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Original Article

Benefit of subcutaneous patient controlled analgesia after total knee arthroplasty

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ABSTRACT

Purpose: Subcutaneous patient-controlled analgesia (PCA) has been widely used for orthopedic surgeries including total knee arthroplasty (TKA). This study aims to clarify the usefulness of subcutaneous PCA in the early phase after TKA.
Methods: Our subjects consisted of 88 osteoarthritis knee patients who underwent primary TKA, and were classified into two groups: 42 patients received a subcutaneous PCA (containing fentanyl and droleptan) after operation (PCA group), and 46 patients were managed without a subcutaneous PCA (control group). We compared the incidence of side effects for 3 days postoperatively, measuring the number of times patients used adjuvant analgesia and range of motion on day 7 between the two groups. 34 of 42 patients in the PCA group tolerated PCA use until POD 3 (continuation sub-group), while 8 patients could not continue PCA (interruption sub-group). Demographic data of the two sub-groups were compared.
Results: The mean number of times adjunctive analgesics were used by the PCA group (3.7 ± 2.2) was significantly less than in the control group (5.4 ± 2.8) ($p = 0.0049$). There were no significant differences in the frequency of side effects between the two groups. There was no significant difference in range of motion between the two groups. Comparing the continuation and interruption sub-groups, patients over 80 years old were at risk to discontinue a subcutaneous PCA ($p = 0.0319$, odds ratio 5.4).
Conclusion: These findings demonstrate that subcutaneous PCA would be a safe postoperative pain regimen for TKA patients, but the effect was not enough to promote early functional recovery.
Levels of evidence: Therapeutic, Level II.

Introduction

Although total knee arthroplasty (TKA) is widely used to treat severely damaged knee joints and to relieve knee pain, TKA has been shown to cause moderate to severe postoperative pain in both the short and long term.[1,2] Pain management is one of the most important keys to achieving successful TKA. Good analgesia following TKA facilitates rehabilitation, which prevents knee contracture, improves patient satisfaction, and may reduce the length of hospital stay.[3] Various methods have been applied to control pain in patients undergoing TKA such as femoral nerve block,[4,5] continuous epidural block,[6] and local infusion analgesia.[7–9]

Patient-controlled analgesia (PCA) involves use of a pre-programmed pump that patients use to self-administer analgesia, usually intravenously (IV). IV PCA has been widely applied in patients following TKA. Although the efficacy of IV PCA has been reported in previous studies, unfavorable problems were side effects.[9,10] Subcutaneous (SC) PCA use has been attempted for

Abbreviations: PCA, Patient controlled analgesia osteoarthritis: OA; TKA, total knee arthroplasty; MRI, magnetic resonance imaging; ACL, anterior cruciate ligament; 3D, three dimensional.

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orthopedic surgeries in order to mitigate postoperative pain after TKA.[11] However, little is known about whether postoperative SC PCA provides clinically important benefits for TKA. We hypothesized that a SC PCA would be effective in mitigating postoperative pain without significant adverse effects. The current study aimed to clarify the benefits of SC PCA use by evaluating the degree of postoperative pain, clinical outcomes at postoperative days (POD) 7after TKA and side effects from analgesia.

Methods

Subjects

We included in our study 88 of 117 patients who underwent primary TKA using a cemented posterior stabilized prosthesis from September 2014 to February 2016. All patients provided written informed consent for this Institutional Review Board approved study. Patients were excluded from the study if they suffered from major complications during and after surgery. They could not be managed with our postoperative pain management due to their comorbidity. Severe deformity required an augmentation such as a metal block or/and a long stem, or they had incomplete data set. Subjects were divided into two groups; one group consisting of 42 patients who received a SC PCA until (POD) 3 (PCA group), and 46 patients who did not undergo a SC PCA (control group). TKA was performed from Sep. 2014 to Apr. 2015 in the PCA group, and from May 2015 to Feb 2016 in the control group. All other aspects of postoperative management and rehabilitation protocol were equal between the two groups. In the PCA group, we defined the 34 patients who had sustained the usage of the PCA until POD 3 as “continuation sub-group”, while the 8 patients who could not tolerate and terminated the usage of continuous PCA due to either suffering from complication or self-removal of subcutaneous catheter earlier than POD 3 as “interruption sub-group”.

Surgical procedures

The same surgical procedures were performed for all patients by 8 surgeons whose career of orthopaedic surgeons ranged 9–34 years (the average was 18 years). The average surgical time was 121 min and average tourniquet time was 95 min. Significant differences of both surgical and tourniquet time among surgeons did not exist. The decision to replace the patella was made by the operating surgeon based on specifics of each case. An air tourniquet was utilized during surgery and was released before skin closure since released tourniquet before skin closure decreases complications compared with released tourniquet after skin closure.[12] Following a midline skin incision, the midvastus approach with measured bone cutting based on anatomic landmarks was used for all knees. An intramedullary alignment rod for the femoral side and an extramedullary guide system for the tibial side were used. After bone cutting, the soft tissues were released on a case-by-case basis to obtain mediolateral balance, and all components were fixed with cement. No drains were utilized in any patients. One ampoule of tranexamic acid (10% Transamin, 10 mL, 1000 mg; Daiichi-Sankyo, Tokyo, Japan) was routinely administered into the joint by an 18-gauge needle after skin closure.

Postoperative pain management

Patients were allowed to start and gradually progress range of motion and full weight-bearing gait exercise on the day after surgery. In the PCA group, the subcutaneous catheter was inserted postoperatively in the sternal region and prepared for use by an Anesthesiologist in the operating room. Analgesia was achieved with fentanyl 1.5 mg (1 mg if the patients were under 50 kg or women over 70 years old), droleptan 50 mg, and saline, up to a total volume of 60 ml. The subcutaneous catheter was left in place until POD 3. Analgesic drugs were infused at a basal rate of 1.0 ml per hour, and when patients wanted to relive pain, PCA was programmed to inject a demand dose of 1.0 ml by themselves with a 30 min lock out time. In both groups, all patients received celecoxib (400 mg/day) from POD 1 and were allowed to use pentazocine (15 mg) and diclofenac sodium supp (50 mg) as adjuvant analgesics if necessary. The number of adjunctive pain killer usage was recorded.

Postoperative assessments

The primary outcome measure was the frequency of adjuvant analgesic use in order to determine the severity of postoperative pain between the PCA and control groups. The incidence of side effects was recorded, including nausea and vomiting, restlessness, cardiac arrhythmia, and respiratory depression through POD 3. The range of knee motion at POD 7 was measured and changes in range of motion (ROM) between pre-operation and POD 7 were calculated (subtracting ROM at pre-operation from ROM at POD7) as an indicator of early progression of rehabilitation.

Statistical analysis

We carried out statistical analyses as followed. The Mann-Whitney test was used to compare the two groups as the data was not normality indicated with Kolmogorov–Smirnov test. A Chi-square test was applied for categorical data. A p-value less than .05 was considered significant. GraphPad Prism v7.04 software (GraphPad Software Inc. La Jolla, CA) was used to perform these statistical analyses. Post hoc power analysis was performed using G-power 3.1 calculation software (Kiel University, Kiel, Germany) as described previously,[13] and it revealed that, with an alpha of 0.05, a power of 0.89 was achieved for number of adjunctive pain killer usage from 0 to 3POD in all patients, and a power of 0.84 was achieved for that in bilateral TKA, whereas only a power of 0.48 was achieved for that in unilateral TKA.

Results

Surgical patients averaged 75 years old (range, 57–90 years). The patients consisted of 23 males and 65 females with 80 cases of osteoarthritis, 5 cases of rheumatoid arthritis and 3 cases of osteonecrosis. Patient demographic data between the two groups were not significantly different (Table 1A). Demographic data of 29 Patients who were excluded from this study was also shown (Table 1B). No significant differences were found with regard to the incidence of side effects between the two groups (Nausea· Vomit: PCA group 40%, control group 31%, Restless: 11%, 10%, Arrhythmia: 2%,2%, Respiratory depression:20%, 24%, respectively) (Fig. 1). The number of adjunctive pain killer usage in the PCA group was significantly fewer than that in the control group between POD 0 and POD 3 ($p = 0.0049$) and between POD 0 and POD 1 ($p = 0.002$) (Table 2A). When the groups were divided into bilateral and unilateral procedure, the PCA group showed better pain control for 3 days postoperatively (Control; 6.2 times, PCA; 4.1, difference; 2.1, $p = 0.0088$) in bilateral procedure. Better pain control was also observed to lesser degree for 3 days postoperatively (Control; 4.1, PCA; 2.9, difference; 1.2, $p = 0.0717$) in unilateral procedure (Table 2B and C). The PCA group was not superior to the control group in terms of range of motion (ROM) at POD 7 (Table 3). 8 of 42 patients, in particular 5 of 8 patients in 80 years old or more, were not able to tolerate PCA use until POD 3 because of complications or

Table 1
Demographic data of two groups.

A			
	PCA (N = 42)	Control (N = 46)	P value
Age	75 ± 8	76 ± 6	0.567
Sex (Men: Female)	15:27	8:38	0.051
Pathology (OA: non-OA)	40:2	40:6	0.177
Procedure (Bilateral:Unilateral)	27:15	29:17	0.904
Preoperative extension	−8.3 ± 6.9	−9.1 ± 6.8	0.532
Preoperative flexion	126 ± 15	125 ± 13	0.246
B			
	PCA (N = 14)	Control (N = 15)	P value
Age	75 (64–81)	77 (68–86)	0.839
Sex (Men: Female)	2:12	1:14	0.501
Pathology (OA: non-OA)	12:0	14:1	0.362
Procedure (Bilateral:Unilateral)	9:5	9:6	0.812

PCA: patient controlled analgesia OA: osteoarthritis.
A: Inclusion patients B:Exclusion patients.
P-values for age and preoperative range of motion were calculated using the Mann-Whitney test. P-values for sex, procedure, and pathology were calculated using the Chi-square test.

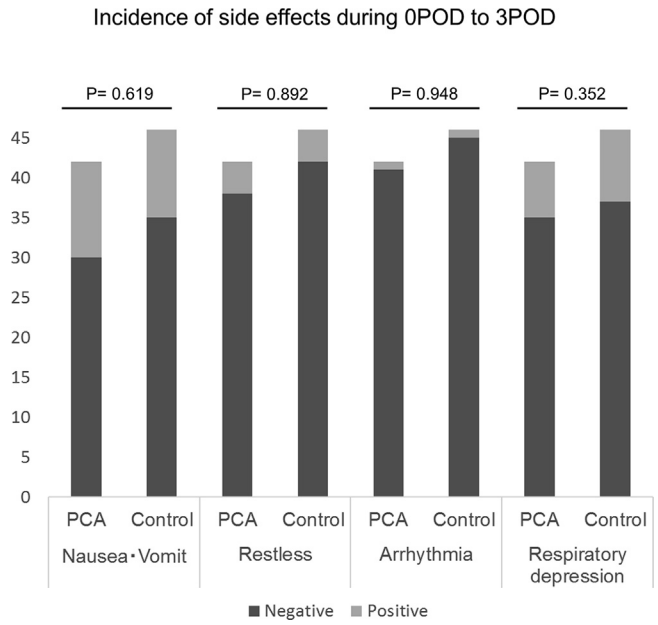

Fig. 1. Incidence of side effects during POD 0 to POD 3.
P-values were calculated using the Chi-square test.

cognitive impairments in the PCA group. Comparing the two subgroups of PCA users who used the PCA continuously (Continuation Group) and those who did not tolerate the PCA for the duration of the study (Interruption Group), there was no significant differences in sex, pathology, or procedure (Table 4). When a cut-off value of 80 years old was applied, a significant difference between these two groups became apparent (p = 0.0319, odds ratio 5.4).

Discussion

The most important finding in this study was SC PCA mitigated post-operative pain in TKA patients as indicated by the number of adjunctive pain killer usages. In addition, SC-PCA did not increase the occurrence of side effects although about 20% patients could not continue PCA until 3POD due to complications and cognitive impairments.

Table 2
Number of adjunctive pain killer usages during postoperative day 0 to day 3.

A. All patients			
	PCA	Control	P value
0 - 3POD	3.7 ± 2.2	5.4 ± 2.8	0.0049**
0 and 1POD	3.1 ± 1.6	4.4 ± 2.0	0.002**
2 and 3POD	0.6 ± 0.9	1.0 ± 1.5	0.0958
B. Bilateral TKA			
	PCA	Control	P value
0 - 3POD	4.1 ± 2.2	6.2 ± 3.1	0.0088**
0 and 1POD	3.4 ± 1.7	5.0 ± 2.1	0.0032**
2 and 3POD	0.4 ± 0.7	1.3 ± 1.8	0.0293*
C. Unilateral TKA			
	PCA	Control	P value
0 - 3POD	2.9 ± 1.9	4.1 ± 1.6	0.0717
0 and 1POD	2.3 ± 1.4	3.5 ± 1.3	0.0322*
2 and 3POD	0.5 ± 0.6	0.6 ± 0.7	0.553

PCA: patient controlled analgesia.
The data was presented as mean ± standard deviation. P-values were calculated using the Mann-Whitney test. **P < 0.01.

Table 3
Changes in range of motion between pre-operation and POD 7.

	PCA	Control	P value
Extension	2.1 ± 7.4	2.9 ± 6.1	0.389
Flexion	−18 ± 14	−19 ± 15	0.528

ROM: range of motion PCA: patient controlled analgesia.
The data was presented mean ± standard deviation. Pvalue was calculated using the Mann-Whitney test.

Traditional postoperative pain control using intramuscular analgesics has several downsides. The intramuscular route is painful, and the absorption rate is not predictable and consistent.[14] Additionally, dosages are not tailored to the individual patient. Its dosage and its administration interval to the experience of pain would be different among each patient. Conversely, PCA provides continuous, customizable analgesia without increasing burden on nursing staff which could lead to adequate pain control and better patient satisfaction.[15–17] It was reported that PCA offered better postoperative pain management after TKA compared with intramuscular analgesics or demanded conventional pain therapy.[18,19] However, opioid IV PCA is associated with side effects such as nausea, vomiting, drowsiness, dizziness, constipation, urinary retention, and respiratory depression.[3] It has been reported that SC and IV PCA achieve equivalent analgesia.[20] Furthermore, Dawson et al. found that SC PCA offered significant advantages compared with IV PCA in terms of frequency of complications and degree of pain reduction in female patients undergoing reconstructive plastic surgery or gynecological surgery.[21]

In this study, we investigated the efficacy and safety of SC PCA in TKA. There was no significant difference in the occurrence of side effects between the PCA group and control group. SC PCA could alleviate post-operative pain following TKA as indicated by decreasing the number of adjunctive pain killer usages. Most likely the patients who underwent bilateral procedures benefited from SC PCA more than those who underwent unilateral procedure, since bilateral procedures gave rise to more pain. Based on our results, subcutaneous PCA might be a safe option in TKA patients. However, approximately 20% patients were not able to continue PCA use until POD 3 due to complications or dementia. The results of this study suggest that alternative modalities should be considered in elderly patients, particularly those over 80 years old who are likely vulnerable to side effect with opioid.

Table 4
Comparison of continuation and interruption sub-groups.

	Continuation (N = 34)	Interruption (N = 8)	P value	Odds ratio of interruption
Age (≧80:<80)	8:26	5:3	0.0319*	5.4
Sex (Men: Female)	12:22	3:5	0.907	1.1
Pathology (OA: non-OA)	33:1	7:1	0.253	4.7
Procedure (Bilateral:Unilateral)	20:14	7:1	0.128	4.9

PCA: patient controlled analgesia OA: osteoarthritis.
Pvalue and odds ratios of interruption were calculated by Chi-square test. *P < 0.05.

In this study, we utilized the number of times of usage with adjunctive pain killer to evaluate the degree of postoperative pain instead of visual analog scale (VAS) or numerical rating scale (NRS) which are commonly used. However, there have been many studies that used consumption of opioid or amount of rescue medication as the indicator of postoperative pain[9,22,23]. It could be reasonable that SC PCA had significant effect of mitigating pain as shown by lower times of adjuvant analgesia in the PCA group than those in the control group.

Many strategies have been developed to control postoperative pain for TKA. Although femoral nerve block is a well-established method of reducing pain substantially, it is technically demanding, time-consuming, and may cause quadriceps muscle weakness and hematoma. These complications are undesirable and should be avoided in increasing risk of thromboembolism, accidental falls and delaying postoperative rehabilitation.[24,25] Alternatively, adductor canal block has been using since it could avoid quadriceps muscle weakness with the equivalent effectiveness of femoral nerve block.[26] Recently, there has been increased interest in intra-operative local infiltration analgesia and post-operative local infusion analgesia techniques in TKA.[9,27] These techniques have several advantages over epidural anesthesia and peripheral nerve block: they are easier and faster to perform while appearing to cause less muscle weakness. Compared to SC PCA containing opioids, local infusion analgesia may cause fewer opioid-related complications such as nausea and vomiting due to decreased systemic exposure to opioids. However, the risk of infection, decreased wound healing, and toxicity associated with the use of local anesthetics remains a concern.[28]

It is clear that better pain management leads to earlier recovery of TKA patients. Use of IV PCA with local infusion analgesia through an intra-articular catheter until 48 h after surgery reduced postoperative pain and led to earlier achievement of straight leg raising compared with only IV PCA in TKA patients.[7] In this study, no significant differences in recovery of knee range-of-motion at POD7 were found between the PCA and control groups. Although use of a SC PCA would reduce postoperative pain, it may not be a significant enough effect to promote early functional recovery based on the results presented in this study suggesting that postoperative pain management until POD3 was insufficient in TKA. Further study is needed to test whether longer term SC PCA improves functional recovery without any harmful effects. SC PCA would provide additional pain relief after TKA without increasing risk of significant complications. Therefore, SC -PCA may be useful as an adjunct to other modalities of pain relief (such as local infiltration of analgesia) to improve functional recovery and patient satisfaction.

This study has several limitations. First, we did not evaluate the degree of postoperative pain by VAS or numerical rating scale NRS as an outcome measure. Second, the ratio of males to females was higher in the PCA group compared to the control group, although no significant difference was shown (p = 0.051). We should consider this difference when interpreting the data obtained by this study. Third, the follow-up period was short. Fourth, the number of patients who underwent unilateral TKA was not adequate indicated by power analysis. Lastly, some important adverse effects of opioids were not recorded such as constipation, dizziness, arterial hypotension, urinary retention and pruritus. Despite these limitations, and recognizing the need for further study to obtain more robust conclusions, we believe that a SC PCA may have favorable outcomes without significant adverse effects for TKA patients.

Conclusions

Our results demonstrate that a SC PCA would be a safe postoperative pain treatment strategy for patients after TKA, but the effect was not enough to promote early functional recovery. Other postoperative pain modalities should be considered in patients over 80 years old who have higher risk of discontinue SC PCA.

Authors' contributions

YN acquisition of data, analysis of data, interpretation of data, drafting the manuscript. YA acquisition of data, analysis of data, drafting the manuscript. TW acquisition of data, interpretation of data, drafting the manuscript, final approved manuscript. MH acquisition of data. TN acquisition of data. KO acquisition of data. MK acquisition of data. IS provided the administrative and financial support. TM acquisition of data. HK participated in the design of the study, provided the administrative and financial support. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare that they have no conflict of interest.

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