A Systematic Review on NSAIDs and Tanezumab efficacy in Chronic Lower Back Pain.

Smaran Kasireddy[1], Sweta Sahu[2], Lyluma Ishfaq[3], Berjis Rahmath[4], Navya Pillikunte Doddareddy[5], Mudit Moondra[6], Mihirkumar P. Parmar[7], Vishal Venugopal[8]

[1]University Hospital Leicester, Leicester, United Kingdom
[2]JJM Medical College, Davanagere, India
[3]Government medical college, Srinagar, Directorate of health services Kashmir Srinagar, J&k , India
[4]Osmania Medical College, Hyderabad, India
[5]Bangalore medical college and research Institute, Bangalore, India
[6]RNT medical College, Rajasthan, Udaipur, India
[7]Gujarat Medical Education and Research Society, Vadnagar, India
[8]Bhaarath Medical College and Hospital, Chennai, India

Abstract

Chronic back pain is a condition that impacts people of all ages and lasts longer than 12 weeks. 7.41% of all years lost to disability (YLD) are attributed to low back pain, which makes it the pathology responsible for the most YLD, surpassing other chronic conditions such as diabetes and depression. Despite the prevalence of drugs such as opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and biologics, the types of drugs administered to individuals differ greatly. We collected data from the PubMed database of the National Library of Medicine, PubMed Central, and Google Scholar. Randomized controlled trials (RCTs) that explicitly evaluate the efficacy of various NSAIDs in adult patients with chronic back pain were selected for this study. After an exhaustive search and examination of numerous publications, only 8 articles met the inclusion criteria. In recent studies that included NSAIDs, they were among the most frequently prescribed medications for the treatment of chronic low back pain. In comparison to placebo, selective COX-II inhibitors such as celecoxib and etoricoxib were found to be efficacious, while valdecoxib was associated with serious side effects. In addition to reducing back pain, COX-II inhibitors with a preference for COX-II, such as aceclofenac and diclofenac, were associated with gastrointestinal side effects. Despite the risk of joint degeneration and accelerated osteoarthritis, intravenous tanezumab may be superior to naproxen and placebo in treating chronic low back pain.

Keywords: Chronic back pain, NSAIDs (Nonsteroidal anti-inflammatory drugs), Efficacy, Tanezumab, COX-2 inhibitors, Treatment options.

Introduction

Lower back pain (LBP) is the primary cause of disability-adjusted life years globally, accounting for 7.41% of all YLD, which is greater than other chronic conditions like diabetes and depression [1]. At any given time, approximately 18% of the population experiences discomfort in the lower region of the back. LBP is one of the most burdensome pain conditions, affecting individuals of all ages due to its wide-ranging prevalence [2]. This burden is a result of its association with high utilization of healthcare resources, reduced function, and decreased work output [3]. When LBP lasts for more than three months, it is referred to as severe or chronic LBP, and this severity considerably elevates the burden when compared to LBP with a brief duration [4].

Chronicity in cases of lower back pain might be paved on by a variety of potential contributory agents, including periods of increased intensity of pain, a higher body mass index, carrying weighted objects at the workplace, awkward working posture, and depression. In addition to these inappropriate attitude practices, prevailing anxiety, smoking, operational restriction during the episode, and physical hard work were also significant predictors of chronicity [5].

***Correspondence:** Mihirkumar P. Parmar, Gujarat Medical Education and Research Society, Department of Internal Medicine, Vadnagar, India. E-mail: mmihir981@gmail.com

***Received:** 23-Nov-2023, Manuscript No. AAAGIM-23-119274; **Editor assigned:** 27- Nov -2023, PreQC No. AAAGIM-23-119274(PQ); **Reviewed:** 12-Dec-2023, QC No. AAAGIM-23-119274; Revised: 15- Dec -2023, Manuscript No. AAAGIM-23-119274(R); Published: 22- Dec-2023, DOI:10.35841/aaagim-7.6.203*

***Citation:** Kasireddy S., Sahu S., et al. A Systematic Review on NSAIDs and Tanezumab efficacy in Chronic Lower Back Pain. Arch Gen Intern Med. 2023;7(6):203*

Although there may be a wide range of causes for chronic back pain, we have chosen to concentrate on studies in which the patient population has no discernible pathology. A multidisciplinary approach is frequently used to treat CLBP. Among the pharmacological alternatives, muscle calming agents, nonsteroidal anti-inflammatory drugs (NSAIDs), and analgesics of opioid nature are the most frequently prescribed medications for lower back pain [6, 7]. A type of monoclonal antibody called tanezumab blocks nerve growth factor (NGF) and is used to treat chronic pain. Studies have shown that tanezumab is efficacious for individuals suffering from non-radicular chronic low back pain [8]. Each medication class has a unique balance of advantages and disadvantages, which complicates the selection of pharmacologic therapy for lower back pain. Moreover, the potential contributing agents and probable benefits of individual pharmaceuticals within a given medication class can vary. We believe it is necessary to quantify and standardize chronic pain treatment protocols in order to provide a more accurate road map, despite the notion that one size does not fit all patients. This study examines the comparative efficacy of nonsteroidal anti-inflammatory medications (NSAIDs) and Tanezumab in the therapeutic procedure for chronic lower back pain.

Methodology

We relied on the PubMed Central (PMC), Cochrane Library, National Library of Medicine (PubMed), and Google Scholar for collecting data through the use of the following medical subject headings (MeSH) terms with the keywords such as “chronic back pain" and “clinical trials" and “low back pain" and as well as various NSAIDs such as “diclofenac”, “aceclofenac”, “ibuprofen”, “paracetamol”, “etoricoxib”, “valdecoxib”. The total number of articles found in electronic databases was 7717. (Figure 1)

Search strategy

Databases like PubMed, PubMed Central, Cochrane Library were utilized and following keywords were utilized in the

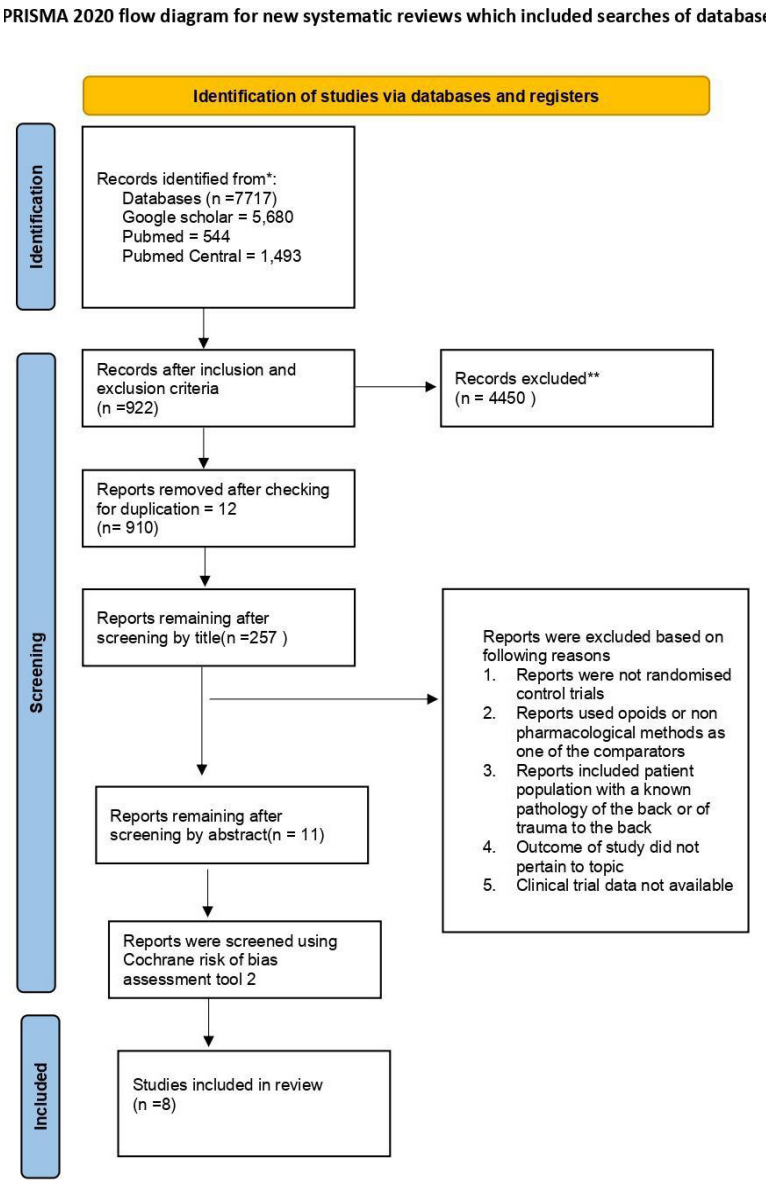

Figure 1. *PRISMA flowchart [9].*

search process of finding relevant articles. Various keywords were employed to explore the investigations for this study. Some keywords are "chronic back pain" OR "low back pain" "ibuprofen" OR "diclofenac" OR "paracetamol" OR "tanezumab" OR "paracetamol" OR "etoricoxib" OR "aceclofenac".

Study Selection

RCTs (Randomized Controlled Trials) that systematically contrast the effectiveness of various NSAIDs based on their chemical structure in patients suffering from chronic back pain. Participants were adult patients (18 years or older) with chronic back pain, which can be reported as a constant pain for at least 12 weeks. Interventions of NSAIDs based on their chemical structure, including cyclooxygenase (COX)-1 or COX-2 inhibitors. A comparison group consisting of either placebo, another NSAID, or Tanezumab were also considered. Studies included were the ones written in English or with English translation. Studies in other languages, absence of the report for utilization of NSAIDs for chronic back pain and with participants with back pain due to specific causes such as infections, tumors, or fractures were excluded. Some other exclusion criteria for studies were use of NSAIDs in combination with other analgesics or therapies, lack report of efficacy of different types of NSAIDs in chronic back pain, animal studies or in vitro studies, minimal sample sizes or short follow-up duration or without a control group or a comparator for comparison. Systematic reviews, meta-analyses, clinical reviews, case reports were not considered.

Main outcome variables

Pain relief and/or functional improvement measured by validated pain scales such as the Roland Morris Disability Questionnaire (RMDQ), Visual Analog Scale (VAS) and Oswestry Disability Index (ODI).

Results

Experimental and control groups were utilized by all the studies included in our documentation. The detailed display of results is written in Table 1. Cochrane Risk of bias assessment was utilized which predicted the results mentioned in Table 2. and Figure 2.

Table 1. *Characteristics of studies included.*

Citation	Year of publication	Focus of Study	Findings
Bedalwi MK et al. [10]	2016	Comparison of celecoxib 200mg twice daily compared to acetaminophen 500mg twice daily	The total back discomfort 33.3% compared 9.1%; ODI 34.8% compared nighttime back pain 41.7% versus 9.1%; (p0.01 for all). According to Guyatt's Responsiveness Index, both ODI, total backache BASDAI, and nocturnal back pain all had receptivity to celecoxib values of 1.62, 1.28, 1.27, and 0.58, correspondingly.
Birbara CA et al.[11]	2003	Comparison of etoricoxib 60mg OD to placebo for control of back pain measured using Visual Analogue Scale.	When compared to the placebo group, etoricoxib significantly reduced the amount of pain experienced after a period of four weeks (12.9mm and 10.3mm for dosages of 60 mg and 90 mg, respectively; p0.01 for each). 12 weeks 10.5mm and 7.5mm for 60mg and 90mg dosages, respectively, with p=0.01 and 0.018.
Coats TL et al. [12]	2004	Valdecoxib 40mg/day versus placebo tablets once daily for four weeks.	Improvements in mean Roland- Morris Disability Questionnaire score with valdecoxib were significantly greater than with placebo at each assessment (p< or =0.03). Although the overall incidence of adverse events (AE) was significantly higher among patients receiving placebo (35.1% vs 24.1% respectively p=0.042) no significant differences were found between groups for the incidence of any individual AE.
Kivitz AJ et al. [13]	2013	Naproxen (500mg twice daily), or placebo vs IV tanezumab 20mg. RMDQ, NRS and LBPI were used to measure efficacy.	Tanezumab 10 and 20 mg substantially raised PGA, LBPI, and Roland Morris Disability Questionnaire scores compared to placebo and naproxen (p 0.05) and exhibited comparable effectiveness profiles.
			Tanezumab 5mg improved PGA ratings compared to placebo (P =.05), while naproxen significantly improved LBPI compared to placebo.
Pallay RM et al. [14]	2009	Etoricoxib 60 mg (n=109), 90 mg (n=106) compared to placebo. Efficacy was measured using RMDQ	Significantly lower LBP intensity was seen in both etoricoxib groups at 4 weeks compared to placebo [-15.15 mm as well as -13.03 mm for 60 and 90 mg, respectively, probability (p) 0.001 for each], and these effects persisted for 3 months. RMDQ ratings significantly improved after treatment as opposed to placebo (etoricoxib 60 mg, -2.82, and 90 mg, -2.38, p0.001 for each).
Taguchi T et al. [15]	2004	Eligible patients were randomized to receive diclofenac sodium patch 75 mg or 150 mg and compared to placebo. Efficacy was measured using visual analogue scale.	Following a period of two weeks of therapy, the initial evaluation of the elementary endpoint revealed that every one of the diclofenac sodium patch's quantities (150 mg and 75 mg) had been more effective to placebo in terms of overall improvement from baseline in the mean 3-day VAS score; the average variance among the active and placebo procedures in this measure was -5.67 [95% confidence interval (CI) -9.34 to -2.00] mm in the 150 mg group and -5.68 (95% CI -9.34 to -2.01 in group of 75mg).
Yang JH et al. [16]	2017	Comparision between aceclofenac CR (200 mg once daily) versus conventional twice daily dose aceclofenac of 100 mg	Aceclofenac CR and aceclofenac both significantly reduced VAS (p=0.028). In both of the groups, the EQ-5D score improved considerably (p=0.037). Both groups' ODI scores had a substantial decline (p=0.012).Comparing pre- and post-treatment, there were no noticeable variations among aceclofenac CR and aceclofenac. When compared to aceclofenac, individuals on aceclofenac CR experienced significantly more indigestion, heartburn, and unfavorable gastrointestinal effects.
Zerbini C et al. [17]	2005	Comparision of etoricoxib 60 mg once daily over 4 weeks compared to high-dose diclofenac 150 mg daily. Efficacy endpoints included: changes in Roland and Morris Disability Questionnaire (RMDQ), Patient Global Assessment of Response to Therapy (PGART) and Low Back Pain Bothersomeness Scale (LBP-BS) scores	Etoricoxib showed considerable effectiveness with a least-squares mean time-weighted decrease from initial LBP-IS score over 4 weeks of -32.94 mm (95% CI -36.25, -29.63). The initial outcome's treatment difference was 2.51 mm (95% CI -1.50, 6.51), which met the predetermined comparability condition of a 95% confidence interval that was entirely within +/- 10 mm.

Table 2. *Bias Assessment of research studies via Cochrane Risk Assessment Tool.*

Study	Randomization Process	Deviation from Intervention	Missing outcome data	Measurement of Outcome	Selection of Reported Result	Overall Bias Risk
	D1	D2	D3	D4	D5	Results
Bedalwi MK et al. 2016	Low	Low	Low	Low	Low	Low risk
Birbara CA et al. 2003	Low	Low	Low	Low	Low	Low risk
Coats TL et al.2004	Low	Low	Low	Low	Some Concerns	Some Concerns
Kivitz AJ et al. 2013	Low	Low	Low	Low	Low	Low risk
Pallay RM et al. 2009	Low	Low	Low	Low	Low	Low risk
Taguchi T, et al. 2004	Low	Low	Low	Low	Low	Low risk
Yang JH et al. 2017	Low	Low	Low	Some Concerns	Some Concerns	Some Concerns
Zerbini C et al. 2005	Low	Low	Low	Low	Some Concerns	Some Concerns

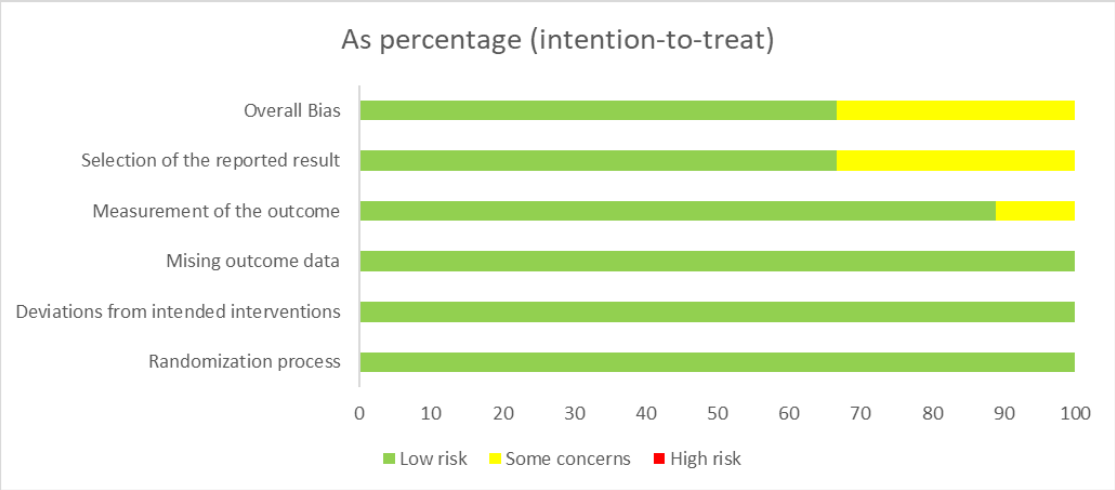

Figure 2. *Cochrane Bias Assessment.*

Discussion

After a thorough search and inspection of the various articles, only nine met the inclusion requirements. Three of these studies assessed the efficacy of etoricoxib, with two comparing it to a placebo and one comparing it to diclofenac. Both studies comparing etoricoxib to a placebo for four weeks revealed statistically significant variations when using the Visual Analog Scale (p 0.001) and the RMDQ (p 0.001). At 4 and 12 weeks, there was a great amount of decrease observed in the symptoms of back discomfort relative to the baseline. According to Zerbini C et al., etoricoxib is as effective as high-dose diclofenac for the treatment of ailment in adult patients with CLBP, with a treatment comparison for the baseline outcome of 2.51 mm (95% confidence interval: -1.50 to 6.50). Comparable adverse effects differences existed among the two groups. The studies indicate that etoricoxib is efficacious in decreasing the intensity of back pain, with significant improvement over placebo at both concentrations tested. It is important to note, however, that the investigation was conducted over a relatively short time duration (12 weeks) and may not provide information about the long-term safety and effectiveness of etoricoxib [17].

In one of the included trials, the COX-2 inhibitor Celecoxib was significantly efficacious than paracetamol in treating persistent nonspecific low back pain (ODI 34.8% vs. 4.5%, nocturnal back pain of lumbar region 41.7% vs. 9.1%, and total back pain 33.3% vs. 9.1%; P = 0.01 for all). Inflammatory lesions of the spine and sacroiliac joints, which commonly accompany nonspecific low back pain, were not crucially different between the two groups [10]. Targeting Nerve Growth Factor (NGF), the human monoclonal antibody tanezumab substantially improved PGA, LBPI, and Roland Morris Disability Questionnaire scores when compared to naproxen and a placebo (p 0.05) [8].

Significantly, tanezumab has been associated with joint degeneration and increased osteoarthritis in a particular group of patients. Therefore, the use of tanezumab should be carefully considered, and patients should be monitored for any adverse effects that may occur. This study indicates that intravenous tanezumab may be a promising option for the therapeutic management of chronic low back pain, with greater efficacy than both naproxen and placebo.

In the study conducted by Taguchi T. et al. (2004), the pain-relieving efficacy of the diclofenac sodium patch at two distinct doses (150mg and 75 mg) was compared to placebo using the visual analogue scale (VAS). The two portions of the diclofenac sodium patch were significantly more productive than placebo at reducing pain, with an observed difference of means as -5.67 mm (95% confidence interval [CI]: -9.34 to -2.00) mm in the 150 mg group and -5.68 mm (95% CI: -9.34 to 2.01) mm in the 75 mg group [15].

In the study conducted by Yang JH et al., participants with pain received either a standard twice-daily dose of traditional aceclofenac (100 mg) or a one dose of controlled functional

dosage of formulated aceclofenac (200 mg). Significantly decreased VAS scores, increased EQ-5D scores, and decreased Oswestry Disability Index (ODI) scores indicated that both formulations were effective at reducing pain. However, there were no significant distinctions in the effectiveness of the two formulations. Patients taking aceclofenac CR experienced more gastrointestinal adverse effects, especially heartburn and indigestion, compared to those taking aceclofenac in its regular form. This may be because the CR formulation contains more aceclofenac per dose, resulting in a faster and longer absorption in the stomach. This study indicates that aceclofenac CR and aceclofenac are equally effective at treating musculoskeletal pain; however, the CR formulation may be more likely to induce gastrointestinal adverse effects. When establishing a treatment plan for a patient, clinicians should consider this aspect of the equation [16].

In contrast to placebo tablets, Coats et al. examined the effectiveness and safety of the chosen COX-2 inhibitor valdecoxib in the treatment of chronic lumbar region ailment. Valdecoxib significantly outperformed placebo at each evaluation in terms of increasing the mean RMDQ score (all P 0.001), according to the study results. This study suggests valdecoxib may be an effective therapy for chronic low back pain. However, the study also revealed that valdecoxib recipients experienced substantially more adverse events than placebo recipients (35.1% and 24.0%, respectively; p=0.042). Given that COX-2 medications have been associated with an increased risk of cardiovascular events such as cardiovascular stroke and myocardial infarction. This conclusion was not unexpected. Importantly, the study found no statistically valuable variations in the incidence of adverse events among the two groups (p=0.042) [12].

We have described in our paper the efficacy of various NSAIDs and compared it to Tanezumab which is a new and viable alternative in the treatment of persistent debilitating lumbar region pain. We believe our paper can influence the change in the types of medications that are routinely prescribed by primary care physicians and can make an impact in better drug choices. While we have not compared the efficacy to opioids, we believe this could be a new avenue for research for future papers and that more work needs to be done on deciding what medications can be prescribed to this population. Selective COX -2 inhibitors and Tanezumab could provide a way forward for these patients suffering from debilitating back pain and hence could be preferred over the usual alternatives of diclofenac and aceclofenac and should be considered as serious alternatives.

Conclusion

We have described in our paper the efficacy of various NSAIDs and compared it to Tanezumab which is a new and viable alternative in the treatment of chronic debilitating back pain. We believe our paper can influence the change in the types of medications that are routinely prescribed by primary care physicians and can make an impact in better drug choices. While we have not compared the efficacy to opioids, we believe this could be a new avenue for research for future papers and that more work needs to be done on deciding what medications can be prescribed to this population. Selective COX -2 inhibitors and Tanezumab could provide a way forward for these patients suffering from debilitating back pain and hence could be preferred over the usual alternatives of diclofenac and aceclofenac and should be considered as serious alternatives.

References

1. Hoy D, Brooks P, Blyth F, et al. The epidemiology of low back pain. Best Pract Res Clin Rheumatol. 2010;24(6):769-81.
2. Andersson GB. Epidemiological features of chronic low-back pain. Lancet. 1999;354(9178):581-5.
3. Stewart WF, Ricci JA, Chee E, et al. Lost productive time and cost due to common pain conditions in the US workforce. Jama. 2003;290(18):2443-54.
4. Becker A, Held H, Redaelli M, et al. Low back pain in primary care: costs of care and prediction of future health care utilization. Spine. 2010;35(18):1714-20.
5. Nieminen LK, Pyysalo LM, Kankaanpää MJ. Prognostic factors for pain chronicity in low back pain: A systematic review. Pain Rep. 2021;6(1).
6. Luo X, Pietrobon R, Curtis LH, et al. Prescription of nonsteroidal anti-inflammatory drugs and muscle relaxants for back pain in the United States. Spine. 2004;29(23):531-7.
7. Luo X, Pietrobon R, Hey L. Patterns and trends in opioid use among individuals with back pain in the United States. Spine. 2004;29(8):884-90.
8. Katz N, Borenstein DG, Birbara C, et al. Efficacy and safety of tanezumab in the treatment of chronic low back pain. Pain. 2011;152(10):2248-58.
9. Sterne JA, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ. 2019;366.
10. Bedaiwi MK, Sari I, Wallis D, et al. Clinical efficacy of celecoxib compared to acetaminophen in chronic nonspecific low back pain: results of a randomized controlled trial. Arthritis Care Res. 2016;68(6):845-52.
11. Birbara CA, Puopolo AD, Munoz DR, et al. Treatment of chronic low back pain with etoricoxib, a new cyclo-oxygenase-2 selective inhibitor: improvement in pain and disability—a randomized, placebo-controlled, 3-month trial. J Pain. 2003;4(6):307-15.
12. Coats TL, Borenstein DG, Nangia NK, et al. Effects of valdecoxib in the treatment of chronic low back pain: results of a randomized, placebo-controlled trial. Clin Ther. 2004;26(8):1249-60.
13. Kivitz AJ, Gimbel JS, Bramson C, et al. Efficacy and safety of tanezumab versus naproxen in the treatment of chronic low back pain. Pain. 2013;154(7):1009-21.

Citation: *Kasireddy S., Sahu S., et al. A Systematic Review on NSAIDs and Tanezumab efficacy in Chronic Lower Back Pain. Arch Gen Intern Med. 2023;7(6):203*

14. Pallay RM, Seger W, Adler JL, et al. Etoricoxib reduced pain and disability and improved quality of life in patients with chronic low back pain: a 3 month, randomized, controlled trial. Scand. J. Rheumatol. 2004;33(4):257-66.

15. Taguchi T, Yamaguchi S, Terahara T, et al. Systemically Acting Diclofenac Sodium Patch for Control of Low Back Pain: A Randomized, Double-Blind, Placebo-Controlled Study in Japan. Pain Ther. 2023;12(2):529-42.

16. Yang JH, Suk KS, Lee BH, et al. Efficacy and safety of different aceclofenac treatments for chronic lower back pain: prospective, randomized, single center, open-label clinical trials. Yonsei Med J. 2017;58(3):637-43.

17. Zerbini C, Ozturk ZE, Grifka J, et al. Efficacy of etoricoxib 60 mg/day and diclofenac 150 mg/day in reduction of pain and disability in patients with chronic low back pain: results of a 4-week, multinational, randomized, double-blind study. Curr Med Res Opin. 2005;21(12):2037-49.

Citation: *Kasireddy S., Sahu S., et al. A Systematic Review on NSAIDs and Tanezumab efficacy in Chronic Lower Back Pain. Arch Gen Intern Med. 2023;7(6):203*