Randomised Controlled Trial

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Effect of ultrasound-guided femoral nerve block with dexmedetomidine and ropivacaine on postoperative analgesia in patients undergoing total knee arthroplasty: a randomized controlled trial

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Background: Dexmedetomidine, a potent and highly selective α2-adrenoreceptor agonist, has become a popular adjuvant to local anesthetics. This study was designed to investigate the effect of dexmedetomidine with ropivacaine for femoral nerve block on postoperative analgesia after total knee arthroplasty.

Methods: Forty-six patients after total knee arthroplasty received ultrasound-guided femoral nerve block with either 0.3% ropivacaine alone (group R) or 0.3% ropivacaine with 0.5 μg/kg dexmedetomidine (group RD). Total 24-h sufentanil consumption, visual analogue scale (VAS) pain scores, frequency of patient-controlled analgesia (PCA) pressed, Ramsay sedation score, the incidence of bradycardia and hypotension, and incidence of postoperative nausea and vomiting (PONV) were recorded.

Results: Compared to group R, the total 24-h sufentanil consumption was significantly reduced (110.76 ± 11.56 vs. 99.09 ± 13.31; $P < 0.05$), the VAS scores were lower at 10 and 12 h postoperatively [3(2–3) vs. 2(1–2) and 3(2–3) vs. 2(1–3), respectively; $P < 0.05$], the frequency of PCA pressed was lower at 8–12 and 12–16-h time intervals [(5(3–6) vs. 2(1–3) and 4(3–4) vs. 2(1–3), respectively; $P < 0.05$]. However, there were no differences in Ramsay's sedation score and the incidence of PONV. Also, no patient experienced bradycardia and hypotension.

Conclusions: 0.5 μg/kg dexmedetomidine with 0.3% ropivacaine for femoral nerve block significantly decreased the total 24-h sufentanil consumption, prolonged and enhanced the analgesic efficacy of ropivacaine, without clinically relevant cardiovascular depression or over-sedation in patients undergoing total knee arthroplasty.

Keywords: dexmedetomidine, femoral nerve block, postoperative analgesia, ropivacaine

Introduction

Total knee arthroplasty (TKA) is considered the gold treatment for end-stage knee osteoarthritis, as it provides considerable benefits in terms of quality of life, pain relief, and functional recovery[1]. Unfortunately, it has been reported that patients undergoing TKA suffer ~60% severe and 30% moderate pain postoperatively; patients even may choose to avoid this surgery when taking this acute postoperative pain into consideration[2]. Moreover, postoperative pain also plays a negative role in rapid postoperative recovery, length of hospital stay, and patient satisfaction[3].

Successful postoperative analgesia is linked to earlier mobilization, shorter length of hospital stay, and lower risk of postoperative complications, as well as better patient satisfaction[4,5]. Patient-controlled intravenous analgesia (PCIA) is an excellent method of postoperative pain relief[6]. To date, opioids are the primary analgesics used in PCIA. Inevitably, the side effects of opioids, such as nausea, vomiting, pruritus, and sedation, may have negative effects on patient comfort and safety as well as delay functional rehabilitation[7]. Thus, it is of great significance to investigate a multimodal analgesia strategy that can minimize the amount usage of opioids.

HIGHLIGHTS

- Ultrasound-guided femoral nerve block (FNB) is an effective component of multimodal analgesia strategy for postoperative analgesia after total knee arthroplasty.
- Dexmedetomidine added to ropivacaine for FNB provides better postoperative analgesia.
- Dexmedetomidine is an ideal adjuvant to ropivacaine for postoperative analgesia.

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Femoral nerve block (FNB), an important complement of the multimodal analgesia strategy, is recommended as the most effective method for postoperative analgesia after TKA[8]. This technique provides excellent postoperative analgesia and reduces opioid consumption[9,10]. Although sciatic nerve block also provides superior analgesia after TKA, it has high technical requirements for operators, especially in obese and elderly patients for deep location[11]. Therefore, FNB is still considered the gold standard for analgesia after TKA. However, as a disadvantage, the short duration of postoperative analgesia provided by single-injection FNB is obvious. Recent studies have demonstrated that adding various adjuvants (e.g. ketamine, fentanyl, dexamethasone, naloxone, and clonidine) to local anesthetics can address this issue[12–16].

Dexmedetomidine is a potent and highly selective α2-adrenergic agonist with sedative, sympatholytic, anxiolytic, and analgesic properties[17]. When added to local anesthetics for various nerve blocks, it can provide a longer duration of analgesia and lower consumption of opioids[18–20]. Under this context, we hypothesized that dexmedetomidine could decrease postoperative sufentanil consumption and increase the analgesic efficacy of ropivacaine when coadministrated with ropivacaine for FNB. Therefore, we designed this study to explore the effect of dexmedetomidine with ropivacaine for FNB on postoperative analgesia after TKA.

Materials and methods

Patients

This prospective randomized study was approved by the Ethics Committee of the First People's Hospital of Lianyungang (LCYJ202010002) and registered at the Chinese Clinical Trial Registry (ChiCTR2000039348) on 24/10/2020. The study was reported in accordance with the rigor of the CONSORT guideline, and all experimental conditions conformed to the Declaration of Helsinki. Patients (45–75 years of age) with American Society of Anesthesiologists (ASA) physical status I–II scheduled for TKA receiving general anesthesia were recruited. Each patient signed an informed consent. Patients with a history of allergy to involved drugs, skin damage, or infection in the ultrasound scan area, severe cardiovascular and respiratory disease, renal or hepatic failure, and inability to communicate were excluded.

Randomization and blinding

Patients were randomized to either ropivacaine (group R) or ropivacaine with dexmedetomidine (group RD) group in a 1:1 ratio according to a computer-generated randomization sequence. The random sequence was generated with sequentially numbered, opaque, and sealed envelopes by an anesthesiologist. Before the performance of FNB, an anesthetic nurse opened a consecutively numbered envelope and prepared the following drug solutions for FNB, that is, 20 ml of 0.3% ropivacaine for group R and 20 ml of 0.3% ropivacaine plus 0.5 μg/kg dexmedetomidine for group RD. The patients, anesthesiologists, surgeons, other nurses, and data collectors were all unaware of the group assignment.

Standard procedure of anesthesia

No patient was premedicated. Once the patient arrived in the operation room, electrocardiogram (ECG), pulse oxygen saturation (SpO_2), blood pressure (BP), and bispectral index (BIS) were monitored. Intravenous (i.v.) access was established and used for drug administration and fluid therapy. General anesthesia was standardized for all patients, and anesthesia was induced with i.v. sufentanil 0.5 μg/kg, propofol 2 mg/kg, and cisatracurium 0.2 mg/kg. After tracheal intubation, mechanical ventilation was initiated with the mode of PVC-VG, and the respiratory rate and tidal volume were regulated to keep the pressure of end-tidal carbon dioxide ($PETCO_2$) at 35–45 mmHg. Anesthesia was maintained using sevoflurane/O_2/air mixture to keep BIS value at 40–60; cisatracurium was administered for muscle relaxation as needed. Patients received tropisetron 5 mg i.v. for postoperative nausea and vomiting after tracheal intubation.

Procedure of ultrasound-guided FNB

FNB was performed postoperatively under the guidance of ultrasound (Philips CX50, Philips Ultrasound, Inc., Bothell, Washington, USA). A 6–13-MHz high-frequency linear probe was placed in the inguinal crease area; the femoral nerve was located laterally to the femoral artery. Moving the probe slightly until the femoral nerve was visualized clearly. Then a 21 G*100-mm insulated needle (UniPlex NanoLine, Pajunk, Geisingen, Germany) was used for the block, and it was advanced using the long-axis in-plane approach. A single dose of 20 ml ropivacaine alone or ropivacaine with dexmedetomidine was slowly injected. After the procedure of the nerve block was completed, extubation was performed when the residual muscular blockade was reversed with 0.04 mg/kg neostigmine and 0.02 mg/kg atropine. Then patients were transferred to the post-anesthesia care unit for further observation.

Postoperative analgesia protocol

An i.v. patient-controlled analgesia (PCA) system was used for postoperative analgesia. The mode of PCA was set to deliver a background infusion of sufentanil 0.04 μg/kg/h (total regimen 2 μg/kg/100 ml). If the VAS > 3 or the patient required at any time, a bolus injection of sufentanil 0.05 μg/kg was given, with a 15-min lockout interval. In the case of the VAS exceeding 3 persistently, an additional 3 μg sufentanil was administrated intravenously.

Outcome measures

Total 24-h sufentanil consumption composed of the PCA delivered and additionally administrated was recorded.

Visual analogue scale (VAS) score (0 = no pain, 10 = worst pain) and Ramsay sedation score (1. patient anxious, agitated, or restless; 2. patient cooperative, oriented, tranquil, and alert; 3. patient responds to commands; 4. asleep, but with brisk response to light glabellar tap or loud auditory stimulus; 5. asleep, sluggish response to light glabellar tap or loud auditory stimulus; 6. asleep, no response) were assessed at 2, 4, 6, 8, 10, 12, and 24 h postoperatively[21].

The frequency of PCA pressed was recorded at 0–4, 4–8, 8–12, 12–16, 16–20, and 20–24-h time intervals postoperatively.

Incidences of bradycardia, hypotension, and postoperative nausea and vomiting (PONV) were recorded for the first 24 h postoperatively.

Hypotension (defined as systolic blood pressure falling >20% from preoperative baseline and/or systolic blood pressure <90 mmHg) was treated with 4–8 μg norepinephrine intravenously. Bradycardia (defined as heart rate falling >20% from preoperative baseline and/or heart rate <50 bpm) was treated with 0.5 mg atropine intravenously.

The primary outcome of the study was the total 24-h sufentanil consumption. The secondary outcomes were the VAS pain score, Ramsay sedation score, frequency of PCA pressed, and incidence of bradycardia, hypotension, and PONV.

Statistical analysis

Our sample size was calculated based on the total 24-h sufentanil consumption. According to a pilot study, the total 24-h sufentanil consumption in group R was 113.7 (22.8). Assuming $\alpha = 0.05$, $\beta = 0.1$ for a 20% difference in total 24-h sufentanil consumption between the two groups, 22 patients in each group were required. Taking a drop-out rate of 10% into consideration, 50 participants were recruited in this study.

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 16.0 (SPSS 16, Chicago, Illinois, USA). All quantitative data were tested for normality by the Shapiro–Wilk test. Normally distributed data were expressed as mean ± standard deviation (SD) and analyzed using an independent two-sample *t*-test. Skewed data were expressed as median (interquartile range, IQR) and analyzed using the Mann–Whitney *U*-test. Categorical data were expressed as numbers (percentages) and analyzed using Pearson's Chi-square test or Fisher's exact test. All tests were two-tailed and statistical significance was considered for $P < 0.05$.

Results

The flowchart is detailed in Figure 1. Among the 50 patients who were assessed for eligibility, 3 did not meet the inclusion criteria, and 1 refused to participate. Consequently, 46 patients were randomized in this study. Patient demographics and duration of operation were comparable between the two groups (Table 1).

The VAS pain scores are shown in Table 2. The VAS pain scores were relatively low in the two groups. Meanwhile, no difference was observed between the two groups at 2, 4, 6, and 8 h postoperatively. However, compared with group R, the VAS pain scores in group RD were lower at 10 and 12 h postoperatively ($P < 0.05$). In addition, Ramsay sedation scores were comparable between the two groups at 2, 4, 6, 8, 10, 12, and 24 h postoperatively (Table 3).

The frequency of PCA pressed are presented in Table 4. Similar to the VAS pain scores, the frequencies of PCA pressed were comparable between the two groups at 0–4, 4–8, 16–20, and 20–24-h time intervals postoperatively. However, the RD group had lower frequencies of PCA pressed than the R group at 8–12 and 12–16-h time intervals postoperatively ($P < 0.05$).

As displayed in Table 5, compared with group R, the total 24-h sufentanil consumption in group RD was lower ($P < 0.05$). Although the incidence of PONV was lower in group RD, no significant difference was observed between the two groups ($P > 0.05$). Besides, no patient experienced hypotension and bradycardia during the first 24 h postoperatively.

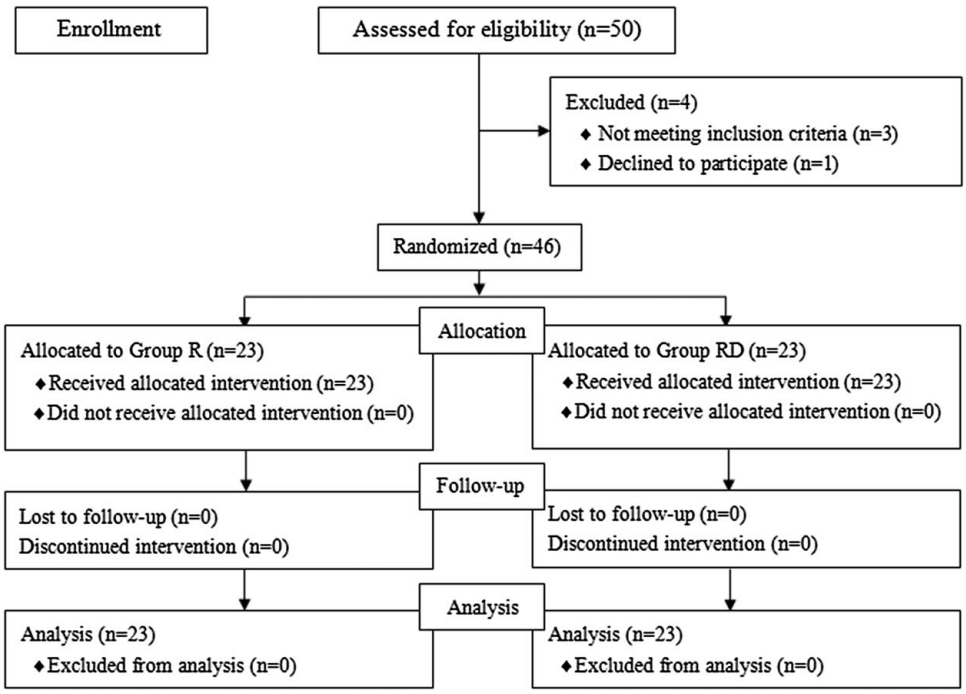

Figure 1. Consolidated standards of reporting trials flow diagram showing the progress of patients through the study. R, ropivacaine; RD, ropivacaine with dexmedetomidine.

Table 1

Patient demographics and duration of operation.

Demographics	Group R ($n=23$)	Group RD ($n=23$)	P
Age (year)	66.7 ± 5.2	67.4 ± 4.8	0.661
Gender, *n* (%)			0.522
Male	6 (26.1)	8 (34.8)	
Female	17 (73.9)	15 (65.2)	
Height (cm)	164.5 ± 6.1	165.1 ± 7.4	0.763
Weight (kg)	71.9 ± 4.2	72.2 ± 4.6	0.816
ASA physical status, *n* (%)			0.475
I	4 (17.4)	6 (26.1)	
II	19 (82.6)	17 (73.9)	
Duration of operation (min)	89.7 ± 9.1	88.4 ± 8.2	0.613

Data are expressed as mean ± SD or number (percentage).
ASA, American Society of Anesthesiologists; R, ropivacaine; RD, ropivacaine with dexmedetomidine.

Discussion

This study demonstrated that dexmedetomidine, when added to ropivacaine for FNB in patients who underwent TKA, significantly reduced the total 24-h sufentanil consumption, prolonged and enhanced the analgesic efficacy of ropivacaine, without clinically relevant cardiovascular depression or oversedation. These findings suggested that dexmedetomidine with ropivacaine for FNB is an effective strategy for postoperative analgesia in patients after TKA.

Dexmedetomidine, a potent and highly selective α2-adrenoreceptor agonist, has been confirmed to be an ideal adjuvant to local anesthetics. Many clinical studies suggested that dexmedetomidine, when added to local anesthetics for various nerve blocks, could provide better postoperative analgesia and reduce postoperative analgesic consumption[22–25]. For femoral nerve block, Li *et al*.[26] reported that adding 1 μg/kg dexmedetomidine to ropivacaine had a significant inhibitory effect on local inflammatory response and showed superior postoperative pain control to ropivacaine alone after TKA. In our study, compared with 0.3% ropivacaine alone, adding 0.5 μg/kg dexmedetomidine to 0.3% ropivacaine for FNB decreased the postoperative VAS pain scores at 10 and 12 h postoperatively and reduced the frequency of PCA pressed 8–12 and 12–16-h time intervals; thus the total 24-h sufentanil consumption was reduced. Our results were in good agreement with the recent study conducted by Yang *et al*.[27], in which they confirmed that 2 μg/kg dexmedetomidine with 0.1% ropivacaine for continuous femoral nerve block preserved quadriceps muscle strength and reduced the total morphine consumption with satisfactory analgesia in patients undergoing TKA.

Although dexmedetomidine has become a popular adjuvant, the exact mechanism of dexmedetomidine for potentiating local anesthetics is still unclarified. Dexmedetomidine may exert systemic effects when administered perineurally due to its absorption and redistribution. In order to clarify this mechanism, Brummett *et al*.[28] demonstrated that the effect of dexmedetomidine to potentiate the analgesic ropivacaine was primarily peripheral in experimental models. In clinical settings, Andersen *et al*.[29] reported that dexmedetomidine exerted a peripheral effect when the systemic effect was controlled in healthy volunteers receiving saphenous nerve block. In another recent study conducted by Jin *et al*., participants after TKA received femoral nerve and sciatic nerve block using ropivacaine, with either 0.5 μg/kg dexmedetomidine perineurally, i.v., or no dexmedetomidine, and the results showed that systemic dexmedetomidine did not prolong the analgesic duration[30]. All these previous findings indicated that the exact mechanism of dexmedetomidine potentiating local anesthetics is peripheral.

In our study, if dexmedetomidine exerted systemic effects, then the Ramsay sedation score and the incidence of bradycardia and hypotension may be higher in group RD. However, our results showed that the Ramsay sedation score was comparable between the two groups, and no patient experienced over-sedation in our study. Furthermore, no patient experienced bradycardia and hypotension during the first 24 h postoperatively. Therefore, our results also indicated that the mechanism of dexmedetomidine potentiating the analgesic efficacy of ropivacaine is peripheral.

PONV are caused primarily due to the use of opioid analgesics, so reducing the opioid consumption may decrease the incidence

Table 2

Postoperative VAS pain scores.

VAS	Group R ($n=23$)	Group RD ($n=23$)	P
2 h	1 (1–2)	1 (1–2)	0.763
4 h	1 (1–2)	1 (1–2)	0.767
6 h	2 (1–2)	2 (1–2)	0.858
8 h	2 (1–2)	2 (1–2)	0.665
10 h	3 (2–3)	2 (1–2)*	< 0.001
12 h	3 (2–3)	2 (1–3)*	0.001
24 h	2 (1–2)	2 (1–2)	0.365

Data are expressed as median (interquartile range).
R, ropivacaine; RD, ropivacaine with dexmedetomidine; VAS, visual analogue scale.
*$P < 0.05$.

Table 3

Postoperative Ramsay sedation scores.

Ramsay	Group R ($n=23$)	Group RD ($n=23$)	P
2 h	2 (2–2)	2 (2–3)	0.091
4 h	3 (2–3)	3 (2–3)	0.810
6 h	2 (2–3)	2 (2–4)	0.645
8 h	3 (2–3)	3 (2–4)	0.549
10 h	4 (3–4)	4 (3–4)	0.861
12 h	4 (3–4)	4 (3–4)	0.636
24 h	3 (2–3)	3 (2–4)	0.356

Data are expressed as median (interquartile range).
R, ropivacaine; RD, ropivacaine with dexmedetomidine.

Table 4

Frequency of PCA pressed at different time intervals.

Frequency of PCA pressed	Group R ($n=23$)	Group RD ($n=23$)	P
0–4 h	1 (0–1)	1 (0–1)	–
4–8 h	0 (0–1)	0 (0–1)	0.561
8–12 h	5 (3–6)	2 (1–3)*	< 0.001
12–16 h	4 (3–4)	2 (1–3)*	< 0.001
16–20 h	1 (1–2)	2 (1–2)	0.151
20–24 h	1 (0–1)	1 (0–1)	0.962

Data are expressed as median (interquartile range).
PCA, patient-controlled analgesia; R, ropivacaine; RD, ropivacaine with dexmedetomidine.
*$P < 0.05$.

Table 5

Postoperative variables during the first 24 h postoperatively.

Postoperative variables	Group R ($n=23$)	Group RD ($n=23$)	P
Total 24 h sufentanil consumption (μg)	110.76 ± 11.56	99.09 ± 13.31*	0.003
PONV, *n* (%)	6 (26.1)	4 (17.4)	0.475
Bradycardia, *n* (%)	0	0	–
Hypotension, *n* (%)	0	0	–

Data are expressed as mean ± SD or *n*(%).

PONV, postoperative nausea and vomiting; R, ropivacaine; RD, ropivacaine with dexmedetomidine.

*$P < 0.05$.

of PONV[31]. Our result showed that the total 24-h sufentanil consumption was reduced in group RD; meanwhile, the incidence of PONV was also lower in group RD than that in group R (26.1 vs. 17.4%). However, we did not determine any significant difference in terms of PONV between the two groups. Our sample size was calculated based on the primary outcome, and the relatively small sample size might be the possible reason that we did not detect the difference in this secondary outcome.

Our study has some limitations. Firstly, we explored only one concentration of dexmedetomidine (0.5 μg/kg); thus, our results may not be appropriate for other different concentrations of dexmedetomidine when added to local anesthetics. Secondly, we did not design an i.v. dexmedetomidine group for comparisons. The presence of such a group could enable us to compare the different effects of dexmedetomidine when administered systemically and perineurally. Thirdly, our trial was one-center designed, so the relatively small sample size may limit the generalizability of our results. Thus, further research is needed to address these limitations.

In conclusion, 0.5 μg/kg dexmedetomidine with 0.3% ropivacaine for femoral nerve block significantly decreased the total 24-h sufentanil consumption, prolonged and enhanced the analgesic efficacy of ropivacaine, without clinically relevant cardiovascular depression or over-sedation in patients undergoing TKA.

Ethical approval

The study was approved by the Ethics Committee of the First People's Hospital of Lianyungang (LCYJ202010002).

Consent

Written informed consent was obtained from the patients for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

C.H. and H.Q.: designed the study, performed the femoral nerve blocks, and wrote the first draft of the manuscript; H.L., P.Z., and X.Z.: analyzed the data and interpreted the results; H.L. and Z.Z.: revised the manuscript. All authors read and approved the final manuscript.

Conflicts of interest disclosure

The authors reported no conflicts of interest in this study.

Research registration unique identifying number (UIN)

1. Name of the registry: Chinese Clinical Trial Registry
2. Unique identifying number or registration ID: ChiCTR 2000039348.
3. Hyperlink to your specific registration (https://www.chictr.org.cn/index.html) The recruitment of the study has been completed.

Guarantor

Hengfei Luan.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Provenance and peer review

The paper was not invited.

Additional information

No additional information is available for this paper.

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