Jurnal Pijar MIPA
https://jurnalfkip.unram.ac.id/index.php/JPM

ISSN 1907-1744 (Print)
ISSN 2460-1500 (Online)

The Effectiveness of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and NSAID-Analgesic Combinations in Optimizing Postoperative Pain Management: A Review

Elsyifa Salsabila, Mally Ghinan Sholih*, Diyanah Fauziyah Tamimah

Department of Pharmacy, Faculty of Health Sciences, Universitas Singaperbangsa Karawang, West Java, Indonesia
*e-mail: mally.ghinan@fkes.unsika.ac.id

Received: November 8, 2025. Accepted: March 3, 2026. Published: April 6, 2026

Abstract: Postoperative pain is a common clinical problem resulting from tissue trauma and inflammatory responses, which can hinder patient recovery. One of the most widely used pharmacological therapies is Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), either as monotherapy or in combination with other analgesics. This study aims to evaluate the effectiveness of NSAIDs, both as single agents and in combination therapy, in reducing postoperative pain. The study employed a Systematic Literature Review (SLR) method, with literature searches conducted in the PubMed and Google Scholar databases. A total of 588 articles were identified, of which 20 studies met the inclusion criteria and were analyzed using a narrative synthesis approach based on pain intensity parameters, including the Visual Analog Scale (VAS) and Numeric Rating Scale (NRS). The results indicate that NSAIDs such as ketorolac, ketoprofen, ibuprofen, diclofenac sodium, and dexketoprofen trometamol effectively reduced postoperative pain intensity, with several studies reporting a decrease in VAS scores from moderate pain levels (VAS >4) to mild pain levels (VAS <2) within 24 hours postoperatively. Furthermore, combination therapy of NSAIDs with paracetamol or tramadol demonstrated superior analgesic efficacy, longer pain-free duration, and reduced opioid requirements compared to NSAID monotherapy, without a significant increase in adverse effects. NSAIDs are effective in postoperative pain management. Combination therapy with other analgesics such as paracetamol or tramadol provides more optimal outcomes compared to monotherapy. However, the selection of analgesic agents, dosage, and duration of therapy should be individualized according to the patient's clinical condition to ensure both safety and therapeutic effectiveness.

Keywords: Combination Analgesics; NSAIDs; Postoperative Pain; Postoperative Pain Management.

Introduction

Surgery is one of the most common medical procedures performed for therapeutic purposes, involving the insertion of instruments into the body to access and treat specific areas. The period following this procedure is called the postoperative phase. During this phase, patients often experience various discomforts, with pain being the most frequently reported symptom [1]. Postoperative pain is a common clinical problem that arises from tissue trauma, surgical manipulation, and inflammatory responses. It represents an unpleasant sensory and emotional experience resulting from tissue damage during surgical procedures, typically lasting for about three to seven days after surgery [2]. Pain is an unpleasant sensory and emotional experience [3]. Patients undergoing surgery commonly experience several postoperative complaints, such as pain at the surgical wound site, which may subsequently lead to fear of movement or early mobilization [4]. Severe pain may hinder the implementation of early mobilization, which is crucial for accelerating recovery and preventing complications such as deep vein thrombosis and pneumonia. Delayed mobilization and prolonged hospitalization can lead to increased healthcare costs. Therefore, postoperative pain management should not only aim to reduce patient discomfort but also play a vital role in promoting faster recovery and improving healthcare efficiency [5].

According to the World Health Organization (WHO) report in 2019, approximately 148 million patients worldwide underwent surgical procedures [6]. WHO also reported that approximately 11% of the global disease burden is attributable to conditions that could be treated surgically. In Indonesia, data from the Ministry of Health (2019) indicated that surgical procedures ranked 11th among 50 disease categories treated in hospitals, accounting for 12.8% of all cases, with an estimated 32% classified as major surgeries [7].

One of the most widely used pharmacological strategies in postoperative pain management is the administration of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). This class of drugs is well known for its analgesic, antipyretic, and anti-inflammatory effects [8]. NSAIDs exert their effects primarily by inhibiting cyclooxygenase (COX-1 and COX-2) enzymes. These enzymes are responsible for catalyzing the production of prostaglandins, which act as inflammatory mediators that increase nociceptor sensitivity and enhance pain perception [9]. By inhibiting COX enzymes, the production of prostaglandins (PGE_2) and prostacyclin (PGI_2) is reduced. These mediators play a crucial role in the inflammatory process. Their reduction may lead to vasoconstrictive effects

How to Cite:
E. Salsabila, M. G. Sholih, and D. F. Tamimah, "The Effectiveness of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and NSAID-Analgesic Combinations in Optimizing Postoperative Pain Management: A Review", *J. Pijar.MIPA*, vol. 21, no. 2, pp. 248–254, Apr. 2026.
https://doi.org/10.29303/jpm.v21i2.10654

and increased sodium retention [10]. In addition, the anti-inflammatory and antipyretic properties of NSAIDs provide additional benefits for postoperative patients, particularly in cases with a strong inflammatory response. Commonly used nonselective NSAIDs include diclofenac, ketorolac, ibuprofen, and meloxicam, whereas the selective cyclooxygenase-2 (COX-2) inhibitor most frequently used is celecoxib. The use of NSAIDs in postoperative pain management has been shown to provide significant and effective analgesia [11].

Multimodal analgesia has emerged as a pain management strategy recommended by the World Health Organization (WHO) and has been widely adopted in clinical practice [12]. This strategy combines different classes of analgesic agents that act on various nociceptive pathways. The primary goal of this approach is to reduce pain intensity while minimizing the use of opioid medications, thereby lowering the risk of opioid-related adverse effects such as nausea, vomiting, constipation, sedation, and respiratory depression [13]. Opioid-related adverse effects have been associated with negative clinical outcomes, including prolonged hospitalization and increased rates of readmission [14].

This concept has also given rise to the idea of opioid-free analgesia, considering that opioid-based analgesic techniques, such as intravenous patient-controlled analgesia (IVPCA) or epidural administration, are not always practical for widespread use. Since its introduction by Kehlet and Dahl (1993) as the term' combined analgesic regimen,' multimodal analgesia has aimed to achieve optimal pain control through additive or synergistic effects [15]. When such combinations produce synergistic interactions, the analgesic benefits can be enhanced. Many combination analgesic regimens are opioid-sparing in nature [16].

According to the Royal Colleges of Surgeons (1996), pain is recognized as the fifth vital sign that should be continuously monitored, alongside other vital parameters [17]. Meanwhile, the World Health Organization (WHO), together with several pain-related organizations, has emphasized that pain management is a fundamental human right. In line with this, the Joint Commission International (JCI) has established pain management as both a patient and family right, as well as an integral component of healthcare service standards [18]. Inadequate pain management in hospitals can lead to serious consequences for both patients and healthcare institutions, including increased patient morbidity and mortality, higher healthcare costs due to complications, reduced quality of care, and lower patient satisfaction [19].

Despite the widespread use of NSAIDs in postoperative pain management, comprehensive review studies that specifically compare the effectiveness of NSAID monotherapy versus NSAID-based combination analgesic regimens remain limited, particularly those incorporating recent clinical evidence. Most existing reviews focus on individual analgesic classes or opioid-sparing strategies without providing a detailed comparison of pain intensity outcomes and safety profiles between single-agent and combination therapies. Therefore, this literature review aims to complement previous research by systematically analyzing and comparing the effectiveness of NSAIDs used as monotherapy and in combination with other analgesics in optimizing postoperative pain management, based on recent studies and clinically relevant pain assessment parameters.

Research Methods

This study employed a Systematic Literature Review (SLR) method, comprehensively searching scientific articles and publications in electronic databases, namely PubMed and Google Scholar, using the Publish or Perish software. The search was conducted using the following adjusted keywords: (“NSAID” or “non-steroidal anti-inflammatory drugs”) and (“analgesic combination” or “multimodal analgesia”) AND (“postoperative pain management” or “pain management after surgery”).

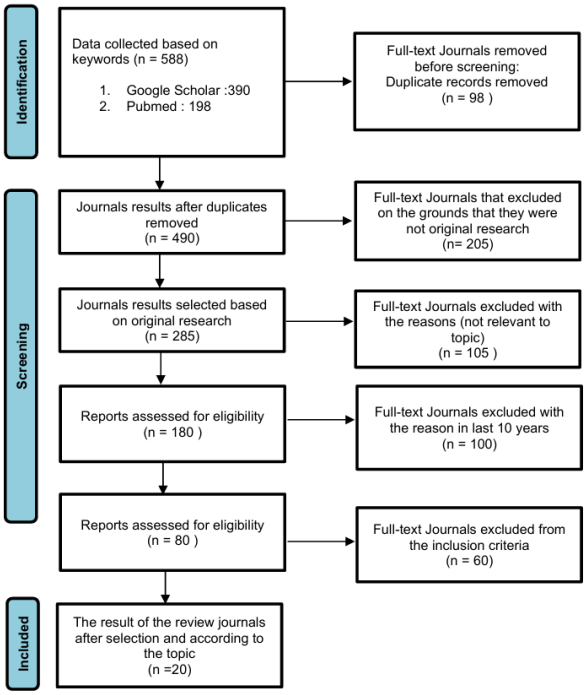

Figure 1. PRISMA Flow Diagram

Table 1. PICO Framework

PICO	Description
P (Population)	Postoperative patient
I (Intervention)	Administration of NSAIDs alone or in combination with other analgesics
C (Comparison)	NSAID monotherapy compared with combination therapy (e.g., NSAIDs + paracetamol or tramadol), or comparison with other analgesic regimens
O (Outcome)	Effectiveness of reducing postoperative pain intensity and side effects

In conducting this review, data were collected using the Publish or Perish software, which identified 588 articles from Google Scholar (390) and PubMed (198) using selected keywords. Of these, 303 articles were excluded for duplication or for not being original research, leaving 285. Subsequently, 105 articles were removed as irrelevant to the topic, leaving 180. A further 100 articles were excluded because they were published more than 10 years ago, leaving

80 articles. Selection was then continued based on the availability of full text and meeting the inclusion criteria, with 60 articles excluded because their full texts were unavailable, leaving 20 articles. After a thorough screening based on the predefined inclusion criteria, 20 relevant articles were identified and analyzed further.

A Systematic Literature Review (SLR) approach was employed to support a PICO-based analytical framework. This method enabled the selection of relevant literature from various scientific databases, ensuring comprehensive coverage of the role of NSAIDs and analgesic combinations in optimizing postoperative pain management. Through this approach, the findings were presented in a structured manner, facilitating readers' understanding, comparison, and interpretation of the evidence, thereby allowing clear conclusions to be drawn from the reviewed studies [20]. The literature search utilized relevant keywords to maintain focus on the effectiveness of NSAID use both as monotherapy and in combination with other analgesic agents in reducing postoperative pain intensity.

The selected articles were analyzed using a narrative synthesis method. Pain intensity was evaluated using the Visual Analog Scale (VAS) and the Numeric Rating Scale (NRS). The VAS is presented as a 10 cm horizontal line, with 0 indicating no pain and 10 representing the worst imaginable pain. The NRS is a numerical rating system ranging from 0 to 10, in which patients are asked to quantify their perceived pain intensity, where higher scores reflect greater pain severity [43]. Study findings were systematically grouped and compared by NSAID type (monotherapy or combination therapy), surgical procedure, pain assessment tools (VAS and NRS), and reported clinical outcomes. The effectiveness of analgesic therapy was evaluated by comparing changes in pain intensity scores, pain relief duration, and the need for additional or rescue analgesics. This approach enabled a structured comparison of postoperative pain management outcomes across different analgesic strategies.

Results and Discussion

Based on the analysis of 20 journals discussing the use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) for postoperative pain management across various surgical procedures, including dental, orthopaedic, abdominal, appendectomy, breast tumor, arthroplasty, and obstetric surgeries, it was found that NSAID administration, either as monotherapy or in combination, effectively reduced postoperative pain intensity. However, most studies reported that combination therapy achieved a greater reduction in pain intensity compared to NSAID monotherapy [21].

Table 2. Monotherapy NSAID

NSAID	Efficacy	Parameter	Reference
Ketorolac	Reduces pain after orthopedic surgery	Pain reduction observed	[22] [23]
Ketorolac	Reduces pain on the first postoperative day	Nilai NTT 30 mg =3.4	[1] [24]
Ketorolac	Reduces pain after cesarean section	VAS from 4.68 ± 1.84 (2h) to 1.52 ± 1.17 (24h)	[25]
Ketorolac	Reduces pain after cesarean section	Ketorolac 30 mg IV comparable to tramadol 1.5 mg/kg IV ($p>0.05$)	[26]
Ketoprofen	Reduces pain after cesarean surgery	VAS from 4.63 ± 2.22 to 1.76 ± 1.40 (2–24h)	[27]
Ketoprofen	Preventive ketoprofen suppository postoperatively	Pain reduction (NRS) 30 min post-op to 12h	[28]
Ibuprofen	Preventive use after tonsillectomy	VAS from 5.93 ± 0.77 (4h) to 1.58 ± 1.41 (7th day)	[29]
Ibuprofen	Preventive use after dental implant surgery	Mean VAS (0–72h) 0.30 ± 0.57 vs placebo 1.14 ± 1.07 ($p<0.001$)	[30]
Ibuprofen	Reduces pain and morphine requirement	Dynamic VAS from 4.32 ± 0.36 → 1.90 ± 0.30 ($p=0.02$)	[31]
Ibuprofen	Preventive use after breast tumor surgery	NRS 5.00 ± 0.73 (1h) → 1.69 ± 0.70 (24h)	[32]

Table 3. Combination Therapy (NSAID + Analgesics)

NSAID	Combination Analgesics	Efficacy	Parameter	Reference
Ketorolac	Tramadol + ketorolac	Combination is effective after abdominal neurosurgery with mild pain at 30 min	No pain and mild pain (VAS 0–3)	[7]
Ketorolac	Tramadol + ketorolac	Combination effectively reduced pain after appendectomy	VAS score combination higher (–3 vs –1; $p<0.05$)	[33] [34]
Ketorolac	Ketorolac + Tramadol	Combination effective for various elective surgeries compared to monotherapy	No severe pain, indicating adequate pain control	[35] [36]
Ibuprofen	Ibuprofen+ Paracetamol	Preventive combination reduced daily morphine requirement after breast tumor surgery and TKA	Combination reduced the morphine requirement the most	[32] [37]

Diclofenac sodium, dexketoprofen trometamol	Diclofenac sodium + dexketoprofen trometamol	Combination use of DT in the early phase and DS in the recovery phase is recommended to enhance postoperative comfort	Effective in reducing pain and additional analgesic needs	[38]

Analgesic agents used in postoperative pain management are generally classified into three main groups: local anesthetics, non-opioid analgesics such as non-steroidal anti-inflammatory drugs (NSAIDs), and opioid analgesics [39]. Pain management is tailored to each individual's pain intensity. These classes of drugs can be administered as monotherapy or in combination, aiming to enhance analgesic efficacy while minimizing the potential adverse effects associated with high-dose single-agent therapy [30].

Findings from several studies indicate that the use of non-steroidal anti-inflammatory drugs (NSAIDs) as monotherapy is effective in reducing postoperative pain intensity, as observed with ketorolac, ketoprofen, and ibuprofen. Among the various NSAIDs, ketorolac is the most frequently used. It exerts its effect by inhibiting prostaglandin synthesis, which plays a key role in inflammation, pain, and fever, making it an effective peripheral analgesic [47]. Ketorolac has been shown to be highly effective in alleviating postoperative pain due to its strong analgesic potency, particularly when administered via intramuscular or intravenous routes, and can serve as an alternative or adjunct to reduce opioid requirements [22]. Ketorolac is recommended as part of the postoperative analgesic regimen for moderate to severe pain. It can be administered as monotherapy due to its lack of respiratory depression or combined with opioids to enhance analgesic efficacy [35].

Ketorolac and ketoprofen have demonstrated significant efficacy in lowering pain scores among postoperative patients. A study conducted by Fudiarti (2018) reported that administration of ketorolac reduced the Visual Analogue Scale (VAS) score from 4.68 ± 1.84 at 2 hours to 1.52 ± 1.17 at 24 hours following cesarean section surgery [27]. Similar findings were reported by other studies, indicating that ketoprofen administration effectively reduced postoperative pain intensity. The Visual Analogue Scale (VAS) score decreased from 4.63 ± 2.22 to 1.76 ± 1.40 within 24 hours after surgery [26]. In addition, preventive administration of ketoprofen suppositories prior to surgery has been shown to effectively reduce postoperative pain intensity for up to 12 hours following the surgical procedure [28]. Preventive administration of ibuprofen has also been proven effective in reducing postoperative pain, particularly following tonsillectomy and dental implant procedures [29][30]. These findings indicate that NSAID monotherapy is sufficiently effective for managing mild to moderate postoperative pain.

In contrast to monotherapy, NSAID combination therapy with other analgesics can provide stronger analgesic effects and extend the duration of pain-free periods compared to NSAID monotherapy. For instance, the combination of ketorolac and paracetamol has been shown to reduce pain intensity more significantly than ketorolac alone. Another study reported that patients receiving this combination experienced no pain at all during the observation period [35]. Another study demonstrated that the combination of ibuprofen and paracetamol significantly reduced Visual Analogue Scale (VAS) scores within 1–8 hours postoperatively. This combination not only extended the duration of pain-free periods but also decreased the need for additional analgesics without causing any notable increase in adverse effects [29][30]. The combination of ketorolac and tramadol is commonly employed for postoperative patients experiencing moderate pain, such as following abdominal surgery [7]. The combination of ketorolac and tramadol is also applied in postoperative patients with appendicitis, and has been shown to provide more effective pain control and reduce opioid requirements compared to ketorolac monotherapy. Furthermore, this combination resulted in a greater reduction in pain scores (VAS–3 vs VAS–1), indicating superior analgesic efficacy [33]. Another study demonstrated that the combination of paracetamol and ibuprofen is more effective than either alone in reducing total morphine requirements. Moreover, the combination of paracetamol and ibuprofen injections provides adequate pain management, thereby facilitating faster patient mobilization [32][37].

The superior analgesic efficacy observed in NSAID combination therapy can be explained by the synergistic pharmacological mechanisms between the combined agents.

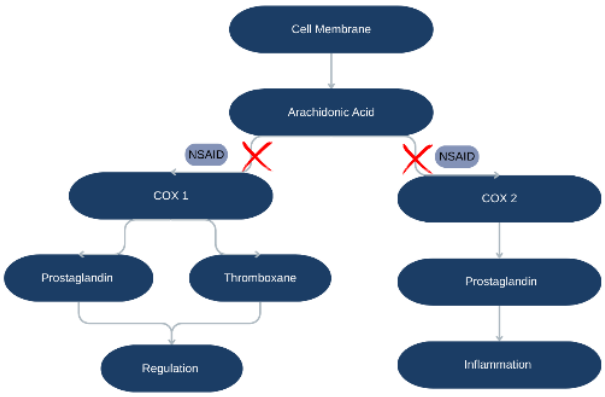

Figure 2. Mechanism of Action of NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs) are a class of medications that alleviate pain by inhibiting prostaglandin synthesis. This mechanism occurs through the suppression of cyclooxygenase (COX) enzymes, which consist of two major isoenzymes: COX-1 and COX-2. COX-1 is constitutively expressed in most tissues and plays a protective role by maintaining gastric mucosal integrity, regulating platelet function, and preserving renal homeostasis. In contrast, COX-2 is inducible and predominantly expressed in inflamed tissues, where its activity significantly increases during inflammatory processes [40]. The inhibition of prostaglandin synthesis leads to a reduction in inflammatory mediators, thereby decreasing vasodilation and attenuating the transmission of pain impulses within both the peripheral and central nervous systems [41].

The efficacy of NSAID combination therapy with other analgesics can be explained by the synergistic

mechanisms between the drugs. NSAIDs act by inhibiting cyclooxygenase (COX) enzymes, thereby reducing prostaglandin production, which plays a key role in inflammation and pain perception. Meanwhile, additional analgesics such as paracetamol exert their effects by inhibiting COX activity in specific cells within the central nervous system, thereby enhancing analgesic efficacy without substantially increasing the risk of systemic side effects [44]. The combination of NSAIDs with other analgesics provides superior pain relief, as pain is addressed through two distinct mechanisms. Additionally, combining NSAIDs with tramadol has been shown to be effective. Tramadol is a weak opioid that acts on the central nervous system by binding to μ-opioid receptors and inhibiting the reuptake of serotonin and norepinephrine, thereby enhancing analgesic efficacy [45]. This mechanism contributes to the reduction of pain signal transmission while increasing the patient's pain threshold, with a lower risk of dependence compared to strong opioids [46].

The use of non-steroidal anti-inflammatory drugs (NSAIDs) as analgesic agents in postoperative patients can significantly reduce opioid consumption, thereby minimizing the risk of adverse effects commonly associated with opioid therapy [27]. These adverse effects include sedation, dizziness, nausea, vomiting, constipation, tolerance, and respiratory depression. Furthermore, prolonged opioid use is associated with psychological and physical dependence, which remains a major clinical concern and an important factor in analgesic selection [33]. Owing to their favorable safety profile and effective analgesic properties, NSAIDs are widely recommended for the management of mild to moderate postoperative pain. However, in cases where first-line NSAID therapy is contraindicated, poorly tolerated, or insufficient to provide adequate pain relief, tramadol or other opioid analgesics may be considered as alternative or adjunctive options to achieve optimal pain control [42].

The use of NSAIDs is also associated with limitations and potential adverse effects that warrant careful consideration. Common side effects include impaired renal function, fluid retention leading to oedema and hypertension, and gastrointestinal bleeding due to inhibition of protective prostaglandins in the gastric mucosa [48]. The risk of NSAID-related adverse effects may be elevated in patients with a history of gastrointestinal disorders, elderly individuals, or those concurrently using medications such as corticosteroids and anticoagulants [49]. Therefore, careful consideration of the NSAID type, dosage, duration of therapy, and the patient's clinical condition is essential to ensure both safety and efficacy.

NSAID use is frequently combined with other medications to minimize the risk of adverse effects. Co-administration of NSAIDs with gastroprotective agents, such as proton pump inhibitors (PPIs) and H_2 receptor antagonists (H_2 blockers), can help prevent gastrointestinal complications commonly associated with NSAID therapy [22]. A similar recommendation is provided by The American College of Gastroenterology, which advises that patients at high risk of gastrointestinal adverse effects should receive a combination of COX-2-selective NSAIDs and/or misoprostol, or high-dose PPIs. Additional studies have demonstrated that administration of misoprostol, PPIs, or high-dose H_2 blockers is effective in preventing gastric and intestinal ulcers associated with NSAID use [50].

Conclusion

Based on the analysis of 20 selected studies, NSAIDs are effective in reducing postoperative pain when used as monotherapy or in combination therapy. However, combination regimens, particularly NSAIDs with paracetamol or tramadol, consistently provide superior analgesic outcomes, including greater pain reduction, prolonged analgesia, and decreased opioid consumption without significantly increasing adverse effects. These findings emphasize the importance of individualized analgesic selection based on patient and surgical factors to optimize safety and efficacy, as well as the clinical value of multimodal analgesia in improving postoperative recovery and patient comfort. Further high-quality randomized controlled trials are required to establish standardized protocols, optimize dosing strategies, and assess long-term safety. Additionally, developing evidence-based clinical guidelines and hospital policies is essential to support effective, consistent postoperative pain management.

Author's Contribution

E. Salsabila: responsible for study design, literature review, and manuscript preparation. M. G. Sholih: supervised the study and interpreted clinical findings. D. F. Tamimah: responsible for the search and selection of scientific articles, as well as data extraction from the selected literature.

Acknowledgements

The authors would like to express their sincere gratitude to Universitas Singaperbangsa Karawang for its support in preparing this manuscript. We also extend our appreciation to Dr. Apt. Mally Ghinan Sholih, M.Farm., for his invaluable guidance and scientific mentorship, as well as to colleagues who contributed constructive feedback in refining this article.

References

[1] K. R. Ramadani, D. Ramadhan, and A. Ibrahim, "Karakteristik Dan Pola Penggunaan Obat Analgesik Nsaid Pada Pasien Pasca Operasi Di Rsud Abdul Wahab Sjahranie Samarinda," in *Proceeding of the 3rd Mulawarman Pharmaceuticals Conferences*, Fakultas Farmasi, Universitas Mulawarman, Samarinda, Apr. 2016, pp. 53–63. doi: 10.25026/mpc.v3i1.66.

[2] D. Y. D. Arna *et al.*, *Kapita Selekta Keperawatan Klinis*, 1st ed. PT Media Pustaka Indo, 2025.

[3] J. Barus, "Revisi definisi nyeri Internasional Association for Study of Pain (IASP) dan kaitannya dengan nyeri pada lansia dengan demensia," in *Menjawab Tantangan Pelayanan Neurologi di Era Adaptasi Kebiasaan Baru*, vol. 1, Perhimpunan Dokter Spesialis Saraf Indonesia (PERDOSSI), 2020.

[4] T. Widyaningrum and A. Vranada, "Penerapan mobilisasi dini terhadap penurunan skala nyeri pasien pasca operasi bedah laminectomy," *nm*, vol. 5, no. 1, p. 82, Apr. 2024, doi: 10.26714/nm.v5i1.14181.

[5] Z. Simsek Yaban, S. Bulbuloglu, G. Kapikiran, H. Gunes, S. Kula Sahin, and S. Saritas, "The effect of bed exercises following major abdominal surgery on early ambulation, mobilization, pain and anxiety: A randomized-controlled trial," *International Wound Journal*, vol. 21, no. 2, p. e14406, Feb. 2024, doi: 10.1111/iwj.14406.

[6] R. Noprianty, R. A. Putri, and H. Manuopo, "Compliance in Filling Surgical Safety Checklist at The Central Surgical Installation," *JAI b*, vol. 16, no. 3, pp. 208–217, Nov. 2024, doi: 10.14710/jai.v0i0.61515.

[7] M. Munawaroh, G. N. Prassetyo, and A. Suryanah, "Gambaran Tatalaksana Pengurangan Rasa Nyeri Pasien Pasca Operasi Bedah Mayor Dengan Anestesi Umum," vol. 7, 2024.

[8] A. Dahlia, A. Abdul, and R. Ariastuti, "Gambaran penggunaan obat analgetik NSAID di Apotek Hidayah Metro Lampung periode Januari-Desember 2022," *Borobudur Pharmacy Review*, vol. 3, no. 2, 2023, doi: https://doi.org/10.31603/bphr.v3i2.10354.

[9] D. R. P. Papeo *et al.*, "Gambaran Penggunaan Obat Antipendarahan dan Antinyeri pada Pasien Rawat Inap Kanker Serviks Di Rumah Sakit X Wilayah Kota Gorontalo Periode 2021-2022," *jmpi*, vol. 9, no. 2, Dec. 2023, doi: 10.35311/jmpi.v9i2.341.

[10] F. P. Imananta, "Artikel Tinjauan: Penggunaan NSAIDs (Non Steroidal Anti Inflamation Drugs) Menginduksi Peningkatan Tekanan Darah Pada Pasien Arthritis," *Farmaka*, vol. 16, no. 1, 2018.

[11] A. Mariatu, M. Verla, and I. Atif, "Multimodal analgesia: Opioid-sparing strategies for pain management," *Baylor College of Medicine, 7200 Cambridge St.*, vol. 32, no. 3, Jul. 2021.

[12] H. Zuo, C. Liu, W. Fan, and X. Lu, "Effects of Multimodal Analgesia Combined with Comfort Management on Pain and Stress Indexes in Patients with Orthopedic Trauma after Intervention: A Retrospective Study," *Ann. Ital. Chir.*, vol. 95, no. 5, p. 886, Oct. 2024, doi: 10.62713/aic.3527.

[13] Irvan, "Penanganan Nyeri Multimodal Post Total Hip dan Knee Arthroplasty," *Continuing Professional Development IAI*, vol. 47, no. 1, 2020.

[14] L. Martinez, E. Ekman, and N. Nakhla, "Perioperative Opioid-sparing Strategies: Utility of Conventional NSAIDs in Adults," *Clinical Therapeutics*, vol. 41, no. 12, pp. 2612–2628, Dec. 2019, doi: 10.1016/j.clinthera.2019.10.002.

[15] P. Kondengis and I. K. Sinardja, "Multimodal analgesia pada manajemen nyeri paska-bedah: sebuah laporan kasus," *medicina*, vol. 50, no. 2, May 2019, doi: 10.15562/medicina.v50i2.626.

[16] J. V. Pergolizzi Jr, P. Magnusson, R. B. Raffa, J. A. LeQuang, and F. Coluzzi, "Developments in combined analgesic regimens for improved safety in postoperative pain management," *Expert Review of Neurotherapeutics*, vol. 20, no. 9, Aug. 2020.

[17] J. Smith and R. Roberts, "Pain: The Fifth Vital Sign," in *Vital Signs for Nurses: An Introduction to Clinical Observations*, Wiley (Wiley Online Library), 2015.

[18] B. suryono Suwondo, L. Meliala, and Sudadi, *BUKU AJAR NYERI 2017*. Perkumpulan Nyeri Indonesia, 2017.

[19] MENKES, "Keputusan Menteri Kesehatan Republik Indonesia Nomor Hk.01.07/Menkes/481/2019 Tentang Pedoman Nasional Pelayanan Kedokteran Tata Laksana Nyeri," Menteri Kesehatan Republik Indonesia, HK.01.07/MENKES/481/2019, Aug. 2019.

[20] M. A. Harahap and S. W. Hasibuan, "Pelatihan Penulisan Artikel Ilmiah Dengan Metode Systematic Literature Review (SLR)," vol. 3, no. 2, 2025.

[21] A. Mobasheri, B. Morlion, V. S. Sethi, M. Cardosa, O. Della Pasqua, and P. Kalita, "Combination vs. single-drug nonprescription analgesics for acute pain management: A narrative review," *Br J Clin Pharmacol*, vol. 91, no. 10, pp. 2796–2816, Oct. 2025, doi: 10.1002/bcp.70180.

[22] V. Anggi, W. Wirawan, and A. Wulandari, "Kajian Penggunaan Obat Pada Pasien Pasca Bedah Ortopedi (Fraktur) Di Upt. Rumah Sakit Umum Daerah Undata," no. 1, 2023.

[23] S. Handayani, H. Arifin, and M. Manjas, "Kajian penggunaan analgetik pada pasien pasca bedah fraktur di trauma centre RSUP M. Djamil Padang," *Jurnal Sains Farmasi &Klinis*. repo.unand.ac.id, 2019. [Online]. Available: http://repo.unand.ac.id/id/eprint/36740/contents

[24] E. K. Abdillah, R. Ismail Abdul Rahman, L. Nugrahini, N. Islamiyah, and T. Tasmin, "Penggunaan Kombinasi Obat Analgetika Pada Pasien Pasca Operasi Di Rumah Sakit X Jakarta," *JFK*, vol. 1, no. 2, pp. 7–13, Jul. 2022, doi: 10.59969/jfk.v1i2.16.

[25] E. D. Antari, U. Nafisah, and W. Sulistyaningsih, "Penggunaan Obat Analgesik Pada Pasien Pasca Bedah Caesar Bangsal Annisa Di Rs Pku Muhammadiyah Surakarta," *Jurnal Farmasindo*, vol. 6, no. 2, pp. 14–18, Dec. 2022, doi: 10.46808/farmasindo.v6i2.143.

[26] D. R. Juwita, N. Faradani, and ..., "Studi Penggunaan Obat Analgesik pada Pasien Pasca Partus Pervaginal dan Sectio Caesarea di RSU Bunda Purwokerto," *... Journal of Indonesia)*, 2019, [Online]. Available: https://jurnalnasional.ump.ac.id/index.php/PHARMACY/article/view/5627

[27] N. H. Furdiyanti, D. O. Oktianti, R. R. Rahmadi, and ..., "Keefektifan ketoprofen dan ketorolak sebagai analgesik pada pasien pasca bedah cesar," *Indonesian Journal of ...*, 2019, [Online]. Available: https://jurnal.unw.ac.id/index.php/ijpnp/article/view/194

[28] L. Lestari, E. Hanindito, and A. Utariani, "Effectiveness of Ketoprofen Suppositoria as Preemptive Analgesia for Postoperative Pain in Patients Undergoing Elective Surgery with General Anesthesia," *IJAR*, vol. 2, no. 1, p. 20, Jan. 2020, doi: 10.20473/ijar.V2I12020.20-26.

[29] A. Jotić *et al.*, "Pain Management After Surgical Tonsillectomy: Is There a Favorable Analgesic?," *Ear, Nose & Throat Journal*, vol. 98, no. 6, pp. 356–361, Jul. 2019, doi: 10.1177/0145561319846065.

[30] G. Pereira, L. Cota, R. Lima, and F. Costa, "Effect of preemptive analgesia with ibuprofen in the control of postoperative pain in dental implant surgeries: A randomized, triple-blind controlled clinical trial," *J Clin Exp Dent*, pp. e71–e78, 2020, doi: 10.4317/jced.56171.

[31] A. Martínez, B. Escontrela Rodriguez, A. Planas Roca, and A. Martínez Ruiz, "Intravenous Ibuprofen for Treatment of Post-Operative Pain: A Multicenter, Double Blind, Placebo-Controlled, Randomized Clinical Trial," *PLoS ONE*, vol. 11, no. 5, p. e0154004, May 2016, doi: 10.1371/journal.pone.0154004.

[32] R. A. A. Aisy, F. Dwimartyono, R. N. Maharani, Muh. W. Harahap, and N. Fadhillah Khalid, "Efektivitas Premedikasi Ibuprofen IV terhadap Skala Nyeri dan Efek Samping Pasca Bedah Tumor Mammae," *UMJ*, vol. 9, no. 1, pp. 31–40, Jun. 2024, doi: 10.33096/umj.v9i1.273.

[33] A. K. Anugrah, L. A. Setiani, and N. M. Nurdin, "Evaluasi Penggunaan Analgetik Pasca Bedah Apendisitis di Rawat Inap RSUP Fatmawati Jakarta," in *Evaluasi Penggunaan Analgetik Pasca Bedah Apendisitis di Rawat Inap RSUP Fatmawati Jakarta*, Jakarta, 2021.

[34] F. Suryaningsih and D. Syamsul, "Patterns of Use of Nonsteroidal Anti-Inflammatory Analgesic Drugs in Emergency Room Pharmacy Services at Regional Hospitals. Dr. Pirngadi Medan," *jisk*, vol. 4, no. 3, pp. 12–17, Dec. 2023, doi: 10.52622/jisk.v4i3.03.

[35] F. Suhaila, M. J. A. Chalil, and A. Yunafri, "Gambaran Manajemen Nyeri Akut Paska Operasi Pada Pasien Yang Menjalani Tindakan Operasi Elektif Di Rsu Haji Medan," *Jurnal Kedokteran dan Kesehatan: Publikasi Ilmiah Fakultas Kedokteran Universitas Sriwijaya*, vol. 11, no. 1, pp. 115–124, 2024.

[36] M. C. N. Setiawati and H. W. Suciati, "Gambaran Penggunaan Analgetika Pada Operasi Orthopedi Di Instalasi Bedah Sentral Rsud Dr. Loekmono Hadi Kudus," *j. ilm. manuntung sains farm. kesehat. jim.*, vol. 7, no. 2, pp. 202–207, Dec. 2021, doi: 10.51352/jim.v7i2.492.

[37] A. M. Lubis, S. Maruanaya, A. R. Tantri, and ..., "The use of combination paracetamol and ibuprofen in postoperative pain after total knee arthroplasty, a randomized controlled trial," *Pain …*. painphysicianjournal.com, 2021. [Online]. Available: https://www.painphysicianjournal.com/current/pdf?article=NzM2Ng%3D%3D\&journal=140

[38] M. Erkal and C. N. Eroglu, "Diclofenac sodium vs. dexketoprofen trometamol: selecting NSAIDs for managing postoperative inflammatory complications after third molar surgery—a randomized clinical trial," *Head Face Med*, vol. 21, no. 1, p. 39, May 2025, doi: 10.1186/s13005-025-00501-0.

[39] D. Milani and D. Davis, "Pain Management Medications," in *StatPearls [Internet]*, Treasure Island (FL): StatPearls Publishing, 2023.

[40] J. Ainun *et al.*, "Pola Penggunaan Analgesik Pasien Bedah Orthopedi di Ruang Gawat Darurat Rs. Ibnu Sina Makassar," *fmj*, vol. 2, no. 7, pp. 496–503, Jul. 2022, doi: 10.33096/fmj.v2i7.99.

[41] Dr. N. J. Dr. Neha Jacob, A. K. A. Aswathy K A, Dr. M. A. M. Dr.Mohammed Asif M, and T. T. Tharuna Thejas, "Potential Drug-Drug Interactions Associated With Nsaids in a Tertiary Care Hospital," *IJPRA*, vol. 10, no. 2, pp. 1041–1053, Feb. 2025, doi: 10.35629/4494-100210411053.

[42] H. Kuroda and Y. Sakao, "Analgesic management after thoracoscopic surgery: recent studies and our experience," *J. Thorac. Dis.*, vol. 10, no. S9, pp. S1050–S1054, Apr. 2018, doi: 10.21037/jtd.2018.04.34.

[43] B. R. Putra, M. A. Yuswar, S. Rizkifani, and J. D. H. Nawawi, "Gambaran Visual Analog Scale (VAS) PASIEN HIPERTENSI DI PUSKESMAS SIANTAN TENGAH PONTIANAK," vol. 1, no. 2, 2024.

[44] Depkes RI, *Pedoman Nasional Pelayanan Kedokteran Tata Laksana Nyeri*. Kementrian Kesehatan Republik Indonesia, 2019.

[45] H. B. A. Putra and A. Subarnas, "Penggunaan Klinis Tramadol Dengan Berbagai Aspeknya," *Farmaka*, vol. 17, no. 2, 2019.

[46] M. Gencer and A. Y. Göçmen, "The relationship between the level of μ-opioid receptor (μORs) and postoperative analgesic use in patients undergoing septoplasty: a prospective randomized controlled trial," *BMC Anesthesiol*, vol. 20, no. 1, p. 230, Dec. 2020, doi: 10.1186/s12871-020-01138-z.

[47] Dr. G. . Bharat, Dr. Tallapudi. Neelima, Dr. Addeapalli. A. S. B. Sarma, Dr. Ujwalasree. Rowthu, and Dr. Kommanapalli. V. Rao, "Comparison Of Ketorolac Versus Ibuprofen For Postoperative Pain Management In Total Abdominal Hystrectomy Surgeries," *IOSRJDMS*, vol. 23, no. 9, pp. 07–12, Sep. 2024, doi: 10.9790/0853-2309080712.

[48] K. Idacahyati, T. Nofianti, G. A. Aswa, and M. Nurfatwa, "Hubungan Tingkat Kejadian Efek Samping Antiinflamasi Non Steroid dengan Usia dan Jenis Kelamin," *JFIKI*, vol. 6, no. 2, p. 56, Mar. 2020, doi: 10.20473/jfiki.v6i22019.56-61.

[49] T.-Y. Chi, H.-M. Zhu, and M. Zhang, "Risk factors associated with nonsteroidal anti-inflammatory drugs (NSAIDs)-induced gastrointestinal bleeding resulting on people over 60 years old in Beijing," *Medicine*, vol. 97, no. 18, p. e0665, May 2018, doi: 10.1097/MD.0000000000010665.

[50] Isnenia, "Penggunaan Non-Steroid Antiinflamatory Drug dan Potensi Interaksi Obatnya Pada Pasien Muskuloskeletal," *PJI*, vol. 6, no. 1, pp. 47–55, Dec. 2020, doi: 10.21776/ub.pji.2020.006.01.8.