Local and Regional Anesthesia

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CLINICAL TRIAL REPORT

Perineural Dexamethasone is More Efficient Than Perineural Dexmedetomidine in Prolonging Popliteal Sciatic and Saphenous Nerve Blocks: A Single-Center, Prospective, Double-Blinded, Randomized Controlled Trial

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Purpose: This study aims to assess and compare the effectiveness of perineural dexamethasone (DEX) and perineural dexmedetomidine (DEM) as adjuvant in popliteal sciatic and saphenous nerve blocks, focusing on the duration of analgesia and side effects following major foot and ankle surgeries.

Patients and Methods: Ninety patients scheduled for major foot and ankle surgeries under general anesthesia, who received popliteal sciatic and saphenous nerve blocks, were randomly assigned to one of three groups: (1) control group receiving 0.375% ropivacaine; (2) DEX group receiving 0.375% ropivacaine combined with 10 mg perineural dexamethasone; (3) DEM group receiving 0.375% ropivacaine combined with 0.75 μg/kg perineural dexmedetomidine. The primary outcome measured was the duration of analgesia, defined as the time from the administration of the nerve block to the onset of the first pain sensation in the surgical area. Secondary outcomes included opioid consumption within the first 48 hours post-surgery and the incidence of side effects such as hypotension and bradycardia. (Clinical trial registration number: ChiCTR2100048127).

Results: The time until the first perception of pain was significantly extended in the DEX group (28.0 (3.3) hours) compared to the DEM group (24.1 (1.3) hours) and the control group (17.5 (3.5) hours, P<0.001). Additionally, opioid consumption within the first 24 hours was markedly reduced in both the DEX and DEM groups compared to the control group (P<0.001). However, opioid usage between 0 to 48 hours post-surgery showed no significant differences among the three groups. The DEM group experienced a higher incidence of hypotension and bradycardia compared to both the DEX and control group (P<0.001).

Conclusion: Both 10 mg dexamethasone and 0.75 μg/kg dexmedetomidine effectively prolonged analgesia in patients undergoing major foot and ankle surgery with a popliteal sciatic and saphenous nerve block. However, dexamethasone (10 mg) provided a significantly longer duration of analgesia compared to dexmedetomidine (0.75 μg/kg).

Trial Registration: Chictr.org.cn identifier: ChiCTR2100048127.

Keywords: foot and ankle surgery, nerve block, dexamethasone, dexmedetomidine

Key Point Summary

- Question: Which adjuvant, dexamethasone or dexmedetomidine, is more effective in prolonging the duration of peripheral nerve block for foot and ankle surgery?
- Findings: This randomized controlled trial demonstrated that dexamethasone is more effective than dexmedetomidine in extending the duration of analgesia for foot and ankle surgery.

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- Meaning: Dexamethasone is superior perineural adjunct for popliteal sciatic and saphenous nerve blocks in terms of analgesic duration.

Introduction

Major foot and ankle surgery are often accompanied by severe postoperative pain.[1,2] Peripheral nerve block (PNB) with local anesthetics is effective and is advantageous for reducing postoperative pain, overall opioid consumption and the rate of opioid-related adverse effects.[3] Nevertheless, the duration of single-injection PNBs is short, hence, many adjuvants have been successfully used to augment the analgesic effect.

Both perineural dexamethasone (DEX), a potent long-acting glucocorticoid with minimal mineralocorticoid activity, and dexmedetomidine (DEM), an alpha-2 adrenoreceptor agonist, have been recognized as effective adjuncts to local anesthetics for prolonging the analgesic duration of PNB.[3–5] Numerous studies have examined the utility of DEX[6–8] and DEM[6,9,10] as adjuvants in PNB. However, the majority of these studies have focused on brachial plexus and trunk nerve blocks, leaving a gap in the literature regarding the comparative effects of perineural dexamethasone verse dexmedetomidine, particularly in the context of lower limb surgeries.

To address this gap, we conducted a prospective, randomized, double-blinded, controlled clinical trial, aiming to assess the postoperative analgesic efficacy of dexmedetomidine versus dexamethasone when combined with 0.375% ropivacaine for popliteal sciatic and saphenous nerve blocks in patients undergoing major foot and ankle surgeries.

The primary objective of this study was to determine the effects of dexamethasone and dexmedetomidine on the duration of analgesia in patients receiving combined popliteal sciatic and saphenous nerve blocks as part of their foot and ankle surgical procedure. Our hypothesis was that perineural administration of dexamethasone would result in a longer duration of analgesia compared to perineural dexmedetomidine.

Methods

Study Design and Participants

This single-center, double-blinded, randomized controlled study comprised three parallel groups and adhered to the Helsinki Declaration. Approval was granted by the Institutional Ethics Committee of Beijing Tongren Hospital (NO. TRECKY2021-054), and the trial was registered at the Chinese Clinical Trial Registry before patient enrollment (ChiCTR2100048127, http://www.chictr.org.cn/showproj.aspx?proj=129550, date of registration: July 3, 2021). Informed consent was obtained from each participant. The study enrolled patients (age 18–75, American Society of Anesthesiologists (ASA) physical status I–III) scheduled for foot and ankle surgery. Exclusion criteria included contraindications to regional anesthesia (coagulation disorder, puncture site infection, allergy to general or local anesthetics), BMI <18 kg/m^2 or > 35 kg/m^2, neuropathy or reduced sensation in the sciatic or femoral nerves, renal dysfunction (creatinine > 1.2 mg/dL), poorly controlled diabetes (fasting glucose > 11 mmol/L), Charcot osteoarthropathy, pathological sinus node syndrome, severe bradycardia (HR< 50 bpm), chronic steroid use for 10 days or longer anytime during the past year or systemic glucocorticoid therapy within 24 hours of surgery, daily opioid use and dementia or psychiatric illness.

Randomization and Blinding

A computer-generated random number sequence allocated participants into three groups (1:1:1). Opaque, sealed envelopes labeled with randomization numbers were kept securely. An investigator not involved in outcome assessments managed enrollment and allocation. Eligible participants were randomized before the surgery using the next numbered envelope in sequence. A nurse, blinded to group assignments, prepared the study drugs in identical syringes: The placebo syringe contained 15 mL of 7.5 mg/mL (112.5 mg) ropivacaine diluted in isotonic sodium chloride for a total volume of 30 mL. The DEX syringe contained 15mL of 7.5mg/mL (112.5 mg) ropivacaine and 2mL of 5 mg/mL (10 mg) dexamethasone diluted in isotonic sodium chloride for a total volume of 30 mL. The DEM syringe contained 15 mL of 7.5 mg/mL (112.5 mg) ropivacaine and 0.75 μg/kg dexmedetomidine diluted in isotonic sodium chloride for a total volume of 30 mL.

No patient received dexmedetomidine or dexamethasone preoperatively. Surgeries were performed by an experienced team. The participants, surgeons, and research staff collecting data remained blinded to group assignments.

Interventions

After establishing i.v. access, standard monitoring (5-lead ECG, noninvasive blood pressure, SpO_2, bispectral index-(BIS)), all patients received 1 mg midazolam and 5 μg sufentanil before the blocks. A specialized research team with over five years of experience in regional anesthesia performed the PNBs.

All regional anesthesia procedures were performed under ultrasound guidance (SonoSite Export, 8–12 MHz linear probe; SonoSite, Bothell, Washington) using a 100-mm needle (Ultraplex; B. Braun, Melsungen, Germany).

Popliteal sciatic nerve block: with the patients in the prone position, the sciatic nerve was localized in the popliteal fossa using a 6–15 MHz linear transducer. Under an in-plane approach, the needle tip was advanced into the paraneural sheath between the tibial and common peroneal nerves. 20 mL of the study medication was then injected, ensuing circumferential spread.

Saphenous nerve block: with the patient in the supine position, a linear transducer was placed at the mid-thigh to identify the saphenous nerve, which appears as a hyperechoic structure anterolateral to the femoral artery. 10 mL of the local anesthetic solution was then administered proximal to the apex of the femoral triangle.

Anesthesia Management and Postoperative Analgesia

All patients received general anesthesia via laryngeal mask and total intravenous anesthesia. Induction involved sufentanil (0.1–0.3 μg/kg), propofol (1–2 mg/kg), and rocuronium (0.6 mg/kg), with propofol and remifentanil maintaining a BIS of 40–60. IV fluids (lactated Ringer's) were administered at 5–7 mL/kg. Mean atrial pressure (MAP) was maintained within 20% of baseline, and ephedrine (6 mg) or atropine (0.5 mg, repeated as needed) was given for hypotension of bradycardia, respectively. After surgery, patients remained in the postanesthesia care unit (PACU) for at least 30 minutes. The integrity of sciatic and saphenous blocks was verified by sensory testing; no patients received preemptive pain medication before pressing the PCIA pump.

The postoperative supplemental analgesia protocol was standardized as follows: the patient-controlled IV analgesia (PCIA) pump containing 1.5 μg/kg sufentanil plus 12 ondansetron in 100 mL was provided to each patient for 48 hours postoperatively (2 mL bolus, 15-minute lockout, 10 mL/ hour maximum, without any baseline infusion). Flurbiprofen axetil (100 g twice daily) was administered after the first PCIA bolus. For uncontrolled pain (NRS>5) or intolerable PCIA side effects (eg, nausea), oxycodone (5 mg) was available as rescue analgesia.

Data Collection

Pain was assessed at rest with an numeric rating scale (NRS) sacle (0–10) at 0.5,2, 6,12,24,36, and 48 hours post-surgery by a blinded investigator. At 48 hours, patients completed the International Pain Out questionnaires, which evaluates pain intensity, functional interference, side effects, and satisfaction. Fourteen days after the surgery, a blinded investigator checked for any persistent pain or adverse events. Opioid usage at 24 and 48 hours (in intravenous morphine equivalents, IMEs) was automatically recorded by the pump.

Outcomes

The primary outcome of this study was the duration of analgesia, defined as the time from block completion until the first reported pain. Patients were instructed to note this time point and communicate it via a dedicated cellphone number. The secondary outcomes included: time to first opioid request, postoperative pain scores, proportion of patients not requiring rescue analgesia within 24 or 48 hours, PCIA opioid consumption, and responses on the International Pain Outcome Questionnaire.[11] This questionnaire encompasses key aspects of postoperative pain management, including pain intensity, physical and emotional functional interference, side effects, and perceptions of care. Potential complications like sensory deficits, nausea/vomiting, respiratory depression, and bradycardia/ hypotension were monitored.

Sample Size Considerations

Based on preliminary data suggesting a larger prolongation with dexamethasone than dexmedetomidine, 27 patients per group were needed for 90% power at a level of significance of 0.05. Allowing a 10% dropout, we enrolled 30 patients per group.

Statistical Analysis

Data normality was checked via the Kolmogorov–Smirnov test. Depending on distribution, variables are presented as mean (SD), median [interquartile] (range), or number (percentage). One-way ANOVA or Kruskal–Wallis test, followed by post hoc testes or pairwise comparisons with Bonferroni corrections (p<0.017), were used as appropriate. Kaplan-Meier analysis with Log rank testing assessed time-to-event data. Categorical variables were compared using chi-square tests or Fisher's exact test. Analyses followed the intention-to-treat principle via SPSS (version 25; SPSS, Inc., Chicago, IL, USA).

Results

Patient Characteristics

A total of 164 patients from Jan 2022 to July 2022 were assessed for eligibility to participate in this study. Thirty-three patients who did not meet the inclusion criteria were excluded. Ultimately, 90 patients were randomized and successfully completed the study protocol successfully (Figure 1). The demographic and intraoperative characteristics were similar across the groups (Table 1).

Primary Outcome

Patients who received perineural DEX had longer time to the first report of pain after PNB than did those in the DEM group and control group (control group, 17.5 (3.5) h; DEM group, 24.1 (1.3) h; and DEX group, 28.0 (3.3) h group; P<0.001) (Table 2). The Kaplan-Meier curves for the primary outcome for patients across groups are shown in Figure 2. The Log rank test also suggested prolongation of the time to first report of pain.

Secondary Outcomes

Time to First Analgesic Request

As shown in Table 2, the mean time to first analgesic request was longer in the DEX group than in the DEM group (31.5 (4.1) h vs 27.2 (3.0) h, P<0.001), and the difference between the control group (20.0 (3.6) h) and the DEX (P<0.001) and DEM (P<0.001) groups was also significant. Twenty-two patients (73.3%) in the control group requested their first analgesic in the first 24 h postoperatively, whereas only 2 patients (6.7%) in the DEX group and 5 patients (16.7%) in the DEM group requested their first analgesic within 24 h postoperatively (P<0.001). No patients in the three groups requested any analgesics in the PACU.

Pain Scores

Difference in pain scores across the three groups was significant only 24 hours after surgery (P<0.001). The actual values at different time points are shown in Supplemental Table 1. The modified rebound pain score (MRPS), the worst pain score during the first 24 hours after surgery minus the lowest score in the PACU, was similar between the DEM group and the control group, but both were significantly higher than that in the DEX group (P<0.001).

Opioid Consumption

Total opioid consumption 24 hours after surgery significantly differed between the control group and the DEX and DEM groups (P<0.001). However, these parameters were similar at 48 hours after surgery among the three groups (P=0.992). Opioid consumption was similar between the DEX group and the DEM group within 24 hours (P=0.419) and 48 hours (P=0.088) postoperatively.

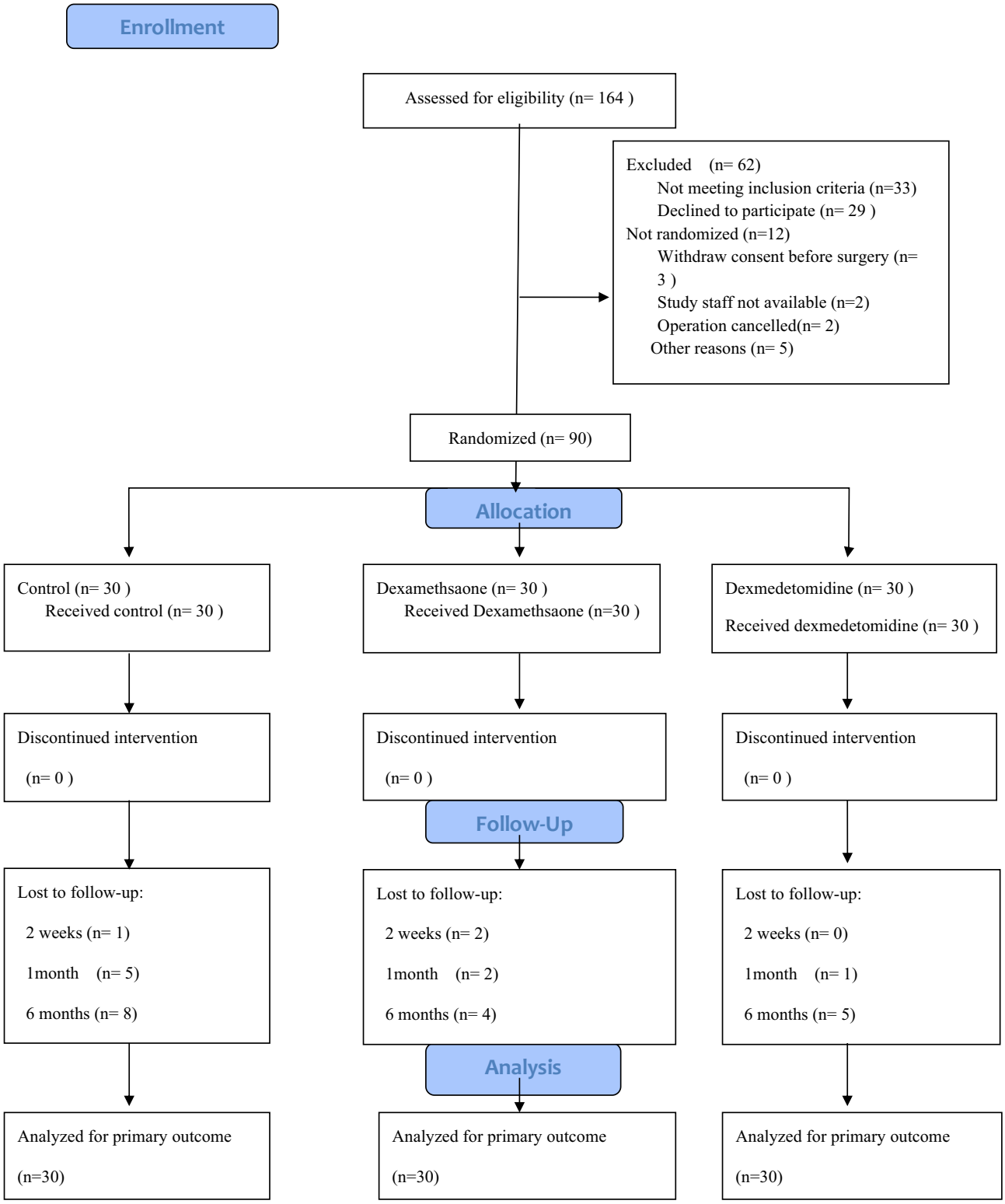

Figure 1 CONSORT flow chart.

Hemodynamic Variables

A comparison of the perioperative hemodynamic variables at different time points are shown in Supplemental Table 2. Heart rate was significantly lower in the DEM group than in the DEX group and control group after intubation (P=0.009) and thereafter.

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Table 1 Demographic and Perioperative Characteristics by Randomization Group

Baseline Characteristics	Control Group	DEX Group	DEM Group
Number, n	30	30	30
Male	10 (33.3%)	8 (26.7%)	9 (30%)
Age, y	53.9 (15.3)	50.8 (13.4)	54.5 (12.6)
Weight, kg	64.8 (11.7)	66.5 (11.2)	67.3 (12.3)
Height, cm	162.1 (7.3)	166.6 (7.0)	163.3 (6.9)
BMI, kg/m^2	24.1 (3.8)	24.9 (4.5)	25.4 (3.2)
ASA physical status			
I	15 (50%)	14 (46.7%)	8 (26.7%)
II	12 (40%)	12 (40%)	21 (70%)
III	3 (10%)	4 (13.3%)	1 (3.3%)
Comorbidities			
Asthma/ COPD	0	1 (3.3%)	1 (3.3%)
Hypertension	6 (20%)	7 (23.2%)	7 (23.3%)
Coronary artery disease	1 (3.3%)	1 (3.3%)	3 (10%)
Diabetes mellitus	2 (6.6%)	2 (6.6%)	1 (3.3%)
Smoker	2 (6.6%)	0	1 (3.3%)
Hyperlipidemia	2 (6.6%)	2 (6.6%)	3 (10%)
Anxiety	1	3 (10%)	2 (6.6%)
Chronic pain	7 (23.3%)	6 (20%)	10 (33.3%)
PNB parameters			
Failed PNBs	0	0	0
Duration of PNB procedure, min	6.5 [4,7]{5,11}	6.7 [5,8]{4,12}	5 [5,6]{5,10}
Duration between the completion of PNB and induction, min	25.6 (10.8)	23.7 (11.7)	24.8 (11.0)
Duration between the completion of PNB and incision, min	33.0 (11.8)	31.0 (11.9)	34.4 (12.5)
Operative parameter			
Type of surgery			
Ankle arthroplasty	3 (10%)	2 (6.7%)	2 (6.7%)
Ankle arthrodesis	4 (13.3%)	6 (20%)	2 (6.7%)
Hallux valgus	15 (50%)	12 (40%)	16 (53.3%)
Subtalar arthrodesis	3 (10%)	4 (13.3%)	3 (10%)
Triple arthrodesis	5 (16.7%)	6 (20%)	7 (23.3%)
History of affected limb surgery	1 (3.3%)	3 (10%)	2 (6.7%)
Length of surgery, min	68.5 [50,92]{33,197}	72.5 [60,95]{30,180}	67.8 [72,100]{45,130}

Notes: Values are expressed as the mean (standard deviation), median (interquartile range){range}, or count (percent).
Abbreviations: DEX, dexamethasone; DEM, dexmedetomidine; BMI, body mass index; ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease.

Table 2 Primary and Secondary Outcome Data by Study Group

	Control Group	DEX Group	DEM Group	*p*-value
Time to first pain, h	17.5 (3.5)	28.0 (3.3) *	24.1 (1.3) *	<0.001#
Time to first analgesic request, h	20.0 (3.6)	31.5 (4.1) *	27.2 (3.0) *	<0.001#
NRS profile				
AUC- NRS $_{0–24\ h}$	42 [24, 57]{0,144}	0 [0,12]{0,96}*	0 [0,39] {0,96}*	<0.001
AUC- NRS $_{0–48\ h}$	72 [24, 72]{0,268}	72 [40,110]{24,192}	70 [38, 86] {0,188}	0.533
Modified rebound pain score€	3 [2, 4.8] {0,10}	0 [0,1] {0,8}*	4 [0, 6] {0,8}	<0.001#

(*Continued*)

Table 2 (Continued).

	Control Group	DEX Group	DEM Group	*p*-value
Postoperative opioid consumption				
IME 0–24 h total, mg	3.0 [0, 6.2]{0,15.2}	0 [0, 0]{0,0.9}*	0 [0, 0.9]{0,7.6}*	<0.001
IME 0–48 h total, mg	9.5 [1.6,15.4] {0.8,29.6}	7.8 [2,14.6] {0.7,28}	8.9 [1.2,10.2] {0.8,32.1}	0.992
Patients not requiring analgesia during the 0–24 h	8 (26.7%)	28 (93.3%)*	25 (83.3%)*	<0.001
Patients not requiring analgesia request during the 0–48 h	1 (3.3%)	5 (16.7%)	3 (10%)	0.183
Hemodynamic adverse events				
Hypotension, n	6 (26.7%)	5 (16.7%)	11 (36.7%)	0.144
Bradycardia, n	2 (6.7%)	3 (10%)*	13 (43.3%)*	0.001
Hemodynamic medications				
Ephedrine, mg	0 [0,0]{0,18}	0 [0,0]{0,12}	0 [0,6]{0,18}	0.170
Atropine, mg	0 [0,0]{0,1}	0 [0,0]{0,0.5}	0 [0,0.5]{0,1}*	<0.001#

Notes: Values are expressed as the mean (standard deviation), median [interquartile range]{range}, or count (percent). €, MRPS, modified rebound pain score, equal to the highest NRS pain score reported in the first 24 hours after PNB minus the lowest NRS score in the PACU.[12] PIOC, pain intensity and opioid consumption, represented as % difference; IME, intravenous morphine equivalents, represented as mg; IME, intravenous morphine equivalents, opioid consumption during the period was recorded for each participant and converted to intravenous morphine equivalents (IMEs). *Statistically significant different compared to the Control group. #Statistically significant difference between the DEX vs DEM groups.

Abbreviations: Dex-PN, dexamethasone perineurally; Dex-IV, dexamethasone intravenously; NRS, numeric rating scales; PACU, postanesthesia care unit; AUC, area under the curve.

Although the incidence of intraoperative hypertension was greater in the DEM group (36.7%), the difference among the three groups was not significant (P=0.144), nor was the difference in the use of ephedrine intraoperatively (P=0.170). The incidence of bradycardia was much greater in the DEM group (43.3%) than in the control (P=0.001) and DEX (P=0.007) groups.

The Pain Outcome Questionnaire

Table 3 shows that the International Pain Outcome Questionnaire profiles included pain intensity, patient satisfaction and other side effects, and no significant differences existed among the three groups.

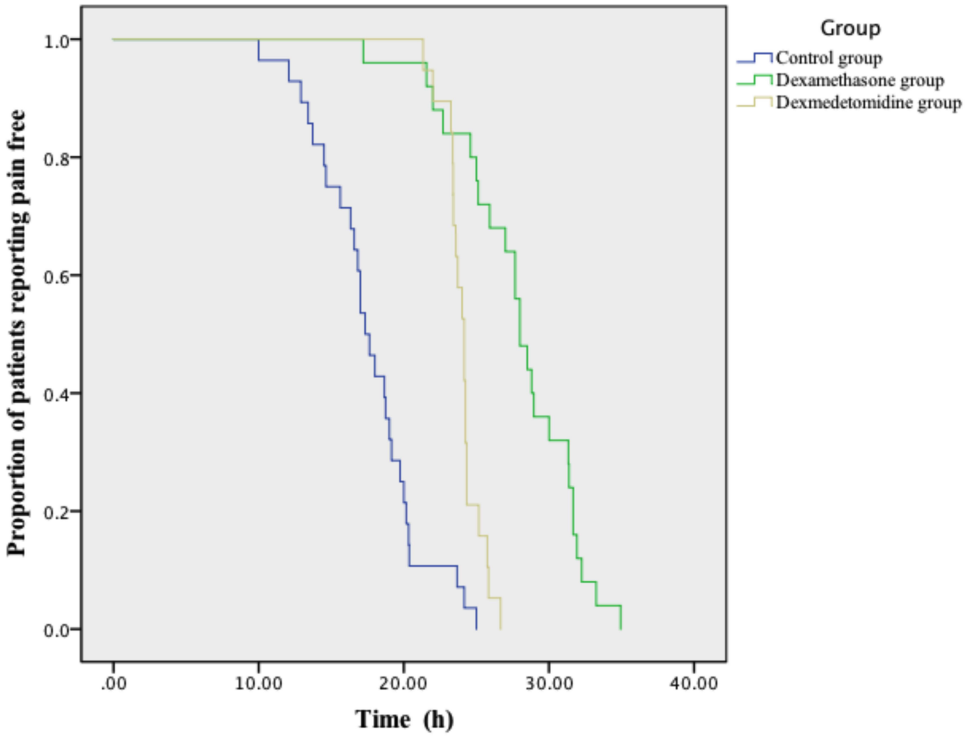

Figure 2 Kaplan-Meier survival plot showing the proportion of patients remaining pain-free over time in the three groups. *P* <0.001 between the control group and the other groups. *P*<0.001 between the dexamethasone group and the dexmedetomidine group.

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Table 3 Descriptive Statistics of Items from the International Pain Outcomes Questionnaire

Baseline Characteristics	Control Group	DEX Group	DEM Group	*p*-value
Postoperative day 2 Pain Outcomes Questionnaire score				
Intensity				
Worst pain [a]	6.2 (4.8,7.2)	6.5 (5.0,7.8)	7.0 (5.7,9)	0.183
Percent time in severe pain [b]	35 [20,40]{10,80}	20 [10,30]{10,50}	20 [10,40]{10,60}	0.461
Percent pain relief [b]	70 [30,50]{5,80}	90 [55,30]{10,90}	90 [70,90]{50,90}	0.857
With activities in bed [a]	0 [0,3]{0,7}	1 [0,4]{0,6}	0 [0,2]{0,5}	0.518
With breathing/coughing [a]	0 [0,0]{0,4}	1 [0,2]{0,6}	0 [0,0]{0,1}	0.619
With sleep [a]	0 [0,3]{0,7}	1 [0,4]{0,8}	0 [0,3]{0,8}	0.418
Effect on emotions				
Anxiety [a]	0 [0,4]{0,6}	0 [0,3]{0,9}	0 [0,1]{0,8}	0.241
Helplessness [a]	0 [0,3]{0,9}	0 [0,2]{0,4}	0 [0,1]{0,5}	0.266
Side effects				
Respiratory depression	0	0	0	1
Acute urinary retention	0	1 (3.3%)	0	1
Nausea [a]	2 [0,4]{0,9}	0 [0,2]{0,4}	0 [0,3]{0,8}	0.167
Vomiting	6 (20%)	2 (6.6%)	3 (10%)	0.366
Drowsiness [a]	0 [0,2]{0,8}	0 [0,1.5]{0,4}	0 [0,2]{0,3}	0.710
Itching [a]	0 [0,0]{0,1}	0 [0,0]{0,0}	0 [0,0]{0,0}	0.445
Dizziness [a]	0 [0,5]{0,9}	0 [0,2]{0,5}	0 [0,2]{0,3}	0.765
Allowed to participate in decision about pain treatment as much as desired				
	15 (50%)	16 (53.3%)	16 (53.3%)	1
Desire for more treatment	12 (40%)	5 (16.7%)*	4 (13.3%)*	0.042
Overall satisfaction with pain management [a]	9 [7,9]{7,10}	9 [8,10]{5,10}	9 [9,10]{6,10}	0.677
Satisfied with results of pain treatment 0–24 h [a]	9 [8.5,10]{7,10}	10 [9.5,10]{9,10}*	10 [9,10]{7,10}	0.036
Satisfied with results of pain treatment 24–48 h [a]	9 [8,9]{7,10}	9 [9,10]{5,10}	10 [8,10]{6,10}	0.061
Patients reporting chronic pain and receipt of opioids before admission to hospital				
How severe was the chronic pain most of the time?				
	4.8 (3.1,8.4)	5.0 (3.0,7.1)	5.2 (3.3,7.2)	0.819
Worst pain after surgery	7.5 (5.5,7.7)	5.8 (4.4,6.5)	6.2 (4.1,7.0)	0.236
Patients with no report chronic pain and no receipt of opioids before admission to hospital				
Worst pain after surgery	5.2 (4.0,7.4)	5.5 (4.0,6.6)	5.8 (3.8,7.1)	0.752
Postoperative neurologic symptoms§				
2 weeks postoperative	4 (13.3%)	8 (26.7%)	6 (20%)	0.429

Notes: Data are expressed as the median [IQR]{range}, mean (95% CI), or count (percent). [a]Assessed using a 0–10 numerical rating scale scale. [b]Assessed using a percentage scale. *Statistically significant different compared to the Control group. §The postoperative neurologic symptoms include any one or more cases of transient or persistent numbness or paresthesia anywhere in the surgical limb, or pain or weakness in the foot or ankle.

Abbreviations: DEX, dexamethasone; DEM, dexmedetomidine; 95% CI, 95% confidence interval; AUC, area under the curve.

Discussion

In this randomized, controlled study, we found that the addition of 10 mg of dexamethasone to 0.375% ropivacaine for popliteal sciatic nerve and saphenous nerve blocks could prolong the duration of analgesia and decrease the incidence of side effects to a greater extent than could the addition of 0.75μg/kg of dexmedetomidine perineurally. Both dexamethasone and dexmedetomidine administration were associated with decreased opioid consumption during the first 24 hours postoperative.

Adjuvants have been used to prolong the analgesic duration of single-injection PNBs and to decrease the incidence of dose-dependent side effects because of their synergistic effects. A variety of medications, including opioids, epinephrine, corticosteroids, α-2 adrenergic receptor agonists, and magnesium sulfate have been investigated for this purpose. However, none of these medications have been found to fulfill all the criteria necessary for an ideal local anesthetic adjuvant. Among the various adjuvants tested, dexamethasone and dexmedetomidine have shown the most promising effects. A considerable number of studies have been conducted on different types of PNBs, such as supraclavicular,[13] interscalene,[14] axillary,[15] interfascial,[9] ulnar nerve blocks,[16] and erector spine plane blocks.[9] Despite this, there is a notable lack of research on popliteal sciatic nerve and saphenous nerve blocks in human subjects. The findings from upper limb blocks and trunk blocks may not be directly applicable to the lower extremity for two primary reasons. First, the efficacy of adjuncts in peripheral nerve blocks can be influenced by site-specific anatomical variations. A previous study indicated that there are differences in systemic absorption of perineural anesthetics between less vascular areas, such as the popliteal sciatic and saphenous nerves, and more vascular areas, like the brachial plexus.[17] This was confirmed by Sehmbi et al,[3] who stratified previous studies based on the location of the block and found inconsistent results between upper and lower limb blocks. Second, the intensity of postoperative pain and surgical inflammation can vary significantly across different surgical populations. For instance, patients undergoing major foot and ankle surgery experience much more severe pain and inflammation compared to those having shoulder arthroscopic surgery,[14,15,18] however, such differences in pain intensity are not observed in volunteer studies,[19,20] which limits the clinical application of findings from these volunteer-based investigations.

A meta-analysis encompassing 100 trials (involving 5728 patients) and a range of local anesthetic adjuncts found that dexamethasone significantly extends the duration of analgesia compared to dexmedetomidine.[3] This finding was corroborated by a subsequent review.[5] Consistent with these reports, our study also observed that both the time to first onset of pain and the time to first analgesic request were markedly longer in the DEX group compared to the DEM group. It is important to note that while the prolonged analgesia achieved with adjuvants is beneficial, it should be balanced against the potential drawback of an extended motor block that could hinder early ambulation after certain surgical procedures, such as knee replacement surgery.[6,10] Nonetheless, in our study, the majority of patients opted for plaster immobilization postoperatively, which they perceived as necessary to ensure sufficient time for proper healing of bones and tissues.

Our findings indicated that the modified rebound pain score (the highest NRS score minus the lowest score in the PACU) was significantly lower in the DEX group compared to both the control and DEM groups. This is agreement with previous studies[12,13,21] and may be attributed to the impact of dexamethasone on the duration of PNB. Patients in the DEX group enjoyed approximately 28 additional hours of pain relief due to the prolonged effect of a single-injection PNB. These results suggest that the inclusion of dexamethasone in PNB may effectively reduce the incidence of rebound pain.

Consistent with Xiao's study,[10] which showed that the addition of 0.5 μg/kg of dexmedetomidine to ropivacaine for femoral nerve block decreased the total morphine consumption in the first 24 hours, we also found a significant reduction in opioid use in the DEX and DEM groups compared to the control group within the initial 24 hours post-surgery. However, at the 48-hour mark, the difference in opioid consumption among the three groups did not reach statistical significance, which may be a consequence of the relatively modest sample size of our study.

In determining the doses of our adjuncts, we referred to the existing human and animal literature at the time of study design. The optimal dose of dexamethasone is a topic of debate, Kirkham et al[22] demonstrated a ceiling effect of dexamethasone at 4 mg, while several dose-response studies have shown that larger doses of perineural dexamethasone (8 to 10 mg) were more effective than small doses (4 to 5 mg).[23,24] Hence, we empirically used 10 mg of dexamethasone as previously reported.[6–8] The ideal adjuvant dose is 1μg/kg of dexmedetomidine,[4,19,25] which has been used in axillary blocks,[19] infraclavicular blocks,[26] erector spine blocks,[27] and femoral nerve blocks.[25] However, considering the potential for synergistic hypotensive effects following tourniquet deflation during lower extremity surgery, particularly in older patients with cardiovascular comorbidities, we chose a more conservative dose of 0.75 μg/kg of dexmedetomidine. Further research is necessary to establish the ideal dose of perineural dexmedetomidine that balances optimal efficacy with minimal toxicity.

In our study, transient hypotension and bradycardia occurred significantly more frequently in the DEM group than in the DEX and control groups, but no patients needed treatment with atropine or ephedrine postoperatively, which coincided with previous studies[4,20] and was in accordance with the pharmacological properties of dexmedetomidine and alpha 2 adrenergic receptors.[6]

No significant differences were observed among groups in terms of the International Pain Outcomes Questionnaire, a well-validated tool designed to evaluate the postoperative pain management.[11,28,29] Satisfaction scores were uniformly high across all groups, making it challenging to detect any statistically significant difference. However, there was a trend towards higher satisfaction in the DEX and DEM groups. This can be attributed to the fact that over 80% of patients in these adjuvant groups did not require analgesics within the first 24 hours and were able to enjoy uninterrupted, restful sleep throughout the night, which likely contributed to a delay in the onset of pain.

Current evidence indicates that dexamethasone provides a longer duration of analgesia than dexmedetomidine. Consequently, it would be reasonable to consider using dexamethasone as an adjuvant to peripheral nerve blocks when the objective is to prolong the analgesic effect. Since perineural dexamethasone use is off-label, clinicians should obtain regulatory approval before use.

Our study has several limitations. Firstly, we did not evaluate the risk of nerve injury associated with the use of the two adjuvants. The reported incidence of postoperative neuropathic complications is relatively low, with one recent large cohort study citing a rate of 8.1%,[30] and Nori reporting a rate of 10% at one year after popliteal block.[31] Given the size of our sample, we were underpowered to detect any differences in long-term nerve complications between the groups. Moreover, preclinical studies have indicated that both dexamethasone[32] and dexmedetomidine[33] may have local anti-inflammatory effects and potential neuroprotective properties Secondly, this study was conducted at a single institution, which may limit the generalizability of our findings to patients undergoing other surgical procedures or populations with different characteristics. Thirdly, the minimum length of stay in our study was 48 hours, so our results may not be directly applicable to patients undergoing ambulatory surgery. Fourthly, the administration of dexmedetomidine and dexamethasone in our study was off-label and not approved by the United States Food and Drug Administration. Nonetheless, these medications are widely used internationally and have been the subjects of numerous clinical trials. Fifthly, the analgesic equivalence between dexamethasone 10 mg and dexmedetomidine 0.75 μg/kg is uncertain. These doses were chosen based on clinical practice and available literature; however, they may not represent equipotent analgesic effects and may influence the interpretation of comparative outcomes. Lastly, our primary outcome, "time to first pain", may introduce potential biases. Although it serves as a proxy for the duration of the sensory nerve block, it could overestimate the actual block duration, particularly if the block dissipates during the night when patients may not awaken until pain reaches a certain threshold. However, this potential bias should be equally distributed across the dexamethasone and the dexmedetomidine groups, thus not affecting the comparative outcomes of the two adjuvants.

Conclusion

Both 10 mg dexamethasone and 0.75 μg/kg dexmedetomidine effectively prolonged analgesia in patients undergoing major foot and ankle surgery with a popliteal sciatic and saphenous nerve block. However, dexamethasone (10 mg) provided a significantly longer duration of analgesia compared to dexmedetomidine (0.75 μg/kg).

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author (Dr.Guyan Wang) or the first author (Dr. Guiyu Lei) upon reasonable request. Please contact the corresponding author (guyanwang2006@163.com) or the first author (zp1643@163.com) for inquiries regarding data access.

Ethics and Consent Statements

Ethical approval for this study (NO.TRECKY2021-007) was approved by the Ethics Committee of Beijing Tongren Hospital, Beijing, China (Chairperson Prof Yan Liu) on 29 June 2021. This trial was registered before patient enrolment at the Chinese Clinical Trial Registry (No. ChiCTR2100048127). This prospective randomized controlled clinical study was conducted from January 2022 to January 2023 at Beijing Tongren Hospital. All participants provided informed consent and they were treated in accordance with the tenets of the Declaration of Helsinki.

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Disclosure

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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