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Özgün Araştırma / *Original Article*

Dexmedetomidine as an Adjuvant to Lignocaine for Intravenous Regional Anesthesia for Forearm and Hand Surgeries: A Prospective, Randomized, Controlled Study

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Ön Kol ve El Cerrahilerinde, Rejyonal İntravenöz Anestezide Lignokaine Deksmedetomidin Eklenmesi: Prospektif, Randomize, Kontrollü Çalışma

ABSTRACT

Objective: *Intravenous regional anesthesia (IVRA) is an effective anesthetic technique for surgical procedures of short duration involving the distal parts of the limbs. Intraoperative tourniquet pain is the major restraint of this technique, and to overcome this limitation, various adjuvants to local anesthetics have been used. This study investigated the effect of a fixed low dose of dexmedetomidine as an adjuvant to lignocaine on intraoperative tourniquet pain, onset of block, duration of block, and patient satisfaction.*
Methods: *A total of 100 adult patients with ASA grade I and II who were scheduled for upper limb surgery of approximately 1 hour in duration were randomly divided into two groups (n=50 in each group). Group A received 35 mL of preservative-free lignocaine alone and Group B received 35 mL of preservative-free lignocaine along with 30 µg of dexmedetomidine. The incidence of tourniquet pain, intraoperative fentanyl consumption, duration of onset and recovery of sensory and motor block after tourniquet deflation, postoperative numeric pain rating scale (NPRS) scores, duration of analgesia, and overall patient satisfaction were noted.*
Result: *The incidence of tourniquet pain and intraoperative fentanyl consumption were significantly lower in Group B. The onset and duration of sensory and motor blocks were faster and longer, respectively, in Group B. Postoperative NPRS scores were lower, duration of analgesia was longer, and overall patient satisfaction was better in the dexmedetomidine group.*
Conclusion: *Dexmedetomidine at a dose of 30 µg as a lignocaine adjuvant significantly reduces tourniquet pain and intraoperative fentanyl consumption in IVRA. Dexmedetomidine shortens the onset of block, prolongs the duration of block, and provides a more satisfactory anesthesia than lignocaine alone.*

Keywords: *Intravenous regional anaesthesia, lignocaine, adjuvant, dexmedetomidine*

ÖZ

Amaç: *Rejyonal intravenöz anestezi (RİVA) distal ekstremitelerin kısa süreli cerrahi girişimlerinde kullanılan etkili bir anestezi tekniğidir. Bu tekniğin başlıca kısıtlaması olan intraoperatif turnike ağrısının giderilmesi için çeşitli adjuvanlar kullanılmıştır. Bu çalışmada, lignokaine eklenen sabit düşük dozda deksmedetomidinin intraoperatif turnike ağrısı, blok başlama zamanı ve blok süresi ile hasta memnuniyeti üzerine etkileri araştırılmıştır.*
Yöntem: *Yaklaşık 1 saat süren üst ektremite cerrahisi geçiren ASA I-II risk grubunda 100 yetişkin hasta randomize olarak iki gruba ayrıldı (her grupta n=50). Grup A'ya sadece 35 mL koruyucusuz lignokain grup B'ye 30 µg deksmedetomidin ile birlikte 35 mL koruyucusuz lignokain verildi. Turnike ağrısı sıklığı, intraoperatif fentanil tüketimi, duyusal ve motor blok başlama zamanları ile turnike indirildikten sonra gerileme süreleri, postoperatif sayısal ağrı skoru (NPRS), analjezi süresi ve genel hasta memnuniyeti not edildi.*
Bulgular: *Turnike ağrısı sıklığı ve intraoperatif fentanil tüketim miktarı Grup B'de anlamlı olarak daha düşüktü. Grup B'de motor ve duyusal blok başlama zamanı daha hızlı ve blok süreleri daha uzundu. Deksmedetomidin grubunda postopertatif NPRS skorları daha düşük, analjezi, süreleri daha uzun ve genel hasta memnuniyeti daha iyiydi.*
Sonuç: *RİVA'da lignokaine adjuvan olarak eklenen 30 µg dozundaki deksmedetomidin, turnike ağrısını ve intraoperatif fentanil tüketimini önemli ölçüde azaltır. Deksmedetomidin eklenmesi, tek başına lignokaine göre blok başlangıcını kısaltır, blok süresini uzatır ve daha tatmin edici bir anestezi sağlar.*

Anahtar kelimeler: *İntravenöz rejyonal anestezi, lignokain, adjuvan, deksmedetomidin*

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INTRODUCTION

Intravenous regional anesthesia (IVRA) can be safely and effectively applied in minor surgical procedures performed on an ambulatory basis involving both the upper and lower extremities [1,2]. Unlike the brachial plexus block, IVRA does not require expertise or instruments such as the nerve stimulator or ultrasound and can be safely used in patients who are not adequately prepared for general anesthesia [3].

Even with its potential advantages such as early onset, rapid recovery, blockade reliability, and cost effectiveness, the use of IVRA has been limited by tourniquet pain and inability to provide postoperative analgesia [3]. To overcome these limitations, various agents such as opioids, dexamethasone, and ketorolac have been used as adjuvants to lignocaine [4,5]. These adjuvants have considerably increased the application potential of IVRA by providing a faster block onset, inhibiting tourniquet pain, and prolonging postoperative analgesia; however, each adjuvant causes some adverse effects. Thus, the search for new adjuvants that can be used in IVRA is ongoing.

The site of action in IVRA presumably exhibits a blockade of small nerves or nerve endings and not major nerve trunks [6]. Dexmedetomidine is a selective α2-adrenergic agonist that can prolong and enhance the local anesthetic action by exerting a direct effect on peripheral nerve activity [7]. Studies have evaluated the use of dexmedetomidine as an adjuvant in IVRA at doses of 1 μg kg^{-1} and 0.5 μg kg^{-1} [8,9].

The present study compared the effect of the addition of 30 μg of dexmedetomidine to 2% lignocaine with 2% lignocaine alone in IVRA on intraoperative tourniquet pain, fentanyl consumption, onset and duration of sensory and motor blockade, duration of postoperative analgesia, and overall patient satisfaction.

MATERIAL and METHODS

This prospective, randomized, double-blind controlled study was approved by the institutional ethics committee. All procedures performed in the study were in accordance with the ethical guidelines of the declaration of Helsinki. Before inclusion in the study, voluntary written informed consent was obtained from all participants.

A total of 100 patients who belonged to American Society of Anesthesiologists (ASA) grade I and II, were aged between 18 and 60 years, and were scheduled to undergo forearm and wrist surgeries of approximately 1 hour in duration were included in this study.

Patients who refused to provide consent; had coagulation disorder, septicemia, peripheral vascular disease, crush injury, compound fractures, and/or local infection in the forearm and wrist; and had a history of allergy to lignocaine were excluded from this study.

Study participants were randomly divided into 2 groups, namely Group A and Group B (n=50 in each group), by using the sealed envelope technique. For IVRA, Group A received preservative-free 2% lignocaine, and Group B received preservative-free 2% lignocaine along with 30 μg of dexmedetomidine.

After a thorough pre-anesthetic evaluation, patients were explained about the procedure and the pain rating score. In the operating room, standard monitors were connected for the continuous monitoring of vital parameters, and baseline values were recorded. Intravenous access was secured in the non-operative limb by using an 18-gauge intravenous (IV) cannula, and a 24-gauge IV cannula was inserted and secured into the peripheral vein of the operative limb as distally as possible. After the complete exsanguination of the arm with the help of the Esmarch bandage, a double-cuffed pneumatic tourniquet was applied on the upper arm, and the proximal tourniquet was inflated to 100 mmHg above the systolic blood pressure of the patient. Circulatory isolation of the limb was confirmed on the basis of the absence of radial pulse on palpation and the loss of pulse oximetry tracing in the ipsilateral index finger.

Group A patients received the local anesthetic solution containing 3 mg kg^{-1} of lignocaine (2% preservative free) diluted to a volume of 35 mL by using 0.9% saline, and the solution was slowly injected through

the 24-gauge cannula. Group B patients received the aforementioned anesthetic solution along with 30 µg of dexmedetomidine. After the injection, the cannula was removed under strict asepsis, and pressure was applied over the site until bleeding ceased. The solution was prepared by personnel not involved in the study in an identical 50-mL syringe, and anesthesiologists who injected the drug and assessed various parameters were unaware of the composition of the injected drug.

Sensory block was assessed by a pinprick performed using a 25-gauge short-bevel hypodermic needle once every 30 seconds. Patients' responses were evaluated in the dermatomes that contain the sensory distribution of medial and lateral antebrachial cutaneous, ulnar, median, and radial nerves, and the time required for the onset of sensory block was noted. Motor block was examined by asking patients to flex and extend their elbows and move the fingers every 30 seconds until the weakness of movements were confirmed, and the time required for the onset of motor block was noted. After the confirmation of both sensory and motor anesthesia, the distal tourniquet cuff was inflated to 100 mmHg above the systolic pressure, the proximal cuff was released, and surgery was commenced.

Vitals were recorded every 3 min for 15 min, then every 5 min for 30 min, and every 10 min thereafter. Patients were observed for tourniquet pain, and intravenous fentanyl was administered as boluses of 25 µg to counteract the tourniquet pain; the total fentanyl consumption was recorded.

After the completion of surgery, the tourniquet was deflated by intermittent deflation and re-inflation over a period of 2 to 3 min. The tourniquet was not released for at least 30 min after injecting the drug even after the completion of surgery and was not kept inflated for more than 90 min. The time of the recovery of sensory and motor blockade postoperatively was noted. Diclofenac injection was administered if required, and the pain score was determined using a numeric pain rating scale (NPRS) of 0-10, where 0 indicated no pain and 10 indicated intolerable pain; the duration of analgesia was also noted.

Definition of outcomes: Primary outcomes were the incidence of intraoperative tourniquet pain and the total consumption of fentanyl intra-operatively. Secondary outcomes included the onset of sensory blockade (time interval from the completion of the local anesthetic injection to the loss of pin-prick sensation), onset of motor blockade (time interval from the completion of the local anesthetic injection to the inability of the patient to move the fingers and flex the elbow in the supine position), duration of sensory and motor blockade after tourniquet deflation, duration of postoperative analgesia (the time from the deflation of tourniquet to the demand of the first dose of the analgesic), NPRS score at the first demand of the analgesic, and overall patient satisfaction (assessed using a four-point scale as highly satisfied, satisfied, fairly satisfied, and dissatisfied).

Sample size calculation and statistical analysis: To determine the number of participants required for adequate study power, sample size was calculated using Clin Calc, an online sample size calculator (www.clincalc.com/stats/samplesize.aspx). Considering an alpha level (probability of type I error) of 0.05 and beta level (probability of type II error) of 0.10 to establish the desired power of 90%, 50 patients were required for each group. The quantitative variables were expressed as mean ± SD and compared using Student's t-test. Qualitative variables were expressed as frequencies and compared using chi-square or Fisher's exact test. Statistical analysis was done using SPSS version 20 software and a p value <0.05 was considered significant.

RESULTS

A total of 110 patients were recruited. Of 110 patients, eight were excluded because they did not meet the inclusion criteria or refused to participate. The remaining 102 patients were included in the study and randomly allocated into two groups. Of these 102 patients, one patient from group A was excluded because the patient's surgery was prolonged, and one patient from group B was excluded because the patient experienced a major leak of the drug from the site where IV cannula insertion was attempted in the ward. Thus, a total of 100 patients were included (n=50 in each group). Both the groups were comparable in terms of age (p=0.798), sex dist-

ribution (p=0.523), weight (p=0.297), surgery duration (p=0.088), and tourniquet application time (p=0.342) (Table I). None of the patients in the study population experienced blockade failure requiring conversion to general anesthesia. The incidence of tourniquet pain was lower in Group B (p<0.001). The consumption of fentanyl intra-operatively was significantly lower in Group B (9.5±19.48 µg) than in Group A (42.54±27.01 µg; p<0.001; Table II).

Table I. Demographic profile of the study participants. Data are expressed as number of participants or mean±standard deviation

	Group A n=50	Group B n=50	p value
Age (years)	34.96±12.81	34±11.71	0.798
Sex (male/female)	35/15	32/18	0.523
Weight (kg)	62.36±10.00	60.26±10.32	0.297
Duration of surgery (min)	45.34±4.45	46.62±3.81	0.088
Tourniquet time (min)	49.33±7.63	50.30±7.95	0.342

Table II. Intra-operative tourniquet pain incidence and fentanyl consumption. Data is represented as number or mean±standard deviation

	Group A n=50	Group B n=50	p value
Tourniquet pain incidence	36/50	11/50	<0.001
Intra-operative fentanyl used (µg)	42.54±27.01	9.5±19.48	<0.001

The onset of sensory block (1.78±0.74 min; p<0.001) and motor block (9.34±1.27 min; p<0.001) was significantly faster in Group B than in Group A (Table III). The duration of sensory and motor block after tourniquet deflation was 13.52±1.31 min (p<0.001) and 26.92±2.36 min (p<0.001), respectively, in Group B which were significantly higher than Group A (Table III). The first demand of an analgesic was earlier in Group A, in addition, the NPRS scores were higher at that time in Group A compared to Group B (Table III). Regarding the overall satisfaction of patients, the majority of patients in Group B were either highly satisfied or more satisfied compared with Group A in which many patients were only fairly satisfied and a few were dissatisfied (p<0.001; Table IV).

Table III. Sensory and motor block and post-operative analgesia characteristics. Data are presented as mean±standard deviation

	Group A n=50	Group B n=50	p value
Onset of Sensory Block (min)	4.82±0.80	1.78±0.74	<0.001
Onsetof Motor Block (min)	14.34±1.17	9.34±1.27	<0.001
Duration of Sensory Block After Tourniquet Deflation (min)	4.64±0.82	13.52±1.31	<0.001
Duration of Motor Block After Tourniquet Deflation (min)	2.54±0.51	26.92±2.36	<0.001
Duration of Analgesia After Tourniquet Deflation (min)	17.14±1.46	35.16±3.04	<0.001
NPRS score at the first demand of analgesic	6.38±1.15	4.2±0.96	<0.001

Table IV. Level of patient satisfaction. Data is represented as number of patients experiencing a particular level of satisfaction in each group

Level of satisfaction	Group A n=50	Group B n=50	p value
Highly satisfied	2	11	<0.001
Satisfied	13	32	
Fairly satisfied	28	7	
Dis-satisfied	7	0	

DISCUSSION

In IVRA, local anesthetics are intravenously administered to one particular limb by occluding the limb proximally to provide conduction blockade. IVRA is a simple and reliable technique that requires little expertise, results in complete and rapid anesthesia, provides a bloodless surgical field, and leads to rapid recovery [1-3]. This anesthetic technique can be used in the emergency department when a patient is not adequately prepared for general anesthesia. However, disadvantages such as the short duration of the block, occurrence of tourniquet pain, and the absence of the analgesic effect after tourniquet deflation limit the use of IVRA. To overcome these limitations, adjuvants such as opioids (fentanyl, sufentanil, morphine, pethidine, and tramadol), non-steroidal anti-inflammatory drugs, neostigmine, midazolam, and dexamethasone have been used; however, these adjuvants can cause some complications such as delayed respiratory depression, pruritis, and nausea [4,5]. This study attempted to overcome these disadvantages by adding 30 µg of dexmedetomidine as an adjuvant to lignocaine. Unlike other studies, the present study used a fixed small dose of dexmedetomidine instead of a dose calculated according to the body weight because the desired outcome was required at the peripheral site for which a specific plasma concentration is not needed.

The demographic characteristics, surgery duration, and tourniquet time were comparable between Group A (administered preservative-free 2% lignocaine only) and Group B (administered a combination of preservative-free 2% lignocaine along with 30 µg of dexmedetomidine). In the present study a rapid onset of sensory and motor blockade as well as a longer duration of sensory and motor blockade after cuff deflation were observed with the use of dexmedetomidine as an adjuvant to lignocaine for IVRA. Subramanya et al. [9] and Memis et al. [10] have reported that the addition of 0.5 µg kg^{-1} of dexmedetomidine to lignocaine for IVRA significantly reduced the duration of the onset of sensory and motor blockade, improved the quality of anesthesia and postoperative analgesia without any side effects. Esmaoglu et al. [8] examined the intraoperative effects and postoperative analgesia of dexmedetomidine when used as an adjunct for IVRA in 40 patients undergoing hand surgery. They reported that the addition of 1 µg kg^{-1} of dexmedetomidine to lidocaine in IVRA improved the quality of anesthesia and reduced analgesic requirements but exerted no effect on the onset and regression time of sensory and motor blockade. Tahawy et al. [11] compared the use of dexmedetomidine with that of magnesium sulfate as an adjuvant in IVRA and observed that the mean time of the onset of sensory block was 2.93±0.86 min in patients who received 20 mL of 1% lignocaine with 0.5 µg kg^{-1} of dexmedetomidine diluted with normal saline to make a total volume of 40 mL. In the present study, the mean time of the onset of sensory block was 1.78±0.74 min, which was considerably lower than that observed by Tahawy et al. [11] this difference in the mean time of the onset can be attributed to the higher concentration of lignocaine used in the present study.

The tourniquet pain, a major limitation of IVRA, was significantly less in the dexmedetomidine group as demonstrated by the lesser incidence and lower intra-operative fentanyl consumption. Nociceptive pain pathways that are most likely stimulated by tourniquet compression are smaller myelinated Aδ fibers (transmission of fast, sharp pain) and unmyelinated C fibers (transmission of slow, dull pain) [7]. Local anesthetics such as lignocaine block larger pain fibers adequately and thereby provide adequate motor and sensory anesthesia. However, the smaller fibers remain relatively unblocked because of repetitive stimulation by the tourniquet. Alpha 2 agonists enhance the peripheral nerve blocks of local anesthetics by selectively blocking Aδ and C fibers and hence are effective in reducing tourniquet pain [7,12]. Nilekani et al. [13] demonstrated a less frequent and delayed onset of tourniquet pain in patients in whom dexmedetomidine was used as an adjunct to lignocaine. Dexmedetomidine was also found to be superior to lornoxicam and ketorolac as an adjuvant to local anesthetic in IVRA in terms of tourniquet pain and intraoperative and postoperative analgesic requirements [14,15].

Both clonidine and dexmedetomidine can potentiate peripheral nerve blocks by strengthening the local anesthetic action. However, dexmedetomidine is more lipophilic than clonidine and is approximately eight times more selective toward α_2A receptors; hence, it shows more favorable results and lower side effects, such as hypotension and sedation, that occur due to the stimulation of α_1 receptors. Yoshitomi et al. [16] evaluated the effects of α_2 agonists on the local anesthetic action of lidocaine and suggested that dexmedetomidine specifically acts through α_2A adrenoceptors. In addition, dexmedetomidine depresses nerve action potentials, particularly in C fibers, by a mechanism independent of the stimulation of α_2 adrenergic receptors [17,18]. This mechanism strengthens the local anesthetic block achieved by peri-neural administration of the drug and could be implicated in the effect observed in the present study. Sardesai et al. [19] reported that dexmedetomidine, when added to lignocaine for IVRA, significantly facilitated the onset of sensory and motor blocks and prolonged the recovery of sensory and motor blocks compared with clonidine.

The systemic analgesic effect of dexmedetomidine is due to its action on α_2 adrenoceptors in the locus ceruleus and the pre-synaptic activation of α_2 receptors inhibiting norepinephrine release, thereby terminating the propagation of pain signals and inhibiting sympathetic activity post-synaptically [13]. After cuff deflation, with the reperfusion of the limb, this systemic effect is probably the reason for lower pain scores at the first demand of the analgesic in the dexmedetomidine group.

Patient satisfaction is a crucial aspect of anesthesia care. In the present study, a significantly higher number of patients were satisfied with the anesthetic technique in the dexmedetomidine group than in the control group. Addition of dexmedetomidine led to better control of tourniquet pain and lower NPRS scores at the time of the first administration of analgesics in the postoperative period; these factors would have led to better patient satisfaction scores. These findings correlate with those of Sardesai et al. [19] who reported that patient satisfaction was better when dexmedetomidine was used as an adjuvant in IVRA instead of clonidine.

The most frequently observed side effects of dexmedetomidine include hypotension, hypertension, bradycardia, dry mouth, and nausea. However, with the use of 30 µg of dexmedetomidine, none of the patients in this study experienced any hemodynamic effects that required specific intervention.

CONCLUSION

The results of this study indicate that the addition of 30 µg of dexmedetomidine to 2% lignocaine for IVRA results in a lower incidence of intraoperative tourniquet pain and a lower need of rescue analgesia. Addition of dexmedetomidine hastens the onset of sensory and motor blockade, prolongs the duration of sensory and motor blockade, enhances the duration of postoperative analgesia, resulting in lower NPRS scores, and improves patient satisfaction without any hemodynamic instability.

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