Clinical and Experimental Health Sciences

Original Article / *Özgün Araştırma*

Does Patient-Controlled Infraclavicular Perineural Dexmedetomidine Increase the Duration of Postoperative Analgesia?

Hasta Kontrollü İnfraklavikülar Perinöral Deksmedetomidin Postoperatif Analjezi Süresini Uzatıyor Mu?

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Abstract

Objective: Peripheral nerve blocks are now used widely for postoperative analgesia, and peripheral nerve catheters are widely utilized. The aim of this study was to retrospectively investigate the effect of perineural infusion of dexmedetomidine on the duration of postoperative analgesia.

Methods: A total of 60 patients aged between 18 and 65 years were included. Group 1 received infraclavicular patient-controlled perineural bupivacaine (0.1%), and group 2 received infraclavicular patient-controlled perineural bupivacaine (0.1%) + dexmedetomidine (200 mic/100 cc). Blood pressure, pulse, peripheral oxygen saturation, modified Ramsay sedation scale, visual pain scores, and the total amount of analgesics were recorded at 0, 30, 60, and 90 min and again at 2, 4, 6, 8, 12, and 24 h.

Results: Systolic blood pressure was higher at 6 h (p=0.007), whereas diastolic blood pressure was higher at 4 and 6 h (p=0.000 and p=0.003, respectively) in Group 1. Heart rate was found to be higher at 8, 12, and 24 h (p=0.004, p=0.002, and p=0.002, respectively) in Group 2. Patients in Group 1 were found to significantly feel pain and need analgesics at 4 and 6 h (p=0.002 and p<0.05, respectively). The mean number of patient requests for analgesia was 5.8±1.4 times in Group 1 and 2.2±0.4 in Group 2 (p<0.05). None of the patients developed sedation/neurological deficits.

Conclusion: The perineural infusion of dexmedetomidine combined with bupivacaine increased the duration of postoperative analgesia, reduced the 24-h need for analgesia and had no adverse effects at low doses.

Keywords: Patient-controlled analgesia, perineural dexmedetomidine infusion, duration of postoperative analgesia

Öz

Amaç: Son zamanlarda postoperatif analjezi amaçlı periferik sinir blokları ve periferik sinir kateterleri yaygın olarak kullanılmaya başlanmıştır. Bu çalışmamızda; deksmedetomidinin perinöral infüzyonunun postoperatif analjeziye etkisini retrospektif olarak araştırmayı amaçladık.

Yöntemler: Distal üst ekstremite cerrahisi geçiren, toplam 60 hasta çalışmaya alındı. Grup 1: infraklavikular hasta kontrollü perinöral bupivakain (%0,1). Grup 2: infraklavikular hasta kontrollü perinöral bupivakain (%0,1) + deksmedetomidin (200 mic/100 cc). 0, 30,60,90, 120. Dk ve 4, 6, 8, 12, 24, saatlerde kan basıncı, nabız, periferik oksijen saturasyonu, modifiye ramsey sedasyon skalası, visüel ağrı skorları, total analjezik miktarı kaydedildi.

Bulgular: Grup 1'de, 6. saat sistolik kan basıncı, grup 2'ye göre yüksekti (p: 0,007). Diyastolik kan basıncı ise 4. ve 6. saatlerde grup 1'de daha yüksekti (p: 0,000, p: 0,003). 8., 12. ve 24. Saatlerde kalp hızı grup 2'de daha yüksek bulundu (p: 0,004, p: 0,002, p: 0,002). 4. ve 6. saatte grup 1'deki hastaların anlamlı olarak ağrı hissettikleri ve analjezik ihtiyaçları olduğu saptandı (p: 0,002, p: 0,000). Grup 2'de ilk ağrı hissedilen zaman 6. saat olarak saptandı. Grup 1'de ortalama 5,8±1,4 defa analjezi ihtiyacı olmuşken, grup 2'de ortalama 2,2±0,4 defa analjezi ihtiyacı olmuştur (p: 0,000). Hiçbir hastada sedasyon / nörolojik defisit gözlenmedi.

Sonuç: Deksmedetomidinin bupivakainle beraber perinöral infüzyonunun postoperatif analjezi süresini artırdığı, 24 saatlik analjezi ihtiyacını azalttığı ve düşük dozlarda hiçbir yan etkiye neden olmadığı görülmüştür.

Anahtar kelimeler: Hasta kontrollü analjezi, perinöral deksmedetomidin infüzyonu, postoperatif analjezi süresi

INTRODUCTION

Regional anesthesia techniques have important advantages than general and systemic analgesia techniques, including excellent pain control, reduced adverse effects, and less length of stay in the post-anesthesia care unit (1-3). Peripheral nerve blocks not only reduce

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the need for intraoperative analgesia but also provide effective analgesia during the postoperative period without significant systemic side effects (4).

Perineural catheters provide early discharge with postoperative analgesia (5). The continuous infusion of local anesthetic through the catheter provides pain control with less opioid consumption and accelerates the healing process along with patient satisfaction (6, 7).

Adjuvant agents are often used in combination with local anesthetics to increase the duration and quality of the block in peripheral nerve blocks (8). Dexmedetomidine is a selective alpha-2 adrenergic receptor agonist and has several effects such as reduced blood pressure, sedation, sleep, analgesia, memory loss, and shivering. Its administration alone or in combination has been tested (9-11). In addition, studies have demonstrated that the perineural administration of dexmedetomidine combined with local anesthetics prolongs the duration of nerve block (12, 13). However, no data related to the perineural infusion of dexmedetomidine is present in the literature.

The present study aimed to investigate the effect of the perineural infusion of dexmedetomidine combined with bupivacaine on the duration of postoperative analgesia, the 24-h need for analgesia, side effects of dexmedetomidine, Ramsay sedation scale, and neurological follow-up.

METHODS

After obtaining the approval from the ethics committee of Erzincan University (decision no. 08/06) and written informed consent was obtained from patients who participated in this study, a total of 60 ASA I–II patients aged 18–65 years who underwent distal upper extremity surgery in our clinic between July 2015 and January 2016 were retrospectively evaluated. American society of anesthesiology (ASA) I included normal healthy patients (non-smoking and no/minimal alcohol use), and ASA II included patients with mild systemic disease [without substantive functional limitations; examples include, but are not limited to, current smokers, social alcohol drinkers, patients with pregnancy, patients with obesity (30<body mass index<40), patients with well-controlled diabetes mellitus/hypertension (DM/HTN), and patients with mild lung diseases]. These operations included all of the upper extremities such as soft tissue, fracture of the distal radius, or carpal tunnel syndrome (ClinicalTrials.gov ID: NCT02550782)

Measurements

Patients were divided into two groups according to the analgesic protocol provided during the postoperative period:

Group 1: n=30, infraclavicular patient-controlled perineural bupivacaine (0.5% marcaine flacon; Astra Zeneca, Sweden) (0.1% bupivacaine; bolus dose, 5 mL; infusion rate, 5 mL/h; and lockout time, 1 h) (14).

Group 2: n=30, infraclavicular patient-controlled perineural bupivacaine + dexmedetomidine (Precedex, 200 mcg; Abbott, USA) (0.1% bupivacaine + 200 mic/100 cc dexmedetomidine; bolus dose, 5 ml; infusion rate, 5 ml/h; and lockout time, 1 h) (15).

The infusion dose of dexmedetomidine was adjusted to not exceed 1 mic/kg.

Patients in groups 1 and 2 were selected from those operated on exactly the same anesthetic protocols. Patients who underwent infraclavicular nerve block and perineural catheter insertion prior to surgery and were given analgesia using the patient-controlled method as well as those who received bupivacaine and bupivacaine + dexmedetomidine infusion via the perineural catheter during the postoperative period were included.

In our clinic, after the patients were bought to their services, patient-controlled analgesia was initiated by an anesthetist when the patient's visual analogue scale (VAS) was ≥4. The time when the first analgesic was administered was considered as 0 min. All patients were informed about the patient-controlled analgesia device and were instructed to push the button of the device if VAS was ≥4. Patients' noninvasive blood pressure (NIBP), heart rate (HR), peripheral oxygen saturation ($SpO_{2)}$, modified Ramsay scale for sedation (1–6: 1, agitated or restless; 2, oriented or cooperative; 3, responding to commands only; 4, brisk response to light glabellar tap; 5, sluggish response to light glabellar tap; and 6, no response) (16), VAS, the first analgesic administration time, the amount of analgesic needed, and nausea/vomiting were recorded at 0, 30, 60, 90, and 120 min and then at 4, 6, 8, 12, and 24 h.

If a patient used 10 ml of analgesics and still felt pain, then 100 mg tramadol HCl (Contramal, Abdi İbrahim, İstanbul, Turkey) was intravenously administered. If a patient still felt pain after 100 mg of intravenous tramadol, then diclofenac sodium (Voltaren IM, Novartis, İstanbul, Turkey) was intramuscularly administered.

Infraclavicular perineural catheter was removed by an anesthetist at the end of 24 h, and all patients with infraclavicular perineural inserted underwent neurological examination of the forearm after 1 month.

Statistical Analyses

The analysis was calculated based on the study by Esmaoğlu et al. (13) in which dexmedetomidine prolonged the duration of analgesia from an average of 670 (70)–880 (70) min. Considering perineural single dose administration, SD of 70 min was taken as 100 min for the perineural infusion of our study. Accordingly, study strength value of 85% was obtained at the significance level of $p<0.0500$ in the two groups with a sample size of 30 each.

One-sample Kolmogorov–Smirnov test was used to determine the normal distribution (Table 3). In the intergroup comparisons, chi-square test was used for categorical variables (Table 2), Student's t-test for normally distributed continuous variables (Tables 1, 3), and Mann–Whitney U-test variance analysis for non-normally distributed continuous variables and ordered variables (Table 3). Statistical analysis was performed using Statistical Package for the Social Sciences 21.0 (SPSS IBM Corp.; Armonk, NY, USA) for Windows package software. $p<0.05$ were considered statistically significant.

RESULTS

The study included a total of 60 (females, 27 and males, 33) patients aged >18 years. The mean age of all patients was 44.57±11.9 years. No significant difference was found between the groups in terms of age and gender (Table 1, 2).

When systolic (SAP) and diastolic (DAP) arterial pressures were compared between the groups, SAP was found to be significantly higher at 6 h in Group 1 than in Group 2 (p=0.007), whereas it was higher at 8 and 12 h in Group 2, but without statistical significance (p=0.920 and p=0.347, respectively). Diastolic arterial pressure values were higher in the first 2 h and at 24 h in Group 1 than in Group 2, but without statistical significance, whereas these were significantly higher at 4 and 6 h in Group 1 (p=0.000 and p=0.003, respectively; Table 3, Figure 1).

Heart rate was higher in Group 2 than in Group 1 at all hours, with statistical significance at 8, 12, and 24 h (p=0.004, p=0.002, and p=0.002, respectively; Table 3, Figure 2).

In none of our patients, SpO_2 dropped under 95%. Sedation was not observed in any patient in the dexmedetomidine group.

When VAS values were compared between the groups, patients in Group 1 were found to significantly feel pain and require analgesics at 4 and 6 h (p=0.002 and p<0.05, respectively), whereas the time of the first sensation of pain was at 6 h in Group 2. There was pain sensation in both groups at 8, 12, and 24 h, but the difference was not statistically significant (p=0.592, p=0.136, and p=0.195, respectively; Figure 3).

When the number of patient-initiated requests for analgesia was examined, the mean numbers were 5.8±1.4 times in Group 1 and 2.2±0.4 times in Group 2 (p<0.05).

Nausea/vomiting occurred in two patients in Group 1 and in three in Group 2. No problems were found in neurological examinations of our patients performed after 1 month.

Table 1. Mean age of patients in the groups.*

	Group	n**	Mean	Standard Deviation	p
Age (years)	1	30	43.40	12.615	0.456
	2	30	45.73	11.435	

*t-test
**Patient number

Table 2. Sex of patients in the groups*

	Group 1	Group 2	Total	p
Male (n**)	16	17	33	0.799
Female (n)	14	13	27	
Total	30	30	60	

*Chi-square test
**Number of patients

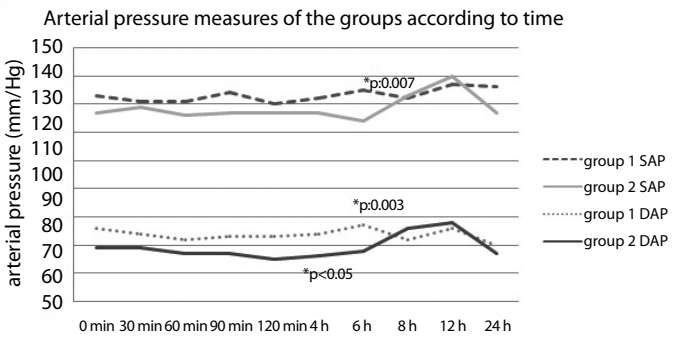

Figure 1. Arterial pressure measures of the groups according to time. Systolic (SAP) arterial pressures was found to be significantly higher in the Group 1 at 6th hour. Diastolic (DAP) arterial pressures were higher in the Group 1 at 4th and 6th hours.

Table 3. Systolic and diastolic arterial pressures and heart rate of patients in the groups according to time

	Systolic arterial pressure			Diastolic arterial pressure			Heart rate		
	Group 1	Group 2	p	Group 1	Group 2	p	Group 1	Group 2	p
0 min	133.50±16.2	127.87±21.0	0.251	86.63±11.3	79.37±14.3	0.347	69.70±14.8	73.73±7.6	0.190
30 min	131.67±15.5	129.23±17.6	0.574	84.77±11.1	79.90±10.3	0.943	70.90±14.8	73.90±8.5	0.342
60 min	131.47±14.1	126.83±18.0	0.273	82.53±8.6	77.20±11.1	0.388	70.70±15.7	74.07±7.2	0.290
90 min	134.20±15.5	127.20±16.8	0.100	83.27±9.6	77.30±10.2	0.976	71.20±15.5	74.20±8.0	0.352
120 min	130.63±15.2	127.13±16.3	0.395	83.07±11.5	75.63±8.4	0.302	70.63±13.4	75.53±6.6	0.79
4 h*	132.83±12.7*	127.20±13.3*	0.100	84.47±8.6*	76.33±11.5*	0.000**	71.90±9.9	76.33±7.0	0.51
6 h*	135.63±16.4	124.67±13.8	0.007**	87.83±13.1*	78.33±10.5*	0.003**	73.30±13.7	75.70±6.7	0.395
8 h	132.67±13.1	133.00±12.6	0.920	82.50±8.9	83.00±9.1	0.832	72.17±12.3	80.27±8.2	0.004**
12 h*	137.00±14.1	140.67±15.7	0.347	86.67±13.0*	88.67±10.4*	0.674	74.47±12.5	83.40±8.0	0.002**
24 h*	128.00±14.7*	124.67±15.4*	0.329	80.00±10.1*	77.33±8.2*	0.301	70.47±10.7	77.07±8.0	0.002**

*Mann–Whitney U-test
**p<0.05 was considered statistically significant. Student's t-test for normally distributed continuous variables and Mann–Whitney U-test variance analysis for non-normally distributed continuous variables and ordered variables.

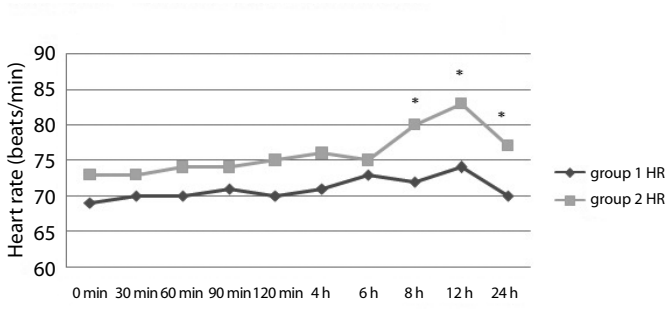

Figure 2. Heart rate measures of the groups according to time.
*Heart Rates (HR) were higher in the Group 2 at all hours. However, these results were found to be statistically significant at the hours 8, 12 and 24 (p: 0.004, p:0.002, p: 0.002).

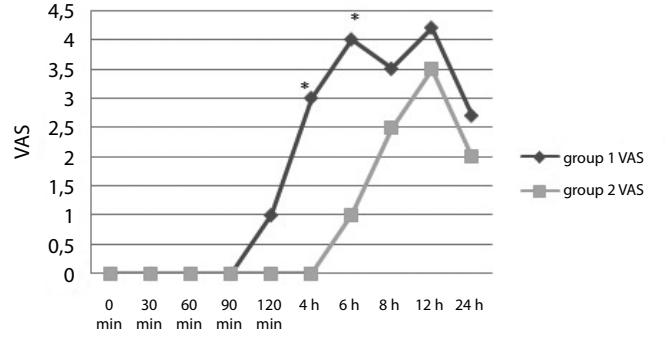

Figure 3. VAS measures of the groups according to time.
*Patients in the Group 1 were found to significantly feel pain and require analgesics at the 4th and 6th hours (p: 0.002, p<0.05).

DISCUSSION

We found that dexmedetomidine combined with bupivacaine infused through an infraclavicular catheter prolonged the time until analgesia was requested and decreased the 24-h need for analgesia without significant systemic side effects (such as sedation, bradycardia, and hypotension) at these doses.

Dexmedetomidine is an alpha-2 agonist affecting the central nervous system. It has several effects such as decrease in blood pressure, sedation, sleep, analgesia, and shivering. In our study, SAP and DAP were lower in Group 2 than in Group 1. These lower values were attributed to the inhibition of sympathetic activity with the postsynaptic activation of alpha-2 adrenoceptor in the central nervous system, resulting in decreased HR and blood pressure (17, 18). In our study, contrary to expectations, HR was higher in Group 2 than in Group 1 over 24 h. This condition monitored at 0 min was attributed to the personal characteristics of patients and decreased dose of dexmedetomidine. Both arterial pressures and HR increased at 8 and 12 h, which were attributed to the increased VAS values.

Several studies have demonstrated that dexmedetomidine increases the duration of postoperative analgesia and prolongs the time of the first need for analgesia (8, 13, 19-23), which is consistent with our findings. Time for the first need for analgesia was found at 4 h in Group 1 and 6 h in Group 2. Furthermore, the total need for analgesics was significantly reduced in Group 2. Masuki et al. (24). have reported that dexmedetomidine reduces local anesthetic absorption, thereby prolonging its effect by inducing vasoconstriction around the injection. Memiş (25) and Esmaoğlu (13) have attributed this prolongation effect to the reduced release of norepinephrine by peripheral alpha-2 agonists, resulting in a decrease in pain because of independent inhibitor effects on the action potential of nerve fibers.

Swami et al. (15) have stated that the administration of perineural dexmedetomidine has a sedative effect. Guo et al. (18) have noted that this sedative effect results from the suppressed release of substance P matter, which plays a role in pain conduction at the dorsal root level and the activation of alpha-2 in the locus coeruleus. In contrast, Bekker et al. (26) have concluded that the perineural administration of dexmedetomidine may be helpful in the case of sedation. In parallel, in our study, the perineural infusion of dexmedetomidine did not cause sedation in any patient, which may be because the infusion of dexmedetomidine resulted in a more peripheral, rather than central, alpha-2 effect (27).

None of our patients developed neurological deficits, which is consistent with animal studies conducted by Brummet (12) in which dexmedetomidine did not cause axon or myelin damage even at high doses (25–40 mic/kg).

Good postoperative analgesia helps patients to return to their normal daily lives in a shorter time, increases patient satisfaction, and reduces the length of hospital stay and costs. Regional anesthesia techniques provide an excellent pain control, contributing to these processes. In recent years, peripheral nerve blocks and even peripheral nerve catheter insertion have been introduced to protect patients against the side effects of opioids used for postoperative purposes (28, 29). However, peripheral nerve catheter takes longer time, is more expensive and painful for patients with a higher rate of complications, and requires more postoperative care (28, 29). Ultrasound guidance reduces the time for catheter insertion and may improve success rates (30). Patients who underwent ultrasonography were included in this study, and the success rate of blocks and insertion of catheters were 100%. There were no technical failures in PCA devices.

Our study has some limitations. First, the number of intragroup patients was small. Further studies with larger number of cases are needed to obtain stronger data. Second, plasma levels of dexmedetomidine that could support its peripheral rather than central effects were not studied. Third, because of feared perineural side effects of dexmedetomidine, the lock-out time was defined at 1 h. This condition may be caused by the ineffectiveness of bupivacaine alone. Fourth, VAS values were evaluated at rest, but not at movement.

CONCLUSION

We found that dexmedetomidine combined with bupivacaine infused through an infraclavicular catheter prolonged the time until analgesia was requested and decreased the need for 24-h analgesia without any side effect (such as sedation, bradycardia, and hypotension) at these doses. Patient-controlled administration of dexmedetomidine at low doses provides a comfortable and good postoperative analgesia and high patient satisfaction and reduces adverse effects.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Clinical Research Ethics Committee of Erzincan University (date 24.08.2016, no: 08/06).

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - İ.K.; Design – İ.K., U.K.; Supervision – S.T., A.S.; Resources – İ.K., U.K., S.T., Z.B.; Materials – İ.K., Z.B.; Data Collection and/or Processing – İ.K., U.K., S.T.; Analysis and/or Interpretation – İ.K., U.K., A.S.; Literature Search – İ.K., U.K., Z.B.; Writing Manuscript – İ.K.; Critical Review – İ.K., U.K., S.T., Z.B., A.S.

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Hasta Onamı: Yazılı hasta onamı bu çalışmaya katılan hastalardan alınmıştır.

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