DEXMEDETOMIDINE PREMEDICATION OF OUTPATIENTS UNDER IVRA

Ayse Mizrak*, Rauf Gul*, Suleyman Ganidagli*, Gunhan Karakurum**, Gulden Keskinkilic* and Unsal Oner*

Abstract

Purpose: Dexmedetomidine is approximately 8 times more selective toward the α-2-adrenoceptors than clonidine. It induces analgesia in patients and decreases anesthetic requirements by up to 90%. The current study aimed to evaluate the effects of dexmedetomidine premedication on tourniquet pain, intraoperative - postoperative analgesic requirements, sedation levels, quality of anesthesia, and the hemodynamic parameters when used as a single dose before intravenous regional anesthesia (IVRA).

Material and Methods: Fifty-four patients undergoing hand surgery (carpal tunnel and tendon release) were randomly divided into 2 groups for IVRA. IVRA was performed with 40 mL of 0.5 % lidocaine in both groups. A single dose of dexmedetomidine 0.5 μg/kg in 20 mL saline was administered to group D (n=27) and placebo solution 20 mL to group C (n=27) through the non-IVRA catheter 15 minutes before IVRA. Sensory and motor block onset and recovery time, hemodynamic variables, tourniquet pain, analgesic requirements according to verbal rating scale (VRS) and visual analog scale(VAS), sedation score, and anesthesia quality were recorded in the intraoperative and postoperative period.

Results: Improved quality of anesthesia, reduced postoperative pain scores, and total analgesic requirements were found in group D during postoperative period. Additionally, the patients experienced a higher degree of sedation during intraoperative and postoperative period.

Conclusion: The premedication of 0.5 μg/kg low dose dexmedetomidine before IVRA improves the quality of anesthesia and decreases the postoperative analgesic requirement of outpatients undergoing hand surgery without any serious side effects.

Keywords: Intravenous regional anesthesia (IVRA), postoperative analgesic requirement, dexmedetomidine, premedication.

* Anesthesiology and Reanimation, Gaziantep University School of Medicine Gaziantep/TURKEY.
** Orthopedics and Traumatology, Gaziantep University School of Medicine Gaziantep/TURKEY.
Corresponding Author: Dr. Rauf GÜL, Gaziantep University Medical Faculty, Department of Anesthesiology and Reanimation, 27310 Sahinbey, Gaziantep, TURKEY. Tel: 00905056327696, Fax: 00903423602244, E-mail: gulrauf@hotmail.com

Introduction

Though tourniquet pain may limit procedures, IVRA provides safe and effective anesthesia for hand surgery of 1- hour duration or less[1]. After tourniquet deflation, a different pain sensation reported as an intense tingling. It is thought to be related to impulse propagation via small, unmyelinated nerve fibers[2]. To improve block quality, prolong post deflation analgesia, and decrease tourniquet pain, various adjuncts having local analgesic effect on peripheral nerves such as clonidine[3], contramal[4], meperidine[5] have been added to the local anesthetic solution. In the same way, the addition of various opioids to local anesthetics have been studied such as fentanyl, sufentanil, morphine and the results of these drugs were found to be deprived of a significant effect[6]. α-2-adrenoceptor agonists have been studied for their sedative, analgesic, cardiovascular stability and perioperative sympatholytic effects with reduced anesthetic requirements[7]. Dexmedetomidine is a selective and specific α-2-adrenoceptor agonist which has beneficial sedative effects for premedication and intensive care sedative procedures, and approximately 8 times more selective toward the α-2-adrenoceptors than clonidine. Dexmedetomidine has been shown to decrease anesthetic requirements by up to 90% to induce analgesia. However, dexmedetomidine may cause hemodynamic side effects such as hypotension and bradycardia[8,9]. It is demonstrated that the addition of low dose dexmedetomidine 0.5 μg/kg to lidocaine for IVRA, improves quality of anesthesia and peroperative analgesia without any side effects[10]. In a previous study, it was reported that the premedication with dexmedetomidine 1 μg/kg preoperatively caused 16% to 20% decreases in systolic blood pressure, diastolic blood pressure, and heart rate, which were mainly abolished within the 4-hour postoperative period[11]. Therefore, this study was designed to evaluate the effect of low dose dexmedetomidine premedication before IVRA for elective hand surgery as an outpatient procedure. The hemodynamic variables, quality of anesthesia, tourniquet pain, postoperative analgesic requirement, and sedation will be investigated in this study.

Material and Methods

After the approval of the institutional review board, written informed consents were obtained from 54 ASA physical status I-II patients. The patients were scheduled to undergo carpal tunnel release or tendon release as an outpatient procedure by the same surgeon under IVRA from April 2007 through October 2007. The work presented has been performed in accordance with the most recent version of the Helsinki Declaration. Patients with Reynaud's disease, sickle cell anemia, history of either allergy to any drug used, or use of opioid analgesics and gabapentin 24 hours before surgery were excluded from the study. Patients were assigned to one of 2 study groups using a computer generated random number table. After the patients had been taken to surgery room, standard monitors including electrocardiography, non invasive blood pressure (SAP, DAP) measurement and pulse oximetry were used. Two intravenous (i.v.) cannulae were inserted, one in the hand to be operated on and the other in the contralateral hand for crystalloid infusion. 15 minutes before placing the tourniquet, 0.5 μg/kg of dexmedetomidine (Precedex®, 200 μg/2 mL; Abbott) in saline 20 mL (Group D, n=27) or placebo solution 20 mL (Group C, n=27) were given to the patients via the non-IVRA catheter intravenously in 15 minutes by a nurse blinded to the study. A double tourniquet (Tourniquet 2800 ELC, UMB; Medizintecknik, GmbH, Germany) was positioned on the upper operative arm. The operative extremity was exanguinated by elevating and wrapping it with a 10-cm Esmarch bandage. The proximal tourniquet was inflated to 100 mm Hg more than the systolic blood pressure to a minimum of 250 mmHg and the Esmarch bandage was removed. Circulatory isolation of the operative arm was confirmed by inspection of the hand, by the absence of the radial pulse, and loss of pulse oximetry tracing of the ipsilateral index finger (Datex Ohmeda, Dash, 5000,ANBL 01373, October-2007). IVRA was achieved with 3 mg/kg lidocaine (0.5% aritmal; TEMS, Turkey). IVRA solutions were administered slowly via the cannula over 3 min. The sensory block was assessed every 30 s after injection of lidocaine using a standardized pin prick technique with a 25-gauge short-beveled needle by an observer who was blind to the drug administered. Patient's response was evaluated in the dermatomal sensory distribution of the medial and lateral antebrachial cutaneus, ulnar, median, and radial nerves. Motor function was assessed by asking the subject to flex and extend their wrist and

fingers at 30 s intervals, and complete motor block occured when no voluntary movement was possible. We recorded the onset time of sensory and motor block. Onset time of sensory and motor block was the time elapsed from injection of study drug to the onset of both blocks. After sensory and motor block were achieved the distal tourniquet was inflated to 250 mmHg, the proximal tourniquet was released, and surgery started. The SAP, DAP, HR, and SPO2 values were recorded before and after tourniquet application at 0, 5, 15, 30, 60, and 120 min. Tourniquet pain, intraoperative-postoperative analgesic requirement, visual analog scale (VAS), verbal rating scale (VRS), anesthesia quality, and Ramsay sedation scores (RSS) of the groups were evaluated at the same measuring times. The assessment of tourniquet-related pain was performed using a 10 cm VAS, with anchors of 0 = no pain and 10 = worst pain imaginable, VRS graded as no pain = 0, mild pain = 1, moderate pain = 2, severe pain = 3 and excruating pain = 4. At the end of the operation, the quality of anesthesia was assessed according to the following numeric scale: 4 = excellent [no complaint from patient); 3 = good (minor complaint without any need for supplemental analgesics); 2 = moderate (complaint which required supplemental analgesics); 1 = unsuccessful (failed block requiring general anesthesia). When the VAS scores of tourniquet pain was reported to be >3 and VRS>2, the patient was administered fentanyl (Fentanil citrate; Abbott) 0.5 µg/kg i.v. boluses, and consumption was recorded during intraoperative period.

In addition, sedation was recorded on a numerical scale; 1 = anxiety and completely awake, 2 = completely awake, 3 = awake but drowsy, 4 = asleep but responsive to verbal commands, 5 = asleep but responsive to tactile stimulus, and 6 = asleep and not responsive to any stimulus.

The distal tourniquet was not deflated until a minimum of 30 min after the lidocaine injection, and it was performed with the cyclic deflation technique. Sensory and motor block recovery time were noted as the time elapsed after tourniquet deflation until return of sensation and movement in the fingers. Intravenous boluses of fentanyl 0.5 µg/kg were administered in the postanesthesia care unit, whenever the visual analog scale score exceeded 3 and verbal rating scale exceeded 2. All the evaluations were performed by a blinded observer who was different from the person who had performed the premedication.

Postoperative nausea, vomiting, dizziness, respiratory depression (defined as a respiratory rate < 10 breaths/min), hypoxemia (defined as SPO2 ≤ 90 %, tachycardia (HR>100 beat/min), bradycardia (HR< 50 beat/min), hypotension (MAP < 60 mm Hg), hypertension (MAP >120 mm Hg) were noted if present.

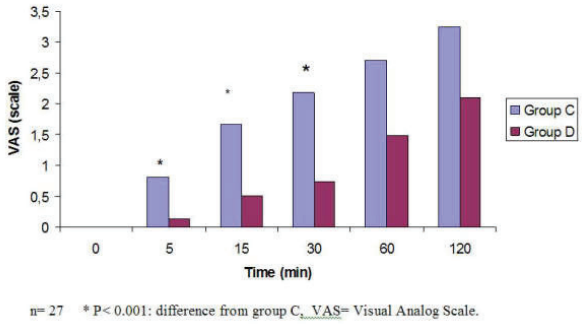
Statistical Analysis

Demographic data, intraoperative and postoperative hemodynamic data, duration of surgery, tourniquet times, the time for the onset and recovery of sensory and motor blocks were analyzed using Student's *t* test. Multiple comparisons were evaluated with Paired Sample *t* test. Gender distribution and non parametrical scale values were analyzed with X^2 test. Summary data are presented as mean (± SD) and median (interquartile ranges) values. Statistical significance was reported when the p value was < 0.05. In the actual power analysis, the sample size was 7. We performed the power analysis to detect the differences of 50 % in number of the patients who need postoperative analgesic between the groups (Power = 0.95, w = 1.40, α = 0.05, Critical Chi^2 = 3.84).

Results

Demographic data was similar in both groups. No differences were seen between the groups with regard to operation and tourniquet time, and surgical operation

Fig. 1
Postoperative VAS scores of the groups



n= 27 * P< 0.001: difference from group C, VAS= Visual Analog Scale.

Postoperative VAS score in the dexmedetomidine group and control group.

Table 1
Demographic Data and The Onset- Recovery times of sensory and motor block

Variable	Group C (n=27)	Group D (n=27)
Gender (F/M) (n)	18/9 (66%/33%)	17/10 (63%/37%)
Age (yr)	33.14±17.84	30.03±14.94
Weight (kg)	67.74±12.03	63.92±8.99
Tourniquet time (min)	57.55±24.37	58.00±17.01
Operation time (min)	45.92±23,02	46.48±16.98
Types of surgical operation (Carpal tunnel, tendon release)	19/8	21/6
Onset time of sensory block (min)	1.87±1.32	4.10±13.03
The recovery time of sensory block (min)	2.34±1.74	2.10±1.54
Onset time of Motor block (min)	2.58±2.25	2.24±1.67
Time to recovery of motor block (min)	**2.21±1.75**	1.87±1.35

Data are presented as means ± SD; NS indicates no significant. n=27 P>0.05.

types of the patients (p>0.05, Table 1). Additionally, there was no statistical difference between the groups when compared for the sensory and motor blocks onset, and recovery time (p>0.05, Table 1). The intensity of pain during tourniquet inflation was not different in group C and group D. According to the baseline assessment, differences in SAP, DAP, SPO_2 and HR values during the intraoperative and postoperative period were not statistically significant in both groups (p>0.05). After tourniquet deflation, postoperative VAS score in the dexmedetomidine group was lower than in the control group and the difference was statistically significant at 5, 15, and 30 min (p<0.001, Fig. 1). Anesthesia quality in group D was higher than in group C in the both intraoperative and postopertaive period (p<0.05, Fig. 2). The percentage of the patients who did not need analgesic drug due to the tourniquet pain during the operation was 92% in group D and 75% in group C. Additionally It was 84% in group D and 25% in group C in the postoperative period (p<0.05, Table 2). Sedation score values during intraoperative and postoperative period at 0, 15, 30, 60, and 120 min were higher for the dexmedetomidine group than the control group (p<0.001, Fig. 3, 4). No adverse effects were observed throughout the intraoperative and postoperative period in either group. None of the patients complained of postoperative nausea or vomiting.

Fig.2
Anesthesia Quality
Intraoperative and postoperative anesthesia quality in the dexmedetomidine (D) and control (C) groups. Values are medians (and interquartile ranges). Anesthesia Quality Scale: 3 = excellent (non complaint from patient); 2 = good (minor complaint without any need for supplemental analgesics); 1 = moderate (complaint which required supplemental analgesics); 0 = unsuccessful (failed block requiring general anesthesia).

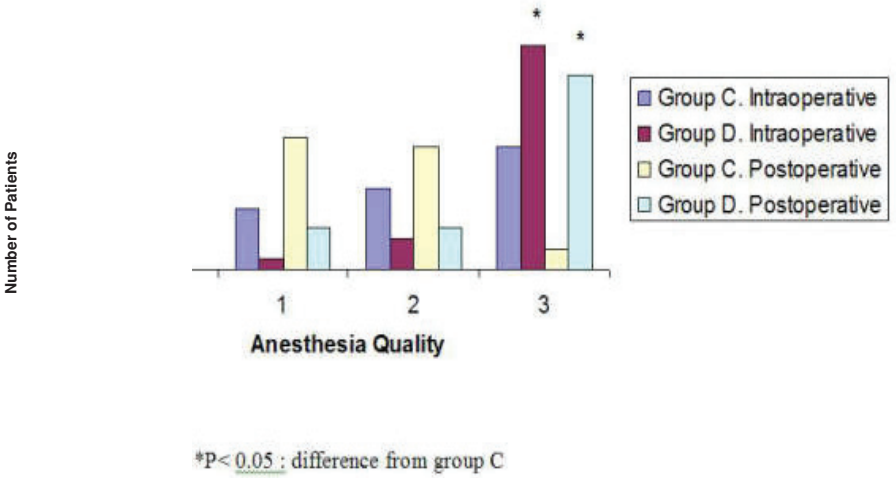
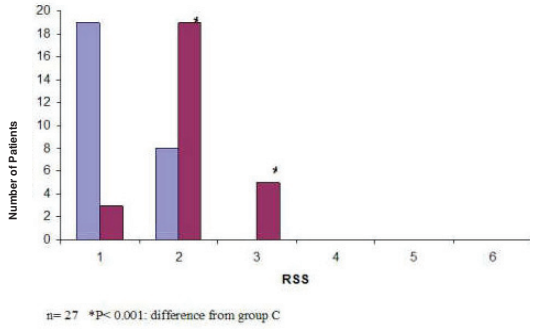


Table 2
Intraoperative And Postoperative Analgesic Requirement

	Group C	**Group D**
	Yes/No	**Yes/No**
Intraoperative (total bolus number of analgesic drug), (µg), %	7/20 (350 µg) (25%/75%)	2/25 (100 µg) (8%/92%)
Postoperative (total bolus number of analgesic drug), (µg), %	20/7* (1000 µg) (75%/25%)	4/23* (200 µg) (14%/86%)

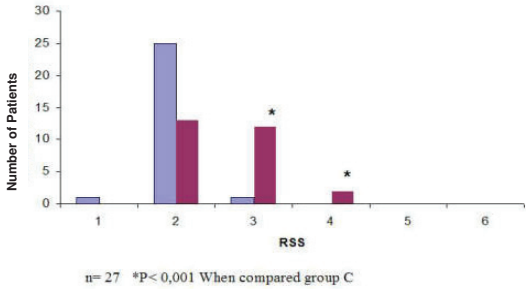
Data are presented as means ± SD; NS indicates no significant. n=27.
** P<0.05 When compared with control groups.*
Yes: Bolus number of analgesic drug according to VRS>2, No: Bolus number of analgesic drug according to VRS≤2.

Fig. 3
Intraoperative Ramsay Sedation Score



Changes of patients' number according to Ramsay Sedation Score during intraoperative period.

Fig. 4
Postoperative Ramsay Sedation Score



Changes of patients' number according to Ramsay Sedation Score during postoperative period. The level of the RSS grade was > 2 significantly in group D (Ramsey Sedation Score of the group D was higher than group group C at the 0.,15.,30.,60., and 120. measuring times.

Discussion

In the present study, it was found that the premedication of single low dose 0.5 µg/kg dexmedetomidine alone before IVRA improved quality of anesthesia and postoperative analgesia without causing considerable side effects. Though tourniquet pain may limit the procedures, IVRA provides safe and effective anesthesia for hand surgery of 1-hour duration or less. Anesthesia during IVRA is produced by multiple complex mechanisms: Initial effect; block of peripheral small nerves and nerve endings, main anesthetic component; block of nerve trunks at a proximal site, blocks nerve conduction and motor end plate function; ischemia, slow component; compression on nerve trunks[6]. Tourniquet pain is a common problem complicating the use of a pneumatic tourniquet during surgical procedures including upper and lower extremities. Although the role of A fibers and unmyelinated C fibers may be considered to be partly involved in tourniquet pain because of the circumferential compression of peripheral nerves enhanced by ischemia[1]. In the present study, the outpatients were observed and evaluated for 2 hours in the postoperative period for the VAS and VRS scores and the postoperative analgesic requirement. The patients with a VAS > 3 were more frequent in group C when compared with group D. The intensity of pain during tourniquet inflation was at similar level in group C and in group D. Postoperative analgesic (Fentanyl) requirements were lower in the dexmedetomidine group than the control group. Preoperative dexmedetomidine administration decreased opioid analgesic requirements in the postoperative period. After tourniquet deflation, a different pain sensation reported as an intense tingling. It is thought to be related to impulse propagation via small, unmyelinated nerve fibers[2]. So far, to improve block quality, prolong postdeflation analgesia, and decrease tourniquet pain, various adjuncts having local analgesic effect on peripheral nerves such as clonidine, tramadol, meperidine have been added to the local anesthetic solution. The addition of some adjuvant drugs to

lidocaine during IVRA may be insufficient or may cause some clinically important side effects as explained. Langlois et al. concluded that tramadol does not reduce tourniquet or postoperative pain when combined with a local anesthetic for IVRA[4]. Reuben et al. arrived at the conclusion that doses of meperidine large enough to produce the most effective postoperative analgesia with IVRA lidocaine causes a significant incidence of side effect, and it limits its clinical usefulness[5]. In the same way the addition of various opioids to local anesthetic such as fentanyl, sufentanil and morphine have been studied, the results of which are found to be deprived a significant benefit on postoperative analgesia[6]. α-2-adrenoceptor agonists have been studied for their sedative, analgesic, cardiovascular stabilizing and perioperative sympatholytic effects with reduced anesthetic requirements[7]. Dexmedetomidine is a potent α-2-adrenoceptor agonist with 8 times higher affinity for the α-2 adrenergic adrenoceptors than clonidine. Dexmedetomidine has been shown to decrease anesthetic requirements by up to 90% to induce analgesia and may cause hemodynamic side effects such as hipotension and bradycardia[8,9]. Clonidine induces analgesia mainly through stimulation of α-2-adrenergic receptors in the dorsal horn of the spinal cord. Gentili and Reuben et al. reported that clonidine could decrease the tourniquet pain as an adjuvant drug under IVRA[12]. Nerve fiber action potentials are depressed especially in small, unmyelinated C fibers[13]. Dexmedetomidine produces sedation, analgesia, and anxiolysis[14] and previous animal studies indicate that dexmedetomidine reduces anesthetic and analgesic requirements in dogs[15] and rats[16]. Electroencephalographic studies confirm the increase with the α2-adrenergic agonists in stage I and II sleep. The hypnotic response probably is mediated by activation of α-2-adrenoceptors in the locus coeruleus, which are coupled via a pertussis toxin-sensitive G protein to a change in conductance through an ion channel[17].

α-2-adrenoceptors located at nerve endings may play a role in the analgesic effect of the drug by preventing norepinephrine release[18]. It was reported that drugs, which stimulate the α-2 adrenoceptors lead to production of analgesia at the spinal cord level[8]. Those studies reveal that both central and peripheral mechanisms are involved in the increased quality of anesthesia and reduction of analgesic requirements when dexmedetomidine is used.

As a result of the mild sedative effect of dexmedetomidine, the patients in group D were more tolerant to the operation and they did not need any other sedative drugs during intraoperative and postoperative period. Turan et al. concluded that premedication with oral gabapentin (1.2 g) before IVRA decreased tourniquet related pain and improved the quality of anesthesia during hand surgery and early postoperative period. However, the trend toward a higher incidence of side effects such as dry mouth, nausea, and dizziness in the study were reported in the study and antiemetic treatment was required[19]. In this study, the quality of anesthesia score reported by the patients was better in the dexmedetomidine group than the control group in the intraoperative and postoperative period. No patient has experienced tachycardia, bradycardia, hypotension, hypertension or arithmia during the study period. Jaakola et al. reported that intravenous premedication of dexmedetomidine 1 μg/kg was an effective premedication before i.v. regional anesthesia, because it reduced patient anxiety, sympathoadrenal responses and opioid analgesic requirements. However, it did not reduce tourniquet pain[11]. It was also indicated that the premedication with dexmedetomidine 1 μg/kg preoperatively caused 16% to 20% decreases in systolic blood pressure, diastolic blood pressure, and heart rate, which were mainly abolished within the 4-hour postoperative period[11]. Apparently, as if two studies are similar. But there are important differences regarding the drug dose, results, and complications. The principal difference between the previous and current studies is that the former reported a high grade of decrease in SAP, DAP, and HR values. On the contrary, in the present study, these hemodynamic variables during the intraoperative and postoperative period were not significantly different in dexmedetomidine and control groups.

Another distinction between two studies is that the previous study did not evaluate the quality of anesthesia of the groups according to the score. In the present study, it was found that the quality of anesthesia in group D was significantly higher than in group C in both intraoperative and postopertaive period. Furthermore, the sedation scale in group D

was higher than in group C during intraoperative and postoperative period. It is thought that the mild sedation and analgesia, dexmedetomidine brought about developes this satisfaction. Similar to the previous study, dexmedetomidine didn't reduce tourniquet pain. VAS scores in group D was lower than in group C in the postoperative period and therefore fentanyl consumption was reduced by the premedication of 0.5 μg/kg dexmedetomidine. The essential thing for the present study is that this study is the first clinical study to demonstrate the usefulness of premedication with dexmedetomidine 0.5 μg/kg for elective hand surgery as an outpatient procedure with IVRA. This study has demonstrated that a single low dose of 0.5 μg/kg dexmedetomidine increases the quality of anesthesia and decreases the analgesic requirements in the postoperative period. In addition to this, it did not change the hemodynamic values, onset time of sensory and motor blocks significantly.

In conclusion it is suggested that low dose of dexmedetomidine 0.5 μg/kg may be used safely for premedication before IVRA in minor outpatient hand surgery.

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