



ORIGINAL INVESTIGATION

Comparison of different local analgesia protocols in postoperative pain management after total knee arthroplasty

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Abstract

Objectives: This study was to compare the effects of different local analgesia protocols on osteoarthritis patients undergoing total knee arthroplasty (TKA).

Methods: Medical records of 148 osteoarthritis patients who underwent unilateral TKA between October 2016 and October 2017 in our hospital were retrospectively analyzed. All these patients were divided into three groups according to the pain management protocol (morphine, morphine + cocktail [100 mg ropivacaine, 10 mg morphine, and 30 mL 0.9% sodium chloride solution containing 2 mL betamethasone (4 mg)], or cocktail). The postoperative visual analog scale (VAS) score, muscle strength, and complications were compared between the groups.

Results: At 6 and 12 hours post-operation, the VAS score in group C was significantly higher than that in group A or group B. In addition, the muscle (quadriceps femoris) strength score of group C (3.7 ± 2.8) was significantly higher than that in groups A and B at 6 and 12 hours post-operation. The VAS score and muscle strength score showed no significant differences among the three groups at 24 and 36 hours post-operation. The time of postoperative first void of group C was significantly shorter than that of groups A and B. Groups A or B had a significantly higher incidence of nausea and emesis compared with group C. The incidence of pruritus was higher in groups A or B than that in group C.

Conclusion: Epidural anesthesia combined with local analgesic cocktail injection is a preferable effective multimodal analgesia for TKA.

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Introduction

Total knee arthroplasty (TKA) is known to be a very successful procedure for advanced osteoarthritis. However, persistent pain after TKA can hamper rehabilitative exercise and functional recovery.¹ Various postoperative pain control protocols have been suggested, each with its pros and cons. For example, orally, intramuscularly, or intravenously administered opioid plays a pivotal role in postoperative pain relief because of their effectiveness in relieving moderate to severe pain, however, opioids may cause respiratory depression, sedation, renal impairment, nausea, emesis, and inhibition of smooth muscle contraction.² Femoral nerve block, one of the commonly used pain control method after TKA, was demonstrated to provide effective analgesia but may lead to muscle weakness, with a possible increase in fall risk.³ In recent years, as surgeons have become more aware of postoperative pain, preemptive analgesia and multimodal analgesia have been widely used in a clinical setting. The multimodal analgesia typically includes a combination of several different pain-alleviating medications, which provide successful pain management, prevent addiction to a single component, and reduce the incidence of side effects associated with high dose analgesia.⁴ Current Enhanced Recovery after Surgery (ERAS) protocols for TKA focus mainly on perioperative care, which includes optimized pain and sleep management, and optimized drainage and urinary catheterization protocol.⁵⁻⁷ To improve perioperative management, enhance postoperative recovery, increase overall satisfaction in TKA patients, we conducted this retrospective clinical study. We reviewed the clinical data of 148 patients who underwent primary TKA surgery and compared the effects of different intraoperative analgesic administration protocols on the postoperative recovery in TKA patients.

Methods

This study was approved by the ethics committee of our hospital. Written informed consent was not required from each patient, as per the institutional review board of our hospital, for this is a retrospective study.

Study subjects

The medical records of osteoarthritis patients who underwent unilateral TKA in our hospital between October 2016 and October 2017 were retrospectively analyzed. Inclusion criteria: (1) age below 80 years; (2) BMI < 35; (3) definite diagnosis of knee osteoarthritis before TKA (Kellgren-Lawrence Grade III-IV), symptoms mainly in one knee and did not respond to non-surgical treatment; (4) overall physical status were I or II according to American Society of Anesthesiologists (ASA) score; (5) TKA approaches were simple midline skin incision or medial parapatellar incision; (6) used stable prostheses without posterior cruciate ligament retention. Exclusion criteria: (1) severe disease in both knees; (2) previous narcotics addiction, history of drug abuse, or current hormonal or opioid treatment; (3) liver or kidney dysfunction before surgery; (4) history of stroke or neurological or psychiatric disorders; (5) uncontrollable

angina or bundle branch block; (6) abnormal coagulation; (7) severely deformed knees or ligamentous instability; (8) postoperative complications, e.g., common peroneal nerve injury; (9) benign prostatic hyperplasia.

All the patients showed similar clinical manifestations, which included severe pain in the affected knee joint, and the inability to walk or stand for long periods. In these patients, the pain worsened when they stood up or climbed stairs. The knee joint had varying degrees of deformity and restricted activity. Preoperative X-ray examination showed significant narrowing of the joint space, subchondral sclerosis, and the formation of osteophytes. The articular valgus deformity was not observed. No patient had a history of knee surgery or knee instability.

In this study, all the selected patients were divided into three groups based on the pain management protocol. The detail grouping information is as follows: patients who received morphine (3 mg) via epidural anesthesia catheter before catheter extraction were assigned to group A, patients who received morphine (3 mg) via epidural anesthesia catheter before catheter extraction plus local analgesic cocktail injection at the knee were assigned to group B, and patients who received epidural anesthesia plus local analgesic cocktail injection at the knee were assigned to group C.

Preoperative care

Before the operation, all the patients were explained to in detail about pain management and trained for pain assessment using VAS. In addition, patients received oral administration of celecoxib once a day for three days at a time of 200 mg.

Surgery

All the surgeries were performed by the same surgeon from a four-member surgical team. During surgery, peripheral intravenous access was established, and vital signs including blood pressure, peripheral capillary oxygen saturation (SpO₂), respiratory rate, and end-tidal carbon dioxide/ETCO₂ (PetCO₂) were monitored. All the patients received the same epidural anesthetic. Continuous epidural anesthesia was given at L₂₋₃ or L₃₋₄ interspaces to achieve bilateral sensory block between T₈ and T₁₀. An intraoperative ropivacaine infusion was used to maintain sedation during surgery, and the anesthesia depth was adjusted according to blood pressure, heart rate, bispectral index, and other parameters. All surgeries were conducted using a standard medial parapatellar arthrotomy with an inflatable tourniquet with pressure set as a patient's systolic pressure plus 100 mmHg (1 mmHg = 0.133 kPa).⁸

A femur resection was performed using the intramedullary alignment technique followed by a four-surface osteotomy of the femur. Tibia resection was performed using the extramedullary alignment technique. The prosthesis was inserted after size measurement. Posterior stabilized knee prosthesis fixed with bone cement (Zimmer Biomet, US) was used in all TKAs. For group A, morphine (3 mg) was administered via the epidural catheter, which was withdrawn at the end of the surgery.

Table 1 Characteristic data of patients who underwent TKA (mean ± SD).

Variables	Group A (n = 50)	Group B (n = 46)	Group C (n = 52)	χ^2/F -value	p-value
Gender (male/female, n)	20/30	16/30	18/34	0.4025	0.8177
Age (years)	65.3 ± 8.3	66.8 ± 7.9	65.5 ± 8.1	0.44	0.6413
BMI (kg. m ⁻²)	25.3 ± 2.3	24.3 ± 2.7	24.3 ± 3.1	0.29	0.7486
Kellgren-Lawrence Grade (III/ IV, n)	19/31	17/29	19/33	1.3488	0.5095
Osteoarthritis site (left/right)	27/23	20/26	25/27	1.0772	0.5085
Osteoarthritis type (traumatic/degenerative, n)	2/48	3/43	4/48	0.6628	0.7179
KSS score	52.2 ± 7.1	53.8 ± 7.9	54.4 ± 6.8	1.80	0.1652
VAS score	4.2 ± 3.2	4.3 ± 3.5	4.0 ± 3.1	0.79	0.4549
Tibiofemoral angle (°)	14.3 ± 5.6	15.6 ± 6.0	15.7 ± 5.7	1.64	0.1938
Knee flexion contracture angle (°)	14.2 ± 8.3	13.5 ± 8.8	13.9 ± 7.9	0.85	0.4267

For group B, morphine (3 mg) was administered via the epidural catheter which was withdrawn at the end of the surgery. In addition, before the prosthesis was inserted, an analgesic cocktail was injected into a periarticular capsule of the knee joint, medial collateral ligaments, peripatellar soft tissue, infra-patella fat pad, and posterior articular capsule. For group C, the patients received an equal volume of saline instead of morphine via the epidural catheter and periarticular injection of the drug cocktail (same as group B). The drug cocktail consisted of 100 mg ropivacaine, 10 mg morphine, 30 mL 0.9% sodium chloride solution containing 2 mL betamethasone (4 mg).

Postoperative care

No intravenous patient-controlled analgesia pump was used. Instead, all patients received intramuscular administration of ondansetron hydrochloride (4 mg). After surgery, the patients received intermittent cooling using an icepack at the incision area during the first 24 hours. A dose of 5 mg dezocine was administered at midnight when VAS > 5. They were asked to raise the affected leg. Meanwhile, patients were asked to start isometric quadriceps exercise, and ankle pumps immediately after surgery. Parecoxib (40 mg) was administered 2 times per day for the first 3 days post-surgery. Then oral celecoxib (200 mg) was administered daily (twice per day) until discharge.

Postoperative evaluations

Postoperative evaluation included the following items: (1) pain level: pain level at 6, 12, 24, and 36 hours post-operation, both at rest and with activity (straight leg raising, bending and flexing the knee in the supine position), were assessed using VAS at each time point. (2) Quadriceps femoris muscle strength: the patients were asked to complete isometric quadriceps exercise and the muscle strength score which was divided into five grades (0-5) were estimated at 6, 12, 24, and 36 hours post-operation. Grade "0" represents absolutely no visible contraction; grade "1" means there was visible contraction but no movement; grade "2" represents some movement but insufficient to counteract gravity; grade "3" represents barely against gravity (inability to resist any additional force); grade "4" represents less than normal (but enough to resist

gravity); grade "5" represents normal. (3) Postoperative complications: the incidence of postoperative nausea, emesis, pruritus, and urinary retention. (The foley catheter was removed 4 hours after surgery. The period during which the patient emptied his or her bladder for the first time after surgery was recorded as postoperative first void. If the postoperative first void was longer than 10 hours, the catheter was reinserted.)

Statistical analysis

Data were analyzed using SPSS 22.0 software. The numerical data were presented as mean ± SD, and categorical variables were expressed as the frequency (%). The inter-group comparison was conducted using paired *t*-test. The multiple means comparison was conducted using F-test when normal distribution was achieved, followed by SNK-q test for post hoc comparisons. If the normal distribution was not achieved, Kruskal-Wallis test was used. The comparison of categorical data was conducted using χ^2 test. A *p*-value less than 0.05 was considered significantly different.

Results

Baseline characteristics of osteoarthritis patients undergoing TKA in each group

A total of 148 osteoarthritis patients were finally included in our study. Baseline characteristics of each group were summarized in Table 1 and described in detail as follows:

Group A: There were 50 patients consisted of 20 men and 30 women in this group. The average age was 65.3 ± 8.3 years old (ranges from 52 to 78 years). The average body mass index (BMI) was 25.3 ± 2.3 kg.m⁻² (ranges from 22.3 to 28.5 kg.m⁻²). Among all the cases, 27 were left knees and 23 were right knees. Two patients had traumatic osteoarthritis and 48 had degenerative osteoarthritis. Nineteen patients were categorized to Kellgren-Lawrence grade III and 31 were categorized to Kellgren-Lawrence grade IV. The mean pre-operative VAS score was 4.2 ± 3.2 (ranges from 3 to 5). The mean knee society score (KSS) was 52.2 (ranges from 40 to 68). Mean tibiofemoral angle (varus deformity) was 14.3 ± 5.6° (ranges from 0 to 25°) and mean knee flexion contracture angle (flexion deformity) was 14.2 ± 8.3° (ranges from 0 to 29°).

Table 2 Comparison of pain level and Dezocine use among patient groups receiving different pain management protocols (mean \pm SD).

Group	N	6 h VAS ($\bar{x} \pm s$)		12 h VAS ($\bar{x} \pm s$)		24 h VAS ($\bar{x} \pm s$)		36 h VAS ($\bar{x} \pm s$)		Dezocine use (n, %)
		At rest	With activity	At rest	With activity	At rest	With activity	At rest	With activity	
Group A	50	2.1 \pm 0.6	2.3 \pm 0.7	2.2 \pm 0.6	3.0 \pm 0.7	2.4 \pm 0.7	4.5 \pm 0.9	3.8 \pm 0.7	4.8 \pm 0.9	6 (12.0)
Group B	46	1.5 \pm 0.6	1.8 \pm 0.5	1.8 \pm 0.6	2.1 \pm 0.7	2.2 \pm 0.7	2.7 \pm 0.8	2.5 \pm 0.7	3.0 \pm 1.1	4 (8.7)
Group C	52	2.9 \pm 0.6	3.0 \pm 0.8	2.8 \pm 0.9	3.4 \pm 1.0	3.0 \pm 1.1	4.1 \pm 0.9	3.8 \pm 1.0	4.7 \pm 1.2	6 (11.5)
χ^2/F value		12.56	13.34	15.23	11.65	2.11	3.02	1.83	1.27	2.48
p-value		< 0.05	< 0.05	< 0.05	< 0.05	> 0.05	> 0.05	> 0.05	> 0.05	> 0.05

Group A: Patients received morphine (3 mg) via epidural anesthesia catheter before catheter extraction. Group B: Patients received morphine (3 mg) via epidural anesthesia catheter before catheter extraction and local analgesic cocktail injection. Group C: Patients received epidural anesthesia and local analgesic cocktail injection. VAS, visual analogue scale; SD, standard deviation.

Group B: There were 46 patients consisted of 16 men and 30 women in this group. The average age was 66.8 ± 7.9 years old (range from 51 to 79 years). The average BMI was $24.3 \pm 2.7 \text{ kg.m}^{-2}$ (ranges from 22.2 to 27.4 kg.m^{-2}). Among all the cases, 20 were left knees and 26 were right knees. Three patients had traumatic osteoarthritis and 43 had degenerative osteoarthritis. Seventeen patients were categorized to Kellgren-Lawrence grade III and 29 were categorized to Kellgren-Lawrence grade IV. The mean average preoperative VAS score was 4.3 ± 3.5 (ranges from 3 to 5). The mean KSS score was 53.8 ± 7.9 (range 43–67). The mean tibiofemoral angle (varus deformity) was $15.6 \pm 6.0^\circ$ (ranges from 0 to 23°). The mean knee flexion contracture angle (flexion deformity) was $13.5 \pm 8.8^\circ$ (ranges from $0-27^\circ$).

Group C: There were 42 patients consisted of 18 men and 34 women in this group. The average age was 65.5 ± 8.1 years old (ranges from 52 to 77 years). The average BMI was $24.3 \pm 3.1 \text{ kg.m}^{-2}$ (range from 23.4–28.4 kg.m^{-2}). Among all the cases, 25 were left knees and 27 were right knees. Four patients had traumatic osteoarthritis and 48 had degenerative osteoarthritis. Nineteen patients were categorized to Kellgren-Lawrence grade III and 33 were categorized to Kellgren-Lawrence grade IV. The average preoperative visual analog scale (VAS) score was 4.0 ± 3.1 (ranges from 3 to 5). The mean KSS score was 54.4 ± 6.8 (ranges from 41–69). The mean tibiofemoral angle (varus deformity) was $15.7 \pm 5.7^\circ$ (ranges from $0-25^\circ$). The mean knee flexion contracture angle (flexion deformity) was $13.9 \pm 7.9^\circ$ (ranges from $0-26^\circ$).

No significant differences were found in terms of all the variables mentioned above among the three groups.

Pain level and dezocine use after unilateral KTA

The VAS scores, both at rest and with activity, at 6 and 12 hours post-operation, were significantly different among the three groups ($p < 0.05$). Further q-test showed no difference in VAS score between groups A and B ($p > 0.05$), however, the VAS in group C was significantly higher than that in group A or B ($p < 0.05$). The VAS scores at 24 and 36 hours post-operation were not different among the three groups ($p > 0.05$). The use of dezocine did not differ among the three groups ($p > .05$) (Table 2).

Muscle strength score in patients underwent unilateral TKA

The muscle strength score at 6 and 12 hours post-operation differed significantly among the three groups ($p < 0.05$). Further q-testing showed no difference in muscle strength between groups A and B ($p > 0.05$), while muscle strength in group C was significantly higher than that in groups A or B ($p < .05$). Muscle strength at 24 and 36 hours post-operation were not different among three groups ($p > 0.05$) (Table 3).

Postoperative complications after unilateral TKA

The incidences of postoperative complications, including urinary retention, nausea, emesis, and pruritus, differed

Table 3 Comparison of muscle strength of the affected leg among patient groups receiving different pain management protocols (mean \pm SD).

Group	N	Muscle strength at 6 h	Muscle strength at 12 h	Muscle strength at 24 h	Muscle strength at 36 h
Group A	50	2.2 \pm 1.2	2.4 \pm 0.8	3.7 \pm 1.1	4.2 \pm 2.6
Group B	46	1.9 \pm 0.7	2.1 \pm 1.2	3.5 \pm 1.9	4.2 \pm 2.7
Group C	52	3.2 \pm 1.9	3.7 \pm 2.8	4.1 \pm 2.1	4.5 \pm 0.9
F-value		8.82	12.23	3.63	2.46
P-value		< 0.05	< 0.05	> 0.05	> 0.05

Group A: Patients received morphine (3 mg) via epidural anesthesia catheter before catheter extraction. Group B: Patients received morphine (3 mg) via epidural anesthesia catheter before catheter extraction and local analgesic cocktail injection. Group C: Patients received epidural anesthesia and local analgesic cocktail injection. SD, standard deviation.

Table 4 Comparison of complications among different patient groups after TKA.

Group	N	Postoperative first void (urinary retention) (mean \pm SD, min)	Nausea and emesis (n, %)	Pruritus (n, %)
Group A	50	442 \pm 112	39 (78)	29 (58)
Group B	46	463 \pm 98	32 (69)	32 (69)
Group C	52	269 \pm 107	12 (23)	20 (38)
χ^2 /F-value		9.39	12.76	10.48
P-value		< 0.05	< 0.05	< 0.05

Group A: Patients received morphine (3 mg) via epidural anesthesia catheter before catheter extraction. Group B: Patients received morphine (3 mg) via epidural anesthesia catheter before catheter extraction and local analgesic cocktail injection. Group C: Patients received epidural anesthesia and local analgesic cocktail injection. TKA, total knee arthroplasty; SD, standard deviation.

significantly among groups A, B, and C ($p < 0.05$). Further q-testing showed that all the incidences of postoperative complications between groups A and B were not significantly different ($p > 0.05$). In addition, all the incidences of postoperative complications in group C were significantly lower than those in groups A or B ($p < 0.05$) (Table 4).

Discussion

The conception of ERAS has drawn more and more attention in total joint arthroplasty.^{9,10} ERAS programs aim to reduce postoperative complications, reduce the stress response to surgical trauma, improve surgical safety, and improve overall patient satisfaction. At present, the perioperative analgesia approaches for patients undergoing TKA include nonpharmacological methods, pharmacological methods, intraspinal analgesia, peripheral nerve blocking, injection of analgesic cocktail around the incision site, and patient-controlled analgesia (PCA). Intrathecal administration of opioids is still the mainstay in postoperative pain management. The common side effects of opioid analgesics are concentrated in the gastrointestinal tract and central nervous systems.¹¹ These side effects include nausea, emesis, constipation, drowsiness and excessive sedation, and respiratory depression. In addition, opioids may cause pruritus, urinary retention, and low blood pressure. Moreover, locally administered anesthetics may block motor neurons and thus affect postoperative rehabilitation exercises. ERAS programs in TKA mainly focus on perioperative care which includes optimization of pain management, prevention of infection and deep vein thrombosis, and optimization of bladder catheterization.⁵⁻⁷ In this study, we compared the effects of a local analgesic cocktail injection on the effects

of epidural morphine injection in pain control. The results showed that local analgesic cocktail injection is more conducive to muscle strength recovery in the first 24 hours post-operation, reducing urinary retention, and lowering the risk of postoperative complications including nausea, emesis, and pruritus.

Pain is considered the fifth vital sign. TKA patients' acute uncontrollable postoperative pain hampers early functional training,¹² which is usually recommended as early as possible after the operation. In our study, epidural morphine and/or local analgesic cocktail injection were/was administered to the patients undergoing total knee arthroplasty. VAS scores, which represent pain levels, were compared among different groups and different time points. VAS scores at 36 hours post-operation, both at rest and with activity, were significantly higher than that at 6, 12, and 24 hours post-operation. The delayed pain may be associated with icepack usage and intravenous administration of parecoxib. The VAS score differed significantly among groups A, B, and C. Further comparison was conducted between pairs of groups. The VAS of groups A and C differed significantly at 6 and 12 hours post-operation, both at rest and with activity, but it did not differ at 24 and 36 hours post-operation. In contrast, the VAS of groups A and B did not differ at any of the time points, either at rest or with activity. These results were consistent with the previous observation that morphine remained within the cerebrospinal fluid for at least 20 hours,¹³ and demonstrated that epidural morphine administration could effectively relieve acute postoperative pain. Among the three groups, patients in group B got maximum pain relief at 6 and 12 hours, followed by group A, and the percentage of dezocine use in group B was the lowest, suggesting that morphine performed better in relieving pain than a cocktail.

Husted et al.⁶ reported that muscle weakness after TKA surgery is positively correlated with the length of stay (LOS). Delayed discharge and prolonged recovery will increase medical expenses. Yan et al.¹⁴ found that epidural morphine administration affects early muscle strength recovery. In this study, the muscle strengths of groups A and B at 6 and 12 hours were significantly lower than those at 24 and 36 hours. In group C, the muscle strength at 6 hours post-operation was significantly lower than that at 12, 24, and 36 hours. Most researches suggested that adding glucocorticoid into the local analgesic cocktail can reduce the time to postoperative straight leg raise and improve the postoperative joint movement.^{15–19} The individuals in group C had significantly greater muscle strength at 6 and 12 hours post-operation than those in groups A and B, although the differences at 24 and 36 hours were not significant. These results suggested that a local analgesic cocktail without epidural morphine administration could facilitate early muscle strength recovery after TKA.

As proposed by current ERAS, no catheterization, no emesis, higher patients' satisfaction, and lower risk of postoperative complications are the future development trend in perioperative care. Indwelling bladder catheter causes patients' discomfort, prevents them from early mobility, prolongs the length of hospital stay, and increases the risk of postoperative venous thrombosis.²⁰ In our study, patients in groups A and B who received morphine administration had a significantly higher incidence of urinary retention, emesis, and pruritus, suggesting local analgesic cocktail injection is superior to morphine administration via epidural anesthesia catheter.

Despite the interesting findings, our study still contains limitations. First, we did not include a non-treatment control group due to ethical reasons. Second, this is a retrospective study with a limited sample size. A further multi-center prospective clinical study with a larger sample size is needed to validate our results.

Conclusion

In summary, both pain protocols, epidural anesthesia plus morphine and epidural anesthesia plus local analgesic cocktail injection, provide satisfactory pain relief. However, within the first 24 hours after operation, epidural anesthesia plus morphine protocol causes reduced muscle strength and higher incidence of urinary retention, nausea, emesis, and pruritus compared with the protocol of epidural anesthesia plus local analgesic cocktail injection. Local analgesic cocktail injection provides better pain relief, prevents the occurrence of postoperative complications, improves patients' early satisfactory rate, and facilitates recovery. Therefore, epidural anesthesia combined with local analgesic cocktail injection is a preferable effective multimodal analgesia for TKA.

Conflict of interest

The authors declare no conflicts of interest.

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