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Original Article

The effect of adding dexmedetomidine to ropivacaine for lumbar plexus and sciatic nerve block

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Abstract: Background and Objectives: Lumbar plexus and sciatic nerve block is a common anesthetic and antalgic technique for lower extremity surgery. However, limited duration of analgesia is hardly sufficient to avoid the demands for opioids. This study we investigate the effect of adding dexmedetomidine to ropivacaine for lumbar plexus and sciatic nerve block. Methods: The double-blind, randomized trial enrolled 90 patients scheduled for lower extremity surgery. Group ropivacaine (R) received 0.5% ropivacaine for lumbar plexus and sciatic nerve block and i.v. normal saline. Group ropivacaine plus perineural demedetomidine (RpD) received 0.5% ropivacaine containing 1 μg/kg dexmedetomidine for nerve block and i.v. normal saline. Group ropivacaine plus systemic demedetomidine (RsD) received 0.5% ropivacaine for nerve block and i.v. normal saline containing 1 μg/kg dexmedetomidine. Sensory and motor block onset times, durations of block and analgesia, haemodynamic parameters and sedation level were recorded. Results: The onset time of sensory and motor block were shorter in group RpD than group R and RpD ($P < 0.05$). The duration of block and analgesia were longer in group RpD than group R and RpD ($P < 0.05$). HR and MAP in group RpD and RsD were lower than group R ($P < 0.05$). Ramsay scores in group RpD and RsD were higher than group R ($P < 0.05$). There weren't bradycardia, hypotension, hypoxemia, in each group. Conclusions: Addition of dexmedetomidine (1 μg/kg) to ropivacaine for lumbar plexus and sciatic nerve block could decrease the onset time of sensory and motor block, and prolong the duration of block, and improve postoperative analgesia without significant side-effects.

Keywords: Dexmedetomidine, ropivacaine, lumbar plexus, sciatic nerve, nerve block

Introduction

Lumbar plexus and sciatic nerve block is a common intra-operative anesthetic [1] and postoperative antalgic technique [2] for surgery of lower extremity. Recent researches indicated that long acting local anaesthetics, such as ropivacaine and bupivacaine, could provide reliable postoperative analgesia about 8 to 14 hours [3-6]. However, the limited duration of analgesia is hardly sufficient to avoid the demands for opioids. Moreover, patients usually complain pain during the first postoperative night, which is negative for rehabilitation, even causes cardio-cerebral events. To prolong the duration of block for postoperative analgesia is an unresolved problem for peripheral nerve block. Continuous catheter technique is a method to increase the duration of analgesia, but there are some complications such as catheter displacement [7] and infection [8-10]. Therefore, an increasing number of anesthesiologists are committed to improving single-shot blocks. Evidences suggest adjuvant drugs, alpha-2 adrenergic receptor agonists and dexamethasone, can increase the duration of local anesthetics for peripheral nerve block [11-13].

Dexmedetomidine, similarly with clonidine, is a highly selective alpha-2 adrenergic receptor agonist. Experimental and clinical researches indicated that adding dexmedetomidine to local anesthetics for peripheral nerve block produced an increase in the duration of sensory and motor block [14, 15]. However, its clinical use in lumbar plexus and sciatic nerve block

Table 1. Demographic data and duration of surgery (n = 30 in each group). Data are expressed as mean ± SD

	Group R	Group RpD	Group RsD
Age (years)	40.23±6.54	41.33±5.52	39.42±7.16
Height (cm)	168.59±9.12	171.16±2.32	172.61±8.74
Weight (kg)	64.31±6.83	68.51±6.43	66.22±7.97
Gender (M/F)	14/16	17/13	15/15
Duration of surgery (minutes)	92.58±14.15	102.61±11.86	104.52±12.28

has not been reported. In this research, we aimed to investigate the effect of adding dexmedetomidine to ropivacaine for lumbar plexus and sciatic nerve block.

Methods

The present study was a prospective, double-blind, randomized controlled trial, which was conducted at the Department of Anesthesiology, the First Central Hospital of Baoding, China. After approved by ethical committee of our institution and informed consent, 90 ASA physical status I-II patients scheduled for lower extremity and foot surgery under lumbar plexus and sciatic nerve block. Exclusion criteria included use of adrenoreceptor agonist or antagonist during the last two weeks, allergy to the study drugs, difficulty in cooperating or quantifying pain using a visual analog scale (VAS), history of cardiac, respiratory, hepatic, or renal impairment, coagulopathy or bleeding diathesis, infection at the injectionsite, and pregnant women.

In the operation room, oxygen was delivered by face mask, and an 18 G intravenous cannula was inserted in patient's left forearm. Patient was monitored by electrocardiogram and pulse oximeter. A right radial arterial catheter was inserted for continuous arterial pressure monitoring. Before lumbar plexus and sciatic nerve block were performed, patients were not premedicated and the basal value of heart rate (HR), mean arterial pressure (MAP), peripheral oxygen saturaton (SpO_2) and sedation levels according to Ramsay score were recorded. The patient was turned to the right lateral position with the hips and knees flexed to approximately 45 degree. The lumbar plexus was located using an 100 mm insulated short-beveled stimulating needle (PAJUNK®, PAJUNK GmbH Medizintechnologie, Germany), connected to a nerve stimulator (PAJUNK®, PAJUNK GmbH Medizintechnologie, Germany), set at an initial amperage of 1.5 mA. Lumbar plexus blockade was done following Winne's approach [16]. The lumbar plexus injection site was confirmed by contraction of the quadriceps and patella with a current less than 0.5 mA at 1 Hz, and then, after negative aspiration, 30 ml study drug was injected. Meanwhile, the sciatic nerve was achieved following the method of Labat [17]. Contraction of gastrocnemius muscle in response to a current less than 0.5 mA at 1 Hz confirmed the sciatic nerve injected site had been reached, and then, after negative aspiration, 20 ml study drug was injected.

Patients were randomly allocated using an online research randomizer (http://www.randomizer.org) into three groups (30 patients each). The ropivacaine (R) group received lumbar plexus and sciatic nerve block with 0.5% ropivacaine 50 ml and i.v. normal saline 50 ml. The ropivacaine plus perineural demedetomidine (RpD) group received 50 ml 0.5% ropivacaine containing dexmedetomidine (1 μg/kg) for lumbar plexus and sciatic nerve block and i.v. normal saline 50 ml. The ropivacaine plus systemic demedetomidine (RsD) received 50 ml 0.5% ropivacaine for lumbar plexus and sciatic nerve block and i.v. normal saline 50 ml containing dexmedetomidine (1 μg/kg). In the RsD group, patients received dexmedetomidine 1 μg/kg in normal saline 50ml systemically over 600 s. In both other groups, 50 ml saline was administered over 600 s. The study drugs were prepared by a nurse who was not involved in block performance or assessment. Patients, anaesthetists performing the nerve block, and investigators evaluating outcomes were unaware of the group assignment and not informed as to the identity of the study drug.

Sensory block of lumbar plexus and sciatic nerve territory was assessed by pinprick test using a 3-point scale: 0 = normal sensation, 1 = loss of sensation of pinprick (analgesia), 2 = loss of sensation of touch (anesthesia). Motor block was evaluated by plantar or dorsal flexion of foot and elevation of thigh using a 3-point scale: 0 = normal motor function, 1 = reduced motor strength, but some perceptible movement, 2 = complete motor block. Sensory and motor blocks were evaluated every 3 minutes

Table 2. Onset time and durations of lumbar plexus block

	Group R	Group RpD	Group RsD
Onset time of sensory block (minutes)	14.52±3.53	9.76±3.21[a,b]	13.82±2.46
Onset time of motor block (minutes)	16.81±2.73	12.65±6.84[a,b]	18.14±3.66
Duration of sensory block (minutes)	721.45±119.32	1198.31±144.15[a,b]	743.52±121.26
Duration of motor block (minutes)	596.75±86.31	872.33±101.09[a,b]	623.11±113.80

Data are expressed as mean ± SD. [a]$P < 0.05$ compared with Group R, [b]$P < 0.05$ compared with Group RsD, n = 30 in each group.

Table 3. Onset time and durations of sciatic nerve block

	Group R	Group RpD	Group RsD
Onset time of sensory block (minutes)	16.73±3.91	11.32±4.64[a,b]	17.56±4.38
Onset time of motor block (minutes)	19.67±4.13	14.26±3.19[a,b]	16.91±4.26
Duration of sensory block (minutes)	659.13±116.58	998.32±94.34[a,b]	683.45±131.98
Duration of motor block (minutes)	553.47±96.72	792.33±142.61[a,b]	538.52±109.15

Data are expressed as mean ± SD. [a]$P < 0.05$ compared with Group R, [b]$P < 0.05$ compared with Group RsD, n = 30 in each group.

Table 4. Durations of analgesia

	Group R	Group RpD	Group RsD
Duration of analgesia (minutes)	1047.23±189.65	1438.98±156.74[a,b]	1056.63±201.72

Data are expressed as mean ± SD. [a]$P < 0.05$ compared with Group R, [b]$P < 0.05$ compared with Group RsD, n = 30 in each group.

for the first 30 minutes after injection. And then, every 30 minutes after surgery, until the return of normal sensory and motor function. Onset time was defined as the time from the end of the local anesthetic injection to complete sensory and motor block (score 2). Duration of sensory block was the time interval between the end of the local anesthetic injection and complete resolution from the sensory and motor block (score 0). The Visual Analog Scale (0-10) was used for evaluation of pain. Pethidine hydrochloride 75 mg was administered IM when the Visual Analog Scale > 4. The time from the end of the local anesthetic injection to the first analgesic request was defined as the duration of analgesia. HR, MAP, SpO_2 and Ramsay score were recorded at 0, 5, 10, 15, 30, 45, 60, 90, 120, 240, 720, 1440 minutes. Bradycardia (HR < 50 beats per minute), hypotension (the decrease of MAP > 20% baseline value), hypoxemia (SpO_2 < 90%), nausea and vomiting were defined as side-effects.

Statistical evaluation

The power analysis based on a previous study, published by Esmaoglu [18], which suggested a calculated sample size of 30 patients in each group would have 80% power of detecting a difference at a 0.05 level of significance, using a confidence interval of 95%. Analysis was performed using SPSS version 17 (Chicago-USA). Data were presented as mean ± SD. Data were tested for normal distribution using the Kolmogorov-Smirnov test. The incidence of complications and gender were analysed using chisquare (χ^2) test. Age, weight, HR, MAP, SpO_2, onset time, duration of sensory and motor block, duration of surgery and duration of analgesia were tested using an analysis of variance (ANOVA) followed by post hoc testing (Newman-Keuls test). Kruskal-Wallis test was used for the comparison between the groups for sedation score. A *P*-value of 0.05 was considered significant.

Results

The demographic data and the duration of surgery were similar in each group (**Table 1**; $P > 0.05$).

The onset time of sensory and motor block of lumbar plexus and sciatic nerve were signifi-

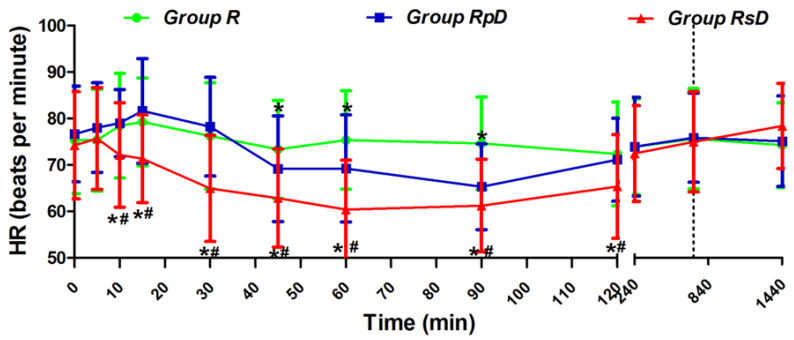

Figure 1. Intraoperative heart rates (mean value) in three groups at various time points. Bar indicates SD. $^{*}P < 0.05$, compared with Group R; $^{\#}P < 0.05$, compared with Group RpD.

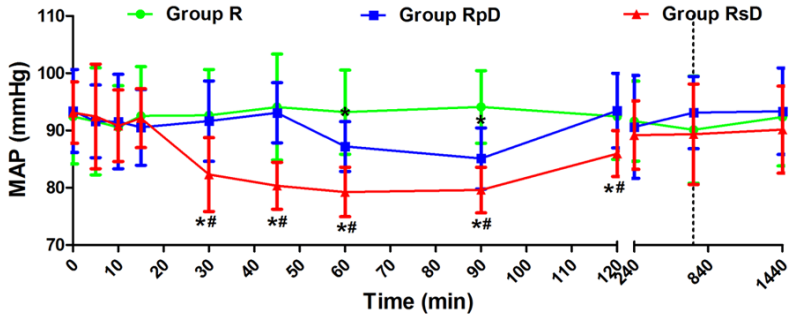

Figure 2. Intraoperative mean arterial pressure (mean value) in three groups at various time points. Bar indicates SD. $^{*}P < 0.05$, compared with Group R; $^{\#}P < 0.05$, compared with Group RpD.

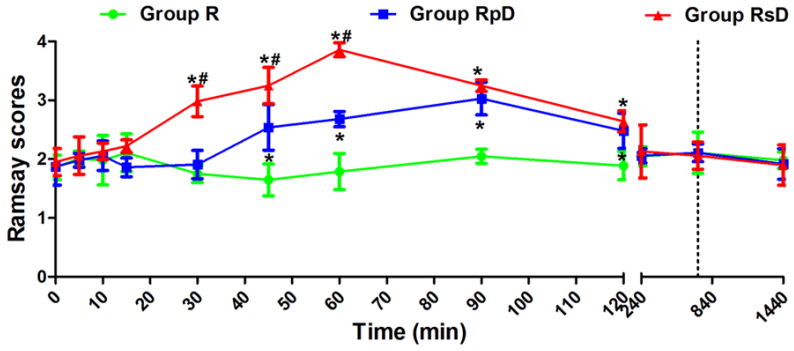

Figure 3. Intraoperative Ramsay score (mean value) in three groups at various time points. Bar indicates SD. $^{*}P < 0.05$, compared with Group R; $^{\#}P < 0.05$, compared with Group RpD.

cantly shorter in group RpD than group R and RpD (**Tables 2**, **3**; $P < 0.05$), but group R and group RpD were comparable with respect to the onset time (**Tables 2**, **3**; $P > 0.05$). The duration of sensory and motor block of lumbar plexus and sciatic nerve were significantly prolonged in group RpD than group R and RpD (**Tables 2**, **3**; $P < 0.05$). The duration of postoperative analgesia was significantly longer in group RpD than group R and RpD (**Table 4**; $P < 0.05$). However, there were no differences in the duration of block and analgesia between group R and group RpD (**Tables 2-4**; $P > 0.05$).

HR levels in group RpD at 45, 60, 90 minutes were significant lower than those in group R (**Figure 1**; $P < 0.05$); HR levels in group RsD at 10, 15, 30, 45, 60, 90, 120 minutes were significant lower than those in group R and group RpD (**Figure 1**; $P < 0.05$). MAP in group RpD at 60, 90 minutes were significant lower than those in group R (**Figure 2**; $P < 0.05$); MAP levels in group RsD at 30, 45, 60, 90, 120 minutes were significant lower than those in group R and group RpD (**Figure 2**; $P < 0.05$). Ramsay scores levels in group RpD at 45, 60, 90, 120 minutes were significant higher than those in group R (**Figure 3**; $P < 0.05$); Ramsay scores levels in group RsD at 30, 45, 60, 90, 120 minutes were significant higher than those in group R and group RpD (**Figure 3**; $P < 0.05$), and 4 patients led to deep sedation. However, there weren't other side-effects such as bradycardia, hypotension, hypoxemia, nausea and vomiting in each group. HR, MAP and Ramsay scores levels were similar in each group at 240, 720, 1440 minutes (**Figures 1-3**; $P > 0.05$).

Discussion

In this study, we found that the addition of 1 μg/kg dexmedetomidine to ropivacaine for lum-

bar plexus and sciatic nerve block could significantly decrease the onset time of sensory and motor block. Moreover, the duration of sensory and motor block and analgesic were significantly prolonged. These results are consistent with the previous researches by Esmaoglu et al. [18] and Bharti et al. [19].

As an adjuvant for local anaesthetics, the analgesia effect of dexmedetomidine was known gradually in clinical, animal and experimental researches [20-22]. Brummett and his colleagues found that adding dexmedetomidine to ropivacaine/bupivacaine extended the duration of sciatic nerve block in rats [20, 21]. Keplinger et al. reported that dexmedetomidine added to ropivacaine for ulnar nerve block prolonged the duration of sensory and motor block in volunteers [15]. Furthermore, Esmaoglu et al. showed that dexmedetomidine added to levobupivacaine shortens the onset time and prolong the duration of axillary brachial plexus block in patients [18]. The analgesic mechanism of α_2-adrenergic receptor agonists is multifactorial. Peripherally [23], α_2-adrenergic receptor agonists produce analgesia by reducing the release of norepinephrine and causing α_2-adrenergic receptor-independent inhibitory effects on nerve fiber action potentials. Centrally [24], α_2-adrenergic receptor agonists produce analgesia by the inhibition of substance P release in the nociceptive pathway at the level of dorsal root neuron and by the activation of α_2-adrenergic receptor in the locus coeruleus. In this study, dexmedetomidine added to ropivacaine for lumbar plexus and sciatic nerve block produced a no less than 50% increase in the duration of sensory block compared with plain ropivacaine. This prolongation of lumbar plexus and sciatic nerve block may be produced by a peripheral mechanism because intravenous infusion of the same dose dexmedetomidine did not caused an extension of peripheral never block duration. The peripheral mechanism also was verified by Brummett et al. in animals [14]. In addition, dexmedetomine may cause contraction of perineural vessel by coupling with alpha-2B adrenergic receptor, reduce the absorption of local anesthetics and then prolong the duration of analgesia. Perineural administration of dexmedetomidine didn't reduce the sensory onset time of ulnar nerve block in Marhofer's study [25], which is in contrast to our research. This may because Marhofer used ultrasound guidance, which decreased the sensory onset time compared with never stimulation used in this investigation.

Sedation without respiratory depression is recognized as superiority of dexmedetomidine in anaesthesia and intensive care medicine. However, side effect associated with dexmedetomidine is not scarce. Dexmedetomidine may cause a dose-related bradycardia, hypotension and excessive sedation when it was used by intravenous injection [26], even perineural administration [15]. In previous study [18], Esmaoglu et al. showed the lower level of BP and HR in dexmedetomidine group (100 μg) from 5 to 90 minutes after injection. Moreover, they observed a high incidence of bradycardia. However, in this study, we found that perineural dexmedetomidine (1 μg/kg) induced to slower HR from 45 to 90 minutes after injection and lower MAP from 45 to 90 minutes. We also observed systemic administration of dexmedetomidine led to slower HR from 10 to 120 minutes after injection and lower MAP from 30 to 120 minutes; nevertheless, none of patients showed bradycardia and hypotension. This may be explained by our smaller dosage of dexmedetomidine than Esmaoglu's protocol. The site of action for sedative effects of dexmedetomidine is locus ceruleus and is mediated by hyperpolarization of noradrenergic neurons thus inhibiting noradrenaline release and inhibiting activity in descending medullospinal noradrenergic pathways. In this research, systemic administration of dexmedetomidine induced to deeper level of sedation from 30 to 120 minutes after injection, and 4 patients led to deep sedation. However, perineural administration of dexmedetomidine led to moderate sedation from 45 to 120 minutes after injection. The reason may be that dexmedetomidine cause contraction of perineural vessel, reduce the speed of absorption of perineural vessel and then reduce the concentration of dexmedetomidine in locus ceruleus [22].

There are some limitations in this research. Firstly, the dosage of dexmedetomidine for lumbar plexus and sciatic nerve block was selected on the basis of previous studies [19, 27]. Up to now, the dose-response study has not been done to assess the optimum dose of dexmedetomidine for lumbar plexus and sciatic nerve

block. Secondly, patients in this study were young and healthy (ASA I-II). It has not been confirmed whether these results were suitable for patients of each age stages or with comorbidities.

Conclusion

In conclusion, the addition of dexmedetomidine (1 μg/kg) to ropivacaine for lumbar plexus and sciatic nerve block could decrease the onset time of sensory and motor block, and prolong the duration of block, and improve postoperative analgesia without significant side-effects.

Disclosure of conflict of interest

None.

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References

[1] Greengrass RA, Klein SM, D'Ercole FJ, Gleason DG, Shimer CL, Steele SM. Lumbar plexus and sciatic nerve block for knee arthroplasty: comparison of ropivacaine and bupivacaine. Can J Anaesth 1998; 45: 1094-6.

[2] Ilfeld BM, Mariano ER, Madison SJ, Loland VJ, Sandhu NS, Suresh PJ, Bishop ML, Kim TE, Donohue MC, Kulidjian AA, Ball ST. Continuous femoral versus posterior lumbar plexus nerve blocks for analgesia after hip arthroplasty: a randomized, controlled study. Anesth Analg 2011; 113: 897-903.

[3] Casati A, Fanelli G, Albertin A, Deni F, Anelati D, Antonino FA, Beccaria P. Interscalene brachial plexus anesthesia with either 0.5% ropivacaine or 0.5% bupivacaine. Minerva Anestesiol 2000; 66: 39-44.

[4] Casati A, Fanelli G, Aldegheri G, Berti M, Colnaghi E, Cedrati V, Torri G. Interscalene brachial plexus anaesthesia with 0.5%, 0.75% or 1% ropivacaine: a double-blind comparison with 2% mepivacaine. Br J Anaesth 1999; 83: 872-5.

[5] Gautier P, Vandepitte C, Ramquet C, DeCoopman M, Xu D, Hadzic A. The minimum effective anesthetic volume of 0.75% ropivacaine in ultrasound-guided interscalene brachial plexus block. Anesth Analg 2011; 113: 951-5.

[6] Vandepitte C, Gautier P, Xu D, Salviz EA, Hadzic A. Effective volume of ropivacaine 0.75% through a catheter required for interscalene brachial plexus blockade. Anesthesiology 2013; 118: 863-7.

[7] Marhofer D, Marhofer P, Triffterer L, Leonhardt M, Weber M, Zeitlinger M. Dislocation rates of perineural catheters: a volunteer study. Br J Anaesth 2013; 111: 800-6.

[8] Aveline C, Le Hetet H, Le Roux A, Vautier P, Gautier JF, Cognet F, Auger P, Bonnet F. Perineural ultrasound-guided catheter bacterial colonization: a prospective evaluation in 747 cases. Reg Anesth Pain Med 2011; 36: 579-84.

[9] Compère V, Rey N, Baert O, Ouennich A, Fourdrinier V, Roussignol X, Beccari R, Dureuil B. Major complications after 400 continuous popliteal sciatic nerve blocks for postoperative analgesia. Acta Anaesthesiol Scand 2009; 53: 339-45.

[10] Ilfeld BM. Continuous peripheral nerve blocks: a review of the published evidence. Anesth Analg 2011; 113: 904-25.

[11] Hutschala D, Mascher H, Schmetterer L, Klimscha W, Fleck T, Eichler HG, Tschernko EM. Clonidine added tobupivacaine enhances and prolongs analgesia after brachial plexus block via a local mechanism in healthy volunteers. Eur J Anaesthesiol 2004; 21: 198-204.

[12] Vieira PA, Pulai I, Tsao GC, Manikantan P, Keller B, Connelly NR. Dexamethasone with bupivacaine increases duration of analgesia in ultrasound-guided interscalene brachial plexus blockade. Eur J Anaesthesiol 2010; 27: 285-8.

[13] Choi S, Rodseth R, McCartney CJ. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials. Br J Anaesth 2014; 112: 427-39.

[14] Brummett CM, Hong EK, Janda AM, Amodeo FS, Lydic R. Perineural dexmedetomidine added to ropivacaine for sciatic nerve block in rats prolongs the duration of analgesia by blocking the hyperpolarization-activated cation current. Anesthesiology 2011; 115: 836-43.

[15] Keplinger M, Marhofer P, Kettner SC, Marhofer D, Kimberger O, Zeitlinger M. A pharmacodynamic evaluation of dexmedetomidine as an additive drug to ropivacaine for peripheral nerve blockade: A randomized, triple-blind, controlled study in volunteers. Eur J Anaesthesiol 2015; 32: 790-6.

[16] Awad IT, Duggan EM. Posterior lumbar plexus block: anatomy, approaches, and techniques. Reg Anesth Pain Med 2005; 30: 143-9.

[17] Dilger JA. Lower extremity nerve blocks. Anesthesiol Clin North Am 2000; 18: 319-40.

[18] Esmaoglu A, Yegenoglu F, Akin A, Yildirim C. Dexmedetomidine Added to Levobupivacaine Prolongs Axillary Brachial Plexus Block. Anesth Analg 2010; 111: 1548-51.

[19] Bharti N, Sardana DK, Bala I. The analgesic efficacy of dexmedetomidine as an adjunct to local anesthetics in supraclavicular brachial plexus block: a randomized controlled trial. Anesth Analg 2015; 121: 1655-60.
[20] Brummett CM, Norat MA, Palmisano JM, Lydic R. Perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. Anesthesiology 2008; 109: 502-11.
[21] Brummett CM, Padda AK, Amodeo FS, Welch KB, Lydic R. Perineural dexmedetomidine added to ropivacaine causes a dose-dependent increase in the duration of thermal antinociception in sciatic nerve block in rat. Anesthesiology 2009; 111: 1111-9.
[22] Wang CG, Ding YL, Han AP, Hu CQ, Hao S, Zhang FF, Li YW, Liu H, Han Z, Guo DL, Zhang ZQ. Adding dexmedetomidine to ropivacaine for lumbar plexus and sciatic nerve block for amputation of lower limb in high-risk patient-a case report. Int J Clin Exp Med 2015; 8: 14184-7.
[23] Gabriel JS, Gordin V. Alpha 2 agonists in regional anesthesia and analgesia. Curr opin Anaesthesiol 2001; 14: 751-3.
[24] Guo TZ, Jiang JY, Buttermann AE, Maze M. Dexmedetomidine injection into the locus ceruleus produces antinociception. Anesthesiology 1996; 84: 873-81.
[25] Marhofer D, Kettner SC, Marhofer P, Pils P, Weber M, Zeitlinger M. Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: a volunteer study. Br J Anaesth 2013; 110: 438-42.
[26] Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effect of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000; 93: 382-94.
[27] Rancourt MM, Albert NT, Cote M, Letourneau DR, Bernard PM. Posterior tibal nerve sensory blockade duration prolonged by adding dexmedetomidine to ropivacaine. Anesth Analg 2012; 115: 958-62.