NSAIDs association with Chronic Pain post TKA: A Systematic Review

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INTRODUCTION: This study compared pharmacological agents used in the management of pain following total knee arthroplasty (TKA) with the purpose of understanding correlates with chronic pain development and identifying the most successful treatments to both decrease expected acute pain and show the least association with prolonged pain following TKA. TKA is completed on many facing end stage osteoarthritis and other conditions with the goal of decreasing pain, restoring functionality, and improving quality of life. TKA is associated with chronic pain in an increasing number of cases, some of which are refractory to care. To date, there are several options to treat pain post-TKA including opioids, non-steroidal anti-inflammatories (NSAIDs), and anesthetics, with NSAIDs as one of the major modulators. Recent literature suggests a link between NSAID use and transition to chronic pain following injury or procedure due to the blockage of necessary healing signals and processes within the body. There is currently minimal investigation into the relationship of chronic pain and the use of NSAIDs following TKA. This study aims to identify all high quality studies on the efficacy of pain analgesics post-TKA with a focus on NSAIDs and other pharmacological agents, then understand correlations with chronic pain occurrence to provide new insights that may guide treatment protocol for TKA and other procedures down the road.

METHODS: To determine the most efficacious treatment of pain post TKA and associations with chronic pain, the key search phrase "Total Knee Arthroplasty AND Chronic Pain OR Total Knee Replacement AND Chronic Pain" was used in the Science Direct, PubMed, and JSTOR databases to pull articles. Inclusion Criteria for abstracts Included Randomized Control Trials, Controlled Clinical Trials, cohort studies, retrospective and prospective studies including subjects that were 18 years or older of any race or gender given pre- or post-operatively pharmacological agents for pain. If studies included animal subjects, systematic review, meta analysis or if it included patients with concurrent conditions or trauma that may be the cause of pain, a history of prior knee hip or back surgery, or focused on acute pain, they were excluded. All articles were reviewed in a blinded fashion, with disagreements reviewed in a non-blind fashion to reach consensus.

RESULTS: A total of 202 articles from ScienceDirect, 761 from PubMed, and 164 from JSTOR were downloaded and added into the Rayyan software for review. There were 144 duplications identified with 140 deleted for this reason.There were 109 disagreements before consensus. PRISMA guidelines were reviewed and accepted throughout each step of the review. A total of 39 full articles were then downloaded for final review. Analysis of 39 selected articles were performed with articles grouped into pharmaceutical and subject categories. Results are as follows: *multimodal (n=15, 38.46%), opioids (n=5, 12.8%), anesthesia (n=4, 10.26%), corticosteroids (n=2, 5.13%), pathogenesis (n=4, 10.26%), Anticonvulsants (n=2, 5.12%), Muscle Relaxants (n=1, 2.56%), Magnesium Sulfate (n=1, 2.56%), NSAIDs (only) (n=1, 2.56%), SNRI (n=2, 5.13%), Radiofrequency ablation (n=1, 2.56%), Ketamine (n=1, 2.56%).* "Multimodal" categories were defined as studies including but not limited to a combination of NSAIDs, Opioid, and acetaminophen. Future Meta-analysis of all included 39 studies will be performed to complete full analysis.

DISCUSSION: Our findings indicate a preliminary correlation between long-term NSAID use post-operatively and chronic pain based on reviewed literature. 39 articles with varying study designs provided a comprehensive understanding of the relationship between NSAID use and the development of chronic pain post Total Knee Arthroplasty. Our preliminary analysis suggests the development of chronic pain is associated with long-term administration of NSAIDs. While research is scarce regarding chronic pain development with prolonged NSAID use, emerging scientific evidence is promising.

SIGNIFICANCE AND RELEVANCE: NSAIDs within a multimodal postoperative regimen have been a staple for surgeons since their inception. Chronic Pain following TKA is well-documented and a relatively common complication arising in an increasing number of patients post-TKA. Our study will provide clinicians with valuable insight to help guide post-operative protocol and improve patient outcomes.