Pain Management in Total Knee and Hip Arthroplasty

Abstract
In recent years, the management and treatment of pain in surgery, especially the painful operation of hip and knee replacement, has been highly sought after by pain and orthopedic surgeons and therefore is of paramount importance. Recently, the majority of valid resources have proposed the use of the multimodal method for pain management as an alternative to taking one or several medications. Today, this technique is used as a guideline by various surgeons, especially orthopedists.

Keywords: Total Joint Replacement, Pain Management and Treatment, Knee Replacement Arthroplasty, Total Hip Replacement

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Introduction
Adequate control of postoperative pain following hip and knee arthroplasty can be a challenging task. Previous studies have shown that over 50% of patients undergoing surgery have reported postoperative pain as a major concern\(^ 1,2\). Patients treated with total knee arthroplasty (TKA) more complain about pain, compared to patients undergoing total hip arthroplasty (THA)\(^ 3,4\). Uncontrolled pain can lead to myocardial ischemia and infarction, pulmonary impairments, paralytic ileus, urinary retention, thromboembolism, infection caused by impaired immune function, anxiety, and chronic postsurgical pain, if takes more than three months. Inadequate control of pain may result in patient dissatisfaction, impaired patient rehabilitation, and prolonged hospitalization\(^ 5\).

The negative effect of pain on rehabilitation causes delay and impairment in the return of muscle function and strength and regaining of the ability to perform normal activities. Several studies have shown that time of recovery and returning to normal activities is longer (about 50 days) in patients with TKA, compared to patients with THA, due to greater level of pain\(^ 6\). Therefore, control of pain in TKA by improving the range of motion and muscle strength is more important than THA\(^ 7\).

Methods
This review study aimed to evaluate approximately 50 valid evidence-based articles published on the treatment and management of pain in patients undergoing TKA and THA during 1988-2017. Results of these studies were presented in terms of various multimodal pain management methods.

Discussion
Inadequate management of acute pain is a risk factor for developing chronic pain. However, it is still unclear how the use of analgesics can reduce or prevent the onset of chronic pain\(^ 7\). Until a few years ago, unimodal or bimodal medicinal methods were used to manage pain in patients after TKA and THA. Nevertheless, the mentioned methods were often associated
with patient dissatisfaction. In addition, they were opioid dependent in most cases, which mainly led to respiratory depression, nausea, and vomiting, constipation, drowsiness and itching. On the other hand, patients and surgeons have always been worried about addiction due to the use of opiates. Moreover, application of high amounts of nonsteroidal anti-inflammatory medications can be associated with several complications, such as digestive problems, gastric ulcer and bleeding, renal disorders, high blood pressure, and heart problems (e.g., myocardial infarction) and cardiovascular complication. Therefore, use of these medications is not suggested. The use of local anesthetics and nerve block is also associated with short-term effects and the high doses of these medications can result in cardiovascular problems, such as vascular collapse and central and peripheral nervous system disorders\(^4\).

In 1993, kehlet & Dahl, finally proposed a multimodal pain management in a colon surgery for the first time, where several analgesics with different mechanisms and pathways were applied\(^7\). The relationship between the analgesics and their effect on prognosis and surgical success is not a new argument, and evaluation of postoperative pain by visual analog scale (VAS) and demand for opiates have been discussed in various studies since the beginning. This has led to the recognition of pain as the fifth vital sign by the American pain association (APS) in 1996\(^10\). In 2012, a meeting was held by the American Society of Anesthesiologists (ASA) in this country to evaluate pain management. Results of this meeting were presented and published in the form of a guideline, which includes the following measures:

1) Patient education before surgery, 2) use of analgesics one-two hours before surgery, 3) neuraxial anesthesia (e.g., spinal, epidural and general), 4) peripheral nerve blocks (femoral and sciatic nerves and both simultaneously), 5) injection of analgesics in the vicinity of the joint in a multimodal mode, 6) intravenous patient-controlled analgesia, and 7) oral analgesics\(^9\).

**Multimodal Pain Management**

This method is a combination of several analgesics, which have different modalities and techniques. The process starts before the surgery and continues to after the surgery, using various medications and methods, such as nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase inhibitors, N-Methyl-D-aspartic acid (NMDA) agonists, anticonvulsants, and centrally acting analgesics (e.g., acetaminophen). In addition, simultaneously with the blocking of the peripheral nerves and injecting local anesthetics in the epidural space and subarachnoid and infiltration, several medications are used around the surgery site and in a multimodal form\(^10-12\). In fact, the mechanism of pain transfer from the brain to the spinothalamic tract and pain receptors must be understood to realize the effectiveness of multimodal analgesics.

Postoperative pain is a consequence of tissue damage and neuropathic stimulation, which is ultimately comprehended and felt by the brain. After a painful stimulation, chemical mediators, such as prostaglandin-2 (PGE2) and Brady Kinine, are released in the damaged area. These chemical mediators stimulate peripheral receptors for pain because of trauma and a rise in the temperature of the place. Through this process, the brain experiences postoperative pain, and a set of multimodal methods and blockage of the passing routes are applied to eliminate or reduce pain after surgery\(^13\) (Figure 1). This strategy is the most important and effective way to manage postsurgical pain that should be applied before the start of operation\(^4\). As mentioned, pain relief has a significant impact on the success of surgical procedures, especially arthroplasty. Therefore, it seems necessary to design and implement a guideline by the surgical team in this regard.
Figure 1. Pain pathways and multimodal analgesic method (adapted from the reference 4) in pre-emptive use of the multimodal approach

The main purpose is to relieve pain and reduce the consumption of opiates and morphine at the same time. However, each surgeon uses his own methods and experiences since there is no ideal protocol in this regard. In addition to reducing pain in patients, application of nonsteroidal analgesics can prevent excessive use of opioids and its relevant complications, which is the main goal of pain management. One of the main problems in using opiates is the development of a complex phenomenon known as “opioid induced hyperalgesia”, which can increase the consumption of opioids, resulting in reduced threshold of pain\(^{14}\). This complication can be prevented by limiting the opiate consumption and use of non-narcotic drugs. This responsibility can be taken up by non-steroid medications, which is known as the opioid-sparing effect\(^ {15}\).

NSAIDs and cox-2 drugs reduce pain by inhibiting prostaglandin synthesis and analgesic receptors\(^ {15-16}\). The major concern of some surgeons is postoperative bleeding due to reduced platelet aggregation with NSAIDs\(^ {17}\). Therefore, the suggestion is to discontinue NSAIDs 7-10 days prior to surgery. In addition, another concern is the emergence of peptic ulcer, renal dysfunction, and delay in healing of wound and bone. As such, use of selective cox-2 inhibitors, such as celecoxib, is recommended due to a lower level of complications and less impact on platelets aggregation, compared to non-selective anti-inflammatory drugs. In a previous research, it was shown that use of cox-2 inhibitors one hour before arthroscopic surgery significantly relieved pain in patients up to 24 hours after the surgery, compared to the placebo\(^ {18}\). In another study, the cox-2 inhibitors were administered from one hour before the arthroscopic surgery to 14 days after the surgery, which resulted in a significant pain reduction in the subjects\(^ {19}\). In the mentioned research, patients required lower amounts of opiates, returned to their normal state faster, and were more satisfied with the surgery outcomes. Recommendations on the proper dose of these medications are presented in Table 1.

**Pregabalin and gabapentin**

These medications are used to treat neuropathic pain in adults. At first, they were applied to treat seizure and neuropathic pain syndromes\(^ {20}\). Studies have shown the effectiveness of these medications on pain reduction in patients after arthroplasty and decrease of opiate consumption. In addition, they reduce anxiety in patients and must be applied an hour before the surgery\(^ {21-24}\). Concomitant use of these medications with NSAIDs has a synergistic effect. In a systematic review, it was concluded that lasting of pain two or more months after TKA and THA could increase the prevalence of chronic postsurgical pain (CPSP) by 20%\(^ {25}\). In another meta-analysis, the effect of pregabline was shown in pain management after surgery. Application of this medication 24-48 hours after TKA reduced pain in patients, especially during rest.
Moreover, a fewer number of patients required morphine, and the range of motion and function of the knees were more improved [26]. The standard amounts of pain inhibitors are presented in Table 2.

### Table 1. Dosage recommendations for individual non-opioid agents that may be administered as part of multimodal analgesia

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose</th>
<th>Route of administration</th>
<th>Time before surgery</th>
<th>Time after Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NSAIDs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketorolac</td>
<td>15-30 mg</td>
<td>PO/IV</td>
<td>1-2 hour</td>
<td>15-30 mg q6hrs</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>800 mg</td>
<td>PO</td>
<td>1-2 hour</td>
<td>800 mg q6hrs</td>
</tr>
<tr>
<td><strong>COX-2 Inhibitors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celecoxib</td>
<td>400 mg</td>
<td>PO</td>
<td>1 hour</td>
<td>200 mg x 1 hrs</td>
</tr>
<tr>
<td>Valdecoxib</td>
<td>40 mg</td>
<td>PO</td>
<td>1 hour</td>
<td>After surgery Bid</td>
</tr>
<tr>
<td><strong>Anti-neuropathic</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>1200 mg</td>
<td>PO</td>
<td>1-2 hours</td>
<td>1200mg x 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(24 hrs after surgery)</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>150mg</td>
<td>PO</td>
<td>1 hour</td>
<td>150 mg x 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(12 hrs after surgery)</td>
</tr>
<tr>
<td><strong>Propacetan 390</strong></td>
<td>2 g</td>
<td>PO/IV</td>
<td>15 minutes</td>
<td>2 g every 4 hours</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>1 g</td>
<td>PO/IV</td>
<td>15 minutes</td>
<td>1 g every 4 hours</td>
</tr>
</tbody>
</table>

### Table 2. Dosages for Preemptive Analgesia

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosage, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxycodone</td>
<td>10</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>400</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>600</td>
</tr>
<tr>
<td>Tramadol</td>
<td>50</td>
</tr>
<tr>
<td>Clonidine patch</td>
<td>0.1</td>
</tr>
</tbody>
</table>

**Primary Intraoperative Period**

In general, regional anesthesia is preferred to general anesthesia. Regional anesthesia has several advantages and can provide proper conditions during and after the surgery. This type of anesthesia contributes to decreased level of bleeding during surgery by keeping the arterial blood pressure down, and there are less complications (e.g., nausea and vomiting) associated with regional anesthesia, compared to general anesthesia. Moreover, regional anesthesia reduces cardiovascular complications and risk of incidence of thromboembolic complications, thereby decreasing the mortality risk in high-risk patients [28-30].

Regional anesthesia includes the following methods:

1- Spinal
2- Epidural
3- Simultaneous use of spinal and epidural
4- Peripheral nerve blocks

Generally, spinal anesthesia is applied in TKA and THA. However, regional anesthesia is not uncomplicated and might be associated with headaches, backaches, neural damages, and subarachnoid epidural hematoma, which are mostly temporary. Several multimodal medications can be used in regional anesthesia. There have always been concerns regarding the use of regional anesthesia in patients receiving anticoagulants. Therefore, it is suggested that use of anticoagulants be discontinued 10 days before regional anesthesia, especially in those who previously consumed thrombolytic drugs. In this regard, complications might emerge in the form of neurological disorders due to local bleeding. This risk increases by using epidural anesthesia and a catheter [31].

**Peripheral Nerve Block**

This method has become increasingly popular for TKA and THA in recent years. Some anesthetists and surgeons prefer this technique to spinal and epidural anesthesia, especially in patients receiving anticoagulants. In addition, there are no complications (e.g., urinary retention and arterial pressure dropping) in the nerve block as observed in the
spinal and epidural anesthesia methods. In this type of anesthesia in TKA, there is a need for blocking of both lumbar nerve (femoral and psoas nerves) and the lumbosacral nerve (sciatic nerve) networks. Nevertheless, adequate anesthesia is often obtained by independent blocking of the lumbar nerve network. It is notable that nerve block is carried out by a single injection or with the help of a catheter or in continuous manner\textsuperscript{32-33}.

Nerve block might be preferred to epidural block method\textsuperscript{34-36}. Some studies recommend femoral and sciatic nerve blocks with the help of a catheter for KTA\textsuperscript{37-38}. However, nerve block is not uncomplicated and might be associated with complications of local infection and neural injury and muscle paralysis, especially when a catheter is applied. Muscle paralysis might emerge in the form of falling, which is dangerous but temporary\textsuperscript{39-40}.

**Intravenous Patient Controlled Analgesia (Iv-pca)**

This method is almost the most commonly used tool for managing pain after TKA and THA\textsuperscript{41}. In the PCA method, a pump is used for injection and transfer of various medications intravenously and through a multimodal technique to relieve postsurgical pain. In addition, the method can be applied as an analgesic during the first postsurgical days. It should be mentioned that the main components of this method are opioids, especially morphine and fentanyl, which can be associated with their own specific complications. The dose and the amount of the prescribed drugs are determined and limited by physicians and healthcare providers. In case of severe pain, patients can receive a higher dose of the medication in a limited amount of time. It should be noted that these medications must be prescribed with caution in older patients due to their possible complications. In order to reduce the use of opioids and morphine in this method, it is possible to use other analgesics in a multimodal method along with the PCA pump (Figure 2).

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{lia.jpg}
\caption{Intra and periarticular local infiltration analgesia (LIA)}
\end{figure}

In recent years, there has been a high tendency toward the use of local angiogenesis infiltration as a method of pain control in patients undergoing hip and knee arthroplasty. In addition, several RCTs related to this issue have been published to this day. In this technique, a multimodal method is applied to inject a combination of several drugs in the vicinity of the surgical site in the form of intra-articular solution during surgery. This method could relieve pain in patients during the first 24 hours after the surgery\textsuperscript{42-45}. Comparison of this technique with morphine injection and block of this epidural led to similar and even more efficient results. Moreover, better analgesic effects were detected in this method, compared to the femoral and epidural block with morphine injection. It is notable that the LIA technique with multimodal method led to a significantly higher reduction in pain after TKA surgery, compared after the THA surgery, which was more confirmed in RCTs\textsuperscript{46}. (Figure 3) (Table 3)
Figure 3. Injection of analgesics during TKA and injection sites

Table 3. Dosages for Deep Intraoperative Injection

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marcaine 0.5% (5 mg/cc)</td>
<td>200-400 mg</td>
</tr>
<tr>
<td>Morphine sulphate (8 mg)</td>
<td>0.8 cc</td>
</tr>
<tr>
<td>Adrenaline 1/1000 (300 μg)</td>
<td>0.3 cc</td>
</tr>
<tr>
<td>Antibiotic</td>
<td>750 mg</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>40 mg</td>
</tr>
<tr>
<td>Normal saline</td>
<td>22 cc</td>
</tr>
</tbody>
</table>

*Maximum dose of marcaine is 400 mg/d.

**Acetaminophen and Paracetamol**

Acetaminophen is a trusted and relatively low-risk drug for the management of pain in patients undergoing arthroplasty and can be a good alternative to NSAIDs and opioids. However, this drug can be used in conjunction with non-steroidal anti-inflammatory drugs in the multimodal method to eliminate the complications of opiates. Complications of acetaminophen, such as bleeding and gastrointestinal problems, are much less than non-steroidal inflammatory drugs and are can be therefore better tolerated by patients.

Today, the intravenous administration of this medication is very common in most countries, including USA (47-49) (Figure 4).

**Conclusion**

Today, TKA and THA are common treatments for the elderly. These surgeries can significantly improve pain, modify joint function and enhance the quality of life of patients. Management of severe pain after this surgery is a huge challenge for patients and surgeons. From the past and even now, opiates have been used as an important factor for reliving pain in patients. However, given the complications of these drugs, especially in older patients, a program must be designed to reduce pain and improve the quality of patients and prevent the unnecessary complications at the same time. As such, application of multimodal analgesics has become prevalent. Selection of multimodal regimens requires complete knowledge about the patient condition and these techniques so that the process could be properly implemented and patients satisfaction would be gained after painful arthroplasty surgeries. This objective is a great ethical responsibility for relevant physicians and healthcare centers.
Figure 4. Multimodal analgesia algorithm for hip and knee arthroplasty at Thomas Jefferson University Hospital and Rothman Institute for Orthopedics (4)

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