مجلهٔ علوم طبّی غالب

MJ

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OPEN ACCESS

پوهنتون غالب

ISSN
E: 3006-094X

دورهٔ اول، شمارهٔ دوم، خزان و زمستان ۱۴۰۳، صص ۱۵ – ۲۳

بررسی مؤثریت دیکلوفناک در کنترل درد و التهاب بعد از جراحی مولر سوم: یک مرور سیستماتیک

رحمت الله نظری[۱]، هدایت الله احسان[۱،۲*] و اسدالله دانشیار[۳]

۱. دیپارتمنت کلینیکی ستوماتولوژی، پوهنځی ستوماتولوژی، پوهنتون چراغ، کابل، افغانستان.
۲. مرکز تحقیقات علوم طبی، پوهنتون غالبِ کابل، کابل، افغانستان.
۳. دیپارتمنت کلینیکی ستوماتولوژی، پوهنځی ستوماتولوژی، پوهنتون طبی کابل، کابل، افغانستان.

اطلاعات مقاله

نوع مقاله: مروری

تاریخ دریافت: ۲۱/ ۰۸/ ۱۴۰۳

تاریخ پذیرش: ۰۱/ ۱۰/ ۱۴۰۳

تاریخ نشر: ۱۰/ ۱۰/ ۱۴۰۳

***شناخت‌نامهٔ نویسندهٔ مسؤول:**

هدایت الله احسان.

مرکز تحقیقات علوم طبی، پوهنتون غالبِ کابل، کابل، افغانستان.

hedayatullah.ehsan@ghalib.edu.af

کُد اختصاصی مقاله/ DOI:

https://doi.org/10.58342/ghalibMj.V.1.I.2.3

چکیده

زمینه و هدف: در جراحی‌های دهانی، درد و التهاب اغلب با استفاده از داروهای ضد التهاب غیر استروئیدی (NSAIDs) کنترل می‌شود. ترکیب آنالژزیک‌های اپیوئیدی با NSAIDs می‌تواند روند کنترل درد را در جراحی‌های تهاجمی، به‌ویژه جراحی‌های مولر سوم، تقویت کند. هدف این مطالعه بررسی مؤثریت دیکلوفناک در کنترل درد و التهاب (از جمله میزان باز شدن دهان) بعد از جراحی مولر سوم و مقایسه آن با سایر داروهای آنالژزیک است.

روش: این مطالعه به‌صورت یک مرور سیستماتیک انجام شده است. منابع تحقیقی شامل GoogleScholar و PubMed بوده و مقالات بررسی شده از سال ۲۰۰۰ به بعد منتشر شده‌اند. تأثیر دیکلوفناک در کنترل درد بعد از جراحی مولر سوم به روش Clinical Randomized Trialارزیابی شده است.

یافته‌ها: پنج مقاله که معیارهای ورود و خروج مطالعه را داشتند، شامل مشارکت کنندگان در گروه‌هایی که دیکلوفناک دریافت کرده بودند و گروه‌هایی که سایر داروهای آنالژزیک را مصرف کرده بودند، مورد بررسی قرار گرفتند. نتایج نشان داد که میانگین شدت درد در ساعت ششم و دوازدهم بعد از جراحی در گروه دریافت‌کننده دیکلوفناک، به ترتیب ۲,۶۳ و ۲,۳۵ بر اساس مقیاس VAS (Visual Analog Scale)بود. این در حالی بود که بیمارانی که داروهای دیگر دریافت کرده بودند، در همان ساعات درد بیشتری را تجربه کردند. همچنین، میانگین میزان باز شدن دهان در روز دوم و هفتم بعد از جراحی در گروه دریافت‌کننده دیکلوفناک به ترتیب ۲۹ و ۲۹,۸۲ میلی‌متر بود، در حالی که میانگین میزان باز شدن دهان قبل از جراحی ۴۳ میلی‌متر بود. بیماران گروه دیکلوفناک نسبت به گروه دریافت‌کننده داروهای دیگر کمی کاهش در باز شدن دهان داشتند.

نتیجه‌گیری: دیکلوفناک تأثیر آنالژزیک کمتری نسبت به دگزامتازون، کترولاک، اتوریکوکسیب و ترکیب کدئین با دیکلوفناک در کنترل درد بعد از جراحی مولر سوم داشت. با این حال، اثر آن در کنترل درد نسبت به ترامادول بیشتر بود. همچنین، تأثیر دیکلوفناک بر میزان باز شدن دهان بعد از جراحی نسبت به اتوریکوکسیب و ترکیب دیکلوفناک با کدئین کمتر بود.

واژه‌گانِ کلیدی: دیکلوفناک، جراحی مولر سوم، درد، التهاب، داروهای ضد التهاب غیر استروئیدی، بررسی سیستماتیک

ارجاع به این مقاله: نظری ر، احسان ه، دانشیار ا. بررسی مؤثریت دیکلوفناک در کنترل درد و التهاب بعد از جراحی مولر سوم: یک مرور سیستماتیک. مجلهٔ علوم طبی غالب. [اینترنت]. ۳۱ دسامبر ۲۰۲٤. [تاریخ برداشت]؛ ۱(۲): ۱۵-۲۳. DOI: 10.58342/ghalibMj.V.1.I.2.3

GHALIB MEDICAL JOURNAL

GHALIB UNIVERSITY

MJ

https://mj.ghalib.edu.af/index.php/mj

OPEN ACCESS

Vol.1, Issue. 2, Autumn and Winter 2024, pp. 15 - 23

ISSN
E. 3006-094X

Efficacy of Diclofenac in Pain and Inflammation Control Following Third Molar Surgery: A Systematic Review

Rahmatullah Nazari[1], Hedayatullah Ehsan[1,2*], Asadullah Danishyar[3]

1. Stomatology Faculty, Cheragh Medical Institute, Kabul, Afghanistan.
2. Clinical Stomatology Department, Medical Sciences Research Center, Ghalib University (Kabul), Kabul, Afghanistan.
3. Stomatology Faculty, Kabul Medical University, Kabul, Afghanistan.

Article Information

Type: Review

Received: 11/ 11/ 2024
Accepted: 21/ 12/ 2024
Published: 31/ 12/ 2024

***Present address and corresponding author:**
Khushal Khan Mina, Kabul, Afghanistan
Hedayatullah Ehsan
Medical Sciences Research Department,
Ghalib University

hedayatullah.ehsan@ghalib.edu.af
hedayatullahehsan@gmail.com

DOI:
https://doi.org/10.58342/ghalibMj.V.1.I.2.3

Abstract

Background: Pain and inflammation following oral surgeries are typically managed with nonsteroidal anti-inflammatory drugs (NSAIDs). The combination of opioid analgesics with NSAIDs has been shown to enhance pain management, particularly in invasive oral surgeries such as third molar extractions. This systematic review evaluates the effectiveness of diclofenac in controlling pain and inflammation after third molar surgery and compares its efficacy with other analgesic treatments. A search of Google Scholar and PubMed databases identified relevant randomized clinical trials published since 2000.

Materials and Methods: This study is a systematic review of randomized clinical trials examining the effects of diclofenac on pain control after third molar surgery. Research articles published from 2000 onwards were sourced from Google Scholar and PubMed. The review focuses on clinical trials that assessed pain levels, mouth opening, and inflammation control in patients receiving diclofenac following third molar extraction.

Results: Analysis of four studies that met the inclusion and exclusion criteria revealed that the average pain intensity at the sixth and twelfth hours post-surgery in the diclofenac group, as measured by the Visual Analog Scale (VAS), were 2.63 and 2.35, respectively. These patients experienced higher pain levels compared to the group receiving alternative analgesics (other than diclofenac) during the same time periods. Additionally, the average mouth opening in the diclofenac group was 29 mm and 29.82 mm on the second and seventh days after surgery, respectively, compared to a preoperative average of 43 mm. Although there was some reduction in mouth opening in the diclofenac group, it was slightly lower compared to the second group, which received other analgesic medications.

Conclusion: Diclofenac demonstrated a relatively weaker analgesic effect compared to dexamethasone, ketorolac, etoricoxib, and the combination of codeine with diclofenac in managing pain following third molar surgery. However, diclofenac's analgesic efficacy was superior to tramadol. Furthermore, while diclofenac did show some effect on reducing mouth opening post-surgery, its impact was less significant compared to etoricoxib and the combination of diclofenac with codeine.

Keywords: Diclofenac, Third Molar Surgery, Pain, Inflammation, Non-Steroidal Anti-Inflammatory Drugs, Systematic Review

To cite this article: Nazari R, Ehsan H, Danishyar A. Efficacy of Diclofenac in Pain and Inflammation Control Following Third Molar Surgery: A Systematic Review. Ghalib Medical Journal. [Internet]. December 31, 2024. [taking date]; 1(2): 15-23: DOI: 10.58342/ghalibMj.V.1.I.2.3

1. Introduction

Pain is a broad term that refers to an unpleasant sensation resulting from stimulation of the nervous system. It can be classified as either acute, which begins suddenly and lasts for a short duration, or chronic, which persists either continuously or intermittently for months or even years. Pain is a common symptom associated with many illnesses and is among the most frequent reasons for seeking medical attention. It is typically experienced in relation to potential or actual tissue damage or occurs as a result of such damage. This revised version ensures clarity, proper grammar, and professional tone suitable for scientific or academic writing. Let me know if you need further refinement [1].

Acute pain emerges suddenly and is typically associated with injuries (surgical or traumatic), acute illnesses, or inflammation. It accounts for approximately 33% of visits to healthcare providers. In contrast, chronic pain is characterized by its persistence or recurrence for at least three months, with its prevalence increasing progressively with age. The psychological impacts of these two types of pain also differ. Acute pain often induces anxiety as it signals immediate harm or injury. Chronic pain, however, is more likely to result in depression due to its prolonged and debilitating nature. Gender differences in pain tolerance and coping mechanisms have also been observed. Men generally exhibit greater tolerance for acute pain, while women tend to manage chronic pain more effectively, possibly due to differences in biological, hormonal, and psychological factors [2].

Pain associated with third molar surgery arises from distinct physiological mechanisms. The third molar, commonly referred to as the wisdom tooth, is the last tooth to erupt and undergoes the most significant anatomical changes during its development. These factors contribute to the complexity of its removal and the intensity of postoperative discomfort [3].

Third molars, commonly known as wisdom teeth, are often extracted for various medical and preventive reasons. These include infections, cellulitis, abscesses, non-treatable periapical lesions, and extensive caries, especially when the tooth is impacted or affects adjacent teeth. Other indications involve unexplained pain, prevention of temporomandibular joint (TMJ) disorders and muscle issues, and pericoronitis, which is inflammation of the soft tissue around a partially erupted tooth. Extraction may also be necessary for cases with deep periodontal pockets, pre-orthodontic treatments to prevent lower dental arch crowding, or to avoid root resorption and caries progression in adjacent teeth. Additionally, third molars are removed to treat associated cysts, tumors, or abscesses, prevent pathological fractures, and facilitate prosthetic work by eliminating potential sources of irritation or sores under dentures. This proactive approach ensures better oral health and minimizes future complications [4].

Another type of pain is nociceptive pain, which occurs due to tissue damage, as seen in cases of cuts, burns, or bruises. In contrast, neuropathic pain results from nerve damage. For instance, pain caused by the compression of a nerve, such as that resulting from a displaced knee joint, is an example of neuropathic pain[5].

The minimum level of pain that a person can detect is referred to as the pain threshold, while the maximum level of pain that a person is willing to tolerate is known as pain tolerance. The most common method for measuring the pain threshold is through thermal stimulation, with a typical threshold around 44 degrees Celsius. While the pain threshold tends to be consistent across individuals, pain tolerance can vary significantly between people [1].

Pain is detected by nerve endings, which are specialized and diverse throughout the body. These nerve endings, known as nociceptors, are not microscopic but rather free nerve endings that vary in their responses to different stimuli. For example, visual receptors in the eyes detect light, auditory receptors in the inner ear respond to sound vibrations, olfactory receptors in the nose sense odors, and taste receptors on the tongue are sensitive to various flavors, each specialized for its specific stimulus [5].

Nociceptors are classified into two main groups: somatic nociceptors and visceral nociceptors. Somatic nociceptors are further divided into two types: superficial nociceptors, which are located on the surface of the skin, and deep nociceptors, found in muscles, joints, and connective tissues. Visceral nociceptors are present in internal organs, with different mechanisms for activation. In hollow organs like the colon and stomach, pain receptors are triggered by distension, while in solid organs, they are activated by pressure. Nociceptors respond primarily to stimuli that cause or threaten tissue damage, meaning stimuli that don’t cause damage do not activate them. Additionally, the conduction speed of impulses in nociceptors is slower (30-50 meters per second) compared to other types of receptors (30-120 meters per second) [6].

Nociceptors are activated by three main types of stimuli: chemical, thermal, and mechanical. Chemical stimuli involve substances that move from inside to outside the cells, triggering pain receptors. These substances include prostaglandins (such as PGD2, PGE1, and PGE2), thromboxanes, leukotrienes, serotonin,

bradykinin, and histamine. Thermal stimuli activate pain receptors directly, while mechanical stimuli, such as pressure and deformation, stimulate nociceptors [5].

In response to nociceptor stimulation, pain signals are transmitted to the spinal cord via Aδ and C nerve fibers. These nerve fibers, responsible for carrying pain impulses, consist of two types: A fibers (large fibers) and C fibers (small fibers). A fibers, which come in different subtypes, play a key role in the modulation of pain [7].

Aβ (A Beta) fibers are the thickest and longest nerve fibers, distinguished by their thick myelin sheath. Thanks to the presence of nodes of Ranvier and the myelin, these fibers transmit nerve impulses at the fastest speeds. They are primarily responsible for sensations of touch, vibration, and pressure, and are involved in the mechanism of Transcutaneous Electrical Nerve Stimulation (TENS). While Aβ fibers do not transmit pain signals, they play a crucial role in pain relief. The transmission speed of nerve impulses in these fibers ranges from 30 to 70 meters per second [8].

Aδ (Delta A) fibers are also myelinated, but to a lesser degree than Aβ fibers. These fibers are smaller and shorter, with a slower transmission speed (12-30 meters per second) compared to Aβ fibers. They transmit pain and temperature signals, making up 25% of nociceptors. Stimulation of Aδ fibers leads to sharp, localized, and sudden pain sensations, which are commonly utilized in acupuncture [8].

C fibers are the thinnest and shortest nerve fibers. Because they lack myelin, their nerve impulse transmission is the slowest, ranging from 0.5 to 2 meters per second. These fibers make up 75% of nociceptors and, like Aδ fibers, are responsible for transmitting pain signals. Stimulation of C fibers leads to diffuse, continuous, persistent, vague, slow, and burning pain sensations [8].

Aδ and C fibers enter the dorsal horn of the gray matter in the spinal cord through the dorsal root. Upon reaching the dorsal horn, they synapse with second-order neurons, which then transmit the information to higher centers in the brain. This synapse involves neurotransmitter mediators, and opioids inhibit further nerve signal transmission by releasing inhibitory neurotransmitters at the synaptic junction [9].

In fact, the modulation of nerve signals occurs at this site. In 1965, two scientists, Melzack and Wall, introduced the Gate Control Theory. They explained that in the dorsal horn of the spinal cord, there is a region known as the substantia gelatinosa, which contains a control gate system involving transmission cells (T cells). When C and Aδ fibers are stimulated, pain messages enter the substantia gelatinosa. This stimulation opens the gate, allowing nerve signals to reach higher brain centers. The more intense the painful stimuli, the more the gate opens. Conversely, certain factors can inhibit the gate, causing it to close [10].

Pain messages originating from the periphery travel to the spinal cord and then to the brain. In response, the brain sends inhibitory messages back to the spinal cord. These messages, mediated by neurotransmitters such as adrenergic substances, gamma-aminobutyric acid (GABA), serotonin, and beta-endorphins, act to close the gate. This reduces the transmission of pain signals from the periphery to the brain, lowering the patient's perception of pain. Additionally, beta-endorphins, endogenous hormones located around the pituitary gland, are released during electrical stimulation. These hormones contribute to gate closure and pain relief [11].

Aδ fibers ascend through the spinal thalamic pathway to the thalamus, where the sensation of pain is initially registered. After synapsing, these fibers continue to the sensory cortex of the brain, where the pain's intensity and nature are evaluated. Factors such as the intensity of stimulation, anxiety, tissue damage, confusion, and distraction can influence pain perception. On the other hand, C fibers ascend via the reticular-spinal pathway to the reticular formation. After synapsing there, they proceed to the thalamus and, subsequently, to the sensory cortex, following a similar route to that of Aδ fibers [10].

The pathway of pain fibers to the sensory cortex of the brain concludes with the brain responding to pain signals by activating descending inhibitory systems. These systems work to close the pain gates and alleviate pain. This process triggers various physiological responses, including sympathetic stimulation, which manifests as increased heart rate and blood pressure, pupil dilation, muscle contraction, rapid breathing, sweating, and pallor. Additionally, parasympathetic responses such as nausea, vomiting, weakness, lethargy, reduced mental alertness, lower heart rate, and decreased blood pressure may occur. Behavioral reactions are also common in response to pain [10].

The gray periaqueductal matter (PAG) plays a crucial role in pain modulation. It contains enkephalins and beta-endorphins, which, when electrically stimulated, can reduce pain. Furthermore, stimulation of the Magnus Raphe nucleus in the brainstem can inhibit pain signals at the spinal cord gate. The administration of morphine into the PAG activates descending pathways, which suppress the transmission of primary pain signals in the dorsal horn of the spinal cord, providing significant pain relief [11].

Pain associated with third molar surgery is influenced by similar mechanisms. These teeth, known for their extensive anatomical changes and being the last to erupt, present unique challenges during extraction. This complexity contributes to the discomfort experienced post-surgery [3].

From an anatomical perspective, 17% of lower third molars have a single root, 77% have two roots, 5% have three roots, and 1% have four roots. For upper third molars, the distribution is slightly different: 15% have one root, 32% have two roots, 45% have three roots, and 7% have four roots. Additionally, the root anatomy of these teeth ranges from straight to C-shaped configurations, further highlighting their variability [12].

The pathway of pain fibers to the sensory cortex of the brain culminates in the brain's response, which activates descending inhibitory systems. These systems work to close pain gates, thereby reducing the sensation of pain. This reaction triggers several physiological changes. Sympathetic responses include an increase in heart rate and blood pressure, pupil dilation, muscle contractions, rapid breathing, sweating, and pallor. Conversely, parasympathetic responses such as nausea, vomiting, fatigue, lethargy, decreased mental alertness, a lowered heart rate, and reduced blood pressure may also be observed. Behavioral responses frequently accompany these physiological changes [13].

The gray periaqueductal matter (PAG) is pivotal in pain modulation. It contains enkephalins and beta-endorphins, which, when electrically stimulated, help alleviate pain. Additionally, stimulating the Magnus Raphe nucleus in the brainstem can suppress pain signals at the spinal cord gate. Injecting morphine into the PAG activates descending pathways that inhibit primary pain signal transmission in the dorsal horn of the spinal cord, significantly easing pain [14].

The classification of the maxillary third molar with respect to the sinus, in terms of angle and proximity, is similar to the maxillary third molar in the upper jaw. The classification regarding the proximity of the sinus to the maxillary third molar is as follows: between the maxillary sinus floor and the tooth, either there is no bony layer or a thin bony layer is visible, or there is no proximity to the sinus, meaning that there is at least 2 millimeters or more of bone present between the maxillary third molar and the maxillary sinus [14].

Pain resulting from third molar surgery is governed by similar mechanisms. These teeth, known for their substantial anatomical changes and being the last to erupt, pose significant challenges during extraction, often leading to postoperative discomfort [4].

Extraction of these teeth, especially the impacted type, requires surgery, and every surgical procedure carries its own risks. Complications specific to the extraction of impacted upper third molars include tuberosity fracture, displacement of the tooth into the maxillary sinus, displacement of the tooth into soft tissues, damage to the adjacent second molar, infection, dry socket, and pain. Complications specific to the extraction of impacted lower third molars include edema, trismus, bleeding, neurological complications, fractures of the lower jaw, lingual plate issues, and postoperative pain [14].

Narcotic analgesics work by affecting specific receptors in the central nervous system and other tissues. These receptors are abundant in the central nervous system and other tissues. Opioid receptors include μ, κ, and δ receptors [15].

Aspirin is a non-selective inhibitor of cyclooxygenase, whereas other drugs are selective competitive inhibitors of this enzyme. There are two types of cyclooxygenase enzymes: COX-1 and COX-2. COX-1 is present in normal cells and plays a role in maintaining cellular homeostasis and tissue function, whereas COX-2 is induced by cytokines and other inflammatory mediators, leading to the stimulation of inflammatory cells. COX-2 catalyzes the production of prostanoids, which are among the mediators of inflammation. Most NSAIDs inhibit both COX-1 and COX-2, while some newer drugs in this group, such as celecoxib and rofecoxib, selectively inhibit COX-2 [16].

During inflammation, arachidonic acid is released from cell membrane phospholipids, which is then converted into prostaglandins by the enzyme cyclooxygenase. Thus, prostaglandins play a crucial role in the inflammatory process. Additionally, prostaglandins sensitize nerve endings in the presence of bradykinin and histamine, leading to the production of intense pain [16].

Diclofenac works by inhibiting the action of the cyclooxygenase enzyme, which leads to a reduction in the production of a chemical called prostaglandin in the body. Prostaglandins are responsible for causing pain and inflammation in the affected area. By inhibiting cyclooxygenase enzymes and reducing prostaglandin production, pain and inflammation are decreased. This medication is considered a very effective analgesic and helps improve the patient's condition by reducing inflammation and relieving pain [17].

2. Materials and Methods

The research method employed in this study was a systematic review. We conducted a comprehensive search for articles using the following keywords: 'diclofenac' or ('third molar' and 'wisdom teeth' and 'third molar

surgery' and 'third molar extraction') and ('pain control' and 'pain management' and 'postoperative pain' and 'oral surgery'). This search was performed across three online databases: Google Scholar, Scopus, and PubMed. To ensure thoroughness, we cross-verified the articles identified in PubMed and Google Scholar by also searching for them in Scopus. After removing duplicate articles, performing title screening, and conducting full-text screening, a total of 4 articles met the inclusion and exclusion criteria and were included in the study.

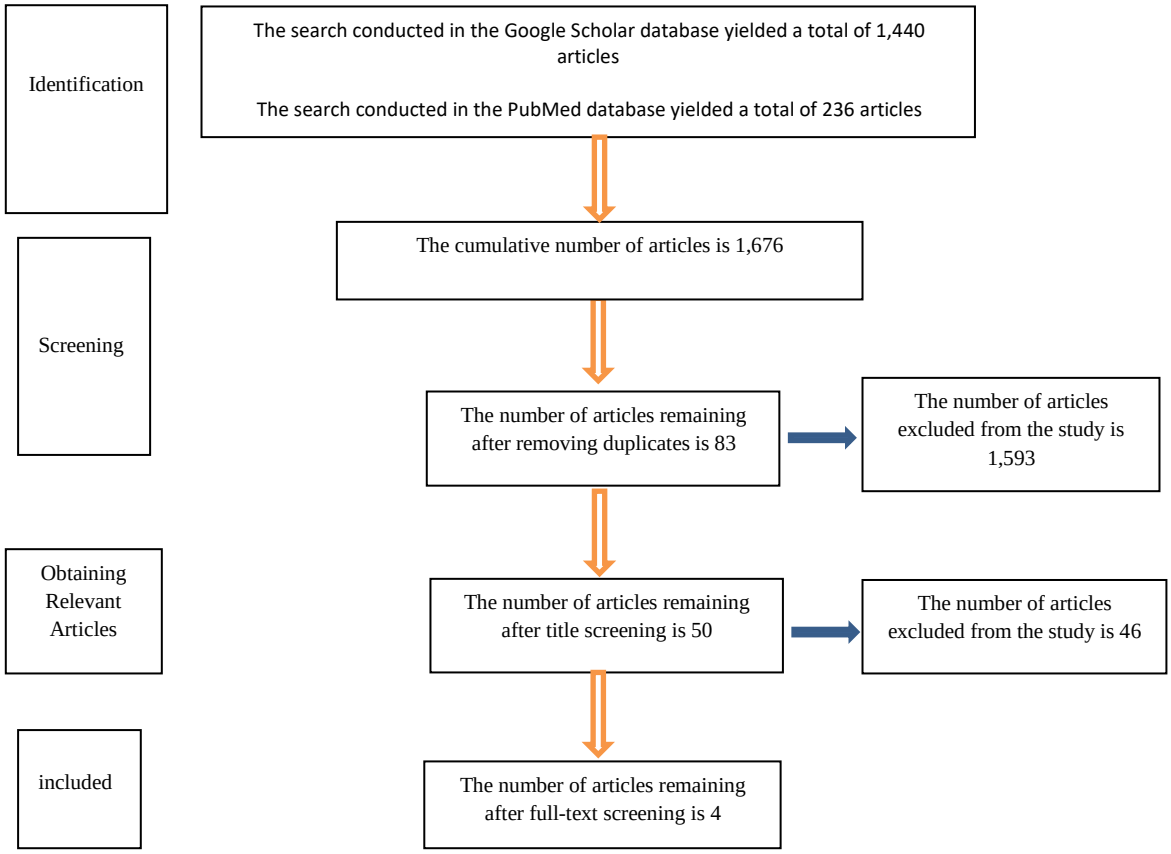

Figure 1. Flow PRISMA diagram

3. Inclusion Criteria

1. Articles that discuss the impact of analgesics (diclofenac) on pain control after third molar surgery, considering the variables relevant to this thesis.
2. Articles published since the year 2000.
3. Articles that investigate the effect of analgesics (diclofenac) on pain control after third molar surgery using a Randomized Clinical Trial (RCT) methodology

Exclusion Criteria:

1. Articles that do not examine the impact of analgesics (diclofenac) on pain control after third molar surgery with respect to the variables of this thesis.
2. Articles that investigate the effect of analgesics (diclofenac) on pain control after third molar surgery using methodologies other than Randomized Clinical Trials (RCTs).
3. Articles published before the year 2000.

Ethical Considerations: As this study was non-interventional, it does not involve ethical considerations.

4. Results

The articles used in this study evaluated pain levels in patients using the Visual Analog Scale (VAS), where a score of 0 represents no pain and 10 represents the maximum pain.

The average pain level at baseline in the first group (patients receiving diclofenac) was 1.27, and in the second group (patients receiving analgesics other than diclofenac) it was 0.11. At the sixth hour after

surgery, the pain level in the first group was 2.63, and in the second group, it was 2.35. At the twelfth hour after surgery, the pain level in the first group was 1.94, and in the second group, it was 1.9. These figures indicate that the average pain level slightly increased until the sixth hour after surgery and then decreased again at the twelfth hour [18,19,20,21].

Comparison between the two groups shows that in the second group, the average pain level at baseline, at the sixth hour after surgery, and at the twelfth hour after surgery was lower than in the first group.

Two articles assessed mouth opening, showing that the average mouth opening at baseline (before surgery) was 43.14 mm in the first group and 44.2 mm in the second group. On the second day after surgery, the average mouth opening was 29 mm in the first group and 29.82 mm in the second group. On the seventh day after surgery, the average mouth opening was 33.8 mm in the first group and 34.63 mm in the second group. This indicates that mouth opening increased from the second to the seventh day after surgery, but it remained less than baseline measurements [20,21].

According to the data, comparison between the two groups shows that the difference in mouth opening on the second and seventh days after third molar surgery is very small, with the second group having slightly more mouth opening than the first group.

Table1. Summary of Analgesic Effectiveness Studies

Author and year	Objective	Participants	Treatment Groups	Measurement Variables	Findings	Conclusion
José Leonardo Simone. (2013)	Compare dexamethasone vs. diclofenac sodium after third molar removal	44 ASA I patients (19 men, 35 women; 16–28 years)	1. Dexamethasone (8 mg) 2. Diclofenac sodium (50 mg) 3. Placebo	Pain (VAS) at various times Total Amount of Rescue Medication (TARM)	Dexamethasone showed lower pain intensity compared to diclofenac and placebo ($p < 0.05$) No significant difference in TARM ($p < 0.05$)	Dexamethasone was effective in controlling postoperative pain
Deepthi Mony. (2016)	Compare pain perception and tablet consumption between Ketorolac and Diclofenac sodium		1. Ketorolac 2. Diclofenac sodium	Pain perception time Number of tablets taken in 3 days	No significant difference in pain perception time ($p = 0.235$) Significant difference in number of tablets ($p = 0.004$	Diclofenac sodium resulted in higher tablet consumption than Ketorolac
Gaetano Isola. (2019)	Compare etoricoxib and diclofenac with placebo on postoperative pain and other outcomes		1. Etoricoxib 2. Diclofenac 3. Placebo	Pain at 2, 12, 48 hours VAS at multiple time points	Significant pain reduction with etoricoxib at 2, 12, and 48 hours No differences in swelling or mouth opening	Etoricoxib was more effective than diclofenac and placebo for pain management
P. Zupelari-Goncalves. (2017)	Compare effectiveness of diclofenac alone vs. diclofenac with codeine for postoperative pain	46 volunteers	1. Diclofenac (50 mg) + Codeine (50 mg) 2. Diclofenac alone (50 mg)	Pain levels within 24 h Rescue medication (paracetamol)	Less pain and rescue medication with diclofenac and codein	Diclofenac combined with codeine was more effective than diclofenac alone

5. Discussion

This study evaluated the effect of diclofenac on pain control and its impact on mouth opening after third molar surgery. It also compared the effects of diclofenac with other analgesics such as etoricoxib, ketorolac, dexamethasone, and tramadol. The findings suggest that the average pain level after third molar surgery was higher in patients receiving diclofenac compared to those in the other group. This was evident at both the sixth and twelfth hours after surgery. Several factors contributed to this result.

Patients who received dexamethasone experienced less pain at the sixth and twelfth hours after surgery compared to those who received diclofenac. The superior performance of dexamethasone compared to diclofenac can be attributed to its mechanism of action. Dexamethasone acts by suppressing neutrophil migration and reducing lymphocyte proliferation. Additionally, it makes capillary membranes less permeable and stabilizes lysosomal membranes. Prostaglandins and certain cytokines (such as interleukins-1, -12, -18,

tumor necrosis factor, interferon-gamma, and granulocyte-macrophage colony-stimulating factor) are inhibited [18].

In another study comparing diclofenac with a diclofenac-codeine combination, diclofenac combined with codeine was found to be more effective for pain control after surgery at the specified hours. This could be explained by the fact that combining diclofenac with codeine inhibits both cyclooxygenase enzymes and activates the central nervous system's descending pain inhibition pathways [21].

Ketorolac, another NSAID with a similar mechanism to diclofenac, was found to be more effective. The higher efficacy of etoricoxib compared to diclofenac in our study was consistent with the findings of Clarke and colleagues [22].

Regarding pain levels over time, both groups experienced an increase in pain at the sixth hour after surgery compared to baseline, which is likely due to the end of the anesthetic effect. Peak pain after third molar surgery is also typically observed between the fifth and sixth hours. Pain levels decreased at the twelfth hour in both groups due to a reduction in inflammatory mediators, which aligns with the results of Simone and colleagues [18].

Mouth opening in both groups was reduced on the second day after surgery but increased on the seventh day. This is related to the production of prostaglandins and cyclooxygenase-2 following surgery, which causes edema and trismus due to the release of arachidonic acid from cell membranes at the surgery site. As the production of inflammatory mediators decreases over time, edema and trismus also diminish, leading to increased mouth opening. Prashar and colleagues also obtained similar results [23].

The articles used in this study are recent, published since 2000, and randomized clinical trials, which are strengths of this study. However, limitations included insufficient time, limited access to the internet, and some articles related to the research topic being unavailable for free.

In conclusion, diclofenac was less effective than dexamethasone, ketorolac, etoricoxib, and the diclofenac-codeine combination in controlling pain after third molar surgery. However, diclofenac was more effective than tramadol. Additionally, the impact of diclofenac on mouth opening after surgery was less compared to etoricoxib and the diclofenac-codeine combination.

6. Strengths and limitations

This study has several strengths. First, we conducted a comprehensive search of major databases including Google Scholar, PubMed, and Scopus. This extensive search strategy aligns with standard practices for systematic reviews and ensures a thorough review of relevant literature. Second, , this review adheres to the PRISMA checklist, ensuring that we followed established guidelines for systematic reviews.

However, the study has some limitations. First, funding constraints may have impacted the scope of our review and the inclusion of some studies. Second, while we conducted a comprehensive review, some relevant information might not have been included. Despite these limitations, our review remains robust and provides valuable insights into the topic.

ORCID

Rahmatullah Nazari https://orcid.org/0009-0001-2011-0691
Hedayatullah Ehsan https://orcid.org/0000-0001-5970-713X

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