DOI: https://doi.org/10.54393/pjhs.v6i8.2981

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (E): 2790-9352, (P): 2790-9344
Volume 6, Issue 08 (August 2025)

Original Article

OPEN ACCESS

Comparative Analysis of Pain Relief and Adverse Effects of Ibuprofen versus Naproxen in Elderly Knee Osteoarthritis

Suhail Marfani[1], Ayesha Khan[2], Muhammad Ali Zubair[3], Nadia Naeem[4], Khawar Anwar[5] and Shabzain Ishrat[3*]

[1]Department of Medicine, Prime Health Care Group, United Arab Emirates
[2]Department of Pharmacology, Bahria University Medical and Dental College, Karachi, Pakistan
[3]Department of Pharmacology, Shahida Islam Medical and Dental College, Lodhran, Pakistan
[4]Department of Pharmacology, Jinnah Sindh Medical University, Karachi, Pakistan
[5]Department of Biochemistry, Shahida Islam Medical and Dental College, Lodhran, Pakistan

ARTICLE INFO

Keywords:
Ibuprofen, Knee Pain, Naproxen Sodium, NSAIDs, Osteoarthritis

How to Cite:
Marfani, S., Khan, A., Zubair, M. A., Naeem, N., Anwar, K., & Ishrat, S. (2025). Comparative Analysis of Pain Relief and Adverse Effects of Ibuprofen versus Naproxen in Elderly Knee Osteoarthritis: Pain Relief and Ibuprofen versus Naproxen in Elderly Knee Osteoarthritis. Pakistan Journal of Health Sciences, 6(8), 57-62. https://doi.org/10.54393/pjhs.v6i8.2981

***Corresponding Author:**
Shabzain Ishrat
Department of Pharmacology, Shahida Islam Medical and Dental College, Lodhran, Pakistan
ishratshabzain@gmail.com

Received Date: 17th March, 2025
Revised Date: 7th August, 2025
Acceptance Date: 18th August, 2025
Published Date: 31st August, 2025

ABSTRACT

Osteoarthritis (OA) has no definitive cure, and to improve the quality of life, analgesic medications are used. **Objectives:** To evaluate ibuprofen and naproxen in elderly patients with knee osteoarthritis in terms of pain relief (primary outcome) and adverse effects (secondary outcome). **Methods:** This comparative analytical study was conducted at the Rheumatology Clinic of Shahida Islam Medical College and Hospital from June to November 2024. Following ethical approval, patients aged over 50 years with stage I-III knee OA willing to participate were included. Exclusion criteria were stage IV OA, systemic or rheumatologic co-morbidities (e.g., hypertension, diabetes), prior use of naproxen or ibuprofen within one month, and history of surgery within the past year. **Results:** A total of 310 participants were enrolled, equally divided between two groups: Naproxen Sodium (440/660 mg, n=155) and Ibuprofen (1200 mg, n=155). Both drugs significantly reduced pain from baseline to day 7 post-medication, including pain at rest, on weight-bearing, during passive movements, morning stiffness, and pain throughout the day and night ($p<0.010$, assessed via Visual Analogue Scale). **Conclusions:** Minimal side effects were observed in both groups. Naproxen and ibuprofen were both effective and well-tolerated options for pain relief in elderly patients with knee OA.

INTRODUCTION

Osteoarthritis (OA) is a chronic musculoskeletal disease which affects synovial joints and manifests in terms of degeneration of cartilage and bony hypertrophy. In developed countries, OA ranks among the top ten most common conditions with significant health impact [1]. Osteoarthritis primarily affects the elderly, with the knee and hip joints most commonly affected. That is why OA is ranked first in the most common factor for musculoskeletal disability in the elderly [2]. Pain in OA is thought to arise from capsular distention, periosteal elevation, synovial inflammation and/or trabecular micro-fractures. OA is becoming an increasingly significant healthcare challenge due to the growing proportion of the elderly population [3]. The pattern of affected joints tends to vary by gender, with male more prone to hip OA while female is more likely to experience a more severe and poly-articular form of disease. The specific area of the body involved in OA plays an important role in terms of pain and degree of disability [4]. For instance, if a person suffers OA of weight-bearing joints such as the knee and hip, the

DOI: https://doi.org/10.54393/pjhs.v6i8.2981

person may be immobilized, potentially reducing the quality of life. In comparison, OA of the inter-phalangeal joints of the hand might lead to less altered activities of daily living (ADL) [5]. The most common reason patients with OA seek medical help is to obtain analgesia during the night. Since there is no definitive cure for OA, current management primarily relies on analgesic medications, educating patients, pain relief, preservation and optimization of joint function [6]. Weight loss encouragement is also advised to such patients in order to decrease stress on weight-bearing joints, which will help to reduce pain while increasing mobility [7]. Nonetheless, evidence supporting the efficacy of various treatment strategies, both individual and in combination, is variable [8]. The first line of treatment in any pain condition is acetaminophen (paracetamol). A maximum of 4000 mg/day is given to patients suffering from OA for pain relief. However, usually, pain relief is limited to paracetamol [9]. After failure or pain relief by paracetamol, the next line of drug is a non-selective non-steroidal anti-inflammatory drug (NSAID), either naproxen 500 mg/day or ibuprofen 1200 mg/day or in combination with acetaminophen [10]. The usual use of NSAIDs is as required rather than as a fixed daily dose. According to the American College of Rheumatology's Subcommittee on Osteoarthritis Guidelines, treatment for patients diagnosed with OA should begin with a low drug dose, which should only be increased if adequate symptomatic relief is not achieved [11, 12]. Even though published data in terms of the contribution of NSAIDs to inflammation of joint pain and cartilage breakdown remains uncertain, there is rising evidence in terms of the role of OA-associated low-grade inflammation for which NSAIDs might be an ideal choice for effective analgesia [13]. The efficacy of NSAIDs in managing knee OA has been studied; however, their effects have been counterbalanced by the broader side effects of NSAIDs on the gastrointestinal tract [14]. Naproxen sodium, a non-selective NSAID, contains smaller naproxen particles compared to standard naproxen, resulting in a faster absorption rate. Naproxen is available over-the-counter (OTC) at doses of 275 mg and 550 mg. Recommended OTC dose for naproxen sodium is 220 mg every 8 to 12 hours with a maximum daily dosage of 660 mg up to 7 days. In elderly individuals greater than 65 years old, the recommended naproxen dose is one 220 mg tablet 12 hourly, with a total daily dose of 440 mg [15]. The maximum dosage of over-the-counter ibuprofen is 1200 mg/day. The efficacy of both naproxen sodium and ibuprofen is reported and recommended in rheumatologic conditions, including OA, in addition to dysmenorrhea and dental pain as well [16]. In developing countries such as Pakistan, where the rate of OA is ever-increasing, coupled with enormous use of OTC drugs such as naproxen and ibuprofen regularly, this study tends to unveil whether the use of OTC ibuprofen and naproxen is effective in terms of pain relief and minimal side effects, especially in the high-risk population of OA, viz., the elderly [17].

Knee osteoarthritis is highly prevalent among the elderly and is a major cause of pain, disability, and reduced quality of life. Although both ibuprofen and naproxen are widely available over-the-counter NSAIDs used for symptomatic relief, comparative data focusing specifically on their short-term efficacy and safety profile in elderly Pakistani patients remain limited. Moreover, real-world evidence evaluating both pain reduction and adverse effects in this high-risk age group is scarce. Therefore, a direct comparative assessment of these two commonly used NSAIDs was necessary to guide safer and more effective clinical decision-making. This study aims to evaluate ibuprofen and naproxen in elderly patients suffering from knee OA in terms of pain relief. The primary outcome was to study the relief of pain, while secondary outcomes were the evaluation of adverse effects by the use of drugs.

METHODS

This comparative analytical study was conducted at the Rheumatology Clinic of Shahida Islam Medical College and Hospital for a period of six months from June 2024 to November 2024. After ethical approval from the Ethical Review Committee of the hospital, IRB no: SIMC/ET.C/00020/24, diagnosed patients with OA (OA of stage I to III) above 50 years of age, willing to participate in the study were included through consecutive sampling while patients with stage IV OA or with other systemic or rheumatologic co-morbidities such as hypertension and diabetes were excluded. Patients already on naproxen sodium and ibuprofen or a history of taking either of the two drugs within the last month were also excluded. Any patient with a history of surgery within the past year was also excluded. The sample size was calculated using G-Power software for sample size calculation. Keeping the test to be applied at a paired t-test (matched pairs) and the following criterion, the sample size came out to be 147. However, due to consecutive sampling, a slightly higher sample size for each group was included, viz. 155 in each group [18]. t-tests - Means: Difference between two dependent means (matched pairs). Analysis (A priori): Compute required sample size. Input (Tail)s: Two, Effect size dz = 0.3, α err prob=0.05 and Power (1-β err prob) = 0.95. Output (Non-centrality parameter, δ): = 3.6373067, Critical t = 1.9763457, Df = 146, Total sample size = 147 and Actual power = 0.9508665. For diagnosis of OA, at least one of the following radiological feature were noted: narrowing of joint space, cyst formation in the knee joint, sub-chondral sclerosis or presence of marginal lipping or sub-chondral sclerosis.

DOI: https://doi.org/10.54393/pjhs.v6i8.2981

Current pain of patients or maximal pain on the visual analogue pain scale (VAS) at nighttime (where pain is highest) was recorded [3]. Patients were advised against using any medication/s which could interfere with pain evaluation or reduce the effects of NSAIDs. These included anti-inflammatories or aspirin-containing medicines, or any other analgesic medicines such as H2 blockers, proton pump inhibitors, antacids, prostaglandin analogues and sucralfate. They were advised to consult with the clinician whenever any symptom arose before taking any medication mentioned above. Informed consent was sought from each patient before inclusion in the study. Using a pre-designed proforma (annexure), data collection was carried out by the principal investigator. At follow-up, the principal investigator also filled out the proforma. Patients were given a list of side effects (as reported in results) and any other side effects observed by them for the duration of follow-up. A pre-designed case-report form (CRF) was provided to the patients for recording any adverse drug reaction (ADR) and/or any drug-drug interaction (DDI), and was directed on how to fill the form and bring it to their follow-up or whenever symptoms arose. Patients were randomly divided into an equal number of patients receiving naproxen and ibuprofen. A daily dose of naproxen sodium 660 mg in patients below 65 years, while 440 mg in patients >65 years of age was advised [19], while ibuprofen 1200 mg all either age group was advised [20]. Treatment was advised for 7 continuous days, and then asked to return for follow-up. Knee pain was assessed at baseline and at follow-up as well. Pain assessment was carried out using VAS [21] (0-No pain, 1=Slight pain, 2=Mild pain, 3=Moderate pain, 4=Severe pain. The clinician assessed the degree of knee pain on three occasions, viz., at rest, on weight-bearing and on passive motion. Along with pain, patients were assessed for joint stiffness in the morning, during the day and at night. Each change in symptom/s was recorded both at baseline and one week after treatment on follow-up. For analysis of data, SPSS version 22.0 was used. For categorical data, frequency and percentages were used. For numerical data, the mean and standard deviation were reported. Data normality was assessed using the Shapiro-Wilk test. For comparison of baseline versus 7-day follow-up data of patients in each group, a paired t-test was applied, keeping $p<0.05$ as statistically significant.

RESULTS

The study included 310 participants, with an equal division between the two treatment groups: Naproxen Sodium (440/660 mg, n=155) and Ibuprofen (1200 mg, n=155). The mean age in the Naproxen group was 62.77 ± 11.67 years, while the Ibuprofen group had a slightly younger mean age of 61.59 ± 12.84 years. Weight and height were similar across groups, with Naproxen patients averaging 78.85 ± 17.72 kg and 165.33 ± 8.98 cm, while the Ibuprofen group averaged 80.29 ± 18.22 kg and 167.6 ± 9.21 cm. The BMI values also aligned closely (Naproxen: 29.26 ± 8.2; Ibuprofen: 28.65 ± 8.58). Gender distribution was comparable, with male constituting 46.45% of the Naproxen group and 48.39% of the Ibuprofen group, while female accounted for 53.5% and 51.61%, respectively (Table 1).

Table 1: Baseline Demographics of Patients Included in the Study (n=310)

Variables		Naproxen Sodium (440/660 mg), n=155	Ibuprofen (1200 mg), n=155
Age (Years) Mean ± SD		62.77 ± 11.67	61.59 ± 12.84
Weight (kg)		78.85 ± 17.72	80.29 ± 18.22
Height (cm)		165.33 ± 8.98	167.6 ± 9.21
BMI (kg/m^2)		29.26 ± 8.2	28.65 ± 8.58
Gender	Male	72 (46.45 %)	75 (48.39 %)
	Female	83 (53.5 %)	80 (51.61 %)

Pain and Stiffness Improvement at Follow-Up: Both treatment groups showed marked improvement in pain and stiffness at the 7-day follow-up. For pain at rest, the Naproxen group showed a reduction from 3.2 ± 0.8 at baseline to 1.5 ± 0.6, while the Ibuprofen group improved from 2.9 ± 0.7 to 1.3 ± 0.5. Pain on passive movement decreased from 4.0 ± 0.9 to 2.1 ± 0.7 in the Naproxen group and from 3.8 ± 0.8 to 2.0 ± 0.6 in the Ibuprofen group. Pain on weight bearing reduced from 4.5 ± 1.0 to 2.7 ± 0.8 for Naproxen and from 4.2 ± 1.1 to 2.5 ± 0.7 for Ibuprofen. For morning stiffness, the mean values in the Naproxen group declined from 3.8 ± 0.7 to 1.9 ± 0.5, and in the Ibuprofen group from 3.5 ± 0.6 to 1.7 ± 0.4. Pain during the day lessened from 4.3 ± 0.6 to 2.3 ± 0.6 in the Naproxen group, and from 4.0 ± 0.7 to 2.1 ± 0.5 in the Ibuprofen group. Similarly, pain at night decreased from 3.6 ± 0.9 to 1.8 ± 0.7 for Naproxen and from 3.3 ± 0.8 to 1.6 ± 0.6 for Ibuprofen (Table 2).

Table 2: Symptoms Improvement of Various Variables in Each Group at Baseline Vs 7th-Day Follow-Up (n=310) Assessed by Visual Analogue Scale

Variables		Naproxen Sodiu (440/660 mg) n=155, Mean ± SD	Ibuprofen (1200 mg) n=155, Mean ± SD	p-Value
Pain at Rest	Baseline	3.2 ± 0.8	2.9 ± 0.7	0.004
	Follow up	1.5 ± 0.6	1.3 ± 0.5	
Pain on Passive Movement	Baseline	4.0 ± 0.9	3.8 ± 0.8	0.003
	Follow up	2.1 ± 0.7	2.0 ± 0.6	
Pain on Weight Bearing	Baseline	4.5 ± 1.0	4.2 ± 1.1	0.003
	Follow up	2.7 ± 0.8	2.5 ± 0.7	
Morning Stiffness	Baseline	3.8 ± 0.7	3.5 ± 0.6	<0.001
	Follow up	1.9 ± 0.5	1.7 ± 0.4	

DOI: https://doi.org/10.54393/pjhs.v6i8.2981

Pain During Day	Baseline	4.3 ± 0.6	4.0 ± 0.7	0.002
	Follow up	2.3 ± 0.6	2.1 ± 0.5	
Pain at Night	Baseline	3.6 ± 0.9	3.3 ± 0.8	<0.001
	Follow up	1.8 ± 0.7	1.6 ± 0.6	

Findings show the frequency and percentage of side effects associated with each treatment group. The most commonly reported side effects in both groups included nausea, dyspepsia, and headache. The Naproxen group had a slightly higher frequency of nausea (12 cases, 34.3%) compared to the Ibuprofen group (10 cases, 28.6%). Dyspepsia was reported by 15 participants (42.9%) in the Naproxen group and 13 (37.1%) in the Ibuprofen group. Headache affected 9 participants (25.7%) in the Naproxen group, slightly lower than the 12 cases (34.3%) in the Ibuprofen group. Additional side effects, such as vomiting, dizziness, and edema, were observed in both groups with relatively lower frequencies and percentages (Figure 1).

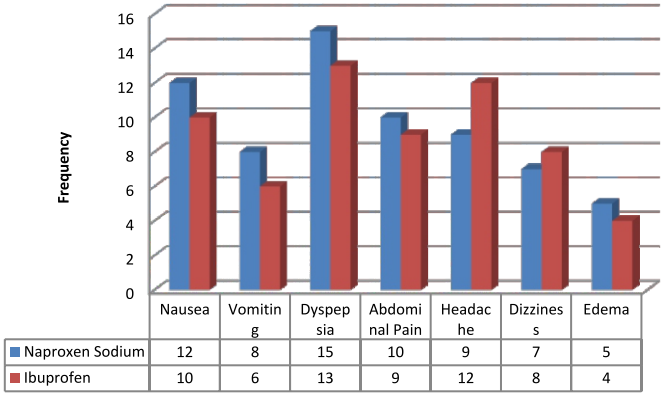

Figure 1: Side Effect Associated with Use of Naproxen Sodium Vs Ibuprofen(n=310)

DISCUSSIONS

The results of the study indicated that both naproxen and ibuprofen were effective in reducing pain in various situations. Both naproxen sodium and ibuprofen were effective in reducing pain at baseline to follow up at the 7th post-medication day in terms of pain at rest, on weight bearing, on passive movements, morning stiffness, pain during the day and at night. A significant difference was observed between the groups ($p<0.010$). Along with that, minimal side effects were reported with both drugs, all of which were tolerable. Similar reports have been reported in other studies as well, wherein the efficacy of various NSAIDs compared to each other and with other lines of treatment for OA, such as opioids and COX-2 inhibitors, was evaluated [19]. In a study on patients administered naproxen sodium and ibuprofen, both demonstrated substantial superior pain relief for mild to moderate knee OA in comparison to placebo [20]. Improvement in pain intensity after 7 days of continuous treatment in this study was observed in between 35-45 %, contrasting with 30 % OA pain improvement in general [21]. In another study, although ibuprofen was effective in alleviating pain in knee OA, some of the side effects were found to be significantly affected in patients [22]. In this regard, naproxen sodium was observed to be highly effective as well as tolerable in terms of side effects [23]. Likewise, results from daily evaluation of naproxen sodium and ibuprofen for reduction of pain-associated symptoms showed that for arthritic pain and control of pain, both ibuprofen and naproxen sodium were significantly beneficial in improving pain in comparison to placebo [24]. In terms of pain evaluation at night, naproxen was reported to show a greater tendency for improving pain, compared to ibuprofen, as evident by the lower pain on VAS by patients on naproxen when compared with ibuprofen [25]. The results were in line with the findings reported in this study. In this study as well, pain relief by naproxen sodium was reported to be for a longer duration than ibuprofen. The possible reason for this might be due to the longer half-life of naproxen sodium as compared to ibuprofen, thereby enabling sustained and optimal relief of pain [26]. The duration of action of naproxen sodium according to published data is long, ranging from 8 to 12 hours [27]. In comparison, the half-life of ibuprofen as reported in literature is around 4-6 hours. Therefore, the use of naproxen sodium for sustained and longer duration of pain relief might be vital in implications such as improving quality of life and day-to-day functioning in knee OA, as naproxen sodium is better than ibuprofen [28]. However, the overall pain relief between naproxen sodium and ibuprofen, as reported in studies, has been equal to each other more or less, with no statistically significant difference between each other. The study highlighted both pain measurements at various timings and situations with the use of naproxen sodium and ibuprofen, both at baseline and at 7th –days follow up along with any side effects observed during the period.

This study was limited by its short duration of follow-up (7 days), which restricts evaluation of long-term efficacy and delayed adverse effects. The single-center design may also limit the generalizability of findings to broader populations. Additionally, long-term gastrointestinal, renal, and cardiovascular safety outcomes were not assessed. Future multicenter randomized controlled trials with extended follow-up periods are recommended to evaluate long-term safety, comparative effectiveness, and impact on quality of life among elderly patients with knee osteoarthritis.

CONCLUSIONS

It was concluded that both ibuprofen and naproxen were effective in providing pain relief among elderly patients with knee osteoarthritis, with only minimal adverse effects observed for each drug.

DOI: https://doi.org/10.54393/pjhs.v6i8.2981

Authors' Contribution

Conceptualization: SM
Methodology: AK
Formal analysis: MAZ, NN
Writing and Drafting: AK, NN, KA, SI
Review and Editing: AK, NN, KA, SI, MAZ, SM

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Long H, Liu Q, Yin H, Wang K, Diao N, Zhang Y *et al.* Prevalence Trends of Site-Specific Osteoarthritis From 1990 To 2019: Findings from the Global Burden Of Disease Study 2019. Arthritis and Rheumatology. 2022 Jul; 74(7): 1172-83. doi: 10.1002/art.42089.

[2] Allen KD, Thoma LM, Golightly YM. Epidemiology of Osteoarthritis. Osteoarthritis and Cartilage. 2022 Feb; 30(2): 184-95. doi: 10.1016/j.joca.2021.04.020.

[3] Hana S, Aicha BT, Selim D, Ines M, Rawdha T. Clinical and Radiographic Features of Knee Osteoarthritis of Elderly Patients. Current Rheumatology Reviews. 2018 Aug; 14(2): 181-7. doi: 10.2174/1573397113666170425150133.

[4] Liu Q, Wang S, Lin J, Zhang Y. The Burden for Knee Osteoarthritis among Chinese Elderly: Estimates from A Nationally Representative Study. Osteoarthritis and Cartilage. 2018 Dec; 26(12): 1636-42. doi: 10.1016/j.joca.2018.07.019.

[5] Clynes MA, Jameson KA, Edwards MH, Cooper C, Dennison EM. Impact of Osteoarthritis on Activities of Daily Living: Does Joint Site Matter? Aging Clinical and Experimental Research. 2019 Aug; 31(8): 1049-56. doi: 10.1007/s40520-019-01163-0.

[6] Adnani H, Hikmawati AN, Sihapark S, Suharyanta D, Widiyaningsih D. Factors of Independent of Activities of Daily Living among Osteoarthritis Elderly. International Journal of Public Health. 2022 Mar; 11(1): 1-7. doi: 10.11591/ijphs.v11i1.21065.

[7] Bobić Lucić L and Grazio S. Impact of Balance Confidence on Daily Living Activities of Older People with Knee Osteoarthritis with Regard to Balance, Physical Function, Pain, and Quality of Life–A Preliminary Report. Clinical Gerontologist. 2018 Aug; 41(4): 357-65. doi: 10.1080/07317115.2018.1453907.

[8] Hermann W, Lambova S, Muller-Ladner U. Current Treatment Options for Osteoarthritis. Current Rheumatology Reviews. 2018 Aug; 14(2): 108-16. doi: 10.2174/1573397113666170829155149.

[9] Conaghan PG, Arden N, Avouac B, Migliore A, Rizzoli R. Safety of Paracetamol in Osteoarthritis: What Does the Literature Say? Drugs and Aging. 2019 Apr; 36(Suppl 1): 7-14. doi: 10.1007/s40266-019-00658-9.

[10] Magni A, Agostoni P, Bonezzi C, Massazza G, Menè P, Savarino V et al. Management of Osteoarthritis: Expert Opinion on NSAIDs. Pain and Therapy. 2021 Dec; 10(2): 783-808. doi: 10.1007/s40122-021-00260-1.

[11] Cooper C, Chapurlat R, Al-Daghri N, Herrero-Beaumont G, Bruyère O, Rannou F *et al.* Safety of Oral Non-Selective Non-Steroidal Anti-Inflammatory Drugs in Osteoarthritis: What Does the Literature Say? Drugs and Aging. 2019 Apr; 36(Suppl 1): 15-24. doi: 10.1007/s40266-019-00660-1.

[12] Schnitzer TJ. Update of ACR Guidelines for Osteoarthritis: Role of the Coxibs. Journal of Pain And Symptom Management. 2002 Apr; 23(4): S24-30. doi: 10.1016/S0885-3924(02)00372-X.

[13] Cioroianu GO, Florescu A, Simionescu CE, Sas TN, Tarniță DN, Rogoveanu OC. The Therapeutic Benefits of NSAIDs and Physical Therapy in Knee Osteoarthritis. Romanian Journal of Morphology and Embryology. 2024 Jun; 65(2): 217. doi: 10.47162/RJME.65.2.08.

[14] Han MH, Nam JH, Noh E, Lee EK. Gastrointestinal Risk of Non-Steroidal Anti-Inflammatory Drugs and Gastroprotective Agents Used in the Treatment of Osteoarthritis in Elderly Patients: A Nationwide Retrospective Cohort Study. International Journal of Clinical Pharmacology and Therapeutics. 2019 Nov; 57(11): 531. doi: 10.5414/CP203377.

[15] Ribeiro H, Rodrigues I, Napoleão L, Lira L, Marques D, Veríssimo M *et al.* Non-Steroidal Anti-Inflammatory Drugs (Nsaids), Pain and Aging: Adjusting Prescription to Patient Features. Biomedicine and Pharmacotherapy. 2022 Jun; 150: 112958. doi: 10.1016/j.biopha.2022.112958.

[16] Wang Y, Fan M, Wang H, You Y, Wei C, Liu M *et al.* Relative Safety and Efficacy of Topical and Oral NSAIDs in the Treatment of Osteoarthritis: A Systematic Review And Meta-Analysis. Medicine. 2022 Sep; 101(36): e30354. doi: 10.1097/MD.0000000000030354.

[17] Said MS, Hashmi AM, Hussain A, ur Rehman S, Mukhtiar M. Clinical Evaluation of Patients Suffering from Osteoarthritis Along with Prevalence, Pharmacological and Non-Pharmacological Treatment. International Journal of Natural Medicine and Health Sciences. 2022 Sep; 1(4). doi: 10.52461/

DOI: https://doi.org/10.54393/pjhs.v6i8.2981

ijnms.v1i4.934.

[18] Amir HQ, Jabeen Z, Khan S, Sultana S, Khan M, Tariq AB. Hematological and Anthropometric features of patients with Knee Osteoarthritis. Bangladesh Journal of Medical Science. 2022 May; 21(3): 682-7. doi: 10.3329/bjms.v21i3.59585.

[19] Couto A, Troullos E, Moon J, Paredes-Diaz A, An R. Analgesic Efficacy and Safety of Non-Prescription Doses of Naproxen Sodium in the Management of Moderate Osteoarthritis of the Knee or Hip. Current Medical Research and Opinion. 2018 Oct; 34(10): 1747-53. doi: 10.1080/03007995.2018.1437029.

[20] Kaufman DW, Kelly JP, Battista DR, Malone MK, Weinstein RB, Shiffman S. Exceeding the Daily Dosing Limit of Nonsteroidal Anti-Inflammatory Drugs among Ibuprofen Users. Pharmacoepidemiology and Drug Safety. 2018 Mar; 27(3): 322-31. doi: 10.1002/pds.4391.

[21] Shega JW, Tiedt AD, Grant K, Dale W. Pain Measurement in the National Social Life, Health, and Aging Project: Presence, Intensity, and Location. Journals of Gerontology Series B: Psychological Sciences and Social Sciences. 2014 Nov; 69(Suppl_2): S191-7. doi: 10.1093/geronb/gbu101.

[22] Varrassi G, Yeam CT, Rekatsina M, Pergolizzi JV, Zis P, Paladini A. The Expanding Role of the COX Inhibitor/Opioid Receptor Agonist Combination in the Management of Pain. Drugs. 2020 Sep; 80(14): 1443-53. doi: 10.1007/s40265-020-01369-x.

[23] Kyerematen K, Troullos E, Paredes-Diaz A. Safety of Naproxen Compared with Placebo, Ibuprofen and Acetaminophen: A Pooled Analysis of Eight Multiple-Dose, Short-Term, Randomized Controlled Studies. Current Medical Research and Opinion. 2019 Oct; 35(10): 1671-1676. doi: 10.1080/03007995.2019.1612338.

[24] Peloso PM, Moore RA, Chen WJ, Lin HY, Gates DF, Straus WL *et al.* Osteoarthritis Patients with Pain Improvement Are Highly Likely to Also Have Improved Quality of Life and Functioning. A Post Hoc Analysis of a Clinical Trial. Scandinavian Journal of Pain. 2016 Oct; 13(1): 175-81. doi: 10.1016/j.sjpain.2016.07.002.

[25] Varrassi G, Pergolizzi JV, Dowling P, Paladini A. Ibuprofen Safety at the Golden Anniversary: Are All NSAIDs the Same? A Narrative Review. Advances in Therapy. 2020 Jan; 37(1): 61-82. doi: 10.1007/s12325-019-01144-9.

[26] Hsueh MF, Bolognesi MP, Wellman SS, Kraus VB. Anti-Inflammatory Effects of Naproxen Sodium on Human Osteoarthritis Synovial Fluid Immune Cells. Osteoarthritis and Cartilage. 2020 May; 28(5): 639-45. doi: 10.1016/j.joca.2020.01.013.

[27] Nakata K, Hanai T, Take Y, Osada T, Tsuchiya T, Shima D et al. Disease-Modifying Effects of COX-2 Selective Inhibitors and Non-Selective NSAIDs in Osteoarthritis: A Systematic Review. Osteoarthritis and Cartilage. 2018 Oct; 26(10): 1263-73. doi: 10.1016/j.joca.2018.05.021.

[28] Maniar KH, Jones IA, Gopalakrishna R, Vangsness Jr CT. Lowering Side Effects of NSAID Usage in Osteoarthritis: Recent Attempts at Minimizing Dosage. Expert Opinion on Pharmacotherapy. 2018 Jan; 19(2): 93-102. doi: 10.1080/14656566.2017.1414802.