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Original article

Local infiltration analgesia versus femoral nerve block in total knee arthroplasty: A meta-analysis



X.-D. Yun¹, X.-L. Yin¹, J. Jiang¹, Y.-J. Teng, H.-T. Dong, L.-P. An, Y.-Y. Xia*

Department of Orthopaedics, Orthopaedics Key Laboratory of Gansu Province, Second Hospital of Lanzhou University, No. 82 Cuiyingmen, Chengguan District, Lanzhou, Gansu, PR China

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ABSTRACT

Introduction: Local infiltration analgesia (LIA) and femoral nerve block (FNB) are both used for the pain management after total knee arthroplasty (TKA). Controversy still remains regarding the optimal technique for pain relief in patients undergoing TKA. The purpose of this meta-analysis was to compare the analgesia achieved with LIA and the one from FNB following TKA.

Hypothesis: LIA achieves better pain control than FNB in patients with TKA.

Methods: Databases, including Pubmed, EMBASE, the Cochrane Library and Web of Science were comprehensively searched to identify studies comparing LIA with FNB for patients with TKA. Two reviewers independently selected trials, extracted data, and assessed the methodological qualities of included studies. Data were analyzed by RevMan 5.2.

Results: Nine RCTs involving 782 patients were included. LIA achieved more rapid pain relief (VAS) at 6 h postoperatively [SMD_{6h} = -0.92, 95% CI (-1.38, -0.47)] than FNB. There were no significant differences at 24 h and 48 h [SMD_{24h} = -0.03, 95% CI (-0.46, 0.40); SMD_{48h} = 0.28, 95% CI (-0.35, 0.91)], VAS with activity at 24 h and 48 h [SMD_{6h} = -0.54, 95% CI (-1.62, 0.54); SMD_{24h} = -0.22, 95% CI (-1.41, 0.96); SMD_{48h} = -0.08, 95% CI (-0.52, 0.69)], opioid consumption at 24 h and 48 h [SMD_{24h} = -0.24, 95% CI (-0.82, 0.34); SMD_{48h} = 0.15, 95% CI (0.25, 0.54)] and length of hospital stay [MD = -0.52, 95% CI (-1.13, 0.09)].

Discussion: LIA may be the better choice in the pain management of TKA for it could achieve fast pain relief and is easier to perform than FNB for patients with TKA.

Level of evidence: Level II, meta-analysis and systematic review.

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1. Introduction

Total knee arthroplasty (TKA) is one of the most common surgical treatments for advanced osteoarthritis of the knee joint. Patients undergoing TKA often experience moderate to severe postoperative pain, leading to immobility-related complications, delay in hospital discharge, and interfere with functional outcome [1]. Effective pain control allows for earlier ambulation and initiation of physiotherapy, which hastens recovery, reduces the length of stay in the hospital, and lowers the risk of postoperative complications [2]. Patient-controlled analgesia (PCA), epidural analgesia (EA) and regional anesthesia are commonly used as analgesic options for TKA [3]. PCA opioids are often used as the primary analgesic for TKA and are frequently associated with side

effects, such as nausea, vomiting, pruritus, and sedation [4]. EA has been popular over recent decades, but patients who received epidurals had more frequent hypotension, urinary retention, and pruritus whereas systemic opioids caused more sedation [5].

Regional anesthesia, such as femoral nerve blocks (FNB) has been used for it reduced the postoperatively need for opioids after TKA [4]. FNB has been part of the standard postoperative pain relief protocols following TKA over recent years, which has many advantages over PCA or EA in TKA [6,7]. However, Fowler et al. [7] revealed that FNB had an improved side effect profile than EA. In addition, Sharma et al. [8] found that femoral neuropathy, neuritis and postoperative falls are complications of FNB after TKA, which can lead to injury requiring reoperation. Besides, vascular puncture and nerve damage were often reported after FNB [3,4,6].

Local infiltration analgesia (LIA) is an alternative regional anaesthesia technique with intraarticular or periarticular drugs injected into the knee joint at the end of the operation, which is simple and avoids potential complications associated with nerve blocks [9]. Several randomized studies have been performed to evaluate the

* Corresponding author. Tel.: +86 93 189 424 60.

E-mail address: xiayylzu@126.com (Y.-Y. Xia).

¹ All first three authors contributed equally to this work.

efficacy of LIA compared with FNB. Some authors demonstrated excellent postoperative pain control after TKA using LIA [10–13]. Opposite conclusions have been reached by other authors who have shown that FNB provides a better analgesia compared with LIA [14,15]. There is still controversy over which of the two techniques leads to better pain relief after TKA.

To investigate which technique is better for pain relief, we undertook a meta-analysis of all available studies comparing LIA with FNB for patients undergoing TKA. The hypothesis of our study was that LIA could achieve better pain relief than FNB after TKA.

2. Methods

This meta-analysis was done in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [16] guidelines.

2.1. Search strategy

A fully recursive literature search was conducted in PubMed, the Cochrane Library, EMBASE, Web of Science up to October 2014. The search items were “peripheral nerve blocks, femoral nerve block, nerve block, local infiltration, wound infiltration, periarticular, intraarticular, knee, arthroplasty and replacement” in combination with the medical subject headings. Further articles that were potentially missed by the search strategy were identified by a manual search of the references from the key articles, related letters, reviews, and editorials. All the searches were conducted independently by two authors without language and publication status restrictions. Differences were resolved by discussion with the third authors.

2.2. Inclusion criteria and study selection

The inclusion criteria for this meta-analysis were comparative studies that compared LIA with FNB for patients with TKA.

The evaluated outcomes were visual analog score (VAS), opioid consumption, length of hospital stay, complications [including venous thromboembolism (VTE), infection]. Studies that reported at least one outcome were included and trials published without the outcome measures of interest were excluded. Two authors independently assessed potentially relevant citations for inclusion and disagreements were resolved with a third author.

2.3. Data abstraction and quality assessment

The extraction of the data was performed independently by 2 reviewers. For each outcome, the number of patients in each treatment arm was extracted for an intention-to-treat analysis. Data unavailable in the included studies were obtained by direct contact with and authorization of the study steering committees. Any disagreement was resolved by consensus or discussion with the other authors.

Study quality was judged by using the Jadad five-point scale [17] for RCTs and the Newcastle–Ottawa Scale [18] quality assessment scale for nRCTs. The Jadad five-point scale contained two questions each on randomization and masking and one question on the reportin of dropouts and withdrawals. The Newcastle–Ottawa Scale assesses population selection, comparability of exposed and unexposed, and adequacy of outcome assessment (including outcome ascertainment and attrition). Discrepancies were resolved by consensus after discussion with the third author.

We used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [19] criteria to evaluate the quality of evidence according to outcomes.

2.4. Statistical analysis and subgroup analysis

Data from all eligible trials were analyzed by Review Manager 5.2. If there were continuous scales of measurement, the mean difference (MD) or standard mean difference (SMD) was recommended to assess the treatment with 95% confidence interval [CI]. For dichotomous outcomes, results were expressed as odds ratio (OR). Data was pooled using the fixed-effect model but the random-effects model was also considered to ensure robustness of the model. Heterogeneity between trials was assessed by the I^2 index, which measures the percentage of the variability in effect estimates that are attributable to heterogeneity. In case of significant heterogeneity, results of the random-effect model were noted. Subgroup analysis was conducted to investigate possible reasons for heterogeneity.

3. Results

3.1. Search results

Among 180 potentially eligible articles that were searched in the databases, we excluded 89 duplicates and 75 citations after screening the titles and abstracts. After reading full texts, 6 citations, which did not fulfill inclusion criteria, were excluded. Nine studies [10–15,20–22] with 782 patients fulfilled our criteria and were included in the analysis (Fig. 1).

Table 1 summarises the characteristics of the 9 included studies. Seven studies was RCTs and the remaining 2 studies was nRCT. The studies were published between 2007 and 2014 and the number of participants per study ranged from 32 to 200. The 9 trials enrolled 782 patients with a mean age of 69.1 years.

The quality scores of the nine trials are summarized in Table 1. The total scores of the seven RCTs showed that the quality of the five trials is high (Jadad score = 5). The last two trials [11,20] were lower quality randomized control trials, due to a lack of information on the blinding of participants. According to the Newcastle–Ottawa Scale, one study [12] scored eight points, which meant that the included trials had high quality while another one [13] was low (score = 5) (Table 1).

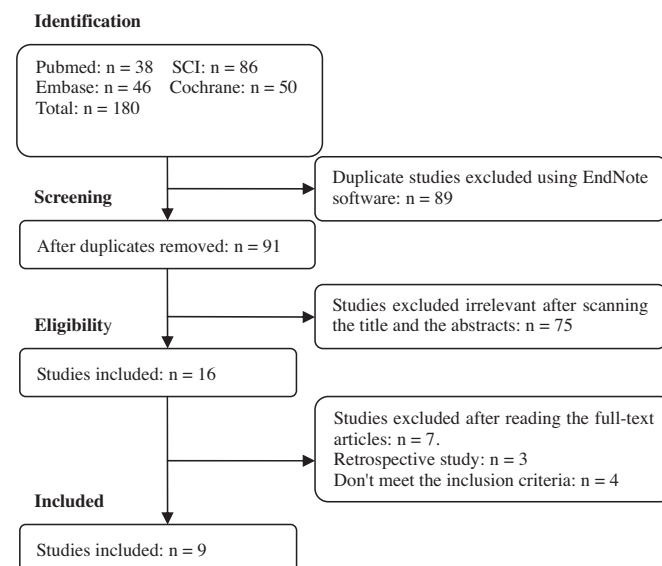


Fig. 1. The flow chart of literature screening.

Table 1
The characteristics of included studies.

Study (year)	No. LIA vs FNB	Age: LIA vs FNB (years)	Anesthesia	LIA group	FNB group	Outcomes	Quality score
Affas et al., 2011 [20]	20/20	67/65	Spinal anesthesia	Ropivacaine 300 mg, ketorolac 30 mg, and epinephrine 0.5 mg	Ropivacaine 60 mg	a, b	3
Antoni et al., 2014 [12]	49/49	66.4/69.7	General anesthesia	Ropivacaine 400 mg	48 h continuous ropivacaine	a, b, c, d	8
Ashraf et al., 2013 [10]	19/21	NR	Spinal anesthesia	150 mL 0.2% ropivacaine, 30 mg ketorolac, 1 mL 1:1000 adrenaline	30 mL of 0.2% ropivacaine	a, b, e	5
Broome et al., 2014 [13]	100/100	NR	Spinal anesthesia	Liposomal bupivacaine	NR		5
Carli et al., 2010 [14]	20/20	70.8/71.1	Spinal anesthesia	Ropivacaine 300 mg, ketorolac 30 mg, and epinephrine 0.5 mg	8 mL of ropivacaine 0.2%	a, b, c	5
Chaumeron et al., 2013 [15]	29/30	67.3/66.6	Spinal anesthesia	400 mg ropivacaine, 30 mg ketorolac, and 0.5 mL adrenaline (1/1000)	20 mL ropivacaine 0.25% (8 to 10 mL/h for 48 to 72 h)	a, b, c, d	5
Moghtadaei et al., 2014 [22]	18/18	64/67.4	Spinal anesthesia	Ropivacaine 300 mg, ketorolac 30 mg, and epinephrine 0.5 mg	200 mg ropivacaine	a, b, c	4
Ng et al., 2012 [21]	16/16	70/70	General anesthesia	Ropivacaine 300 mg, adrenaline 1 mg, and isotonic sodium chloride solution 70 mL	0.2% ropivacaine	a, b	5
Toftdahl et al., 2007 [11]	40/37	70/72	Spinal anesthesia	Ropivacaine 300 mg, ketorolac 30 mg, and epinephrine 0.5 mg	ropivacaine 20 mg	a, b	3

a: pain score; b: morphine consumption; c: length of hospital stays; d: complication; NR: not reported.

3.2. VAS score

Data from eight studies [10,12–15,20–22] counting 545 patients were available to examine the pain score with rest. LIA had significantly lower pain score than FNB postoperatively 6 h [$SMD_{6h} = -0.92$, 95% CI (-1.38, -0.47)] while there were no statistical differences at 24 h and 48 h postoperatively between the two groups [$SMD_{24h} = -0.03$, 95% CI (-0.46, 0.40); $SMD_{48h} = 0.28$, 95% CI (-0.35, 0.91)].

A total of six studies [11,14,15,20,21] involving 244 patients reported the results of pain score with activity. There were no significant differences in pain score with activity between LIA and FNB at 6 h, 24 h and 48 h postoperatively [$SMD_{6h} = -0.54$, 95% CI (-1.62, 0.54); $SMD_{24h} = -0.22$, 95% CI (-1.41, 0.96); $SMD_{48h} = -0.08$, 95% CI (-0.52, 0.69)].

3.3. Opioid consumption

Eight studies [10–12,14,15,20–22] with 419 patients reported the results of opioid consumption. There were no significant difference in opioid consumption between LIA and FNB at 24 h and 48 h postoperatively [$SMD_{24h} = -0.24$, 95% CI (-0.82, 0.34); $SMD_{48h} = 0.15$, 95% CI (0.25, 0.54)].

3.4. Length of hospital stay

Data were available from six studies [10,12–15,22] involving 464 patients. There were no statistical differences in length of hospital stay between the two groups [$MD = -0.52$, 95% CI (-1.13, 0.09)].

3.5. Complications

Six studies reported the rate of complications, including nausea or vomiting, deep infection, VTE and falls. There were no significant

difference in nausea or vomiting [OR = 1.64, 95% CI (0.70, 3.84)], deep infection [OR = 0.99, 95% CI (0.16, 5.95)], VTE [OR = 0.30, 95% CI (0.05, 1.61)] and falls [OR = 0.33, 95% CI (0.01, 8.52)] between the two groups.

3.6. Subgroup analysis

To eliminate the heterogeneity, nine trials were under subgroup analysis based on the study type (RCT or nRCT). The results of meta-analysis of RCTs were consistent with the results of total included studies.

3.7. Quality of the evidence by GRADE system

All outcomes in this meta-analysis were evaluated using the GRADE system. The evidence quality for each outcome was mostly moderate or low. The reason for downgrade was mostly the small sample sizes. The results of evidence of outcomes were listed in Table 2.

4. Discussion

Based on nine studies involving 782 patients, the most important findings of this meta-analysis were that: LIA has lower VAS score at 6 h postoperative surgery than FNB, while there are no statistical differences in pain score at 24 h and 48 h, opioid consumption at 24 h and 48 h, length of hospital stay and complications between the two groups.

FNB has been recommended for pain control after TKA. Some meta-analyses have proved the advantage of FNB over EA or PCA [5–7]. However, 0.1% to 2.5% of patients experience complications associated with nerve blocks, including muscle weakness, nerve damage, local infection with peripheral nerve blocks and tourniquet [15]. Besides, 15% of femoral nerve blocks are unsuccessful, which is depending on the experience of anesthetists

Table 2
The outcomes of meta-analysis and subgroup analysis.

Outcomes	No. included studies	No. of patients		MD or OR (95% CI)	Heterogeneity	GRADE quality
		LIA	FNB			
VAS with rest at 6 h						
Total	4	86	89	−0.92 (−1.38, −0.47)	$I^2 = 51\%$	Low
VAS with rest at 24 h						
Total	8	271	274	−0.03 (−0.46, 0.40)	$I^2 = 82\%$	Low
RCTs	6	122	125	−0.17 (−0.41, 0.76)	$I^2 = 80\%$	Low
VAS with rest at 48 h						
Total	5	214	215	0.28 (−0.35, 0.91)	$I^2 = 89\%$	Low
RCTs	3	65	66	0.77 (−0.24, 1.78)	$I^2 = 86\%$	Low
VAS with activity at 6 h						
Total	2	49	50	−0.54 (−1.62, 0.54)	$I^2 = 75\%$	Low
VAS with activity at 24 h						
Total	5	123	121	−0.22 (−1.41, 0.96)	$I^2 = 73\%$	Moderate
VAS with activity at 48 h						
Total	4	102	100	−0.08 (−0.52, 0.69)	$I^2 = 44\%$	Moderate
Opioid consumption at 24 h						
Total	8	208	211	−0.24 (−0.82, 0.34)	$I^2 = 88\%$	Moderate
RCTs	7	159	162	−0.33 (−1.00, 0.34)	$I^2 = 88\%$	Moderate
Opioid consumption at 48 h						
Total	6	172	170	0.15 (−0.25, 0.54)	$I^2 = 69\%$	Low
RCTs	5	123	121	0.26 (−0.19, 0.71)	$I^2 = 66\%$	Low
Length of hospital stay						
Total	6	235	229	−0.52 (−1.13, 0.09)	$I^2 = 69\%$	Low
RCTs	4	86	89	−0.21 (−0.79, 0.37)	$I^2 = 69\%$	Low

[23]. Conversely, LIA is a convenient, easy, and quick technique to clinician, and a recent meta-analysis [24] has proved its efficacy in pain management in TKA and THA versus placebo. This technique only affects the surgical area with limited interference of the muscle strength. It might offer several advantages over traditional methods, such as easier rehabilitation of the operated extremity and earlier discharge from the hospital [9].

Our primary outcome measure was VAS score with rest/activity and opioid consumption. Ashraf et al. [10] showed the LIA group had significantly lower pain scores at 4 h postoperatively than FNB. Toftdahl et al. [11] reported lower pain and morphine consumption in the LIA group on the first day postsurgery. Chaumeron et al. [15] found lower opioid consumption in the LIA group during the first 8 postoperative hours. The pain score with rest at 6 h was found to be marginally lower in the LIA group compared to FNB group. However, there were no significant differences in pain score at 24 h and 48 h, opioid consumption at 24 h and 48 h between the two groups. These results indicated that the sensitive sciatic nerve territory of the knee is covered not only by a FNB alone, but also by the sciatic block or obturator block [23]. However, a combination of these procedures made it complexity to clinicians and patient care.

Regarding the length of hospital stay, our study failed to demonstrate any significant difference in length of hospital stay between the two groups. Length of hospital stay following TKA is dependent on many factors, including preoperative haemoglobin, age, and gender [14,15,20]. At present, there is no conclusive evidence that LIA could reduce hospital stay than FNB.

Major complications, including nausea or vomiting, deep infection, DVT and falls were observed in two groups. Totally two deep infections were found in FNB group and two in LIA group. Six DVTs were found in FNB group and two in LIA groups. Although the results of meta-analysis showed no significant differences in complications was found between the two groups, LIA seemed to be safer in reducing venous stasis and thrombosis [15].

Eight out of included nine studies used a cocktail regimen, consisting of a long-acting local anesthetic (usually ropivacaine), ketorolac, an opioid (epimorphine) while two studies only used local anesthetic (ropivacaine [25] or levobupivacaine [26]). Some concern exists regarding the maximum dose of local anesthetics and its side effects. In our included studies, the dose of local anesthetics used varies from 300 to 400 mg, however, local anesthetics

plasma concentrations were not assessed. Vendittoli et al. [27] revealed that the maximum concentration of ropivacaine in plasma is much lower than the toxicity threshold concentration and no risk of local anesthetic systemic toxicity was found. The addition of epimorphine to local anesthetics could slow ropivacaine release in the vascular system and prolong its local action [15]. It is noteworthy that ketorolac, a kind of NSAIDs, has been shown effective when given locally [28]. Ketorolac in a multimodal analgesic regime is approved for intraarticular use for a positive effect on soft-tissue healing and prevention of heterotopic ossification [29]. However, it needed further study to determine the exact cardiovascular risk when ketorolac is given for a short period of time, because ketorolac has been recently associated with increased cardiac risks [30].

In addition, the optimal site of administration of local anaesthetics should be concerned. Andersen et al. [31] compared the extraarticular wound infiltration or intraarticularly LIA after TKA and found there was no statistical difference between the two groups. Dobrydnjov et al. [32] compared the effects of continuous intraarticular and extraarticular administration of LIA following TKA and reported that continuous intraarticular reduced the incidence of high pain intensity during first exercises. Future studies should continue to investigate which optimal site of administration is better.

Besides, the cost-effectiveness of LIA and FNB should be carefully considered. Some authors suggested that LIA might be considered to be superior to femoral nerve block due to the fact that it is both cheaper and less technically demanding. For example, administration and onset of a FNB can take up to 20 to 30 minutes, which may not be reproducible if used by practitioners with less experience [21]. In addition, it also requires extra operating time for catheter placement, risk of catheter dislodgement, weakness of the quadriceps muscle and other side effect [33]. These factors may delay procedures and add to patient discomfort. Based on the comparable results in pain relief and morphine consumption between LIA and FNB for patients undertaking TKA, LIA may be the better choice.

This meta-analysis is the first study to evaluate the efficacy and safety of LIA versus FNB for patients undergoing TKA. There are some strength in our study. It follows the PRISMA guidelines and GRADE system was applied to grade the evidence of the results, which makes it convenient for clinician.

This study also has several potential limitations. Firstly, the quality of included studies were not well and the sample sizes of each studies were small. Five of the nine trials had 50 or less participants in each allocation arm. While small studies suffer lack of power, they also often have a very selected participant group (higher adherence that would be expected in the clinical situation), concentrated researcher attention resulting in a greater risk of inflated effect sizes. In words, large sample RCTs were still needed. Secondly, the inhomogeneity among included studies still existed. For instance, different regimens of LIA and FNB might limit the conclusion. So, future studies should investigate the efficacy of different regimen of LIA or FNB in the pain control of TKA. Thirdly, the observation period of follow-up may be too short, especially with regard to adverse events, such as infection and VTE. Long-term followed-up studies should be conducted in the future.

5. Conclusions

Based on the current evidence, LIA seems to be as effective as FNB, even better during the first 6 h after TKA. But due to poor statistical power of the studies, no recommendation can be made. Large sample and high quality RCTs are still needed to confirm the efficacy of LIA compared with FNB.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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