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Article – Review**Redefining Recovery: Multimodal Analgesics and Tranexamic Acid in Orthopedic Surgery**

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Introduction

As the demand for joint replacements continues to rise, optimizing patient outcomes and enhancing recovery have become paramount goals for orthopedic surgeons. Patients used to have minimal mobility following a Total Knee Arthroplasty (TKA) or Total Hip Arthroplasty (THA) due to pain or the effects of sedation from anesthesia. This would lead to longer hospital stays, more complications, and higher opioid use.¹ These surgeries also resulted in levels of blood loss that required transfusion therapy postoperatively.² In recent years, there has been a paradigm shift in postoperative care for total joint arthroplasty (TJA), marked by significant advancements in the use of multimodal analgesics and tranexamic acid (TXA).

The integration of multimodal analgesic approaches, combining various analgesic agents and techniques, has shown promise in effectively managing postoperative pain while minimizing opioid consumption.³ Concurrently, the administration of TXA, an antifibrinolytic agent, has gained widespread recognition for its role in reducing blood loss and transfusion requirements in TJA procedures.⁴

Multimodal Analgesics

The management of postoperative pain poses a significant challenge in TKA, impacting mobility, rehabilitation, and overall patient satisfaction. The conventional approach involving general anesthesia and postoperative epidural with patient-controlled opioid analgesia is fraught with undesirable adverse effects, including nausea, vomiting, hypotension, urinary retention, respiratory depression, delirium, and an increased risk of infection.⁵ This goes without mentioning the US Department of Health and Human Services declaring the opioid crisis a national public health emergency, in 2017.⁶ Multimodal analgesics helps tackle this problem by encouraging the use of NSAIDs, Acetaminophen, Gabapentinoids, Ketamine, Corticosteroids, and regional nerve blocks.

Acetaminophen

Acetaminophen has been used for decades to manage pain. It safely reduces postoperative pain and opioid use, but there is not sufficient data to support the efficacy or safety after discharge. When IV acetaminophen was compared to a placebo, there was a significant reduction in postoperative pain scores. There was also a reduction in postoperative 24-hour opioid use. No significant differences were found between oral or IV acetaminophen reductions in pain or opioid use following TJA. Postoperative complications were comparable between the two acetaminophen groups and placebo.⁷ However, according to the Clinical Practice Guidelines, there is not overwhelming evidence supporting the superiority of oral acetaminophen over placebo, so the recommendation for its use is only moderate. Additionally, the use of IV acetaminophen is only moderately recommended, as well, due to the significantly higher price.⁸ However, as a generic version of IV acetaminophen becomes available, the medication cost may become less of a barrier to its widespread utilization.

Gabapentinoids

Gabapentinoids operate through analgesic mechanisms that encompass the direct attenuation of excitatory neurotransmission within the spinal cord, achieved by inhibiting neuronal ion channels. Additionally, they employ indirect mechanisms, including descending inhibition and the prevention of injury-evoked synaptogenesis. The multifaceted actions of gabapentinoids contribute to their effectiveness in pain management, making them an intriguing consideration for pain control in TKA.⁹ However, according to Clinical Practice Guidelines, there was not a significant reduction in postoperative pain during the preoperative period with gabapentinoids compared to placebo, but pregabalin did have a decrease in opioid consumption. After discharge, pregabalin also showed decreased postoperative and neuropathic pain while gabapentin did not. Pregabalin is recommended for use due to its reduction in opioid use and postoperative and neuropathic pain, while a weaker gabapentinoid, gabapentin, is not as effective.¹⁰ Even though gabapentinoids can be used for pain management, the FDA warns that they can depress respiratory function, especially in patients concomitantly using opioid medication. This is especially true in patients with pre-existing risk factors since there were 12 deaths from respiratory depression associated with gabapentinoids from 2012 to 2017.¹¹ Therefore, extreme caution must be considered when prescribing a gabapentinoid for a postoperative patient.

Ketamine

Ketamine is an N-methyl-D-aspartate (NMDA) receptor antagonist that acts at the dorsal horn of the spinal cord.¹² It does not exhibit the typical opioid-related complications, such as respiratory depression.¹³ The efficacy of its use was shown in a study done by Brinck et al, where perioperative intravenous ketamine reduced the pain at rest by 5/100 mm on a visual analog scale up to 24 hours after surgery. It also reduced opioid consumption by 8mg morphine equivalents over 24 hours post-operation.¹⁴ A Clinical Practice Guideline written on Ketamine use in TJA strongly recommended the use of Ketamine to reduce opioid consumption post-operatively. However, they only have a moderate recommendation for its use in the reduction of pain due to mixed results in their meta-analysis. Interestingly, ketamine was shown to significantly reduce nausea and vomiting, but they only have a moderate recommendation for the use of ketamine as an antiemetic because this is a secondary effect of ketamine. Ketamine was not found to have an increase in adverse events, but it should be used cautiously with the elderly due to a higher rate of hallucinations and nightmares.¹⁵

Periarticular Injection

Periarticular Injection (PAI) is becoming a popular pain management tool for TJA that can be performed directly by the surgeon. PAI involves the technique of injecting a combination of medications directly into the tissue surrounding the joint.¹⁶ This has the benefit of targeting specific pain receptors, instead of taking an oral anesthetic that can have more systemic effects. PAI was shown to be effective in a study that analyzed patients through visual analogs. They showed low visual analog scores for pain and high visual analog scores for patient satisfaction. Reduced firing from the targeted pain receptors allows for movement sooner after an operation. These patients also showed to reduce their use of patient-controlled analgesia at six, twelve, and twenty-four hours post-operation.¹⁷ Through a meta-analysis conducted by Hannon et al, PAI decreased pain and opioid use post-operatively without an increase in adverse events. They also found that a PAI cocktail of a long-acting local anesthetic with adjuvant medications further decreased these two parameters more than using a long-acting local anesthetics alone. Two additional adjuvant medications that were very effective were corticosteroids and ketorolac, whereas morphine did not provide the same benefit.¹⁸ The localized effects of PAI allow patients to ambulate sooner after the operation. This reduces the risk of adverse events like clotting and stiffness while also improving the blood flow to the affected parts of the body. Additionally, the sooner a patient mobilizes after surgery, the sooner they can begin rehabilitation to accelerate their recovery.¹⁹

Tranexamic Acid

A complication that can extend the hospital stay and recovery time for a patient is bleeding, especially when transfusions are needed. TXA is an antifibrinolytic agent that inhibits plasmin from breaking down fibrin in blood clots. There may be some concerns about adverse events from the use of TXA due to its method of action, but it has proven to be safe as a blood clot stabilizer and not a blood clot promoter. In a meta-analysis completed by Yang et al, there were no significant differences in deep vein thrombosis, pulmonary embolism, prothrombin time, or activated partial thromboplastin time compared to a placebo group.²⁰ TXA was proven to be effective through a meta-analysis performed to support a clinical practice guideline.²¹ For TKA, it was found that the need for transfusion was reduced by 66% for topical TXA, 61% for oral TXA, 81% or 55% for IV TXA when given before or after surgery, and 75% when multiple doses were given compared to placebo. There was also a reduction in blood loss and the need for transfusion for different volumes of dosing. TXA has been proven to be effective through multiple forms of administration and dosing volumes.²² These observed benefits of using TXA ultimately resulted in a strong recommendation for its use in TJA from the Clinical Practice Guidelines written by Fillingham et al.²³ A multivariate regression analysis completed by Hamidreza et al showed reduced complications associated with TXA use as well, specifically Periprosthetic Joint Infections (PJI). The rate of PJI dropped from 3.4% to 1.6% with the use of TXA. They believed that this reduction is due to a reduction in blood loss and the need for allogeneic blood transfusions, which can lead to surgical infections.²⁴

Conclusion

The dynamic landscape of postoperative care for TKA and THA responds to the escalating demand for joint replacement surgeries with significant advancements in patient outcomes and recovery. The paradigm shifts towards multimodal analgesics, encompassing diverse agents and techniques, presents a promising path for effective pain management while mitigating the adverse effects associated with traditional opioid medications. Notably, the integration of medications such as acetaminophen, gabapentinoids, ketamine, and the innovative PAI technique showcases a multifaceted approach to addressing postoperative pain and opioid consumption. Furthermore, the strategic use of TXA emerges as a crucial factor in reducing blood loss and transfusion requirements, ultimately contributing to improved patient safety and decreased complications. As these advancements are embraced, the dedication to optimizing orthopedic surgical care remains unwavering, promising a future

where patients experience enhanced mobility, shortened recovery times, and elevated overall satisfaction.

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