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Original Article

Perineural administration of dexmedetomidine in combination with ropivacaine prolongs axillary brachial plexus block

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Abstract: To evaluate the hypothesis that adding dexmedetomidine to ropivacaine prolongs axillary brachial plexus block. Forty-five patients of ASA I~II and aged 25-60 yr who were scheduled for elective forearm and hand surgery were randomly divided into 3 equal groups and received 40 ml of 0.33% ropivacaine + 1 ml dexmedetomidine (50 μg) (Group DR_1), 40 ml of 0.33% ropivacaine + 1 ml dexmedetomidine (100 μg) (group DR_2) or 40 ml of 0.33% ropivacaine + 1 ml saline (group R) in a double-blind fashion. The onset and duration of sensory and motor blocks and side effects were recorded. The demographic data and surgical characteristics were similar in each group. Sensory and motor block onset times were the same in the three groups. Sensory and motor blockade durations were longer in group DR_2 than in group R ($P < 0.05$). There was no significant difference in the sensory blockade duration between group DR_1 and group R. Bradycardia, hypertension and hypotension were not observed in group R and occurred more often in group DR_2 than in group DR_1. Dexmedetomidine added to ropivacaine for an axillary brachial plexus block prolongs the duration of the block. However, dexmedetomidine may also lead to side effects such as bradycardia, hypertension, and hypotension.

Keywords: Dexmedetomidine, ropivacaine, brachial plexus

Introduction

Dexmedetomidine is a highly selective α2 adrenoceptor agonist that has been shown to have both sedative and analgesic effects [1, 2]. Compared with clonidine, dexmedetomidine has an α2:α1 adrenoreceptor ratio of approximately 1600:1 (seven to eight times higher than clonidine) [3]. Multiple clinic studies have reported that clonidine prolongs the duration of anesthesia and analgesia in peripheral nerve blocks [4-7]. Only a few clinical studies have reported the administration of dexmedetomidine in combination with bupivacaine and levobupivacaine but not with ropivacaine [8-15]. Animal studies show that dexmedetomidine added to ropivacaine increases the duration of analgesia [16, 17]. It is unknown whether administering dexmedetomidine in combination with ropivacaine can prolong axillary brachial plexus block in patients.

In this study, we evaluated the hypothesis that adding dexmedetomidine to ropivacaine would prolong axillary brachial plexus block.

Material and methods

The study was a prospective, randomized, controlled and double-blinded trial, which was approved by the Research Ethics Committee of the First Affiliated Hospital of Harbin Medical University. Forty-five physical status ASA I~II patients aged 25-60 yr who were scheduled for elective forearm and hand surgery were involved in this study. Informed consent was obtained from the patients before the operations. Patients who had contraindications for axillary brachial plexus block or the study medications; a history of alcohol or drug abuse; significant cardiovascular, pulmonary, hepatic, or renal diseases; peripheral neuropathy; or hypertension were excluded—as were pregnant or lactating women.

Patients were assigned using a random number table to one of three groups (n = 15): Group R received 40 ml of 0.33% ropivacaine plus 1 ml of 0.9% NaCl; Group DR_1 received 40 ml of 0.33% ropivacaine plus 1 ml of dexmedetomi-

Table 1. Patient characteristics

	Group R	Group DR_1	Group DR_2
Age (yr)	40.66±14.13	38.06±7.39	44.86±13.34
Height (cm)	165.13±9.05	168.80±7.69	168.93±6.87
Weight (kg)	62.80±13.31	65.47±12.14	66.40±7.85
Sex (M/F)	8/7	10/5	10/5

R = ropivacaine + saline; DR_1 = ropivacaine + dexmedetomidine (50 μg); DR_2 = ropivacaine + dexmedetomidine (100 μg); M = male; F = female. Values are expressed as the mean ± SD. There were no significant differences between the groups.

dine (50 μg); Group DR_2 received 40 ml of 0.33% ropivacaine plus 1 ml of dexmedetomidine (100 μg). The anesthetic solution was prepared by an anesthesiologist who was not involved in the study, and the anesthesiologist who performed the block was also blinded to the treatment groups.

Standard monitoring was maintained (electrocardiography, pulse oximetry, and automated sphygmomanometry; Cardiocap II, Datex) after the patient entered into the operating room. Two milligrams midazolam was administered via the peripheral vein, which was located on the contralateral arm by a 20-gauge cannula. In addition, oxygen was delivered via a Venturi face mask at a rate of 4 L/min. Next, the basic blood pressure, heart rate and SpO_2 were recorded. Each patient was placed in a supine position with the arm abducted to 75° and externally rotated in all cases. Subsequently, an axillary perivascular plexus block was performed by a single experienced anesthesiologist using a nerve stimulator (Stimuplex HNS 12, Germany). The stimulation frequency was set at 2 Hz, and the duration of stimulation was set at 0.3 ms. The intensity of the stimulating current, initially set to deliver 1 mA, was gradually decreased to < 0.5 mA after the appropriate motor response was observed (thumb abduction for the radial nerve, thumb opposition for the median nerve, thumb adduction or ulnar deviation of the hand for the ulnar nerve and flexion of the forearm on the arm for musculocutaneous nerves). The area of the identified axillary pulse was shaved and disinfected. The site of injection was subcutaneously infiltrated with 1 ml of 2% lidocaine.

Three points of axillary brachial plexus blockade were adopted in our study. The identified order of nerves was as follows: median, radial or ulnar, and musculocutaneous. Thirteen milliliters of the local anesthetics was injected at the site of the median, radial or ulnar nerves after identification. Nine milliliters of the local anesthetics was injected at the site of the musculocutaneous nerves. The remaining 6 ml was injected subcutaneously when the needle was withdrawn to block the intercostobrachial nerve. The patient was excluded if the anesthesia was insufficient after 40 min. Blocks were evaluated every 5 min during the first 40 min from the moment of needle withdrawal. The sensory block was evaluated using the pain sensation in the median and radial nerve distribution of the hand. A 3-point scale for pain using a pinprick with a 23 G needle (0 = sharp sensation, 1 = blunt sensation, and 2 = no sensation) was applied. The motor block was assessed by a modified Bromage scale, as follows: 0 = no movement, 1 = finger movement, 2 = flexion of the wrist against gravity, and 3 = extension of the elbow against gravity. The sensory block onset was defined as the time from the injection to the disappearance of sharp pain by the prick test. The motor block onset was defined as the time between injection and motor paralysis distal to the injection site. The duration of the sensory block was defined as the time interval between administration of the local anesthetic and the complete recovery of sensation.

At the above-mentioned time points, blood pressure, oxygen saturation, and ECG lead II were measured. The baseline values were recorded a few minutes after midazolam premedication. Any episodes of hypotension or bradycardia were noted and defined as a 20% decrease in pressure or heart rate in relation to the baseline value. All patients were kept in the hospital overnight, and a printed assessment chart for the timing and distribution of the return of movement and pain was given to the patients for completion with the aid of the nurse. The patients were also assessed for total block failure, unblocked nerve distributions, necessity of supplementing the block, time to the first postoperative analgesia and total postoperative analgesia requirements.

The sample-size calculation revealed that at least 14 subjects in each group were necessary to detect a 35% increase in the analgesia duration with a power of 0.9 and a significance level of 0.05. The data are presented as the

Table 2. Sensory and Motor Block Onset Times

	Group R	Group DR_1	Group DR_2
Sensory block onset time (min)	18.54±5.24	15.46±3.67	13.34±6.43
Motor block onset time (min)	20.00±7.56	16.66±6.99	14.00±5.07

R = ropivacaine + saline; DR_1 = ropivacaine + dexmedetomidine (50 μg); DR_2 = ropivacaine + dexmedetomidine (100 μg). Values are expressed as the mean ± SD.

Table 3. Sensory and Motor Block Durations

	Group R	Group DR_1	Group DR_2
Sensory block duration (min)	689.00±269.00	804.00±340.00	1190.00±456.00*
Motor block duration (min)	511.86±135.51	737.73±135.99*	1033.8±273.76**

R = ropivacaine + saline; DR_1 = ropivacaine + dexmedetomidine (50 μg); DR_2 = ropivacaine + dexmedetomidine (100 μg). Values are expressed as the mean ± SD. (*$P < 0.05$, **$P < 0.01$ compared with Group R).

mean ± SD. The statistical analysis was performed using SPSS 13.0 (serial number 5031432, Stats Data Mining Co., China). The onset time and duration of the motor and sensory block was evaluated using one-way ANOVA followed by the Student-Newman-Keuls test. Analysis of the categorical data and proportions was performed using the X^2 test. $P < 0.05$ was considered significant.

Results

The analysis of the patient clinical characteristics demonstrated no significant differences between the groups (**Table 1**).

The sensory and motor block onset time was similar in each group (**Table 2**). The sensory blockade duration was significantly longer in group DR_2 than in group R ($P < 0.05$). By contrast, there was no significant difference in the sensory blockade duration between group DR_1 and group R. The motor blockade duration was longer in group DR_2 than in both group DR_1 and group R ($P < 0.01$) (**Table 3**).

The incidence of side effects was significantly higher in group DR_2 compared with group R and DR_1. In group DR_2, bradycardia was observed in all patients, and 9 of them were treated with atropine. Hypertension was observed in 6 patients, and hypotension was observed in 3 patients. In group DR_1, bradycardia was observed in 8 patients, and four of them were treated with atropine; hypotension was observed in 2 patients, and no hypertension was observed in this group. ($P < 0.01$) (**Figures 1** and **2**). No side effects (including bradycardia, hypotension, and hypertension) were observed in group R.

Discussion

In this study, the analgesic and side effects of 50 μg and 100 μg of dexmedetomidine mixed with 40 ml of ropivacaine 0.33% were evaluated in axillary brachial plexus blockade for forearm and hand surgery. The results demonstrated no difference in the sensory and motor block onset time among three groups. Adding 100 μg of dexmedetomidine to ropivacaine prolonged the sensory and motor blockade duration compared with group R and concurrently increased the incidence of hypotension and bradycardia. Adding 50 μg of dexmedetomidine to ropivacaine also prolonged the motor blockade duration but not the sensory blockade duration and led to bradycardia.

To our knowledge, most human studies of dexmedetomidine as an adjuvant to local anesthetics involved combinations with bupivacaine or levobupivacaine [8-15]. Bupivacaine, levobupivacaine and ropivacaine are all long-acting local anesthetics. Because of its unique pharmacologic properties and fewer side effects, ropivacaine has been accepted by an increasing number of anesthesiologists for peripheral nerve blocks. However, there is no published study on dexmedetomidine in combination with ropivacaine. A previous study demonstrated that the addition of dexmedetomidine to bupivacaine in greater palatine nerve blocks in children undergoing cleft palate repair causes a 50% increase in the duration of postoperative analgesia, with no adverse side effects [8]. More recently, Aliye Esmaoglu et al. [9] showed that dexmedetomidine added to levobupivacaine for axillary brachial plexus blocks shortens the onset time and prolongs the durations of the blockade and postoperative analgesia, which also leads to bradycardia. However, no difference in the onset time with or without the use of dexmedetomidine was found in our study, possibly because of the different local anesthetics.

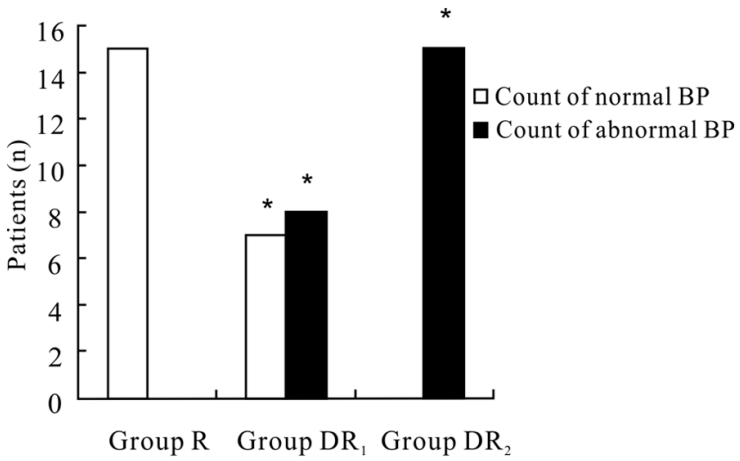

Figure 1. Number of patients with normal versus abnormal blood pressures. BP = blood pressure; R = ropivacaine + saline; DR_1 = ropivacaine + dexmedetomidine (50 μg); DR_2 = ropivacaine + dexmedetomidine (100 μg). *P < 0.05 when the group was compared with Group R.

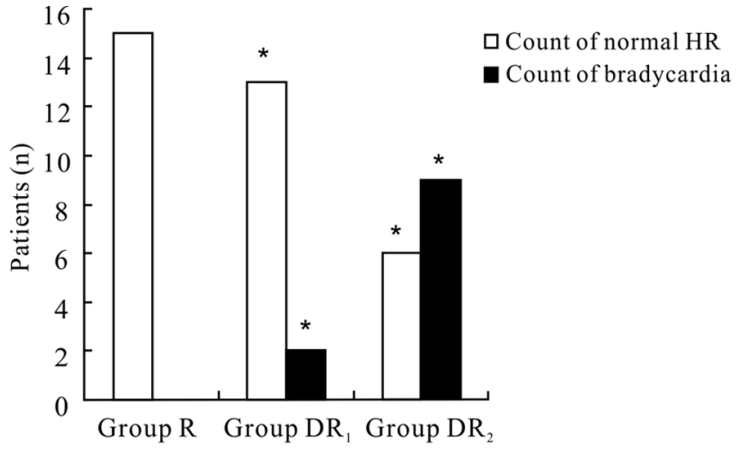

Figure 2. Number of patients with a normal heart rate versus bradycardia. HR = heart rate; R = ropivacaine + saline; DR_1 = ropivacaine + dexmedetomidine (50 μg); DR_2 = ropivacaine + dexmedetomidine (100 μg). *P < 0.05 when the group was compared with Group R.

An animal study revealed that the perineural administration of clinically relevant doses of dexmedetomidine in combination with ropivacaine increases the duration of sensory blockade in a dose-dependent fashion [16]. The findings are an essential corroboration of our human studies. In this clinical study, we also found that dexmedetomidine increased the duration of sensory and motor blockades when added to 0.33% ropivacaine in a dose-dependent fashion.

The mechanism by which dexmedetomidine mediates axillary brachial plexus blockade is not fully defined. However, it may be similar to the mechanism suggested for clonidine.

There are several hypotheses concerning clonidine administered in peripheral nerve blocks: First, clonidine may induce a direct effect on the nerve fiber, consequent to a complex interaction between clonidine and axonal ionotropic, metabolic, or structural proteins [18-21]. Second, clonidine blocks Aδ and C fibers and increases potassium conductance in isolated neurons, thus intensifying the local anesthetic conduction block. Third, clonidine may cause local vasoconstriction, thus decreasing local anesthetic spread and removal around neural structures. A previous study demonstrated that dexmedetomidine enhances the local anesthetic action of lidocaine via α2A adrenoceptor [22], whereas Chad M et al. reported that during sciatic nerve blockade in rats, dexmedetomidine added to ropivacaine causes an approximately 75% increase in the analgesia duration, which is reversed by pretreatment with an Ih current enhancer [17]. The analgesic effect of dexmedetomidine is not reversed by an α2-adrenoceptor antagonist.

There are certain limitations in our study. First, we did not observe the degree of sedation during the procedure, which might have provided us more information on dexmedetomidine. Second, we did not administer the dexmedetomidine intravenously; whether it has the same effect is unknown.

In conclusion, dexmedetomidine added to ropivacaine for axillary brachial plexus blockade prolongs the duration. However, dexmedetomidine may also cause side effects such as bradycardia, hypertension, and hypotension.

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Disclosure of conflict of interest

None.

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