



Comparative Study of the Efficacy of Dexmedetomidine and Fentanyl as Adjuvants to Ropivacaine in Ultrasound-Guided Supraclavicular Brachial Plexus Block

Ultrason Eşliğinde Supraklaviküler Brakiyal Pleksus Bloğunda Ropivacaine Yardımcı Olarak Deksmetomidin ile Fentanilin Etkinliğinin Karşılaştırmalı Çalışması

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Objective: Supraclavicular brachial plexus block is preferable to general anaesthesia in upper limb surgeries. Various adjuvants have been added to improve the quality of the block and prolong postoperative analgesia. The aim of the present study was to compare the onset and duration of sensory and motor blockade with the quality of perioperative analgesia and postoperative complications provided by dexmedetomidine and fentanyl as adjuvants to ropivacaine under ultrasound (USG) guidance in supraclavicular block.

Methods: A total of 80 patients with American Society of Anesthesiologists grade I/II scheduled for elective upper limb surgeries were randomly allocated into two groups. Group A received 30 mL of 0.5% ropivacaine with 1 µg kg⁻¹ dexmedetomidine, and group B received 30 mL of 0.5% ropivacaine with 1 µg kg⁻¹ fentanyl for supraclavicular brachial block using USG guidance. The onset and duration of sensory and motor block, time for requirement of rescue analgesia and adverse events during the perioperative period were noted.

Results: The onset of sensory blockade was 13.95±1.34 min in the dexmedetomidine group and 14.18±1.41 min in the fentanyl group. There was a highly significant statistical difference in terms of the duration of the sensory blockade, i.e. 801.75±46.07 min with dexmedetomidine compared to 590.25±40.41 min with fentanyl (p<0.0001). The duration of motor blockade was highly statistically significant with 649.56±42.73 min in group A compared to 456.75±32.93 min in group B.

Conclusion: Dexmedetomidine prolongs the duration of sensory and motor block and postoperative analgesia as compared to fentanyl when used as an adjuvant to ropivacaine in supraclavicular brachial plexus block and is not associated with any major adverse events.

Keywords: Ropivacaine, dexmedetomidine, fentanyl, supraclavicular brachial plexus block

Amacı: Supraklaviküler brakiyal pleksus bloğu, üst ekstremité ameliyatlarında genel anesteziye tercih edilebilir. Bloğun kalitesini artırmak ve postoperatif analjeziyi uzatmak için çeşitli yardımcı tedaviler eklenmektedir. Bu çalışmanın amacı supraklaviküler blokta ultrason eşliğinde ropivacaine yardımcı olarak verilen deksmedetomidin ile fentanil, duyuşal ve motor blok başlangıcı ve süresi, perioperatif analjezinin niteliği, ve postoperatif komplikasyonlar açısından karşılaştırmaktır.

Yöntemler: ASA (American Society of Anesthesiologists) I/II sınıfında yer alan ve elektif üst ekstremité cerrahisi planlanan toplam 80 hasta rasgele iki gruba bölündü. Ultrason eşliğinde supraklaviküler brakiyal blok için, A grubuna 1 µg kg⁻¹ deksmedetomidin ile birlikte 30 mL %0,5 ropivacain, B grubuna ise 1 µg kg⁻¹ fentanil ile birlikte 30 mL %0,5 ropivacain verildi. Duyusal ve motor bloğun başlangıç ve süreleri, kurtarma analjezi gereksiniminin zamanı, ve perioperatif dönem boyunca yan etkiler kaydedildi.

Bulgular: Duyusal bloğun başlaması deksmedetomidin grubunda 13,95±1,34 dakika, fentanil grubunda 14,18±1,41 dk olarak bulundu. Duyusal bloğun süresi açısından istatistiksel olarak oldukça anlamlı bir farklılık izlendi (deksmedetomidin 801,75±46,07 dk, fentanil 590,25±40,41 dk) (p<0,0001). Grup B ile (456,75±32,93 dk) ile kıyaslandığında, motor bloğun süresi Grup A'da (649,56±42,73 dk) istatistiksel olarak oldukça anlamlı derecede farklıydı.

Sonuç: Fentanil ile kıyaslandığında Deksmetomidin, supraklaviküler brakiyal pleksus bloğunda ropivacaine yardımcı tedavi olarak kullanıldığında, duyuşal ve motor bloğun ve postoperatif analjezinin süresini uzatmaktadır ve ayrıca herhangi bir majör yan etkisi bulunmamaktadır.

Anahtar Kelimeler: Ropivacain, deksmedetomidin, fentanil, supraklaviküler brakiyal pleksus blok

Introduction

Brachial plexus block provides adequate muscular relaxation and maintains stable perioperative haemodynamics for upper limb surgeries (1). Ropivacaine, a long-acting amide local anaesthesia, has better safety profile than bupivacaine with reduced cardiotoxic effects (2, 3). Adjuvants have been administered to achieve prolonged block with improved quality of anaesthesia and local anaesthesia (4). In the present study, blocks were performed under ultrasound (USG) guidance for optimal success rates of the block. The aim of the present study was to compare the two adjuvants, dexmedetomidine and fentanyl, in terms of efficacy, duration of postoperative analgesia and any side effects.

Methods

This was a prospective, randomised clinical trial study. The Institutional Ethics Committee approved the study. Written informed consent was obtained from all of the patients.

A total of 80 adult patients were randomly allocated into two groups (n=40) using a computerised random number table. Patients with American Society of Anesthesiologists (ASA) grades I and II, aged between 18 and 60 years, either gender and who underwent elective orthopaedic surgeries of the elbow, forearm and hand were included in the study.

Patients with coagulopathies or on anticoagulants; severe renal, hepatic, respiratory or cardiac diseases; infection at the site of the block; pregnancy and neuromuscular disorders were excluded from the study. Any contraindication to ropivacaine, dexmedetomidine or fentanyl and patient refusal were also excluded.

Patients in group A received 30 mL of 0.5% ropivacaine with 1 µg kg⁻¹ of dexmedetomidine, and those in group B received 30 mL of 0.5% ropivacaine with 1 µg kg⁻¹ of fentanyl under supraclavicular brachial plexus block using USG guidance.

Preoperative assessment included detailed history, general physical examination, systemic examination, airway assessment and routine investigations, such as haemoglobin, total white blood cell count, differential white blood cell count, bleeding time, clotting time, platelet count, blood glucose, blood urea and serum creatinine. Electrocardiography and chest X-ray were also performed. All patients received tab alprazolam 0.5 mg orally the night before surgery, and a preoperative fasting status of 8 h was ensured. The block procedure and the Visual Analogue Scale (VAS) score were explained to the patient. Preoperative baseline vital parameters were recorded. Intravenous line was secured with an 18G cannula, and infusion of lactated ringers was started. Premedication was given with inj. ondansetron 4 mg iv, inj. ranitidine 50 mg iv and inj. midazolam 0.03 mg kg⁻¹ iv. After aseptic precautions, skin infiltration was given with 1 mL of 2% lignocaine. Supraclavicular brachial plexus block was performed with USG guidance (SonoSite) by in plane technique with the volume and adjuvant according to the study groups. The onset of sensory and motor blockade was assessed every 5, 10, 15, 20 and 30 min until complete sensory or motor block. The onset of sensory block was assessed by a pinprick method and defined as the time from the completion of local anaesthesia injection to the time when sensory block was detected. The onset of motor block was measured as the time between the completion of local anaesthesia injection to the achievement of score 3 of the modified Bromage scale. If anaesthesia was found inadequate after 30 min of administration of the drug, such patients were excluded from the study. The duration of sensory and motor block was assessed at 1, 2, 3, 5, 12 and 24 h. The total duration of sensory block was measured as the duration between the onset of complete sensory block to the

appearance of pain and institution of rescue analgesia in the postoperative period. The total duration of motor blockade was calculated as the time between the onset of motor block to the complete recovery of motor activity. Degree of sedation was noted using the Ramsay Sedation Scale. Bradycardia was defined as heart rate <50/min and hypotension <30% of the baseline parameters. Complications, such as intravascular injection, arrhythmias, pneumothorax and paresis, were noted. Heart rate, respiratory rate, oxygen saturation and blood pressure were recorded every 5 min to 30 min and then every 30 min to the regression of the block. Rescue analgesia was given with a VAS score ≥4 cm with inj. diclofenac 75 mg iv infusion over 30 min. If pain persisted even after 2 h of infusion, inj. tramadol 2 mg kg⁻¹ and inj. paracetamol 1 g iv infusion were used for supplemental analgesia. The total analgesia given in 24 h was noted.

Sample size and statistical analysis

The calculated sample size of each group was 49 based on the study by Soma et al (5). The mean±SD of the onset of motor block of two groups was 3.06±0.25 and 3.26±0.45 minutes respectively. Considering 95% confidence level and 80% power with anticipated mean difference of 0.2 and common standard deviation of 0.35.

$$n = \frac{(Z_{\alpha} + Z_{\beta})^2 \times 2 \times SD^2}{d^2}$$

where:

Z_{α} =confidence level at α level,

Z_{β} =power of the study,

SD=standard deviation,

d=difference between two means.

The total sample size was 98 (49 + 49). With 40 cases in each group, we checked power using post hoc test, and adequate power with 80 patients was seen. Using a random number table, 80 patients were allocated into two groups: group A (ropivacaine with dexmedetomidine) and group B (ropivacaine with fentanyl), with 40 patients in each group. Statistical Package for the Social Sciences software, version 16 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

At the end of the study, all data were compiled and analysed statistically. Statistical tests for continuous data, unpaired t-test (normally distributed) and Mann-Whitney U test (skewed data) were used. For categorical data, the chi-square test was applied to determine the significant difference between the groups. A p-value of <0.05 was considered as statistically significant. Both groups were compared with regard to age, weight, gender, ASA grade and duration of surgery. Age was analysed statistically by the Student's unpaired t-test and weight by using the Mann-Whitney U test. In both groups,

Table 1. Demographic variables

Variable	Group A Mean±SD	Group B Mean±SD	p
Age (years)	39.5±13.41	38.4±11.35	0.693*
Weight (kg)	59.5±6.33	58.42±6.17	
Min–Max	48-67	50-69	0.5731†
Median	62.0	56.5	
Gender			
Male	23	18	0.3709‡
Female	17	22	
ASA grade			
I	30	32	0.7889‡
II	10	08	
Duration of surgery (min)	84.83±2.87	85.13±2.61	*0.6921 NS

*Unpaired t-test. †Mann–Whitney U test. ‡Chi-square test. NS: not significant; SD: standard deviation; Min: minimum; Max: maximum

Table 2. Onset and duration of sensory block (min)

	Group A	Group B	p
Onset of sensory block	13.95±1.34	14.18±1.41	
Min–Max	12-16	11-17	*0.4544 NS
Median	14	14	
Duration of sensory block	801.75±46.07	590.25±40.41	
Min–Max	750-900	540-660	*<0.0001 HS
Median	780	570	

*Mann–Whitney U test. NS: not significant; HS: highly significant; Min: minimum; Max: maximum

gender and ASA grade were analysed statistically by the chi-square test. The onset and duration of sensory and motor block were compared using the Mann-Whitney U test. The Fisher's exact test was used for the analysis of adverse effects, such as nausea, vomiting and hypotension.

Results

The 80 patients included in the study were comparable with respect to demographic variables, such as age, gender distribution and weight. There was no statistically significant difference among the two groups (Table 1). There was no statistically significant difference among the two groups with regard to the duration of surgery and the distribution of cases of ASA I and II (Table 1). The onset of sensory blockade was 13.95±1.34 min in the dexmedetomidine group compared to 14.18±1.41 min in the fentanyl group (Figure 1). There was no statistically significant difference between the two groups

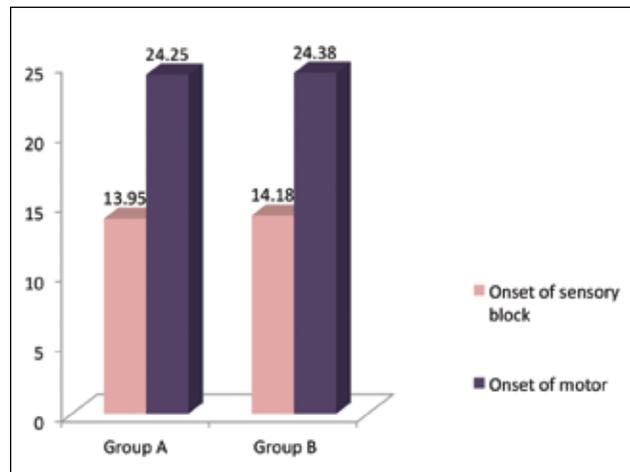


Figure 1. Onset of sensory and motor block (min)

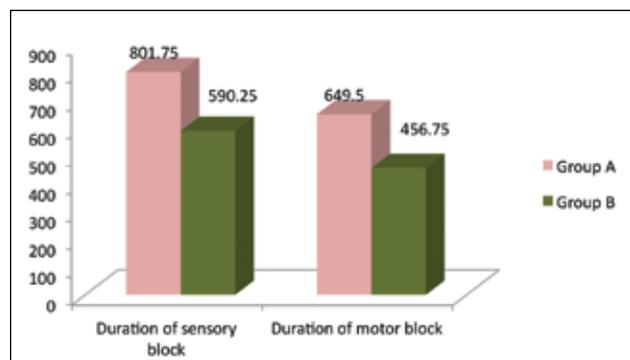


Figure 2. Duration of sensory and motor block (min)

(p=0.45). Although there was no difference in the onset of action of sensory blockade among the two drugs studied, there was a highly significant statistical difference in terms of the duration of the sensory blockade, i.e. 801.75±46.07 min with dexmedetomidine as adjuvant compared to 590.25±40.41 min with fentanyl (p<0.0001) (Table 2). The onset of motor blockade was not statistically significant among the two study groups, but the duration of motor blockade was highly statistically significant with 649.56±42.73 min in group A compared to 456.75±32.93 min in group B (p<0.0001) (Table 3). Sensory blockade lasted for a longer duration than motor blockade (Figure 2). Bradycardia was seen intraoperatively in 3 patients and postoperatively in 2 patients in group A compared to none in group B (p=0.054). One patient in group A had hypotension that responded to two bolus doses of inj. mephentermine 3 mg. In group A, 6 patients had a sedation score of 3, but there were no cases of respiratory depression in any of the patients in both groups. Nausea and vomiting were seen in 3 patients in group A and 2 patients in group B (Table 4). These patients were given inj. metoclopramide 10 mg iv. Patients in the dexmedetomidine group received lower doses of diclofenac, tramadol and paracetamol injections than those in the fentanyl group, but the difference was not statistically significant (Table 5).

Discussion

In the present study, we studied the intraoperative and post-operative anaesthesia effects of two adjuvants added to ropivacaine in a USG-guided supraclavicular brachial plexus block. When local anaesthesia is used solely, they have a shorter duration of action (6). The duration of analgesia with local anaesthesia alone can be prolonged with the use of indwelling catheters, but misplacement, migration and infection are the inherent problems with catheter placement (7, 8). Adjuvants to local anaesthesia provide the benefits of prolonging the duration of action without the need of an additional procedure and risks of catheter insertion (9). Adjuvants, such as opioid and non-opioids, have been used for supraclavicular block to enhance the duration of analgesia and minimise the use of systemic analgesia (10, 11).

Table 3. Onset and duration of motor block (min)

	Group A	Group B	p
Onset of motor block	24.25±1.56	24.38±1.46	
Min–Max	22-27	22-28	0.776 NS
Median	24	24	
Duration of motor block	649.5±42.73	456.75±32.93	
Min–Max	570-720	390-510	*<0.0001 HS
Median	645	450	

NS: not significant; HS: highly significant; Min: minimum; Max: maximum

Table 4. Adverse effects

	Group A No. of patients (%)	Group B No. of patients (%)	p
Bradycardia	5 (12.5)	0 (0)	0.054, significant
Nausea/vomiting	3 (7.5)	2 (5)	1.00* NS
Hypotension	1 (2.5)	0 (0)	1.00* NS
Sedation	6 (15)	0 (0)	0.025 significant
Respiratory depression	-	-	-

*Fisher's exact test. NS: not significant

Table 5. Rescue analgesia in the postoperative period. Demographic characteristics of the three groups

Groups	Inj. diclofenac No. of patients (%)	Inj. tramadol No. of patients (%)	Inj. paracetamol No. of patients (%)	p
Group A	6 (12.5)	4 (10)	0 (0)	0.1582 NS
Group B	10 (25)	16 (40)	6 (12.5)	

NS: not significant

A USG-guided peripheral nerve block is one of the accurate and safe methods in modern anaesthesia practice. Side effects, such as intraneural and intravascular injections, can be avoided with USG-guided regional nerve blocks (12).

Ropivacaine (2, 7), an amide-linked local anaesthesia and an S(-) enantiomer, is less lipophilic than bupivacaine and hence a decreased potential for cardiotoxicity and central nervous system (CNS) toxicity. It has less penetration of large myelinated nerve fibres due to less lipophilicity, resulting in greater degree of motor sensory differentiation. In the present study, 30 mL of 0.5% ropivacaine was used. It was observed from previous studies that increasing the concentration of ropivacaine from 0.5% to 0.75% fails to improve the onset or duration of the block, and using 0.25% ropivacaine for subclavian perivascular brachial plexus block requires frequent analgesia and supplementation (6). Adjuvants to ropivacaine that enhances the motor and sensory blockade, therefore, provide adequate surgical anaesthesia (13, 14).

Dexmedetomidine is a centrally acting α_2 agonist mediating antinociception via peripheral α_2 adrenoceptors. Clonidine, another centrally acting α_2 agonist that is much less selective, has also been used as an adjuvant to local anaesthesia (15-17). The activation of inwardly rectifying G1 protein-gated potassium channels, resulting in membrane hyperpolarisation and decrease in the excitability of the CNS cells and the reduction of calcium conductance into the cells, inhibiting neurotransmitter release, are the probable mechanisms of action of dexmedetomidine. The effect of the addition of dexmedetomidine to bupivacaine (18, 19) and levobupivacaine (20, 21) has been studied and found to be effective with no postoperative neurological deficits.

Fentanyl is a potent synthetic opioid analgesia with a strong agonistic action at the μ -opioid receptor with a rapid onset and short duration of action. Fentanyl, when added to local anaesthesia in peripheral nerve blocks, potentiates the local anaesthesia action via central opioid receptor-mediated analgesia by the peripheral uptake of fentanyl to the systemic circulation (8, 22). In the present study, 1 $\mu\text{g kg}^{-1}$ of fentanyl was used together with 30 mL of 0.5% ropivacaine. The onset of sensory and motor blockade was similar in both the study groups, but the duration of postoperative analgesia was significantly prolonged with dexmedetomidine as adjuvant compared to fentanyl.

Marhofer et al. (23) added dexmedetomidine as adjuvant to ropivacaine in a USG-guided ulnar nerve block and showed that the time for the onset of motor block is decreased without effect on time to the onset of sensory block. The duration of both sensory and motor block was prolonged.

Yoshitomi et al. (24) studied alpha-2 adrenoceptor agonists, including dexmedetomidine, clonidine and oxymetazoline, combined with lidocaine in male guinea pigs. It was found that adrenoceptor agonists enhance the degree of local anaesthesia of lidocaine in a dose-dependent manner.

Rancourt et al. (25) did a prospective, randomised, controlled, double-blind, crossover trial in 14 healthy volunteers who received a USG-guided tibial nerve block. Ropivacaine alone and in combination with dexmedetomidine was studied. It was observed that dexmedetomidine added to ropivacaine for tibial nerve block prolongs the duration of sensory blockade.

Das et al. (26) studied 84 patients posted for elective forearm and hand surgeries to evaluate the effect of adding dexmedetomidine to ropivacaine for supraclavicular brachial plexus blockade. It was found that the onset of the block is earlier, and the duration of action is prolonged in dexmedetomidine than ropivacaine alone. Various studies (27-29) that evaluated the combination of dexmedetomidine and ropivacaine for peripheral nerve blocks have shown that dexmedetomidine is a safe and effective adjuvant (30).

In our study, 5 patients in the dexmedetomidine group had bradycardia that responded to atropine. Although the difference was statistically significant (Table 4), there was no clinically significant difference and was managed with single doses of inj. atropine 0.6 mg iv. Nausea and vomiting were seen in 3 patients and hypotension in 1 patient that were treated. Sedation was seen in 6 patients in the dexmedetomidine group compared to none in the fentanyl group. The difference was not statistically significant and clinically did not require any intervention.

The limitations of our study are that the plasma level of the study drugs was not measured, and patients in the paediatric and geriatric age groups and patients with comorbid conditions were not included in the study.

Conclusion

Dexmedetomidine prolongs the duration of sensory and motor block and postoperative analgesia as compared to fentanyl when used as an adjuvant to ropivacaine in supraclavicular brachial plexus block and is not associated with any major adverse events.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of The Institutional Ethical Committee, BLDEU Shri B M Patil Medical College.

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

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