Effects of Intravenous Patient-Controlled Analgesia with Morphine, Continuous Epidural Analgesia, and Continuous Three-in-One Block on Postoperative Pain and Knee Rehabilitation After Unilateral Total Knee Arthroplasty

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In this study, we assessed the influence of three analgesic techniques on postoperative knee rehabilitation after total knee arthroplasty (TKA). Forty-five patients scheduled for elective TKA under general anesthesia were randomly divided into three groups. Postoperative analgesia was provided with IV patient-controlled analgesia (PCA) with morphine in Group A, continuous 3-in-1 block in Group B, and epidural analgesia in Group C. Immediately after surgery, the three groups started identical physical therapy regimens. Pain scores, supplemental analgesia, side effects, degree of maximal knee flexion, day of first walk, and duration of hospital stay were recorded. Patients in Groups B and C reported significantly lower pain scores than those in Group A. Supplemental analgesia was comparable in the three groups. Compared with Groups A and C, a significantly lower incidence of side effects was noted in Group B. Significantly better knee flexion (until 6 wk after surgery), faster ambulation, and shorter hospital stay were noted in Groups B and C. However, these benefits did not affect outcome at 3 mo. We conclude that, after TKA, continuous 3-in-1 block and epidural analgesia provide better pain relief and faster knee rehabilitation than IV PCA with morphine. Because it induces fewer side effects, continuous 3-in-1 block should be considered the technique of choice. **Implications:** In this study, we determined that, after total knee arthroplasty, loco-regional analgesic techniques (epidural analgesia or continuous 3-in-1 block) provide better pain relief and faster postoperative knee rehabilitation than IV patient-controlled analgesia with morphine. Because it causes fewer side effects than epidural analgesia, continuous 3-in-1 block is the technique of choice.

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Postoperative pain after total knee arthroplasty (TKA) is a major concern. It is severe in 60% of patients and moderate in 30% (1), and it hinders early intense physical therapy, the most influential factor for good postoperative knee rehabilitation (2,3).

After TKA, postoperative pain relief can be achieved by a variety of techniques, such as IV patient-controlled analgesia (PCA) (4), epidural analgesia with narcotics and/or local anesthetics (5,6), and lumbar plexus blockade (7,8). Few studies compare the analgesic efficacy of these techniques and their influence on postoperative knee mobilization.

The aim of the present study was to compare IV PCA with morphine with continuous epidural analgesia and continuous 3-in-1 block in terms of analgesic efficacy and postoperative knee rehabilitation after unilateral TKA.

Methods

After informed consent and with institutional approval, 45 ASA physical status II or III patients scheduled for elective unilateral TKA under general anesthesia (GA) were included in this study. Patients were excluded if they met any of the following criteria: contraindications to regional anesthetic technique (e.g., local infection, sepsis, coagulation abnormality), age <18 or >80 yr, weight <50 or >100 kg, allergy to local anesthetic and/or opioid, preexisting neurological deficit, diabetes, or inability to comprehend pain scales or to use a PCA device.

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Patients were divided into three groups of 15 in a randomized fashion using a computer-generated list of random permutations. During the first 48 h postoperatively, analgesia was provided on the ward by using IV PCA with morphine (concentration 2 mg/mL, dose 1.5 mg, lockout 8 min) in Group A, continuous 3-in-1 block in Group B, and continuous epidural analgesia in Group C.

In Group B, continuous 3-in-1 block was performed before inducing GA, following the guidelines of Winnie et al. (9). The femoral artery was located below the inguinal ligament, and an 18-gauge, short-beveled cannula (Alphaplex® set; Sterimed, Saarbrucken, Germany) was inserted just lateral to the artery. The femoral nerve was accurately located with a peripheral nerve stimulator (Anaestim; MK III, Meda, Belgium). Using a Seldinger technique, a 20-gauge catheter was threaded 10–15 cm into the psoas compartment. After a negative aspiration test for blood and cerebrospinal fluid (10), 37 mL of 0.25% bupivacaine with epinephrine 1:200000 was injected, followed by a continuous infusion of 0.125% bupivacaine with sufentanil 0.1 μg/mL and clonidine 1 μg/mL at the rate of 10 mL/h. To verify the correct position of the catheter, the cutaneous sensibility in the area of the femoral nerve was assessed by using a cold test before the induction of GA.

In Group C, epidural analgesia was performed before inducing GA, at L2-3 or L3-4 level. A 18-gauge catheter (Minipack Portex®; Portex Ltd, Hythe, UK) was threaded 4–5 cm into the epidural space. After a negative test dose of 3 mL of 0.25% bupivacaine with epinephrine 1:200000, 10 mL of the same solution and 10 μg of sufentanil were injected, followed by the same continuous infusion as in Group B. The extent of upper sensory blockade was assessed by cold testing before inducing GA.

In all groups, GA was induced with 0.3 μg/kg sufentanil, 3–5 mg/kg thiopentone, and 0.5 mg/kg atracrium. The trachea was intubated, and controlled ventilation was started. Anesthesia was maintained with sufentanil infused at a rate of 0.0025 (Groups B and C) or 0.005 (Group A) $\mu g \cdot kg^{-1} \cdot min^{-1}$ (stopped 45 min before the end of the procedure) and a mixture of nitrous oxide (66%) and isoflurane (0.2%–1%) in oxygen.

The intensity of pain at rest and on movement was assessed by the patients using a visual analog scale (0 = no pain, 10 = worst possible pain) 4, 24, and 48 h after the operation. A postoperative pain score (PPS) (0 = no pain; 1 = moderate pain only when moving; 2 = moderate pain at rest, severe pain when moving;3 = constant severe pain) was also recorded by nurses 4, 8, 12, 24, 36, and 48 h postoperatively. Supplemental postoperative analgesia was standardized. If the PPS was ≥1, 1 g of propacetamol (Prodafalgan®; Upsamedica s.a, Brussels, Belgium) was administered IV, followed by 10–20 mg of IM piritramide (DIPI), a synthetic μ-agonist opioid (Dipidolor®; Janssen Pharmaceutica, Beerse, Belgium) if PPS remained unchanged after 30 min in Groups B and C. Pain scores, supplemental analgesia, and side effects were recorded for each group.

Immediately after surgery, all three groups started identical physical therapy regimens. During the first 48–72 h postoperatively, a continuous passive motion machine was applied, with the range of motion set at levels tolerated well by the patient. From the day after surgery until discharge, the patients performed active and assisted knee and hip flexion and extension exercises against gravity twice daily. Getting up from bed was encouraged as soon as possible, followed by ambulation with a walker.

The degree of knee flexion tolerated by each patient was recorded by the physical therapist twice a day until discharge. The day of first ambulation, the number of postoperative days required to obtain 90° of knee flexion, the need for knee manipulation under GA, and the duration of hospital stay were recorded for each group.

The surgeons reviewed the patients 6 wk and 3 mo after the procedure, and assessed knee flexion by goniometry.

Data from the three groups were compared by using analysis of variance and the least significant difference test or by using χ^2 analysis when appropriate. Results are expressed as mean ± SD. A P value <0.05 was considered significant.

Results

Population data (age, weight, height, gender ratio) were comparable in all groups.

In Group B, a block of the femoral nerve was obtained in all patients. In Group C, upper sensory level (before the induction of GA) was higher than T12 bilaterally in all patients.

The VAS score at rest and on movement and the PPS 4, 24, and 48 h are presented in Table 1. Compared with Group A, all pain scores were significantly lower in Groups B and C. Compared with Group B, significantly better scores were noted in Group C, but only in the immediate postoperative period (4 h).

In Group A, the total consumption of morphine during the first 48 h postoperatively was 67 ± 26 mg (45 ± 13 mg on Day 1; 22 ± 15 mg on Day 2). Supplemental analgesia was comparable in the three groups (propacetamol 1.8 ± 1.5 vs 1.7 ± 1.1 vs 1.1 ± 1.5 g/48 h (P = 0.37) and DIPI 0 vs 1.9 ± 4.1 vs 2.3 ± 6.2 mg/48 h (P = 0.29), for Group A versus Group B versus Group C).

Side effects are presented in Table 2. Compared with Group B, urinary retention and catheter-related

Table 1. Pain Scores at 4, 24, and 48 Hours in the Three Groups

	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	P value
VAS_R				
4 h	45 ± 18 (0–70)	32 ± 18 (0–60)*	11 ± 15 (0–45)*†	<0.001
24 h	27 ± 14 (10–60)	17 ± 10 (0–35)*	16 ± 14 (0–40)*	0.04
48 h	20 ± 14 (0–50)	10 ± 6 (0–20)*	12 ± 10 (0–30)*	0.03
VAS_M				
4 h	66 ± 15 (40–90)	48 ± 20 (0–80)*	20 ± 21 (0–50)*†	<0.001
24 h	52 ± 19 (30–100)	36 ± 11 (20–60)*	33 ± 23 (0–70)*	0.01
48 h	42 ± 17 (15–80)	25 ± 12 (10–45)	30 ± 25 (0–80)	0.06
PPS				
4 h	1.6 ± 0.5 (1–2.5)	1.2 ± 0.6 (0–2)*	0.4 ± 0.5 (0–1)*†	<0.001
24 h	1.1 ± 0.2 (1–1.5)	0.8 ± 0.3 (0–1)	0.6 ± 0.5 (0–1.5)*	0.002
48 h	0.9 ± 0.2 (0.5–1)	0.5 ± 0.5 (0–1)	0.5 ± 0.6 (0–2)	0.06

Values are mean ± SD (range).
VAS_R = visual analog scale score at rest, VAS_M = visual analog scale score on movement, PPS = postoperative pain score.
* Significantly different compared with Group A.
† Significantly different compared with Group B.

Table 2. Technical Problems and Percentage of Patients with Side Effects in Each Group

	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	P value
Nausea/vomiting	40	33	27	0.74
Arterial hypotension	0	0	7	0.36
Urinary retention	13	0	40*	0.05
Catheter problems	0	0	40*†	<0.001
Lateralization on nonoperated side	—	0	13*†	<0.001
Difficult insertion	—	0	7	0.07
Kinked catheter	—	0	20*†	<0.001

Values are expressed as percentages.
* Significantly different compared with Group B.
† Significantly different compared with Group A.

problems were significantly more frequent in Group C.

The degree of knee flexion obtained daily in each group are presented in Table 3. Compared with Group A, significantly better knee flexion was noted in Groups B and C from Day 1 until discharge. No difference was noted between Groups B and C. Six weeks after the procedure, patients in Groups B and C had significantly better knee flexion than patients in Group A. However, at 3 mo, no difference was noted among the groups.

The number of days required to obtain 90° of knee flexion (discharge criteria) was significantly higher in Group A compared with both other groups (17 ± 7 vs 9 ± 6 vs 8 ± 5 days [$P < 0.001$] for Group A versus Group B versus Group C). Five patients in Group A, one patient in Group B, and no patients in Group C were discharged with <90° of knee flexion. This difference was statistically significant ($P = 0.02$). Two patients in Group A and none in Groups B and C required manipulation under GA for stiff knee during the observation period. Patients in Groups B and C walked significantly earlier than those in Group A (4.3 ± 0.7 vs 3.5 ± 0.6 vs 3.5 ± 1 days [$P = 0.02$] for Group A versus Group B versus Group C).

The duration of hospital stay (including rehabilitation phases of recovery) was significantly longer in Group A (21 ± 3 days) than in Groups B (17 ± 3 days) and C (16 ± 4 days) ($P < 0.001$).

Discussion

Postoperative pain is a major concern after TKA. It is severe in 60% of patients and moderate in 30% (1). When inadequately treated, it intensifies reflex responses, which can cause serious complications, such as pulmonary or urinary problems, thromboembolism, hyperdynamic circulation, and increased oxygen consumption (11). Moreover, it hinders early intense physical therapy, the most influential factor for good postoperative knee rehabilitation (2,3).

Postoperative pain relief can be achieved by a number of techniques, such as IV PCA (4), epidural analgesia with narcotics and/or local anesthetics (5,6), and lumbar plexus blockade (7,8). Epidural analgesia with

Table 3. Knee Flexion Obtained Daily in Each Group

	Group A (n = 15)	Group B (n = 15)	Group C (n = 15)	P value
Day 1	33 ± 15 (10–60)	56 ± 22 (20–85)*	48 ± 20 (10–90)*	0.009
Day 2	44 ± 14 (20–70)	65 ± 15 (30–85)*	61 ± 16 (30–90)*	<0.001
Day 3	53 ± 17 (25–85)	74 ± 11 (55–90)*	71 ± 12 (50–90)*	<0.001
Day 4	62 ± 18 (30–90)	81 ± 7 (65–90)*	79 ± 12 (50–90)*	<0.001
Day 5	68 ± 19 (25–95)	84 ± 6 (75–90)*	86 ± 7 (70–95)*	<0.001
Day 6	72 ± 15 (35–95)	85 ± 5 (75–90)*	87 ± 6 (70–95)*	<0.001
Day 7	73 ± 14 (45–95)	85 ± 5 (75–90)*	90 ± 4 (80–95)*	<0.001
Day 8	73 ± 14 (40–95)	86 ± 5 (75–90)*	90 ± 5 (80–100)*	<0.001
Day 9	76 ± 11 (55–95)	87 ± 5 (75–90)*	92 ± 6 (80–105)*	<0.001
Day 10	77 ± 11 (55–95)	88 ± 6 (75–95)*	91 ± 5 (80–100)*	<0.001
Discharge	88 ± 7 (75–100)	94 ± 4 (85–100)*	97 ± 4 (90–105)*	<0.001
6 wk	103 ± 12 (80–125)	116 ± 12 (100–135)*	114 ± 14 (90–135)*	0.03
3 mo	116 ± 11 (90–130)	124 ± 12 (95–135)	121 ± 12 (90–135)	0.22

Values are expressed in degrees of knee flexion as mean ± SD (range).
* Significantly different compared with Group A.

opioid and/or local anesthetics provides superior pain relief compared with conventional IM opioids or IV PCA with morphine (12–15). However, it is associated with side effects, such as nausea, pruritus, urinary retention, and respiratory depression with opiates, and bilateral motor blockade and arterial hypotension with local anesthetics. Continuous 3-in-1 block provides better pain relief than systemic (IM or IV PCA) opioids (16,17). It is as efficient as epidural analgesia and induces fewer side effects; it is thus considered the analgesic technique of choice after open knee surgery (17).

In the present study, we demonstrate that continuous 3-in-1 block and epidural analgesia provide better pain relief than IV PCA with morphine after TKA. Except in the immediate postoperative period (4 h), these loco-regional anesthetic techniques provide comparable analgesia. Continuous 3-in-1 block induces nearly 4 times fewer side effects than epidural analgesia. This was observed in the limited number of patients in the present study, but was recently confirmed in more than 500 patients (18). Thus, we can conclude from both studies that continuous 3-in-1 block is the technique of choice for providing postoperative analgesia after TKA.

After knee surgery, poorly managed pain may inhibit the early ability to mobilize the knee joint. This, in turn, may result in adhesions, capsular contracture, and muscle atrophy, all of which may delay or permanently impair the ultimate functional outcome (19). Few studies have assessed the influence of the postoperative analgesic technique on knee rehabilitation after TKA. Compared with conventional IV or IM opioid treatment, epidural analgesia is associated with more rapid achievement of all postoperative rehabilitative milestones and, in some studies, a shorter hospital stay (20–22). Compared with IV PCA with morphine, continuous femoral nerve block improved the range of motion, but only in the early postoperative period. This benefit did not affect the outcome at 6 wk (23).

In the present study, we demonstrate that continuous 3-in-1 block and epidural analgesia equally allow better and faster postoperative knee rehabilitation (earlier fulfillment of discharge criteria [90° of knee flexion], earlier ambulation, no stiff knee) and shorter duration of hospital stay than IV PCA with morphine after TKA. However, these benefits do not affect the outcome at 3 mo.

With both loco-regional anesthetic techniques, better knee flexion is recorded not only during the administration of the technique, but also after it. Pain relief alone cannot explain this prolonged beneficial effect. After open knee surgery, pain can be associated with severe reflex spasms of the quadriceps muscle, causing further pain and impaired muscle function. Rather perplexingly, these spasms begin as soon as the patient begins to ambulate, and their mechanisms are unknown. Animal data suggest that the massive nociceptive input from stimulation of nociceptive afferents produces sensitization not only of the peripheral nociceptors, but also of dorsal horn neurons. This increased excitability in the spinal cord is strong and prolonged. Consequently, nonnociceptive input (e.g., touch, proprioception) triggers increased reflex excitability with consequent spasm of the muscles supplied by the same and adjacent spinal segments (24). With regional anesthesia, the massive afferent nociceptive input is blocked; consequently, these reflex responses do not occur. Thus, prevention of quadriceps muscle spasm could explain the prolonged beneficial effect observed in our study with the loco-regional anesthetic techniques. However, this hypothesis should be confirmed by specific studies.

Added to the local anesthetic solution, sufentanil reduced the onset time of the block (25) and clonidine prolonged duration of both anesthesia and analgesia (26) after a single-shot brachial plexus block. Their

inclusion in our continuous infusion is based on unpublished data that supports enhanced onset and prolonged duration of continuous peripheral nerve block. This observation must be confirmed by a large randomized study.

This randomized study demonstrates that continuous 3-in-1 block and epidural analgesia provide better pain relief and allow better and faster knee rehabilitation than IV PCA with morphine after elective unilateral TKA. Because it induces fewer side effects than epidural analgesia, a continuous 3-in-1 block is the technique of choice to provide postoperative analgesia after TKA.

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References

1. Bonica J. Postoperative pain. In: Bonica J, ed. The management of pain. 2nd ed. Philadelphia: Lea & Febiger, 1990:461–80.
2. Shoji H, Solomonow M, Yoshino S, et al. Factors affecting postoperative flexion in total knee arthroplasty. Orthopedics 1990; 13:643–9.
3. Ryu J, Saito S, Yamamoto K, Sano S. Factors influencing the postoperative range of motion in total knee arthroplasty. Bull Hosp Joint Dis 1993;53:35–40.
4. Ferrante FM, Orav EJ, Rocco AG, Gallo J. A statistical model for pain in patient-controlled analgesia and conventional intramuscular opioid regimens. Anesth Analg 1988;67:457–61.
5. Baker MW, Tullos HS, Bryan WJ, Oxspring H. The use of epidural morphine in patients undergoing total knee arthroplasty. J Arthroplasty 1989;4:157–61.
6. Ilahi OA, Davidson JP, Tullos HS. Continuous epidural analgesia using fentanyl and bupivacaine after total knee arthroplasty. Clin Orthop 1994;299:44–52.
7. Schultz P, Anker-Møller E, Dahl JB, et al. Postoperative pain treatment after open knee surgery: continuous lumbar plexus block with bupivacaine versus epidural morphine. Reg Anesth 1991;16:34–7.
8. Edwards ND, Wright EM. Continuous low-dose 3-in-1 nerve blockade for postoperative pain relief after total knee replacement. Anesth Analg 1992;75:265–7.
9. Winnie AP, Ramamurthy S, Durrani Z. The inguinal paravascular technique of lumbar plexus anesthesia: the "3-in-1" block. Anesth Analg 1973;52:989–96.
10. Singelyn FJ, Contreras V, Gouverneur JM. Epidural anesthesia complicating continuous 3-in-1 lumbar plexus blockade. Anesthesiology 1995;83:217–20.
11. Kehlet H. Surgical stress: the role of pain and analgesia. Br J Anaesth 1989;63:189–95.
12. Gustafsson L, Friberg-Nielsen S, Garle M, et al. Extradural and parenteral morphine: kinetics and effects in postoperative pain: a controlled clinical study. Br J Anaesth 1982;54:1167–74.
13. Loper K, Ready L. Epidural morphine after anterior cruciate ligament repair: a comparison with patient-controlled intravenous morphine. Anesth Analg 1989;68:350–2.
14. Raj P, Knarr D, Vigdorth E, et al. Comparison of continuous epidural infusion of a local anesthetic and administration of systemic narcotics in the management of pain after total knee replacement. Anesth Analg 1987;66:401–6.
15. Soubiron L, Singelyn F. Postoperative analgesia after elective orthopaedic surgery: comparison between IV PCA, continuous peripheral nerve blocks and continuous epidural analgesia [abstract]. Br J Anaesth 1997;78:A414.
16. Edwards N, Wright E. Continuous low-dose 3-in-1 blockade for postoperative pain relief after total knee replacement. Anesth Analg 1992;75:265–7.
17. Serpell M, Millar F, Thomson M. Comparison of lumbar plexus block versus conventional opioid analgesia after total knee replacement. Anaesthesia 1991;46:275–7.
18. Singelyn F, Gouverneur JM. Postoperative analgesia after open knee surgery: comparison between continuous "3-in-1" block (CB) and continuous epidural analgesia (EA) [abstract]. Anesthesiology 1997;87:A803.
19. Akeson W, Amiel D, Abel M, et al. Effects of immobilization on joints. Clin Orthop 1987;219:28–37.
20. Williams-Russo P, Sharrock N, Haas S, et al. Randomized trial of epidural versus general anesthesia: outcomes after primary total knee replacement. Clin Orthop 1996;331:199–208.
21. Mahoney O, Noble P, Davidson J, Tullos H. The effect of continuous epidural analgesia on postoperative pain, rehabilitation, and duration of hospitalization in total knee arthroplasty. Clin Orthop 1990;260:30–7.
22. Buechele Pati A, Perme D, Trail M, Henry P, et al. Rehabilitation parameters in total knee replacement patients undergoing epidural vs. conventional analgesia. J Orthop Sports Phys Ther 1994;19:88–92.
23. Ganapathy S, Wasserman R, Watson J, Moote C, et al. Efficacy of continuous femoral block following total knee arthroplasty [abstract]. Anesthesiology 1997;87:A773.
24. Woolf C, Wall P. The brief and the prolonged facilitatory effects of unmyelinated afferent input on the rat spinal cord are independently influenced by peripheral nerve injury. Neuroscience 1986;17:1199–205.
25. Singelyn FJ, Contreras V, Lefebvre B, et al. Adding sufentanil to mepivacaine results in faster but not prolonged anesthesia and analgesia after brachial plexus blockade [abstract]. Anesthesiology 1993;79:A832.
26. Singelyn FJ, Gouverneur JM, Robert A. A minimum dose of clonidine added to mepivacaine prolongs the duration of anesthesia and analgesia after axillary brachial plexus block. Anesth Analg 1996;83:1046–50.