivering in group I in our study has been attributed to dexmedetomidine possibly preventing shivering. In group II we observed shivering in 30% of the patients, which is in agreement with literature reports.

After spinal anesthesia, the incidence of nausea has previously been reported to range between 2 and 18%, whereas that of vomiting has been reported to range between 0 and 7% [25]. In our study, the extent of nausea and vomiting were 10 and 0%, respectively, which is in agreement with literature reports. Complications such as paresthesia, PDPH, allergy, total spinal anesthesia, and voiding difficulty were not observed in any of our patients.

In conclusion, we have found that intravenously administered dexmedetomidine prolonged the duration of sensorial and motor blockade, provided sufficient sedation, and had few side effects. We therefore believe its application during spinal anesthesia is appropriate, although extreme attention should be paid to bradycardia.

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