Research Article

An Overview of Multimodal Analgesia in Orthopedic Surgery

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Abstract: Most patients undergoing orthopedic surgeries experience moderate to acute pain. Initially, opioids were the main medication that targeted mechanisms of pain transmission. However, the use of opioids has a lot of risks, including addiction, respiratory depression, urinary retention, vomiting, and nausea. Over the years, multimodal analgesia has become the preferred pain control or management strategy in orthopedic practice. Administering more than one mode to address postoperative pain by recruiting several receptors via various medications decreases the need for opioids and speeds up the recovery process. Implementation of effective analgesic interventions and strategies reduces preoperative opioid intake, subsequently preventing addiction to pain drugs and the risk of opioid overdose. Multimodal analgesia has been a crucial component of pain management in orthopedic surgery since early opioid consumption. This essay explores the concept of multimodal analgesia as a pain management mechanism in orthopedic surgery. It provides an overview of the elements of multimodal analgesia and also highlights the opioids.

Keywords: orthopedic surgery, multimodal analgesia, opioid addiction, anesthesia

Introduction

Orthopedic surgery is one of the most painful operations a patient can experience. According to the International Association for the Study of Pain, pain refers to an unpleasant emotional or sensory experience related to or resembling that related to potential or actual tissue damage (Garcia et al., 2023). Improvement in pain management remains among the most significant developments in replacement surgery. Effective pain management accelerates healing, improves quality of life after surgery, and speeds up recovery. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) declared pain as the fifth vital sign during patient treatment; hence, poor pain control is economically wasteful, clinically unsound, and unethical. Therefore, a healthcare organization is mandated to actively respond to pain...
management (Sherman et al., 2020). Postoperative pain is a common element after orthopedic surgery and is often a limiting factor for patient recovery. Postoperative pain incidences can vary based on the technique and type of surgery. Spine and joint replacement surgeries are the most painful postoperative surgeries. Arefyane et al. (2020) report that 70.5 percent of orthopedic emergency surgery patients experience moderate to severe postoperative pain. Additionally, orthopedic patients with preoperative anxiety have a 6.42 times higher chance of developing moderate to severe postoperative pain than those without anxiety. Other factors that increase the likelihood of an orthopedic patient experiencing postoperative pain include the history of preoperative pain, duration and type of anesthesia, intraoperative use of a tourniquet, and patient expectation about postoperative pain.

Healthcare organizations have employed several strategies to manage postoperative pain in orthopedic surgeries, including opioid use. Although opioids are an effective postoperative analgesia, they have significant drawbacks. Shultz et al. (2019) report a connection between intraoperative exposure to opioids and hyperalgesia in the immediate postoperative phase, creating early development of tolerance and potential risks. Researchers have also studied the relationship between periods of opioid use and the risk of misuse. Brat and his colleagues discovered that an additional week of opioid use and every refill increases the risk of abuse by forty-four percent. The negative effects of prolonged exposure to opioids include respiratory depression, constipation, vomiting, and nausea (Shultz et al., 2019). Excessive prescription of opioids post-surgery increases the risks of dependence, overdose, diversion, abuse, and misuse, contributing to the national opioid crisis that exerts huge economic and health burdens for patients, their relatives, the healthcare system, and society in general (Bronstone et al., 2022). Due to these effects of opioid use for postoperative pain, multimodal analgesia is a pain management strategy that the medical community has turned its attention to manage postoperative pain and reduce opioid consumption effectively. This essay aims to review multimodal analgesia as a pain management strategy in orthopedic surgery.

Need for Multimodal Analgesia in Opioid Crisis

Physicians have depended on opioids as the standard of care for managing postsurgery pain, resulting in overprescription that has worsened the opioid epidemic in the United States. Over six hundred thousand individuals succumbed to drug overdose, mostly associated with opioids administered or prescribed for pain between 1999 and 2000. Almost half of patients who consume opioids for at least three months tend to remain on opioids for five years, and there are possibilities for them to stay on opioids for the rest of their lives (Chunduri & Aggarwal, 2022). In 2020, around 9.5 million individuals from the age of twelve misused opioids in the U.S., which accounts for 3.4 percent of the country’s population (Deshler et al., 2023). The increased accessibility of opioid drugs and the measures to sufficiently reduce or manage pain has resulted in a significant increase in opioid consumption in the U.S. Subsequently, the effects associated with opioid have increased. Although the U.S. accounts for 4.4 percent of the global population, it consumes eighty percent of the

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global opioid supply. In 2016, the Centers for Disease Control and Prevention (CDC) approximated that 32445 deaths occurred resulting from opioid consumption, which is equal to around eighty-nine deaths daily (Shultz et al., 2019).

Moreover, orthopedic surgeons administer or prescribe approximately seven percent of opioid prescriptions in the U.S. Orthopedic surgeons prescribe more opioids for their patients than the majority of the other specialty physicians due to the pain related to orthopedic treatment procedures. According to Shultz et al. (2019), the biggest challenge in postoperative opioid administration is mastering the management of the amount required for pain control at an unpredictable period. Besides abuse and causing deaths, opioids can cause serious adverse drug effects such as nausea, constipation, and vomiting, which impede the use in pain management. The greatest concern when focusing on the medication’s negative consequences is the risk of sedation after opioid intake and their development into respiratory depression, which may lead to death or injury.

Physicians have implemented various approaches to prevent opioid addiction and overdose. Multimodal analgesia is the most effective strategy to address opioid-related issues. The strategy includes post, peri, and preoperative components. It seeks multidisciplinary cooperation between relevant parties using more than one mode, including nonopioid medication, regional anesthesia, psychotherapy, physical therapy, and local injection to tackle postoperative pain, resulting in a quicker recovery process with less need for opioids and superior pain control, reducing the potential risk of abuse (Chunduri & Aggarwal, 2022).

The Concept of Multimodal Analgesia

Multimodal Analgesia, also called balanced analgesia, employs several analgesic medications, cognitive approaches, and physical modalities to impact the central and peripheral nerve loci for pain treatment (Garcia et al., 2023). The concept of multimodal or balanced first emerged years ago, and it rejects the notion that the use of a single drug (monotherapy) is an adequate strategy for pain management. The concept argues combining several analgesics provides superior pain control (Sherman et al., 2020). Perioperative pain entails multiple subtypes of pain, making it impossible to treat it with a single medication effectively. Surgical pain can be idiopathic, psychogenic, nociceptive, mixed, or neuropathic based on the surgery (Schwenk & Mariano, 2018). The strategy integrates multiple analgesic agents, each targeting a different pain-related receptor, thereby exhibiting its pain-reducing effect via other mechanisms of action. The combination of two or more analgesic medications for pain relief allows the administration of lower doses of each drug, hence minimizing the risk of negative drug effects (Sherman et al., 2020). An effective multimodal analgesia protocol standardizes analgesic categories while facilitating some flexibility in the separate components based on patient allergies, previous surgical experiences, medications, and comorbidities (Schwenk & Mariano, 2018).

Golubovska et al. (2014) report that many studies have determined the effectiveness of multimodal strategies for postoperative analgesia. Large-scale meta-analyses also
discovered that the strategy result in enhanced pain control, fewer side effects, and lower narcotic consumption.

The American Society of Anesthesiologists (ASA) proposes the use of multimodal analgesia for pain management, stating that patients should receive around-the-clock paracetamol, NSAIDs, or COX2 inhibitors. Moreover, the American Society for Pain Management Nursing proposes for nurses to be strong advocates for pain management approaches that integrate opioid dose-sparing techniques initiated early in the treatment plan, even before the operation (Golubovska et al., 2014). The Society of Critical Care Medicine (SCCM) recommends the use of nonopioids to reduce the amount of opioids administered or to remove the need for IV opioids altogether. The Joint Commission also suggests a multimodal strategy combining nonopioid pain medications, non-pharmacologic methods, care coordination, psychosocial support, and promoting healthy behaviors (Golubovska et al., 2014).

**Figure 1.** Shows the potential benefits of opioid-sparing multimodal analgesia. (Sullivan et al., 2016)

The biggest challenge in the implementation of multimodal analgesia is the crisis of drug shortages. Consequently, perioperative physicians have to look for alternative medication within the same classes since only a few firms manufacture the major intravenous medicines used in the U.S., including perioperative drugs, stressing the significant downstream that a production issue within one firm can cause. The American Society of Health-System Pharmacists has listed several medications used in anesthesia as being in shortage, including hydromorphone, fentanyl, and ketamine, which are analgesics commonly used in multimodal protocols (Schwenk & Mariano, 2018).
Preemptive Analgesia

The concept of preemptive analgesia involves the performance of procedures or administration of pain medication before surgical incision to avoid surgical pain, which is more effective than a similar intervention post-surgery. Preemptive analgesia aims to decrease the intensity of post-surgery pain, reduce hyperalgesia incidents, and prevent central and peripheral hypersensitivity (Li et al., 2019). More than a century ago, Crile introduced preemptive analgesia based on clinical observation that Woolf and Wall later studied. Initially, the concept was mainly based on animal studies. Still, later human studies followed. Preemptive analgesia protects the nociceptive system, significantly decreasing pain levels and reducing the risk for chronic pain development (Chunduri & Aggarwal, 2022). Administration of pregabalin and COX-2 combination between thirty minutes and one hour before the operation promotes faster recovery. It reduces the intensity of post-surgery pain after complete joint replacements.

Moreover, administration of ketamine before incision, occasionally followed by an infusion, significantly decreases the need for post-surgery pain drugs and appears to prevent neuromodulation, hence reducing chronic pain development. Conducting peripheral nerve blocks before surgery reduces the need for supplemental pain drugs after and during the surgery. The concept of preemptive analgesia is an essential component of multimodal analgesia protocols despite initial clinical trials being inconclusive (Chunduri & Aggarwal, 2022).

Surgical Site Infiltration

Surgeons occasionally use infiltration of local anesthetics in combination with other drugs to prolong the period of regional analgesia—the medication function by directly stopping the conduction and generation of pain signals from the incision area. Studies have demonstrated that intra-articular injections of slow-release bupivacaine formulations reduce the need for supplementation and lengthen the period of pain relief (Joshi & Machi, 2019). Developing newer combinations of local anesthetics with anti-inflammatory features is ongoing. The techniques are operator-reliant, hence the possibility of success rate variations. Despite this approach’s role in reducing the need for supplemental medication and extending the period for pain relief, the potential for chondrolysis when injected into the joints and the risk of toxicity, especially during the administration of local anesthetics in large doses, limit its use. However, surgical site infiltration is essential to multimodal analgesia and can be an effective adjuvant to systemic analgesics (Chunduri & Aggarwal, 2022).

Multimodal Analgesic Agents for Orthopedic Surgery

A multimodal analgesia procedure should be based on individual surgery functioning like a checklist, not a recipe, with options to modify to the individual patient. According to Schwenk & Mariano (2018), nonopioid analgesics are the foundation for building an effective perioperative multimodal analgesia protocol. Besides eliminating
the side effects of opioids, many of the agents are highly efficient in reducing perioperative pain, promoting meeting medical objectives, and faster mobilization.

**Acetaminophen**

Acetaminophen is a nonopioid analgesic agent with a proven track record of safety when used in suitable doses for the years it has been in clinical use. Most multimodal protocols entail acetaminophen, and the lack of contraindications outside severe liver illness and its opioid-sparing effects make it appealing. The agent is a cheap and useful component of the multimodal protocol. However, when used alone, it is inadequate for painful procedures such as total knee arthroplasty (TKA). A meta-analysis to establish the impact of one dose of acetaminophen for severe postoperative pain discovered that thirty-six percent of patients reported that they experienced relief for four hours.

According to Yin et al. (2022), acetaminophen administration intravenously is better than rectal or oral administration since it bypasses the gastrointestinal tract, thereby quickly attaining maximum concentration in the central nervous system. In 2010, the United States Food and Drug Administration (FDA) approved the administration of acetaminophen IV. Schwenk and Mariano (2018) report evidence supporting the oral use of acetaminophen instead of the intravenous approach. They explain that the medication can be appropriate for intravenous use in specific indications such as a patient’s inability to take the drug orally and long surgical procedures. Some studies have shown the advantages of using acetaminophen intravenously, including fewer discharges and shorter hospital stays (Schwenk & Mariano, 2023). Due to the medication’s hepatotoxicity, the FDA proposes a maximum daily dosage of four grams for adolescents and adults weighing at least fifty kilograms (Richette et al., 2015). The European Union also recommends a maximum daily dosage of three grams for older people at risk for hepatotoxicity who have more than fifty kilograms in body weight (Mian et al., 2018).

On the other hand, the Chinese Center for Drug Evaluation proposes a maximum dosage of two grams daily for all adults due to the lower body mass index of the Chinese population than other ethnic populations and the negative effects connected to acetaminophen dosage, including hepatotoxicity (Yin et al., 2022). Researchers have well established the effectiveness of opioid-sparing intravenous acetaminophen at a daily dose of four grams in patients undergoing orthopedic surgeries, including knee arthroplasty and total hip arthroplasty. However, the safety and effectiveness of the maximum daily amount of two grams of intravenous acetaminophen remains unclear despite recommendations from the Chinese Center for Drug Evaluation (Yin et al., 2022).

**Non-steroidal anti-inflammatory drugs (NSAIDs)**

NSAIDS are a well-developed group of analgesics that are highly effective additions to the multimodal analgesic approach of pain management, particularly for patients undergoing orthopedic surgery involving extensive inflammation. Inhibition of
prostaglandin synthesis and cyclooxygenase (COX) allows NSAIDs to exert their effects. Schwenk and Mariano (2018) report that the combination of 1000 milligrams of paracetamol and 400 milligrams of ibuprofen had 1.5 as the number required to treat to attain fifty percent or more postoperative pain relief. While the universal use of paracetamol is acceptable due to negligible negative effects, NSAIDs are associated with a higher risk of negative impacts, hence limiting their use. There have been increasing concerns about the high risk of postoperative bleeding associated with NSAIDs, but there is a lack of evidence to support this claim. In 2014, Gobble and colleagues conducted a meta-analysis that found that ketorolac does not increase the risk of perioperative bleeding (Schwenk & Mariano, 2018). However, there is a need for warranting caution in patients with pre-existing gastrointestinal ulcers, renal disease, and chronic kidney disease. Patients with gastrointestinal ulcers can use a substitute for COX-2 inhibitor, like a nonselective NSAID, for risk reduction. All NSAIDs increase the risk for cardiovascular incidents such as myocardial infarction; therefore, there is a need to consider careful scheduling of NSAID doses (Wick et al., 2017; Schwenk & Mariano, 2023). Additionally, surgeons have raised concerns related to poor bone healing or possible nonunion in orthopedic patients exposed to NSAIDs, but there is no evidence to support these concerns. While reviews on the impact of NSAIDs on soft tissue healing in the field of sports medicine surgery have been unable to make definitive conclusions, they have stated a possibility that NSAIDs may not affect the healing rate after most procedures except for celecoxib, possibly impeding tendon to bone healing in rotator cuff repair surgery (Schwenk & Mariano, 2023).

**Gabapentinoids**

Gabapentinoids is commonly used group of analgesic agents and include pregabalin and gabapentin. The agents are anticonvulsants, exerting their clinical effects through their interaction with voltage-gated calcium channels (Schwenk & Mariano, 2023). Gabapentinoids play a significant role in the prevention of acute nociceptive pain injury. The analgesic agents induce sedation without having adverse side effects and reduce postoperative opioid requirements and preoperative anxiety (Khetarpal et al., 2016). Tsai et al. (2023) report that while the two types of analgesic agents have the same chemical structures and mechanisms of action, pregabalin is stronger and takes effect quicker than gabapentin. High-quality evidence from various studies has indicated the safety and efficacy of gabapentinoids in neuropathic pain treatment after spinal cord injury. The search for pros such as reduction of anesthetic consumption, post and preoperative agitation, pain, postoperative vomiting, and nausea is promising in pediatrics. However, only gabapentin is available for children of all ages (Pinto Filho et al., 2019). Although gabapentin is an amino acid with the same structure as the neurotransmitter Gamma-aminobutyric acid (GABA), it does significantly interact with this transmitter or other neurotransmitters, thereby facilitating a reduction in the amalgamation of the neurotransmitter glutamate and the reduction of calcium influx via linking the voltage-reliant calcium channels’ alpha-2-delta subunit. Consequently, side effects include ataxia, drowsiness, dizziness, and diplopia (Pinto Filho et al.,

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On the other hand, gabapentin used in adult patients has a relative risk of producing sedation of 1.22, and preoperative administration appears to weaken the hemodynamic pressure of orotracheal intubation (Pinto Filho et al., 2019).

**N-methyl-D-aspartate (NMDA) antagonists**

NMDA antagonists are other agents considered during multimodal analgesia protocols with a specific focus on magnesium and ketamine. The agents are potent antihyperalgesics that control opioid-induced analgesia and central sensory processing of pain. They reduce central sensitization implicated when surgical pain signs develop (Polomano et al., 2017). Ketamine has a clear effect involving the reduction of opioid use during the perioperative period. It can reduce long-term consumption of opioids in opioid-tolerant patients and persistent postoperative pain when administered intravenously (McNicol et al., 2014). The American Society of Regional Anesthesia and Pain Medicine (ASRA) published national guidelines suggesting ketamine infusions for opioid-tolerant patients and those undergoing painful surgeries (Schwenk & Mariano, 2023). Although reviews on pre-surgical ketamine and psychomimetic negative drug effects have reported inconsistent findings, healthcare professionals should factor in these effects when making treatment decisions and exercise caution when using ketamine. These effects include out-of-body experiences, nightmares, and hallucinations (Schwenk & Mariano, 2018; 2023). The benefits of ketamine are maximized during painful surgeries like TKA and in patients with high opioid tolerance. Benzodiazepine and clonidine reduce the chances of severe adverse drug effects since it seems patients who have not received an adjuvant have the highest risk of experiencing adverse drug effects. The Prevention of Delirium and Complications Associated with Surgical Treatments (PODCAST) trial findings concluded that a single large dose of ketamine did not reduce pain or delirium post-surgery. Still, they increased nightmare and hallucination incidents among elderly patients. These findings have led to questioning the analgesic benefit of one intraoperative large dose of ketamine (Schwenk & Mariano, 2023). Generally, an infusion is preferable to minimize the risk of adverse drug effects and maximize analgesia in post and intraoperative ketamine use.

The use of magnesium as an analgesic agent has demonstrated inconsistent findings but has shown synergism when combined with ketamine or morphine. Magnesium exerts its clinical effects through spinal NMDA receptors and seems more effective when administered intrathecally instead of intravenously (Helander et al., 2017). Anesthesiologists administer magnesium as a bolus dose of between thirty to fifty milligrams per kilogram intravenously, followed by six to twenty mg/kg/hour infusion for four hours. Extracellular magnesium prevents the development of central sensitization by blocking the NMDA receptor in a voltage-reliant way (Chunduri & Aggarwal, 2022). Despite the inconsistency in the findings about magnesium use as a postoperative agent, it remains a cheap addition to the multimodal analgesia approach that is considered if allergies or contraindications limit the use of other nonopioid agents. Studies show that magnesium can reduce opioid and anesthetic requirements when administered perioperatively with little to no negative effects and may offer
more stable hemodynamic parameters during the surgery. Magnesium administration via intravenous infusion before or after anesthesia induction is a useful adjunct when used alongside other components of a strong multimodal analgesia protocol (Schwenk & Mariano, 2023).

Table 1. The table below shows the dosing recommendation of nonopioid drugs used in multimodal analgesia. (Parvizi & Bloomfield, 2013)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route of Administration</th>
<th>Preoperative Dosing</th>
<th>Postoperative Dosing</th>
<th>Common Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ketorolac</td>
<td>Intravenous</td>
<td>15-30 mg</td>
<td>15-30 mg every 6 h for 7 doses</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Oral</td>
<td>800 mg</td>
<td>800 mg every 6 h</td>
<td>Gastric ulcers</td>
</tr>
<tr>
<td>COX-2 inhibitor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Celecoxib</td>
<td>Oral</td>
<td>400 mg</td>
<td>200 mg every 12 h</td>
<td>Sulfur allergy</td>
</tr>
<tr>
<td>Anti-neuropathic</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Oral</td>
<td>300 mg</td>
<td>300 mg every 12 h</td>
<td>Renal insufficiency</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>Oral</td>
<td>75 mg</td>
<td>75 mg every 12 h</td>
<td></td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>Oral/ intravenous</td>
<td>1000 mg</td>
<td>650 mg every 6 h</td>
<td>Liver disease</td>
</tr>
</tbody>
</table>

Opioids

Despite the side effects associated with opioids, such as a dangerous risk of addiction, urinary retention, respiratory depression, pruritus, vomiting, nausea, and ileus, opioids remain the backbone for postoperative pain control and management. Since nonopioids have shown to be highly effective, surgeons mainly use opioids as a rescue medication in situations where other pain management methods do not control the pain well.
Table 2. Shows the most common opioid medications in orthopedic surgery. (Chunduri & Aggarwal, 2022)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Dose</th>
<th>Analgesic Duration</th>
<th>Metabolism</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine</td>
<td>2–4 mg IV</td>
<td>3-4 hours</td>
<td>Liver glucuronidation - Active metabolites are renally cleared</td>
<td>Causes Histamine release, can induce vagally mediated venodilation, hypotension, bradycardia</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>0.5–1 mg IV/SC</td>
<td>2-4 hours</td>
<td>Liver—Glucuronidation</td>
<td>Can be used in renally impaired patients - Avoid in patients suffering from hypovolemic shock - Contraindicated in Genitourinary Obstructions</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>1–2 mcg/kg IV</td>
<td>30 minutes- 1 hour</td>
<td>Liver—CYP3A4 and CYP3A5</td>
<td>Up to 100× more potent than morphine - Can be used in renally impaired patients - Can be used in patients with hemodynamic instability or bronchospasm</td>
</tr>
<tr>
<td>Meperidine</td>
<td>50–150 mg IV</td>
<td>2-3 hours</td>
<td>Liver—CYP3A4 and CYP3A5</td>
<td>Active metabolite, normeperidine, can cause seizures - Contraindicated with monoamine oxidase inhibitors - Elderly have a slower elimination Rate.</td>
</tr>
<tr>
<td>Codeine</td>
<td>15–60 mg PO</td>
<td>4-6 hours</td>
<td>Liver—CYP2D6</td>
<td>Avoid in pediatric patients - Causes increased intracranialPressure</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>2.5–10 mg PO</td>
<td>4-6 hours</td>
<td>Liver—CYP2D6 and CYP3A4</td>
<td>Avoid in pediatric patients - Causes increased intracranial Pressure</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>5–10 mg PO</td>
<td>3-6 hours</td>
<td>Liver—CYP2D6</td>
<td>Avoid with CYP3A4</td>
</tr>
</tbody>
</table>
Local Anesthetics

Discussions involving techniques to reduce opioid consumption during pain management and multimodal analgesia protocols must include regional anesthesia. Regional anesthesia is a reversible and pharmacologically induced loss of skeletal reflexes and responsiveness, reduced stress response, or all these concurrently affecting a part of a body (Obalum & Ibeanusi, 2018). Regional anesthesia employs local anesthetics in the form of neuraxial (epidural and spinal) blocks and peripheral nerve blocks to control pain after orthopedic surgery. Moreover, it offers superior pain control than traditional opioid-based techniques in several types of surgeries, including ankle and foot surgery, TKA, and shoulder surgery. It can reduce the time spent in the post-anesthesia unit and decrease vomiting and nausea (Schwenk & Mariano, 2018). Research has established the efficacy and safety of regional anesthesia. It has been demonstrated that regional anesthesia significantly reduces the opioid intake in arthroscopy, fracture treatment, and arthroplasty (Shultz et al., 2019).

According to Kamel et al. (2022), regional anesthesia in orthopedic surgeries alleviates some of the complications related to general anesthesia, including the risk of pulmonary aspiration, hypoxia, respiratory depression, vomiting, nausea, and airway trauma. They further report benefits of regional anesthesia in orthopedic surgeries to include a reduction in postoperative ileus development and urinary retention, decreased intraoperative loss of blood, reduced unexpected admissions resulting from uncontrolled pain, quicker recovery, early initiation of physical therapy, shorter hospital stays, reduced opioid consumption, superior post-surgery pain control, higher patient satisfaction, and improved intraoperative muscle relaxation (Kamel et al., 2019). Peripheral nerve blocks may be more appealing than neuraxial blocks in contemporary orthopedic surgery since they only affect the surgical extremity, have better compatibility with anticoagulation, and are unrelated to hypotension.

In TKA, peripheral nerve blocks offer effective analgesia, and newer methods like the IPACK (interspace between the popliteal artery and posterior capsule of the knee) block help surgeons address knee pain that other nerve blocks do not address. Despite the benefits mentioned above, nerve blocks risk complications such as infection, bleeding, rebound pain, and nerve injury; hence, it is important to weigh these risks

<table>
<thead>
<tr>
<th></th>
<th>Tramadol</th>
<th>Oxymorphone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td>50–100 mg PO</td>
<td>5–10 mg PO</td>
</tr>
<tr>
<td>Time</td>
<td>3–6 hours</td>
<td>3–6 hours</td>
</tr>
<tr>
<td>Route</td>
<td>PO</td>
<td>PO</td>
</tr>
<tr>
<td>Liver</td>
<td>CYP2D6 and CYP3A4</td>
<td>None known</td>
</tr>
<tr>
<td>and</td>
<td>and</td>
<td></td>
</tr>
<tr>
<td>CYP3A4</td>
<td>CYP3A4</td>
<td></td>
</tr>
<tr>
<td>and</td>
<td>and</td>
<td></td>
</tr>
<tr>
<td>CYP3A4</td>
<td>CYP3A4</td>
<td></td>
</tr>
<tr>
<td>inhibitors (macrolide antibiotics/azole-antifungal agents)</td>
<td>inhibitors (macrolide antibiotics/azole-antifungal agents)</td>
<td></td>
</tr>
<tr>
<td>Causes increased intracranial Pressure</td>
<td>- Causes increased intracranial Pressure</td>
<td></td>
</tr>
</tbody>
</table>

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against potential advantages (Schwenk & Mariano, 2023). To prolong the period of nerve blockade, anesthesiologists may add adjuvants like dexmedetomidine or dexamethasone to the perineural mixture or position a continuous nerve block. Although the United States has not approved perineural dexamethasone indication, studies have shown that it extends the period for brachial plexus block by six to eight hours and for sciatic block by thirteen hours (Rehangdale et al., 2014). Although dexmedetomidine can also prolong blockade with a mechanism that is the same as clonidine, there may be a risk of bradycardia (Schwenk & Mariano, 2018). Orthopedic surgeons have widely adopted the use of peripheral nerve blocks in their practice. However, they must collaborate with anesthesiologists. Kamel et al. (2022) explain that collaboration is crucial since it allows orthopedic surgeons to comprehend the relevant clinical aspects of the blocks to maximize perioperative efficacy and patient safety and enhance clinical outcomes.

Conclusion
Multimodal analgesia seeks to eliminate overdependence on opioids for pain management and reduce their related adverse effects. A multimodal analgesia routine must be surgery-centric, acting more like a checklist with options to modify the medication for individual patients, accounting for the potential risks and benefits. Elements of multimodal analgesia include gabapentinoids, NSAIDs, NMDA antagonists, and acetaminophen. Although various healthcare agencies have recommended the application of multimodal analgesia perioperatively to reduce long-term intake of opioids after surgery, the simultaneous crisis of drug shortage presents an additional problem. Consequently, anesthesiologists must expand their clinical experience and knowledge to include analgesic agents they have not traditionally used. Therefore, multimodal analgesia protocols should be flexible. The importance of multimodal analgesia strategy has never been greater than during the present opioid epidemic, and with the emerging evidence that short perioperative opioids can increase the risk of long-term opioid intake.

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Authors Contribution: Dr. Ahmed Mohamed Ahmed, Dr. Hai Ping Ma, and Dr. Sakarie Mustafe Hidig Conceived and designed this article and wrote the initial draft of it. The authors have read and approved the final version of the manuscript.

References


