

IN BRIEF

The Role of Periarticular Injections for Postoperative Pain after Total Knee Arthroplasty

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Abstract

Periarticular multimodal drug injection (PMDI) is better than FNB (femoral nerve block) in pain relief after total knee arthroplasty (TKA). PMDI of bupivacaine [20 mL 0.5% bupivacaine hydrochloride - HCl (100 mg) following implantation plus incisional injection of 10 mL 0.5% bupivacaine HCl (50 mg) before wound closure] is more efficacious than PMDI after implantation. PMDI leads to less postoperative pain than IAI (intraarticular injection) and IAI + PMDI. PMDI of magnesium sulfate and sodium bicarbonate added to a conventional PMDI (ropivacaine, epinephrine, and dexamethasone) prolongs analgesia. No differences exist between gonyautoxin (GTX)2/3 (40 µg GTX 2/3 diluted in 30 mL of sodium chloride 0.9%) and a combination of 300 mg of levobupivacaine, 1 mg of epinephrine, and 60 mg ketorolac diluted in 150 mL of sodium chloride 0.9%.

Level of evidence: I

Keywords: Periarticular multimodal drug injection, Postoperative pain, Total knee arthroplasty

Introduction

Periarticular multimodal drug injection (PMDI) in total knee arthroplasty (TKA) has been associated with short-run benefits in terms of pain alleviation.¹ The purpose of this article has been to analyze randomized control trials (RCTs), meta-analysis, non-inferiority trials and studies with level 1 of evidence on the role of PMDI in the treatment of postoperative pain after TKA. On 21 August 2024 a PubMed search was conducted using the following keywords: "periarticular injection TKA". Of the 216 articles found only 12 were analyzed because they were RCTs, meta-analysis of RCTs or other studies with level 1 of evidence.

Main body

RCTs, meta-analysis of RCTs and other studies with level 1 of evidence

In a study (Fu et al, 2017) PMDI was superior to femoral nerve block (FNB).² In 2020 Altay et al reported that the combined injection of bupivacaine [20 mL 0.5% bupivacaine hydrochloride - HCl (100 mg)] after implantation plus incisional injection of 10 mL 0.5% bupivacaine HCl (50 mg) before wound closure was more effective than the periarticular injection alone.³

Chan et al (2021) found that the combination of intravenous and periarticular corticosteroids improved pain

control after one-stage bilateral TKA.⁴ Compared to PMDI alone, Li et al found that the addition of corticosteroids to PMDI diminished pain at postoperative days 1, 2, and 3.⁵

The study of Bagderi Fard et al (2022) did not support the benefit of including a steroid (Depo-Medrol) in the periarticular injection cocktail for pain control after the TKA.⁶

In 2022 Mortazavi et al compared three types of injections: intraarticular injection (IAI), PMDI, and combined IAI + PMDI. PMDI led to less early postoperative pain compared with the other two methods.⁷

The study of Minaei et al (2023) showed that subperiosteal injection of lidocaine, dexmedetomidine, and marcaine was more effective than periarticular injection, providing effective postoperative pain management after TKA.⁸

Chen et al (2023) found that PMDI with liposomal bupivacaine (LB) was not superior to traditional PMDI (without LB).⁹

In 2023 Motifard et al compared three treatments: (1) PMDI of bupivacaine, morphine, epinephrine, and ketorolac, (2) only epinephrine (placebo group), and (3) 400 mg celecoxib orally (control group). The injections and oral therapy were carried out within 15 minutes prior to the surgical procedure. Preemptive PMDI led to considerable postoperative pain alleviation in comparison to placebo

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(only epinephrine) or oral celecoxib (400 mg).¹⁰

In 2023 Wang et al recommended a multimodal analgesic (MA) protocol for diminishing the occurrence of motor blockade and numbness in individuals following TKA. The MA protocol ensured early rehabilitation while maintaining appropriate pain alleviation. The study compared the clinical efficacy and adverse effects of the proposed MA protocol versus patient-controlled epidural analgesia (PCEA).¹¹

In 2023 Hinzpeter et al compared a PMDI of 40 µg

gonyautoxins (GTX) 2/3 diluted in 30 mL of sodium chloride 0.9% to a PMDI (300 mg of levobupivacaine, 1 mg of epinephrine, and 60 mg ketorolac diluted in 150 mL of sodium chloride 0.9%). Pain scores were similar at all time intervals.¹²

RCTs, meta-analysis of RCTs and other studies with level 1 of evidence on PMDI to improve pain control after TKA are summarized in [Table 1].

Table 1. Periarticular multimodal drug injection (PMDI) to improve pain control after total knee arthroplasty (TKA): randomized controlled trials (RCTs), meta-analysis of RCTs and other studies with level 1 of evidence.

AUTHORS [REFERENCE]	YEAR	TYPE OF PMDI (MIXTURE OF THE INJECTION MATERIAL)	RESULTS	CONCLUSION
Fu et al ²	2017	This review article with level 1 of evidence evaluated the efficacy of various types of PMDI in comparison with femoral nerve block (FNB).	Lower pain score on the day of surgery was detected after PMDI.	PMDI had superiority to FNB in the management of pain control after TKA.
Altay et al ³	2020	This study compared the efficacy of combined periarticular [20 mL 0.5% bupivacaine hydrochloride - HCl (100 mg) after implantation] plus incisional injections [10 mL 0.5% bupivacaine HCl (50 mg)] before wound closure versus periarticular injection alone of bupivacaine [20 mL 0.5% bupivacaine HCl (100 mg) after implantation].	The mean VAS score in the combined group-periarticular and incisional injections) within the first 4 hours was lower than that in the group of periarticular injection alone.	The combined injection of bupivacaine was more effective than its periarticular injection alone and provided effective postoperative pain management after TKA.
Chan et al ⁴	2021	All patients received 16 mg of dexamethasone intravenously. One knee was randomized to receive LIA (local infiltration analgesia) with 40 mg of triamcinolone, while the other knee received LIA without corticosteroids. For each patient, one knee was affected by intravenous steroids only, while the other was under the combined effect of intravenous and periarticular steroids (IVPAS).	IVPAS knees showed lower VAS scores from day 1 to 6 weeks.	IVPAS improved pain control after TKA with no increase in wound complications up to 1 year.
Li et al ⁵	2021	This meta-analysis of RCTs evaluated the effect of periarticular injection of corticosteroids on postoperative pain relief and knee functional recovery in patients undergoing TKA. Various types and doses of corticosteroids were used.	Compared with the control group, the VAS score at rest of the corticosteroid group decreased significantly at postoperative days 1, 2, 3. The morphine equivalent of postoperative analgesia was significantly reduced.	The addition of corticosteroids to multimodal cocktail periarticular injection relieved pain intensity.
Bagheri Fard et al ⁶	2022	In this double-blinded RCT, its authors investigated whether including a steroid (Depo-Medrol) in the periarticular injection cocktail for pain control after TKA was beneficial. A total of 42 TKA individuals were included in this study. The individuals of each group were randomly allocated into cohort A (cocktail+Depo-Medrol) and cohort B (cocktail alone). The outcome measures were a VAS for pain at five different time points for TKA, ROM and straight leg raise (SLR). Individuals were followed for 3 months to observe infection, wound complications, and any venous thromboembolic event.	The preoperative VAS, 12, 24, 48h, and 72h postoperative VAS were not statistically different between cohorts A and B. The mean scores of knee ROM and ability to perform SLR were not significantly different between individuals in the steroid and non-steroid groups. The only observed complication was one surgical site infection in the non-steroid cohort.	This study did not support the benefit of including a steroid (Depo-Medrol) in the periarticular injection cocktail for pain control after the TKA.
Mortazavi et al ⁷	2022	This study compared three injections: intra-articular (IA), periarticular (PA), and combined intra-articular and periarticular (IA+PA). In the IA group, 400 mg of ropivacaine, 5 mg of morphine, 0.6 mL of 1:1,000 epinephrine, and 30 mg of ketorolac were diluted with sterile normal saline solution to create 100 mL of analgesic cocktail. Then, the cocktail was injected through the joint space after suturing of the knee capsule. In the PA group, after bone cut preparation and prior to inserting the component, 30 mL of the cocktail was injected into the posterior capsule; 10 mL, into the medial collateral ligament; and 10 mL, into the lateral collateral ligament. While the cement was curing, another 20 mL was injected into the quadriceps and medial and lateral retinacular tissue. The remaining 30 mL of the cocktail was injected into the infrapatellar fat pad and subcutaneous tissue. In the IA+PA group, 30 mL of the cocktail was injected into the posterior capsule and lateral and medial collateral ligaments after bone cut preparation but before component insertion. While the cement was curing, another 10 mL was injected into the quadriceps, patellar tendon, and medial and lateral retinacular tissue. Also, 10 mL was injected into the infrapatellar fat pad and subcutaneous tissue. Finally, after watertight capsular closure, the remaining 50 mL was injected into the knee joint space.	The morphine consumption was lowest in the PA group and highest in the IA group. The PA group had significantly lower VAS pain at rest than either IA or PMDI + IA. The PA group had also lower VAS pain during activity compared with IA and IA + PMDI.	This study found that PA was associated with less early postoperative pain compared with the other 2 analgesic methods.

Table 1. Continued

Minaei et al ⁸	2023	This randomized double-blind prospective study compared the efficacy of subperiosteal and periarticular injections of a local anesthetic for postoperative pain management after TKA. Individuals were randomly divided into two cohorts, with a local anesthetic (21 mL) administered either in periarticular (P cohort) or subperiosteal (S cohort) forms prior to wound closure. The local anesthetic consisted of lidocaine 2% (15 cc), dexmedetomidine (1 cc), and marcaine 0.5% (5 cc). VAS was recorded at 6, 12, 24, and 48 hours after surgery.	A total of 40 individuals (P and S cohort; N=20 each), consisting of 10 males (mean age=67.4 years old), were included in this study. The intensity of pain in the S cohort was substantially lower than in the P cohort 24 hours after surgery (mean VAS scores in the P cohort: 4 vs. the S cohort: 3.3). Moreover, VAS scores at 6, 12, and 48 hours post-surgery were lower in the S cohort compared to the P cohort; however, the difference was not statistically significant.	This study indicated that subperiosteal injection of lidocaine, dexmedetomidine, and marcaine was more effective than periarticular injection, providing effective postoperative pain management after TKA.
Chen et al ⁹	2023	This meta-analysis of RCTs studied whether liposomal bupivacaine (LB) offered better efficacy than traditional PMDI following TKA. A total of 16 RCTs with 1629 participants were involved. Ten RCTs used standard bupivacaine as the control drug, whereas 6 RCTs used a cocktail.	No significant difference was observed in pain relief between the two groups.	LB administration during TKA was not superior to PMDI.
Motififard et al ¹⁰	2023	This study compared the efficacy of preemptive PMDI [50 mg bupivacaine hydrochloride 0.5%, 1 mL morphine sulfate 10 mg/mL, 300 mcg epinephrine (1:1000), and 30 mg ketorolac diluted by 0.9% sodium chloride solution to make a total 100 mL of injection drug] versus placebo [300 mcg epinephrine (1:1000)] and oral celecoxib (400 mg orally) on postoperative pain. The injections and oral therapy were performed within 15 minutes before the surgical procedure.	All the studied groups showed a statistically significant trend of improvement in VAS, while the comparison of the three groups in terms of VAS revealed remarkable superiority of multimodal injection to the other treatments.	Preemptive PMDI, led to considerable postoperative pain relief in comparison to placebo or oral celecoxib.
Wang et al ¹¹	2023	These authors proposed a multimodal analgesic (MA) protocol: administration of ultrasound-guided nerve block (NB) in the femoral and obturator nerves prior to spinal anesthesia plus periarticular injection (PAI) with 30 mg of ketorolac, 5 mg of morphine, 100 mg of ropivacaine, and 0.1 mg of epinephrine intraoperatively plus intravenous patient-controlled analgesia (IVPCA) postoperatively (fentanyl 4 µg/mL). The study compared the clinical efficacy and adverse effects of the proposed MA protocol versus patient-controlled epidural analgesia (PCEA) made of 0.16% ropivacaine with fentanyl 1.5 µg/mL in normal saline, PCEA drug: 500 mL/bag, bolus doses: 4–5 mL, background infusion: 4–5 mL/hour, lock out interval: 15–20 mL, 4 hours limit: 40–55 mL.	A lower proportion of individuals in the MA cohort experienced motor blockade (7% vs. 23%) compared to those in the PCEA cohort on the first postoperative day. Moreover, a lower proportion of individuals in the MA cohort experienced numbness (18% vs. 43%) than those in the PCEA group on the first postoperative day.	The MA protocol can be recommended for diminishing the occurrence of motor blockade and numbness in individuals following TKA. Therefore, the MA protocol ensures early rehabilitation while maintaining appropriate pain alleviation.
Hinzpeter et al ¹²	2023	This study compared the efficacy of PMDI of gonyautoxin 2/3 (GTX 2/3) and a mixture of levobupivacaine, ketorolac and epinephrine. Patients were randomly allocated to receive periarticular infiltration of 40 µg GTX 2/3 diluted in 30 mL of sodium chloride 0.9% (study group) or a combination of 300 mg of levobupivacaine, 1 mg of epinephrine, and 60 mg ketorolac diluted in 150 mL of sodium chloride 0.9% (control group). Postoperatively, all patients received PCA (morphine bolus of 1 mg; lockout interval of 8 minutes), acetaminophen, and ketoprofen for 72 hours.	No differences between groups were found.	This study showed that GTX 2/3 was a safe and efficient drug for pain control after TKA.

VAS = Visual Analog Scale; ROM = Range of motion; PCA = Patient-controlled analgesia

Conclusion

PMDI is better than FNB in pain relief after TKA. PMDI of bupivacaine after implantation plus incisional injection before wound closure is more effective than PMDI after implantation.

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