Special Article

Contemporary Pain Management in Total Knee Arthroplasty

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Pain management has become a very important part of postoperative care for total knee arthroplasty patients. Contemporary pain control has evolved from high-dose opioid in the past to state-of-the-art multimodal regimens. These include multiple non-opioid medication such as NSAIDs, COX-2 inhibitors, and gabapentinoid, and novel anesthetic techniques such as preemptive analgesia and ultrasound-guided peripheral nerve blocks. Another method which is gaining popularity is intraarticular injection of anesthetic cocktail during surgery. Pre-op education can also help patients cope with their pain better.

Keywords: *Total knee arthroplasty, Pain management, Multimodal regimens, Intraarticular injection*

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Pain management is a major aspect of post-operative care. Total knee arthroplasty (TKA) is associated with moderate to severe postoperative pain[1]. Adequate pain control will undoubtedly improve early postoperative outcomes. This statement is proven by the fact that pain isa major evaluating domain of many knee scoring systems[2-4]. The purpose of this article is to review current strategies of pain management in TKA.

Mechanism of pain in total knee arthroplasty

Bone and surrounding soft tissue inflammations produced by TKA causes reduction of nociceptive pain threshold, a process called peripheral sensitization. Whenpain is prolonged, spinal cord and brain will be persistently exposure to stimuli, causing central sensitization. Inadequate acute pain control can lead to chronic pain, which will be very difficult to resolve[5].

From traditional pain control to contemporary pain managements

Strong opioids play a major role in traditional post-operative pain control[6]. Although opioids are very effective for pain control, most patients are suffered from their side effects, ranging from common and minor ones such as nausea, vomiting, dizziness, pruritus, somnolence, constipation, urinary retention to the more serious and life-threatening one like respiratory depression. In order to minimize those adverse reactions, patient-controlled anesthesia (PCA) has been introduced for post-op pain control. Nonetheless, the aforementioned side effects are still common with PCA[7].

Contemporary pain managements are focused on multimodal analgesia. Key aspects of multimodal regimen include preemptive medication, continuous regional anesthesia,local injection of anesthetic agent, multiple pain medication and novel technique such as ultrasound-guided peripheral nerve block. Using relatively low doseof multiple medications can block the pain signals at different part of pain pathway. This method resulted in less pain and fewer side effects from opioids, allowing patients to ambulate sooner than previously possible[8].

Preemptive analgesia

Preemptive analgesia consists of various analgesic methods given before the beginningof painful stimuli. Preemptive analgesia can reduced sensitization of the pain receptor, limitingafferent transmission of the noxious stimuli from peripheral to central nervous systems[9]. The timing of preemptive intervention has been defined as before surgerywith some regimens starting as early as a day before surgery. Preemptive

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analgesia includes both anesthetic procedure and medication. Regional anesthesia such as spinal and epidural blocks are technically preemptive procedures. A meta-analysis regarding efficacy of preemptive analgesia demonstrated that epidural anesthesia can significantly lower postoperative pain score and reduce opioid consumption[10]. Medications that can be used for preemptive pain controlinclude opioid, non-steroidal anti-inflammatory drugs (NSAIDs), acetaminophen and gabapentinoid.

Although the benefit of preemptive analgesia is well-documented, administration of such medications should be done in concordance with anesthesiologist.

Anesthetic techniques

Although general anesthesiais a viable options for TKA, many literatures clearly support superior benefits of regional anesthesiain terms of postoperative pain control[11-13]. Spinal and epidural anesthesia are both popular regional anesthetic techniques for total knee arthroplasty. The authors preferred epidural anesthesia for our patients due to its potential advantages over spinal anesthesia such as lower hemodynamic change and ability to infuse additional opioid or anesthetic agent[11]. Nonetheless, it is more technical demanding, has longer on set of action and incomplete motor or sensory blockade may occur[12]. Meta-analysis by Block et al suggested that epidural anesthesia provided superior postoperative pain control than parenteral opioids[13]. Other variants of epidural anesthesia include continuous epidural infusion and patient-control epidural anesthesia (PCEA). Recent randomized study from Hospital for Special Surgery found that PCEA and femoral nerve block cansignificantly reduce side effect of regional block[14].

Peripheral nerve block

Peripheral nerve block is another regional anesthetic method to enhance postoperative pain control. Multiple techniques areavailable such as femoral nerve, sciatic nerve, lumbar plexus and obturator nerve blocks. Femoral nerve block is the most popular technique for TKA (Fig. 1). The administration of anesthetic agent can be given assingle dose, continuously-orpatient-controlled perineural anesthesia. The superior pain control after TKA with femoral nerve block alone or in combination with sciatic nerve block were demonstrated in many studies[15-17]. Furthermore, the prolonged analgesic effect after infusion catheter removal have also been reported[18].

Fig.1 Femoral nerve block with catheter placement in patient undergoing total knee arthroplasty. Additional anesthetics can be administered post-operatively.

Downsides of femoral nerve block are technical difficulty, quadriceps motor weakness, less predictable pain relief, and inadequate coverage of posterior aspect of the knee. Serious complications from femoral nerve blockinclude compartment syndrome and vascular injury[19]. Fall due to muscle weakness is another potential serious complication of femoral nerve block. Continuous femoral block with lower concentration of anesthetic agent have been recommended in orderto minimize quadriceps weakness[20].

Intraarticular injection and continuous intraarticular infusion

Intraarticular injection is a technique to reduce postoperative pain by infiltrating the anesthetic agent to the soft tissue around the knee, also called pericapsular injection, andlocal infiltrative anesthesia (LIA). This techniquehas recentlygained popularity in TKA (Fig. 2).

Recent studies demonstrating lower pain score and fewer opioid consumption after intraarticular injection have been published[21-24]. The mixtures of infiltrative agents, nicknamed “cocktails” are varied among studies. Commonly used formulas usually include bupivacaine or its variants, epinephrine, clonidine, NSAIDs, steroid and morphine. Diclofenac and ketorolac are two available injectable NSAIDs inThailand. Due to the fact that diclofenacmay precipitate crystallization when mixed with other agents, ketorolac seems to be a safer choice for periarticular infiltration.

Dalury et al[25] suggest a combination of the

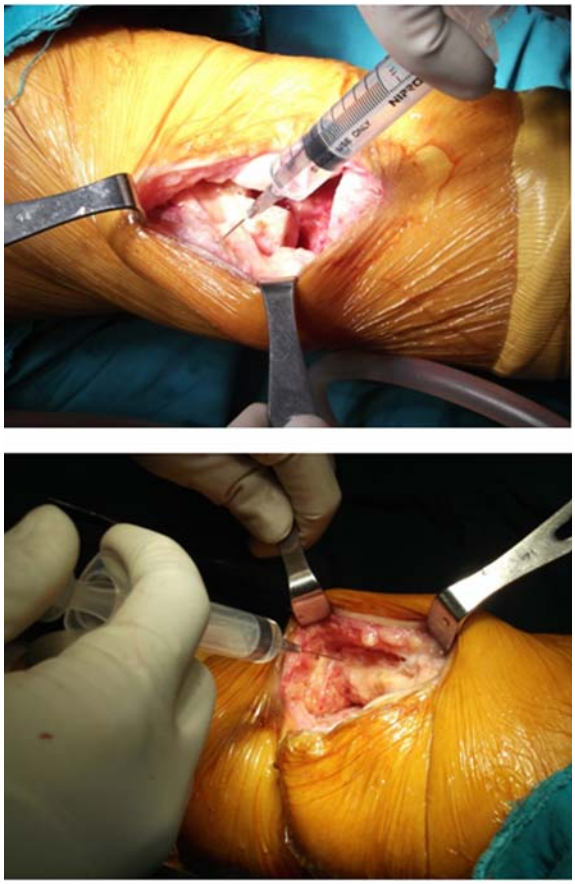

Fig. 2 Intraarticular injection with analgesic cocktail before final component implantation.

ropivacaine,epinephrine, ketorolac, clonidine and normal saline mixtures for intraarticular injection. Recommended injection sites are posterior capsule, medial periosteum, medial capsule, lateral periosteum, lateral capsule, skin and soft tissue.

The authors routinely used intraarticular injection for patients who do not receive continuous femoral nerve block. Our formula consists of 0.5% bupivacaine 20 ml, epinephrine 1 mg/ml (0.3 ml), morphine 10 mg/ml (0.5 ml) and normal saline solution 20 ml. Injecting the cocktail at posterior capsule should be done cautiously to avoid possible neurovascular structure injury.

Recent studies demonstrated similar pain control between intraarticular injection and femoral block, butintra articular injection is preferred because it is more economical and easier to perform[23,24].

An alternative method to intraarticular injection is local infusion analgesia. A randomized control study by Ikeuchi et al demonstratedthat local infusion analgesia via intraarticular double lumen catheter significantly reduced postoperative TKA pain[26]. In contrast, meta-analysis by Gupta et al, showed that local anesthetic injected via wound catheters did not reduce pain intensity[27].

Surgical technique & postoperative pain

Since pain in TKA is related to soft tissue injury and inflammation, it is strongly related to operative techniques. The popularity of minimally invasive surgery (MIS) concept, which focused on lowering soft tissue trauma than conventional technique, is due mainly to this reason. The principles of MIS TKA consisted of mobile skin window of limited incision, multiple knee position during surgery, patella subluxation rather than eversion and smaller instruments. Previous study at our institute demonstrated significantly lower postoperative pain with MIS TKA[28]. Another study by Dabboussi et al also confirmed our findings[29].

Effect of different knee arthrotomies are also topic of discussion. There are some studies demonstrating the relationship between pain and different surgical approaches[30-35]. Early report by Dalury and Jiranek demonstrated lower pain in midvastus approach than medial parapatellar arthrotomy[32]. However two recent randomized-control studies reported no not find such advantage[33,34]. Another study comparing subvastus and medial parapatellar approaches showed no difference of postoperative pain[35].

Tourniquet and postoperative pain is another interesting topic. There are reports of lower degree of pain in TKAs without tourniquet[36,37]. Duration of tourniquet also affects post-operative pain. Releasing the tourniquet before closing soft tissue and skin resulted in less pain than releasing the tourniquet after skin closure[38]. Drain placement, on the other hand, does not cause significant difference of early post-operative pain[39].

Comparison studies of pain in other aspects of surgery such as patella resurfacing versus non-resurfacing, or in regards to implant design (fixed-bearing versus mobile bearing, or cemented versus cementless fixation) are currently not available.

Multimodal analgesia

Various medications use for post-operative pain control include strong opioid (morphine, pethidine and fentanyl), weak opioid (tramadol, codeine), aceta-

minophen, conventional NSAIDs, COX-2 inhibitors, gabapentinoid[40,41]. When use in combination, lower dosage of each medicine are usually required, especially opioids. The strong opioids play a major role in early postoperative period but weaker opioid are used in the later days after surgery.

Conventional NSAIDs and COX-2 inhibitors have major role in multimodal analgesia. Parenteral NSAIDs such as ketorolac, diclofenac and parecoxib can be use peri-operatively. Efficacy of ketorolacin multimodal regimens to reduce post operative pain has been reported[42]. Dalury et al[25] suggest using ketorolac both for intraarticular injection and postoperatively. Even though COX-2 inhibitors have less gastro-intestinal side effects than conventional NSAIDs, there are concerns regarding renal and cardiovascular disturbance from COX-2 inhibitor in older patients. Regarding this matter, Tanavalee et al demonstrated that three doses of Parecoxib can be safety administered during early postoperative period without causing oliguria when patients received adequate hydration[43].

Gabapentinoids are gaining popularity in multimodal post-op pain regimens. Apart from usual pain receptor-blockade mechanism, Gabapentinoidsalso have role in pain-related sleep disturbance[44].

The authors are currently using both COX-2 inhibitor (celecoxib 200 mg or etoricoxib 90 mg) and gabapentinoids (gabapentin 300 mg or pregabalin 75 mg) for post-op pain control. The dosages are lower than those recommended for each medicine due to our interpretation of multimodal therapy.Our multimodal analgesic regimens are shown in Table 1.

Physical methods

Cold compression is an additional method for post-operative pain control. The potential benefits of cold compression are pain relief and reduction of edema. Systematic review suggested that both cooling and compression should be supplemented for

Table 1. Authors' TKA pain control regimen

Medication	Dose	Frequency
Day of surgery		
Intraarticular injection		
Bupivacaine	0.5% 20 ml	
Epinephrine	1 mg/ml (0.3 ml)	
Morphine	10 mg/ml (0.5 ml)	
Normal saline solution	20 ml	
Postoperative		
(with neuraxial opioid)		
Parecoxib	20-40* mg	IV every 12 hour, 3 doses
Tramadol	50 mg	IV as needed every 6 hour(as rescue pain medication)
Acetaminophen	650 -1000 mg	oral every 6 hour
Postoperative day 1		
Morphine	1-1.5** mg	IV every 3 hour
Etoricoxibor Celecoxib	90 mg200 mg	oral once daily oral once daily
Gabapentinor Pregabalin	300 mg75 mg	oral once daily before bed time oral once daily before bed time
Tramadol	50 mg	IV as needed every 6 hour (as rescue pain medication)
Postoperative day 2,3		
Acetaminophen plus codeine	300mg/15 mg	1 tablet every 8 hour
Etoricoxibor Celecoxib	90 mg200 mg	oral once daily oral once daily
Gabapentinor Pregabalin	300 mg75 mg	oral once daily before bed time oral once daily before bed time
Home medications		
Acetaminophen plus codeine	300mg/15 mg	1 tablet every 8 hour
Etoricoxib or Celecoxib	90 mg200 mg	oral once daily oral once daily
Gabapentin or Pregabalin	300 mg75 mg	oral once daily before bed time oral once daily before bed time
Acetaminophen	650-1000 mg	oral as needed every 4 hour

IV = intravenously, * Adjusted to renal function, ** Adjusted to pain score and side effects

postoperative analgesia following TKA[13]. However, another study demonstrated no superiority in terms of pain, knee and calf swelling and knee flexion in patients with cold compression therapy[45]. Anovel thermal therapy using far infrared ray (FIR) resulted in lower discomfort experience after TKA[46].

Patient education and careteams

The patient careteam including surgeons, anesthesiologists, internists, physical therapists, pharmacists and nursing staffs all play important role for maximized the operative result.

With the multidisciplinary approach, many centers have developed protocols for patients undergoing TKA such as Enhanced Recovery Programs (ERP) in United Kingdom[47] and Joint Replacement Program (JRP) in USA[48].

These protocols consisted of a pre-operative class, standard pathways for medical care, comprehensive peri-operative pain management, aggressive physical therapy (PT) and proactive discharge planning. Patients following these protocol were able to achieves better clinical results, including pain score, range of motion, shorten length of stay and fewer complications.

Patient education is also important. Many patients arenervous about surgery and afraid of post-operative pain. Pre-operative education which provides better understanding of hospital course and methods of pain control can serve as a psychological support for the patient.

Preoperative education has been successfully adopted at our institute with multiple media for patients scheduled for TKA, including video presentation, group seminar and patient handbook.

Conclusion

Pain control after total knee arthroplasty is one major key to a successfulsurgery. An evolution from traditional method using only strong opioid to contemporary management with multimodal regimen has improve early outcomes and patient satisfaction greatly. This new trend consists of preemptive analgesia, multiple analgesic medications, peripheral nerve block, intraarticular injection and physical devices. Patient education and care teams can also assist patients to achieve excellent and not-so-painful TKAs.

Potential conflicts of interest

None.

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วิธีร่วมสมัยในการควบคุมอาการปวดในผู้ป่วยที่ได้รับการผ่าตัดข้อเข่าเทียม

ยุทธนา คณาสุข, สีหธัช งามอุโฆษ

การผ่าตัดข้อเข่าเทียมถือเป็นการผ่าตัดที่มีความเจ็บปวดรุนแรง ดังนั้นการควบคุมความเจ็บปวดหลังการผ่าตัดถือเป็นสิ่งสำคัญยิ่งในการการดูแลผู้ป่วย ปัจจุบันมีแนวคิดในการความเจ็บปวดต่างจากเดิมซึ่งใช้ยาในกลุ่มมอร์ฟีนเป็นตัวหลักเพียงตัวเดียวโดยการปรับเพิ่มปริมาณตามความเจ็บปวด ซึ่งมักจะมีผลทำให้เกิดผลข้างเคียงจากยาได้บ่อย ในปัจจุบันมีแนวคิดการควบคุมความเจ็บปวดโดยใช้ยาหลายชนิดในปริมาณที่ค่อนข้างน้อยร่วมกัน ซึ่งจะช่วยลดผลข้างเคียงจากยาตัวใดตัวหนึ่งได้ บทความนี้เป็นการรวบรวมงานวิจัยที่เกี่ยวข้องกับการบริหารยาแก้ปวดรวมไปถึงนวัตกรรมใหม่ๆ ที่นำมาใช้สำหรับการควบคุมความเจ็บปวดหลังการผ่าตัดข้อเข่าเทียม