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Perioperative Pain Management in Total Hip Arthroplasty: Korean Hip Society Guidelines

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Effective perioperative pain management techniques and accelerated rehabilitation programs can improve health-related quality of life and functional status of patients after total hip arthroplasty. Traditionally, postoperative analgesia following arthroplasty was provided by intravenous patient-controlled analgesia or epidural analgesia. Recently, peripheral nerve blockade has emerged alternative analgesic approach. Multimodal analgesia strategy combines analgesics with different mechanisms of action to improve pain management. Intraoperative periarticular injection of multimodal drugs is one of the most important procedures in perioperative pain control for total hip arthroplasty. The goal of this review article is to provide a concise overview of the principles of multimodal pain management regimens as a practical guide for the perioperative pain management for total hip arthroplasty.

Key Words: Pain control, Total hip arthroplasty, Analgesics

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INTRODUCTION

Total hip arthroplasty (THA) is one of the most common major surgical procedures, and efficacious and cost-effective interventions as well as improving health-related quality of life and functional status of patients[1,2]. However, despite these advantages, THA can be associated with significant postoperative pain. Postoperative pain after THA can adversely affect early postoperative patient recovery. Moreover, pain can negatively impact postoperative mobility, increasing the risk of venous thromboembolic

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disease, and also may impair rehabilitation. As a result, these consequences of pain can prolong patient recovery and can increase hospital length of stay and cost. Therefore, adequate postoperative pain management after THA should be emphasized to enhance patient well-being and to minimize the physiologic consequences of pain[3,4].

The preemptive use of multimodal approach is the most important concept of pain management, and has been widely accepted as a gold standard approach of pain management following THA[5,6] Preemptive means that initial pain management should be performed before surgical stimuli, and multimodal approach means that multi-drugs or multi-modalities with different mechanisms or sites should be applied to get synergetic effect. Using two concepts, it has been known to be effective for postoperative pain management, reduction of the opioid consumption, and early initiation of rehabilitation eventually.

PAIN PERCEPTION

Pain is an unpleasant feeling that is conveyed to the brain by sensory neurons. The discomfort signals actual or potential injury to the body. The pain pathways form a complex, dynamic, sensory, cognitive, and behavioral system that evolved to detect, integrate, and coordinate a protective response to incoming noxious stimuli that

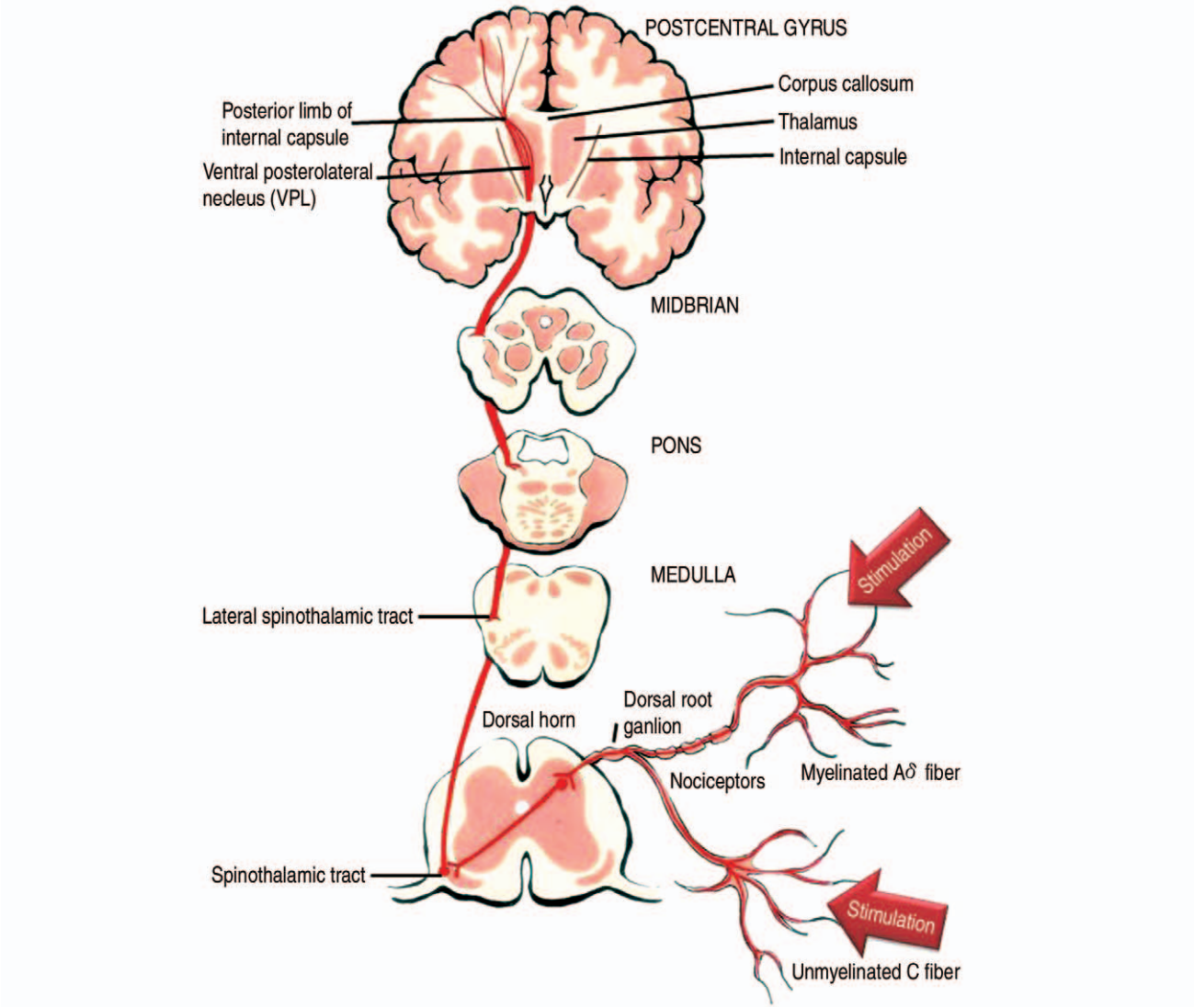

Fig. 1. Spinothalamic tract. Pain transmission from receptors in the skin ascends in the spinal cord to the postcentral gyrus via the lateral spinothalamic tract. First-order neurons transmit this sensory information and enter the spinal cord. Second-order neurons from the dorsal horn then decussate at the ventral commissure and ascend in the lateral spinothalamic tract before ending in the ventral posterolateral nuclei of the thalamus. Third-order neurons then project to the postcentral gyrus.

threatens tissue injury or organism survival[7].

Nociceptors are the specialized sensory receptors responsible for the detection of noxious (unpleasant) stimuli, transforming the stimuli into electrical signals, which are then conducted to the central nervous system (CNS). They are the free nerve endings of primary afferent Aδ and C fibers. Distributed throughout the body (skin, viscera, muscles, joints, meninges), they can be stimulated by mechanical, thermal or chemical stimuli. Transmission is divided into two categories, fast and slow. A-delta fibers detect and transmit pain quickly. These fibers are relatively small (1-6 m), thinly myelinated neurons that can conduct at speeds of 6 to 30 m/sec. C fibers are small (<1.5 m) and unmyelinated, conducting pain at 0.5 to 2 m/sec[8]. Complex interactions occur in the dorsal horn between afferent neurons, interneurons and descending modulatory pathways. Sensory neuron cell bodies are located in the dorsal root ganglia (DRG). DRG neurons are classically pseudo unipolar; one process extends into the peripheral nerve and the other process extends centrally, transmitting information through the dorsal root into the spinal cord. Most sensory fibers project from the DRG through the dorsal root and into the dorsal root entry zone (DREZ). At the DREZ, most unmyelinated and small myelinated axons project laterally to enter. Lissauer tract[9] fibers then extend vertically in this tract for several spinal segments before synapsing. There are two main pathways that carry nociceptive signals to higher centers in the brain. The spinothalamic tract: secondary afferent neurons decussate within a few segments of the level of entry into the spinal cord and ascend in the contralateral spinothalamic tract to nuclei within the thalamus. The spinothalamic tract transmits signals that are important for pain localization. The spinoreticular tract fibers also decussate and ascend the contralateral cord to reach the brainstem reticular formation, before projecting to the thalamus and hypothalamus. This pathway is involved in the emotional aspects of pain (Fig. 1).

Historically, osteoarthritis pain has been considered a nociceptive pain related to the degree of structural damage to the affected joint. Even though patients with osteoarthritis present structural anomalies, the severity of these changes is not always proportional to the degree of pain or disability. A significant proportion of these patients show signs of central sensitization, with pain modulation and processing altered at the CNS level. Central sensitization is defined as "an increased response of CNS neurons which inform of pain when faced with inputs coming from low threshold mechanoreceptors"[10]. One of the characteristics of central sensitization is that, once installed, it can persist in time despite the lack of new painful stimuli from the periphery. In clinical practice, it is not uncommon to find patients with osteoarthritis who show symptoms even after prosthetic substitution. It has been noted that patients suffering with osteoarthritis and a high degree of pain and low pain thresholds before surgery run a greater risk of continued pain after getting a prosthetic knee, which has been interpreted as an accurate reflection of central sensitization[11].

PATIENT EDUCATION AND REHABILITATION

The purpose of arthroplasty of hip joint is to restore painless hip joint and provide early functional recovery. The rehabilitation protocol after THA is mandatory to improve range of motion and strengthen the muscle power around hip joint. This should include preoperative education, post-acute rehabilitation, such as early ambulation with walking aids and muscle strengthening exercise, and balancing exercise[11]. The structured post-acute rehabilitation should be provided by trained professionals with knowledge at proper timing after THA. And for the early application of acute rehabilitation, well-designed multimodal pain management is necessary[11]. Also, the preoperative education can influence patient's perception of postoperative pain, walking and whole rehabilitation program. Consequently preoperative education can promote early discharge and reduce the total amount of analgesics usage. So, the preoperative education should be provided for patients and their family before THA[11]. The content should include the overall surgical procedure and rehabilitation protocol, expected benefits of THA, postoperative pain level and pattern, and pain management methods. Usually verbal format or small group sessions and is accompanied by a booklet as an adjunct to the verbal presentation[12].

For the pain management after THA, it is more important to give information about postoperative pain than information about pathoanatomy, biomedical model of anatomy, and biomechanics of the disease and THA[12]. Educational sessions which aim to enhance patient knowledge of pain science and pain processing by the nervous system may help patients experience less fear and anxiety, and ultimately help alleviate postoperative pain[12,13]. Increasing a patient's knowledge of pain science

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may alter their perception of threat and they may then experience less fear and anxiety. Additionally, the increased knowledge and understanding of pain science may help modulate the pain experience. The patients also felt less pain perhaps because they were less stressed and better prepared to cope with pain. Anxiety has been reported to increase sensitivity to pain and to reduce anxiety decrease[14].

CRYOTHERAPY

Cryotherapy involves the application of bag of ice or cooled water to the skin surrounding injury and operation area, and has been traditionally used in the post-operative recovery. The cold penetrates the soft tissues and, when applied over a joint, decrease in tissue metabolism associated with a reduction in enzymatic activity, and preventing tissue damage caused by injury[15,16]. Cryotherapy can reduce leukocyte migration and slow down nerve signal transmission, providing a reduction of inflammation and producing a short-term analgesic effect. Local hypothermia induces vasoconstriction and reduces extravasation of blood into surroundings tissues, local inflammation and edema production[17,18]. Many studies examining the benefits of cryotherapy on recovery after TKA have shown a reduction in blood loss[19-21].

However, the clinical benefits on pain and range of motion have been equivocal, with some studies showing a benefit[19-23] and others showing no difference in the treatment group[19,24,25]. Because most of the studies includes limited number of subjects and are nonrandomised, unblinded, cohort studies, and there are scanty of studies about the hip arthroplasty, further evaluation about the benefit of cryotherapy is needed.

MULTIMODAL ANALGESIA

Multimodal analgesia strategy combines analgesics with different mechanisms of action to improve postoperative pain management. This approach targets the various pathways and neurotransmitters involved in nociception and may allow a reduction in the dose of each individual analgesic. By using non-opioid adjuncts, perioperative opioid requirements and opioid-related side effects can be reduced such as nausea, vomiting, sedation, respiratory depression, urinary retention, and constipation[26]. In this section, we review the following multimodal analgesic adjuncts: acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), selective cyclo-oxygenase-2 (COX-2) inhibitors, and gabapentinoid.

1. Acetaminophen

Acetaminophen is a weak analgesic with minimal opioid-sparing ability but this agent is the most basic adjunct of a multimodal analgesia regimen due to its safety. According to literature review of meta-analyses and a Cochrane review, regular dosing significantly lowers visual analogue pain score (VAPS), decrease opioid requirements, reduces opioid-related adverse effects, and improve postoperative mobility[27,28]. A NSAIDs or COX-2 inhibitors can be added in the absence of contraindications. Hepatotoxicity can occur when $\geq$4 g are administered in 24 hours in healthy adults. Therefore, dose reduction is recommended in elderly patients, and its use should be limited in patients with compromised hepatic function.

2. Nonsteroidal Anti-inflammatory Drugs and Cyclo-oxygenase-2 Inhibitors

The NSAIDs has strong evidence supporting the efficacy for perioperative analgesia, and there are numerous NSAIDs with different onset, duration, route of administration, efficacy, and side-effect profile[27]. The Procedure-Specific Postoperative Pain Management Group summarized the relevant literature on perioperative analgesia specifically for patients undergoing THA[3]. They found that NSAIDs reduced morphine consumption and VAPS by 4 to 10 mm up to 32 hours postoperatively when compared with placebo[3]. The side-effects of NSIADs include gastrointestinal mucosal damage, renal dysfunction, and platelet dysfunction. Selective COX-2 inhibitors have minimal adverse gastrointestinal and hemostatic effects; consequently, these agents may be preferred in the perioperative setting. Several studies have shown that COX-2 inhibitors improve postoperative analgesia and reduce opioid consumption in patients undergoing THA[29]. Many COX-2 inhibitors have withdrawn from the market due to adverse cardiovascular effects. Celecoxib and meloxicam remain in use because the cardiovascular risk associated with these agents has been shown to be no higher than that associated with nonselective NSAIDs. However, widespread use of COX-2 inhibitiors still has been known to be associated to an increase of cardiovascular events, especially in elderly

populations[30]. Recently, some authors have reported a cost-effectiveness and the safety of using a fixed-dose combination of NSAIDs and a proton pump inhibitor compared to COX-2 inhibitors[31]. Therefore, the use of NSAIDs in combination with a proton pump inhibitor could be an alternative treatment option in high risk of cardiovascular events. There are also concerns about inhibitory effects of NSAIDs and COX-2 inhibitors on bone healing because animal research showed that these agents may reduce new bone formation by inhibiting osteoblast and osteoclast function[32], but the effect of small doses administration for short periods of time to human has yet to be determined conclusively.

3. Gabapentinoids

The gabapentinoids are effective postoperative analgesics that reduce opioid consumption by up to 50% compared with placebo[33]. Gabapentin and pregabalin are currently classified as a gabapentinoid. Pregabalin has been known to offer faster onset and more reliable, dose-dependent bioavailability than gabapentin due to improved absorption profile. The most common side effects of the gabapentinoids include somnolence and dizziness and can be minimized with dose reduction[34]. According to published data, the use of gabapentinoid alone for analgesia following major orthopedic surgery decreased opioid consumption but there were no differences in pain scores compared with placebo[33]. In addition to analgesia and reduced opioid consumption, gabapentinoids may confer other ancillary benefits throughout the early perioperative period.

ANESTHESIA AND NERVE BLOCK

1. Anesthesia

The most recent trend recommends the use of two or more analgesic modalities with different mechanisms of action that will provide analgesia while limiting side effects and adverse events to decrease pain in total joint arthroplasty[35]. It has been recommended that regional anesthesia offers significant advantages over general anesthesia with regard to intraoperative blood loss, deep vein thrombosis, and postoperative pain management[11,35]. Regional anesthesia during hip arthroplasty could be performed by spinal anesthesia, epidural anesthesia with or without indwelling catheters for 24 or 48 hours, intrathecal morphine, and epidural anesthesia in combination with spinal anesthesia or general anesthesia[11,35-37].

Generally, single-shot spinal anesthesia is preferred typical method for hip arthroplasty[11,35,38]. Additionally, epidural anesthesia results in significantly less pain in perioperative period than other analgesic modalities for total joint arthroplasty. Compared with systemic analgesia, epidural analgesia results in excellent improvement for pain regulation and earlier mobilization, however higher rates of postoperative urinary retention, hypotension, and itchiness[39,40]. Uncorrected hypovolemia, increased intracranial pressure, infection or allergy to local anesthetic agent, and coagulopathy are absolute contraindications of regional anesthesia[11,35,38,40]. Furthermore, epidural hematoma, which is a rare but potentially serious complication of epidural analgesia, remains a concern among patients having hip arthroplasty who receive postoperative thromboprophylaxis[38-41]. When performing regional anesthesia, it should be considered that appropriate anesthesia level and safe analgesic dose with skillful procedure, to minimize complications related to anesthesia.

2. Nerve Block

Peripheral nerve blocks are effective adjuvant options for pain management for hip arthroplasty[11,35,38,40,42].The use of nerve blocks has been proven to be very effective at controlling pain and minimizing narcotic requirements after hip arthroplasty[11,43,44]. Nerve block options include femoral block, sciatic block, posterior lumbar plexus block, fascia iliaca block, and periarticular local anesthesia infiltration[41]. Peripheral nerve block provides as good-quality analgesia as epidural anesthesia and it is superior to systemic opioids for pain relief[38,43,45]. Peripheral nerve blocks are associated with preserved contralateral limb strength that may facilitate postoperative rehabilitation when compared with the bilateral lower extremity sensorimotor block that can result with epidural analgesia[38,45]. Furthermore, peripheral nerve block has fewer complications, including hypotension and urinary retention with epidural anesthesia. The disadvantages of nerve blocks are increased time taking to place the blocks during perioperative period, and possibilities of injury associated motor blockade that limits functional recovery and delays rehabilitation[44]. Peripheral nerve blockade could be the assistant options regulating pain for postoperative analgesia after hip arthroplasty[46,47]. Both single-injection and continuous peripheral nerve block techniques are proven to reduce

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perioperative complications, reduce hospital length-of-stay, conserve hospital resources, and enhance patient satisfaction[36,48-51].

PATIENT CONTROLLED ANALGESIA AND EPIDURAL INJECTION

Patient controlled analgesia (PCA) is a delivery system, based on the use of a sophisticated microprocessor-controlled infusion pump, with which patients self-administer small, predetermined dose of analgesic medication to relieve their pain. PCA was developed in the early 1980s[52,53]. Since its introduction, it has become widely used for the management of postoperative pain in major orthopedic surgery. Basic composition of PCA models include initial loading dose, bolus (demand) dose, lockout interval, and background infusion rate. The initial loading dose is titrated to achieve a minimal level of analgesia in the recovery room until the VAPS is ≤ 4. The bolus (demand) dose is the small amount of analgesia the patient receives each time. Optimal efficacy and safety of the analgesia depends on balance between the dose small enough to minimize adverse effect and the dose large enough to achieve analgesic satisfaction. The lockout period is defined as the length of time during which there will be no drug delivery. The lockout period is generally recommended between 5 and 10 minutes regardless of the opioid used. The background infusion rate is a constant rate of infusion administered to deliver the equivalent of the usual opioid dose, but it may cause respiratory depression.

Baseline characteristics of common opioids for PCA are summarized in Table 1. The common adverse effects of PCA include nausea and vomiting, pruritus, respiratory depression, sedation and confusion, and urinary retention. In recent decades, alternative routes of PCA have extensively been developed, although the intravenous (IV) PCA is the most widely used method of PCA delivery. Variable modalities of PCA such as peripheral regional, intranasal, and transdermal PCA have been introduced[54]. The characteristics of IV and epidural PCA, which is the two major delivery methods of PCA, are summarized in Table 2.

Epidural analgesia has been considered as one of the most effective methods for pain relief after surgery. Medical route of epidural blockage is directed to the epidural space of the spinal cord. Comparing to spinal block, a large dose of drug is typically necessary and the onset of analgesia is slower with epidural analgesia than with spinal anesthesia[41]. Contraindication of epidural block is uncorrected hypovolemia, increased intracranial pressure, coagulopathy, and prior spinal surgery. Adverse events include tachycardia, high blood pressure, light headache, metallic taste in mouth, ring in ears, and facial numbness.

Table 1. Common Opioids for Patient Controlled Analgesia

Drug	Background infusion rate	Bolus dose	Lockout period (min)
Morphine	≤0.5 mg/h	1-2 mg	5-10
Hydromorphone	≤0.5 mg/h	0.25-0.5 mg	5-10
Fentanyl	≤50 μg/h	20-50 μg	5-10
Sufentanil	≤5 μg/h	3-6 μg	5-10

Table 2. Characteristics of PCA Modalities

Modality	Analgesics used	Advantages	Disadvantages
IV PCA	Morphine Fentanyl Hydromorphone	Rapid effect Programmable Uniform & sustainable	Invasive Require staff monitoring
Epidural PCA	Opioids Local anesthetics	High efficacy Programmable	Invasive Require staff monitoring Catheter problem Rebound pain Hematoma

PCA: patient controlled analgesia, IV: intravenous.

Table 3. Common Compositions and Sites of Intraoperative Periarticular Injection

Compositions	Local anesthetics (bupivacaine, ropivacaine)
	Non-steroidal anti-inflammatory drug (ketololac)
	Opioid (morphine)
	Steroid (methylprednisolone)
	Additional drugs (epinephrine, antibiotics, clonidine)
Injection sites	Capsule
	Synovium
	Iliopsoas tendon and insertion site
	Abductors
	Fascia lata
	Short external rotators
	Subcutaneous tissue

PERIARTICULAR INJECTION

Intraoperative periarticular injection of multimodal drugs is one of the most important procedures in multimodal pain control protocol[11,55,56]. Injection using opioid and local anesthetics into injured or stretched nerves or tissues under the guidance of a surgeon can block axonal sodium channels and inhibit the conduction of pain messages. Wound infiltration with local anesthetic can act locally to reduce peripheral nociception with few systemic adverse effects[38,56,57]. Several authors reported its effectiveness on reducing postoperative pain and improving postoperative mobility after THA[11,55,58-61]. However, there is disagreement of the proper dosage and composition of injection drugs and techniques of injection and its efficacy on reduced opioid consumption is also unclear[56,61]. The most commonly used drugs for periarticular injections include local anesthetics (bupivacaine and ropivacaine), ketorolac, morphine, clonidine, and steroids (Table 3). These components can activate directly the mu-opioid receptor near the surgical site inhibiting the local inflammatory response and relieving the pain by preventing the production of pain transmitters[61]. Steroids are effective for lengthening the duration of action of the periarticular injection but care should be taken using in patients with high risk of infection, such as diabetes or immunocompromised patients[11,56]. Additional drugs can be used to prolong the effect (epinephrine) and to reduce the risk of infection (antibiotics). Authors also use periarticular injection as a part of multimodal pain control protocal since 2006[62]. Components of authors' protocol are summarized in Table 4.

Table 4. Components of Periarthicular Injection in Authors' Protocol

1. Morphine HCl 5 mg
2. Methylprednisolone acetate 40 mg
3. Ropivacaine 6.8 mg
4. Dilute with 0.9% normal saline to total volume of 90 mL

CONCLUSION

Although patient education and rehabilitation protocols are important in facilitating a patient's recovery after total joint arthroplasty, it cannot be overemphasized that the focus of rehabilitation protocol after joint replacement should be in controlling perioperative pain. Multimodal pain management has become an important part of the perioperative care of patients undergoing total joint arthroplasty. The principle of multimodal therapy is to use different techniques that target several different steps of the pain pathway, allowing more effective pain control with fewer side effects.

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This clinical practice guideline was approved by Korean Hip Society on November 17, 2015. It is based on a systemic review of published articles on the management of perioperative pain control after total joint arthroplasty. This comprehensive review provided some suggestions of how orthopedic surgeons may serve as the ideal experts to deal with perioperative pain control after total joint arthroplasty. These suggestions will be revised regularly following further developments

and innovations in this field.

CONFLICT OF INTEREST

The authors declare that there is no potential conflict of interest relevant to this article.

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