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Literature Review: *Effectiveness of NSAIDs in Osteoarthritis Patients*

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Abstract: Pain, stiffness, swelling, and decreased joint function are some of the clinical signs of osteoarthritis, a disease that affects numerous anatomical and physiological aspects of joint tissue, cartilage degradation, bone remodeling, and osteophyte development. This literature review's objective is to ascertain the efficacy of NSAIDs in osteoarthritis by searching for journals from PubMed. The method used was to search for articles through pubmed using the keywords "NSAID", "osteoarthritis", "Therapy" with a filter added for the last 5 years (2019-2024) obtained 103 articles. Then with the keywords "NSAID", "osteoarthritis", "therapy", "efficacy" obtained 71 articles. After analysis, there are 13 journals that can be include into inclusion requirement. NSAIDs preparations are particularly helpful for osteoarthritis therapy, both in knee and hip osteoarthritis. NSAIDs medications in a variety of dose forms, including oral, topical, spray, injection and plaster, are useful in relieving pain in osteoarthritis patients

Keywords: Osteoarthritis, NSAID, Knee, Therapy, Efficacy

INTRODUCTION

Pain, stiffness, swelling, and reduced joint function are some of the clinical signs of osteoarthritis, a disease that affects several anatomical and physiological features of joint tissue, including cartilage degradation, bone remodeling, and osteophyte production. 10% of males and 18% of women aged 60 and over have symptomatic OA, which affects an estimated 240 million people globally (Roux & Ferrero, 2024).

Hereditary 60% of hand and hip OA and 40% of knee OA are caused by causes. Numerous genes might contribute to the illness's development, opening the door to potential pharmacological treatments in the future. Several dietary factors are thought to raise the chance of developing OA, including deficiencies in vitamins D, C, and K (Nguyen & Poiraudeau, 2016). To fully comprehend the connection between OA and these dietary factors, additional investigation is necessary. risk factors at the joint level. Damage The knee is one of the most often damaged joints. After ten to fifteen years, 13% of patients get early-onset knee OA due to anterior cruciate ligament (ACL) rupture. The frequency of knee OA is greater, ranging from 21% to 40%, when such a rupture is connected to compromised cartilage, bone underneath the chondral, collateral ligaments, and/or menisci, it happens in around 65–75% of knees with ACL injuries. Hip

osteoarthritis was associated with extended periods of standing and lifting, while hand osteoarthritis was prevalent in tasks requiring more manual dexterity, and knee osteoarthritis was more frequent in professions involving crouching and kneeling (Nguyen & Poiraudeau, 2016).

Medications such analgesics, exercise, orthotic therapy, and surgery are the primary forms of treatment. One of the most important therapeutic choices for osteoarthritis is oral analgesics; however, because of age-related pharmacokinetic alterations and polypharmacy, adverse events are more likely to occur in older patients (Endo et al., 2023). Nonsteroidal anti-inflammatory medicines (NSAIDs) constitute the mainstay of pharmacologic therapy since they have been shown in short-term clinical studies to be effective for OA-related pain and are usually advised above other pharmacological therapies. However, their usage is not advised in patients who are susceptible to gastrointestinal, cardiovascular, or renal issues, and it is not advised for any patient to take them for a long time owing to the possibility of these adverse events (AEs) (Neogi et al., 2022).

METHODS

In this study, the method used was to search for articles through pubmed using the keywords "NSAID", "osteoarthritis", "Therapy" with a filter added for the last 5 years (2019-2024) obtained 103 articles. Then with the keywords "NSAID", "osteoarthritis", "therapy", "efficacy" obtained 71 articles. After analysis, there are 13 journals that can be include into inclusion requirement. Table 1 then provides an explanation of the literature review's findings.

RESULT AND DISCUSSION

In a review of 13 articles, it was discovered that NSAID preparations are particularly helpful for osteoarthritis therapy, both in knee and hip osteoarthritis. NSAID medications in a variety of dose forms, including oral, topical, spray, injection and plaster, are useful in relieving pain in osteoarthritis patients. A brand-new topical NSAID patch called S-flurbiprofen plaster (SFPP) was created. The active version of the often used FP, SFP, is present in the plaster. SFP is an analgesic, anti-inflammatory, and cyclooxygenase (COX) inhibitor (Tomatsu et al., 2022).

Ibuprofenamine hydrochloride spray was well tolerated in the Phase I research alone dosages at repeated dosages of up to 140 mg twice day and up to 280 mg. The dosage selection and upcoming clinical assessment of phase II ibuprofenamine hydrochloride spray research are supported by these results (Xie et al., 2021). According to the main outcome after three months of therapy, diclofenac etalhyaluronate (DF-HA) injection was more effective than a placebo at reducing pain (Nishida et al., 2021b).

Other NSAID formulations, like meloxicam, may be used as an analgesic after orthopedic surgery, such as complete ankle and shoulder replacement. Meloxicam has shown efficacy in alleviating postoperative pain after complete hip replacement. Conversely, meloxicam shown no impact on long-term postoperative discomfort in patients who have total knee replacements (TKA) (Hu et al., 2021). studies by Choi and Choi (2023) A safe and efficient method of treating osteoarthritis symptoms, diacerein and celecoxib treatment may be beneficial in the early stages.

Table 1. The Results Of The Analysis in 13 Scientific Articles

Author	Title	Method	Sample	Result
(Ren et al., 2020)	Preoperative meloxicam versus postoperative meloxicam for pain control, patients' satisfaction and function recovery in hip osteoarthritis patients who receive total hip	A controlled, randomized study is the methodology used.	Each group has to have a minimum sample size of 60.The minimal sample size, taking into account a 10% drop-out rate, was established at 66 in each group, for a research total of 132.	When it comes to hip OA patients who had THA, preoperative meloxicam is better than postoperative meloxicam in terms of postoperative pain management, patient satisfaction, and safety and hip joint function recovery.

	arthroplasty: a randomized, controlled study			
(Kubo et al., 2022)	Diclofenac–hyaluronate conjugate(diclofenac etalhyaluronate) intra-articular injection for hip, ankle, shoulder, and elbow osteoarthritis: a randomized controlled trial	The method used a randomized, controlled trial	Participants in this research were to be OA anyone over 20 with hip, For target joint discomfort, an average 11-point (0–10) NRS of 5–9 throughout the screening period and at least six months of elbow, shoulder, or ankle joint discomfort.	Patients with hip OA responded quickly to intra-articular Diclofenac etalhyaluronate (DF-HA), which was safe and sustained analgesia for 12 weeks when given every 4 weeks.
(Neogi et al., 2022)	Observed efficacy and clinically important improvements in participants with osteoarthritis treated with subcutaneous tanezumab: results from a 56-week randomized NSAID-controlled study	The technique is based on a recent multicenter, phase 3 randomized, double-blind, active-controlled research.	BMI < 39 kg/m2, age > 18, and, according to the central reader, a KL level ≥ 2 in the index joint, were requirements for eligibility.	This trial indicates that in individuals with mild to severe osteoarthritis of the hip or knee with a documented insufficient reaction to the standard osteoarthritis analgesics, therapy with SC tanezumab (2.5 mg and 5 mg) or oral NSAIDs provide promp and persistent (56 weeks or more) effectiveness compared to baseline. For a significant percentage of subjects, improvements in function and pain were clinically significant. Although the majority of individuals handled tanezumab well, joint safety events had a dose dependent relationship and occurred more often with tanezumab compared to NSAIDs, warranting consideration in the assessment of the drug's overall risk-benefit profile.
(Tomatsu et al., 2022)	Efficacy and safety of S-flurbiprofen plaster in knee osteoarthritis patients: A 2-week randomized controlled Phase III clinical trial compared to diclofenac gel	The research was designed as a Phase III, open-label, randomized, active controlled, multicenter, and non-inferiority research.	For this investigation, individuals with Grade II or III knee OA were examined. Participants in this research required to be able to walk, have unilateral knee discomfort, understand visual analog scales (VAS), and be at least 40 years old at the time of consent. As a pre-treatment, the patients took 200 mg/d of celecoxib for two weeks between the first and second visits.	SFPP to diclofenac gel was shown to be effective in reducing pain while getting out of a chair. The majority of efficacy outcomes showed groups' statistically substancial differences, suggesting that SFPP is a very effective treatment for individuals with knee OA. Additionally, SFPP was accepted favorably by individuals with knee OA.
(Nishida et al., 2021a)	Efficacy and Safety of Diclofenac–Hyaluronate Conjugate (Diclofenac Etalhyaluronate) for Knee Osteoarthritis: A Randomized	50 locations around Japan participated in a phase III multicenter, Double blind, randomized, placebo controlled research.	Participants using knee OA who were between the ages of 40 and 75 and had a radiographically diagnosed a WOMAC pain subscale score, a K/L level of 2 or 3, and at the time of screening, the target knee's pain	When administered once every four weeks, DF-HA, a linked to molecule that combines the benefits of IA HA and NSAIDs, significantly reduced symptoms and had long-lasting, fast-acting effectiveness in individuals with knee OA. Additional safety assessment is required since anaphylactic responses were

	Phase III Trial in Japan		score must be between 50 and 90 mm (on a 100-mm VAS) and the contralateral knee's pain score must be less than 30 mm.	noted. DF-HA is anticipated became new therapeutic agent that will address an unfulfilled require to pharmacotherapy for knee OA, even if further research is required to confirm its clinical utility.
(Li et al., 2023)	Efficacy and safety of flurbiprofen cataplasms versus loxoprofen sodium cataplasms in knee osteoarthritis: a randomized controlled trial	This randomized controlled study was open-label and non-inferiority.	This study was open-label, randomized, controlled, and non-inferiority. 250 patients with radiographic confirmation of knee osteoarthritis were recruited by the orthopedic outpatient clinic at Peking University Shougang Hospital (KLS II–III) between October 2021 and April 2022.	Patients with knee OA may effectively reduce their pain levels by using topical NSAIDs. In China, FPC and When treating knee OA, two of the most often recommended topical NSAIDs are LSC. According to the results of the present research, patients may benefit more from FPC than LSC when it comes to pain reduction, improved joint function, and safety when used in a therapy choice for knee OA discomfort.
(Xie et al., 2021)	Safety, Tolerability, and Pharmacokinetics of Ibuprofenamine Hydrochloride Spray (NSAIDs), a New Drug for Rheumatoid Arthritis and Osteoarthritis, in Healthy Chinese Subjects	Ibuprofenamine hydrochloride's pharmacokinetics, safety, and tolerability in healthy Chinese individuals were examined in a single and multiple ascending dosage trial.	A total of 34 people participated in the trial (20 participants in the multiple dose trial and 34 participants in the single dose study). Eligible participants were healthy adults aged 18–45 with a BMI of 19.0–28.0 kg/m2. Each participant was deemed healthy based during a physical assessment, medical history, 12-lead ECGs, crucial indications, and lab examinations.	In healthy Chinese patients, the novel transdermal NSAID ibuprofenamine hydrochloride spray showed good pharmacokinetic and safety characteristics. Ibuprofenamine hydrochloride spray was well tolerated in this Phase I investigation at solitary concentrations > 280 mg and recurrent doses > 140 mg twice day. These findings provide help with to the Phase II study's dosage the choice and additionally clinical assessment of ibuprofenamine hydrochloride aerosol.
(Hu et al., 2021)	Evaluation of analgesic effect, joint function recovery and safety of meloxicam in knee osteoarthritis patients who receive total knee arthroplasty A randomized, controlled, double-blind study	The approach is a double blind, randomized, controlled trial.	The 128 eligible patients were categorized into two categories at random: the meloxicam group (N=65) and the control group (N=63). The blind realization, randomization design/procedure, and sample size calculation were conducted by a third party (Shanghai QeeJen Bio-Tech, China). Guangzhou Boji Medical & Biotechnological Co., Ltd. (China) supplied the placebo, whereas Shanghai Boehringer Ingelheim Pharmaceutical Co., Ltd. (China) supplied meloxicam (7.5 mg per tablet).	A study that was randomized, double blind, and placebo commanded to examine the postoperative analgesic consequences of meloxicam impact demonstrates that the medication may relieve pain after orthopedic surgery, such as total ankle and shoulder replacement. Meloxicam has also been proved to be effective in managing postoperative pain after total hip replacement. However, meloxicam had no effect on patients' long-term postoperative pain following TKA. This could be because pain could decrease using time and the healing of the patient's laceration, and meloxicam was stopped 72 hours after TKA; as a result, no change in pain was observed after day 7.

(Choi & Choi, 2023)	Efficacy and safety of diacerein and celecoxib combination therapy for knee osteoarthritis A double-blind, randomized, placebo-controlled prospective Study	The approach is a prospective, randomized, double-blind, placebo-controlled research.	Across many medical locations, 87 individuals over 50 individuals were tested for knee pain who was identified as having primary osteoarthritis in their knees and whose visual analog scale (VAS) score was more than 40 mm were included. inflammatory inflammation, such as gout and rheumatoid arthritis, secondary osteoarthritis of the knee, and any other conditions that might have an impact on the study's findings were the exclusion criteria.	There was no discernible change in the VAS ratings comparing the comparation and monotherapy groupings, according to the study's main outcome data. However, compared to the other groups, the combination treatment group's absolute value of the VAS score enhancement was larger. There were no severe adverse effects in this trial, they happened seldom, and there were no significant variations between the groups. Consequently, a safe and efficient treatment approach for osteoarthritis symptoms is diacerein and celecoxib combination therapy, which may also have an advantage in early symptom alleviation.
(Multicenter et al., 2021)	Comparison of the Efficacy and Safety of Ketoprofen Plaster and Diclofenac Plaster for Osteoarthritis-Related Knee Pain: A Multicenter, Randomized, Active-Controlled, Open-Label, Parallel-Group, Phase III Clinical Trial	This phase III study was multicenter, parallel-group, open-label, randomized, active-controlled, and noninferiority.	Adult male or female patients between the ages of 40 and 75 who had participants in this study had to have idiopathic OA of the knee and the baseline pain level in the index knee during walking is ≥40 mm on the VAS.	In the current clinical investigation, it was shown that giving patients with knee OA 30 mg of ketoprofen plasters twice a day for three weeks did not significantly worsen their pain than giving them 15 mg of diclofenac plasters once a day. The safety profile of the ketoprofen plaster was good and it was well tolerated. There were no unexpected tolerability results, and the frequency of adverse events.
(Park et al., 2020)	A comparative study of the efficacy of NAXOZOL compared to celecoxib in patients with osteoarthritis	This research was a prospective, double-blind, double-dummy, randomized controlled one preliminary experiment that was two-arm parallel, active-controlled, and	The following were the requirements for inclusion: (1) 50 years of age; (2) radiographs showing symptomatic osteoarthritis with a pain VAS score greater than 4. Based on the patient's history, clinical examination, and radiographic abnormalities, osteoarthritis was diagnosed.	A novel naproxen and esomeprazole strontium tetrahydrate combination is called NAXOZOL. Naproxen has anti-inflammatory, analgesic, and antipyretic properties because, like others NSAIDs, it primarily inhibits the activity of COX-2, which lowers the production of prostaglandin and thromboxane from arachidonic acid. The pharmacokinetics of naproxen were similar to those of VIMOVO, according to a clinical research comparing the two medications' safety and pharmacokinetics. There were no safety concerns and both medications were well accepted.
(Nishida et al., 2021b)	Sustained-release diclofenac conjugated to hyaluronate (diclofenac etalhyaluronate) for knee osteoarthritis: a	This multicentre, randomized, placebo-controlled, double-blind, parallel-group	During the screening process, eligible patients were between the ages of 40 and 75 and had pain for 12 weeks, with a mean VAS index of 30 mm at the knee on the other	InjectioAccording to the main outcome after three months of therapy, DF-HA was more effective than a placebo at reducing pain. The WOMAC pain subscores, the 50-foot walk test pain score, and the daily pain score obtained from the patients' diaries were the three

	randomized phase 2 study	comparison phase 2 study	side (100-mm VAS), a mean Kellgren-Lawrence radiographic score of a mean WOMAC pain subscore of 50 to 90 mm (inclusive) at the target knee, a score of 2 or 3, and a diagnosis of knee OA from the American College of Radiology. Furthermore, in the middle of the study, the pain score from the 50-foot walk test was included in the qualifying parameters since several Patients' pain assessments were inconsistent; for example, they had a high WOMAC pain subscore but a low 50-foot walk test score.	main end measures of pain severity used in the research. Both the DF-HA group and the placebo group saw a substantial reduction in baseline WOMAC pain subscores, daily pain scores, and 50-foot walk test pain ratings after the first injection. Since the IA injection itself was shown to have a significant placebo effect, these decreases were assumed to be placebo effects. The 50-foot walk test pain score showed a tendency toward better pain reduction twelve weeks after the first injection, while the DF-HA group's daily pain score and WOMAC pain subscores demonstrated noticeably superior pain mitigation.
(Shin et al., 2020)	Efficacy and safety of short-term use of a pelubiprofen CR and aceclofenac in patients with symptomatic knee osteoarthritis: A double-blinded, randomized, multicenter, active drug comparative, parallel-group, phase IV, non-inferiority clinical trial	double-blinded, randomized, multicenter, active drug comparative, parallel-group, phase IV, non-inferiority clinical trial	191 individuals in all were chosen at random to get either aceclofenac 200 mg (n = 96) or 90 mg of pelubiprofen CR (n = 95). The primary outcome variable, measured with a 100 mm VAS, was the Pain decrease from baseline to week four was not inferior.	When compared to the baseline, the pain VAS values at week four were considerably lower in both groups who received either aceclofenac 200 mg or pelubiprofen CR 90 mg. Nonetheless, non-inferiority was confirmed by the aceclofenac group's and pelubiprofen group's respective pain VAS alterations of -21.8 therefore -21.7 in the entire analysis set and -22 therefore -21.9 in the pre-protocol set. When compared to aceclofenac 200 mg, the incidence of adverse events was lower with pelubiprofen CR 90 mg (p = 0.005).

CONCLUSION

NSAIDs preparations are particularly helpful for osteoarthritis therapy, both in knee and hip osteoarthritis. NSAIDs medications in a variety of dose forms, including oral, topical, spray, injection and plaster, are useful in relieving pain in osteoarthritis patients. Combining celecoxib with diacerein treatment is a secure and efficient way to relieve osteoarthritis symptoms, with potential benefits in early stages.

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