

THE SYSTEMATIC REVIEW OF NON-OPIOID ANALGESICS IN ADULTS AFTER MAJOR SURGERY

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ABSTRACT

Background: Following surgery, chronic postsurgical discomfort is frequent. Finding non-opioid analgesics that may be able to stop persistent pain following surgery is crucial, even if these trials frequently lack sufficient funding.

Aims : This systematic review is to review the effects of non-opioid analgesics in adults after major surgery

Methods: By comparing itself to the standards set by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, this study was able to show that it met all of the requirements. So, the experts were able to make sure that the study was as up-to-date as it was possible to be. For this search approach, publications that came out between 2014 and 2024 were taken into account. Several different online reference sources, like Pubmed and SCIENCE DIRECT, were used to do this. It was decided not to take into account review pieces, works that had already been published, or works that were only half done.

Result: In the PubMed database, the results of our search brought up 234 articles, whereas the results of our search on SCIENCE DIRECT brought up 803 articles. The results of the search conducted for the last year of 2014 yielded a total 67 articles for PubMed and 29 articles for SCIENCE DIRECT. In the end, we compiled a total of 6 papers, 5 of which came from PubMed and 1 of which came from SCIENCE DIRECT. We included six research that met the criteria.

Conclusion: In summary, this systematic review contains the postoperative outcomes in patients after treated with intravein non opioid analgetics after surgery than in controls in terms of 24 hours post operative of opioid use, the pain score, hospitalization prior and the occurrence of opioid related adverse events.

Keyword: Non-opioid analgetic, major surgery

INTRODUCTION

General surgery is a medical specialty that includes the surgical treatment of a wide range of diseases, injuries, and disorders. Specializing in operations on the belly, breasts, skin, digestive tract, endocrine system, and other body parts, general surgeons are highly qualified medical specialists. When it comes to the diagnosis, monitoring, and treatment of surgical problems, they frequently take on the role of chief surgeon. General surgery includes both urgent and elective procedures. Elective treatments are prearranged to treat non-life-threatening conditions such as benign tumors, appendicitis, gallbladder diseases, and hernias. Conversely, life-threatening conditions include trauma, perforations, bleeding, and infections are treated with urgent operations.¹

General surgeons manage every step of the surgical care process, including preoperative diagnosis and evaluation, surgical intervention, postoperative care, and follow-up. They work together with other medical professionals, including anesthesiologists, surgical assistants, nurses, and specialists in related fields, to provide comprehensive patient care.¹

The discipline of general surgery is always evolving due to advancements in technology, less intrusive treatments, and surgical methodologies. General surgeons have two options for doing open surgery: they can employ minimally invasive methods like robotic surgery or laparoscopy, which need fewer incisions and specialized equipment. These less intrusive procedures often result in shorter hospital stays, less pain following surgery, and quicker recovery times for the patients. In addition to their surgical expertise, general surgeons provide vital non-operative care, including wound care, managing acute and chronic diseases, and counseling patients on lifestyle modifications and preventative measures. They work along with specialists in several fields, such as vascular surgery, gastrointestinal, oncology, and more, to organize interdisciplinary patient care.^{2,3}

Different levels of acute pain and tissue stress following surgery can have a detrimental effect on a patient's comfort, recovery, and overall well-being. Effective pain management is essential to minimize suffering, promote early mobilization, facilitate rehabilitation, and prevent issues associated with inadequate pain control. The goal of postoperative pain management is to minimize side effects, encourage a speedy recovery, and offer the greatest pain relief available. It uses a multimodal approach that combines a number of techniques and therapies tailored to the patient's needs. A comprehensive pain management plan should consider the patient's general health, the operation, the expected duration of pain (usually two to three months in chronic instances), and the possible risks and benefits of different medications.⁴

One of the mainstays of postoperative pain management is the application of a multimodal analgesic approach. This approach involves the administration of many analgesic medicines with different mechanisms of action to target different pain circuits at different levels. Synergizing medications from different classes, such as opioids, non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, and local anesthetics, can result in higher pain relief with lower dosages of each medication. Negative impacts are less likely as a result. Opioids such as morphine are commonly used to relieve adverse postoperative pain. By affecting the central nervous system, they provide analgesia; however, they also have unfavorable side effects such as constipation, respiratory depression, sleepiness, and the potential for addiction.^{5,6}

Consequently, in order to provide targeted pain relief while reducing the requirement for systemic opioids, opioid-sparing treatments are widely employed. Using localized anesthesia procedures like epidural or peripheral nerve blocks is one of these strategies. Non-opioid analgesics like NSAIDs and paracetamol are majorstays of multimodal analgesia. NSAIDs decrease inflammation via prostaglandin inhibition, which produces prostaglandins, which are inflammatory mediators implicated in pain signaling. Acetaminophen, also referred to as paracetamol, modifies the central nervous system's perception of pain. Both types of medications have analgesic properties and can be used alone or in conjunction with opioids to treat patients with mild to severe pain.^{5,6}

The goal of enhanced recovery after surgery (ERAS) protocols is to expedite recovery and enhance perioperative care. In recent years, there has been an increased focus on these protocols. Pain treatment is an essential component of ERAS protocols, and methods including proactive analgesia, early oral medication intake, and preoperative education are employed to improve pain management and patient outcomes. Healthcare practitioners can effectively manage pain by combining many analgesic modalities, such as opioids, non-opioids, and regional anesthesia, while minimizing side effects and promoting early recovery. Better rehabilitation plans are put into practice, which further enhances pain management and patient outcomes. Tailored pain management regimens based on patient characteristics and surgical procedures are necessary to provide optimal pain relief and improve the surgical experience overall.^{7,8}

METHODS

Protocol

By following the rules provided by Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020, the author of this study made certain that it was up to par with the requirements. This is done to ensure that the conclusions drawn from the inquiry are accurate.

Criteria for Eligibility

For the purpose of this literature review, we review published literature contains the effect of non opioid analgesics on adults after major surgery. This is done to provide an explanation and improve the handling of treatment at the patient. As the main purpose of this paper, to show the relevance of the difficulties that have been identified as a whole.

In order for researchers to take part in the study, it was necessary for them to fulfil the following requirements: 1) The paper needs to be written in English. In order for the manuscript to be considered for publication, it needs to meet both of these requirements. 2) The studied papers include several that were published after 2013, but before the time period that this systematic review deems to be relevant. Examples of studies that are not permitted include editorials, submissions that do not have a DOI, review articles that have already been published, and entries that are essentially identical to journal papers that have already been published.

Search Strategy

We used "non-opioid analgetic" and "major surgery" as keywords. The search for studies to be included in the systematic review was carried out using the PubMed and SCIENCE DIRECT databases by inputting the words: (*"analgesics non narcotic"[Pharmacological Action] OR "analgesics, non narcotic"[MeSH Terms] OR ("analgesics"[All Fields] AND "non narcotic"[All Fields]) OR "non-narcotic analgesics"[All Fields] OR ("non"[All Fields] AND "opioid"[All Fields] AND "analgesic"[All Fields]) OR "non opioid analgesic"[All Fields]) AND ("major"[All Fields] OR "majored"[All Fields] OR "majoring"[All Fields] OR "majorities"[All Fields] OR "majority"[All Fields] OR "majors"[All Fields]) AND ("surgery"[MeSH Subheading] OR "surgery"[All Fields] OR "surgical procedures, operative"[MeSH Terms] OR ("surgical"[All Fields] AND "procedures"[All Fields] AND "operative"[All Fields]) OR "operative surgical procedures"[All Fields] OR "general surgery"[MeSH Terms] OR ("general"[All Fields] AND "surgery"[All Fields]) OR "general surgery"[All Fields] OR "surgery s"[All Fields] OR "surgerys"[All Fields] OR "surgeries"[All Fields])) AND ((clinicaltrial[Filter]) AND (2014:2024[pdat])) used in searching the literature.*

Data retrieval

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

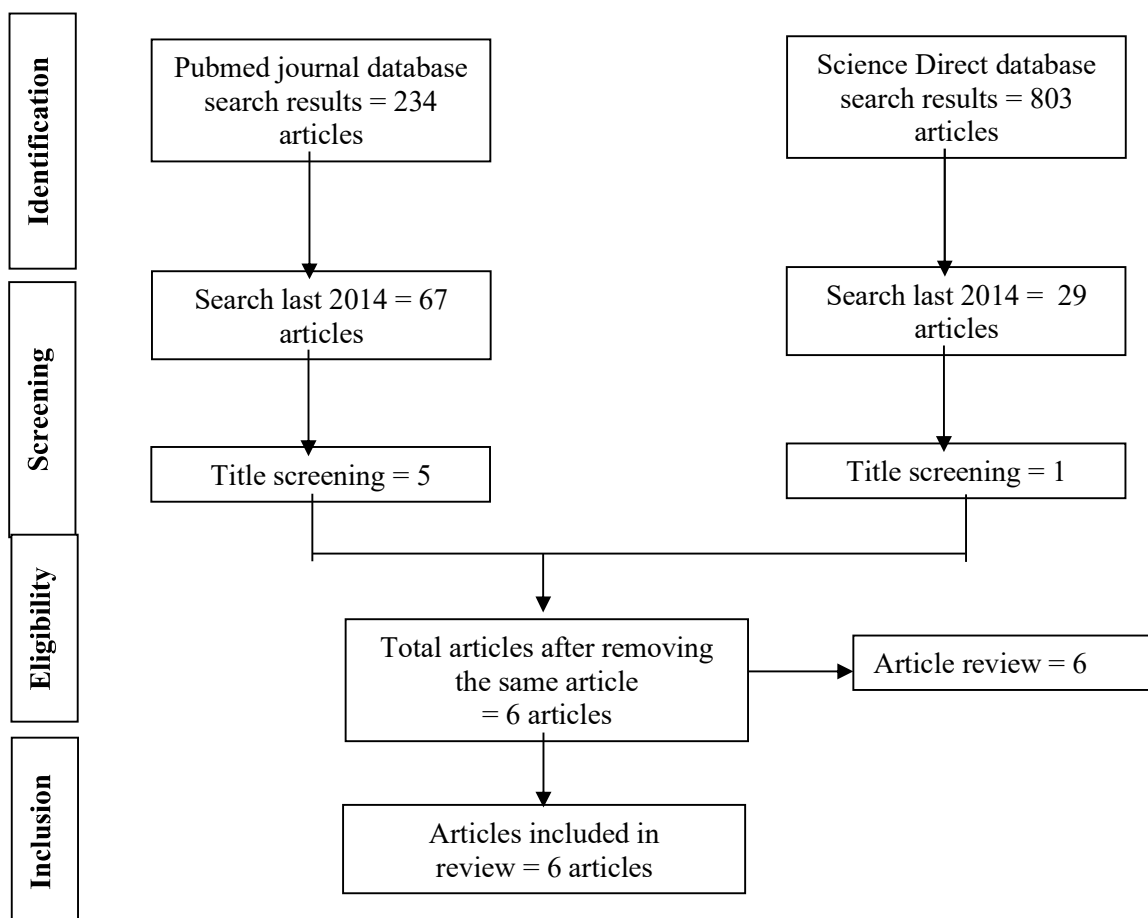


Figure 1. Article search flowchart

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 234 articles, whereas the results of our search on SCIENCE DIRECT brought up 803 articles. The results of the search conducted for the last year of 2014 yielded a total 67 articles for PubMed and 29 articles for SCIENCE DIRECT. In the end, we compiled a total of 6 papers, 5 of which came from PubMed and 1 of which came from SCIENCE DIRECT. We included six research that met the criteria.

Beloil, et al⁹ (2019) showed that when three NOAs—paracetamol, nefopam, and ketoprofen—are combined with morphine, there is a notable reduction in morphine use for 48 hours following surgery, which is linked to better analgesia during the first 24 hours following surgery.

Takeda, et al¹⁰ (2019) showed that following initial total hip arthroplasty (THA), postoperative intravenous acetaminophen (IA) treatment dramatically decreased both the postoperative pain score and the amount of opioids consumed. After THA, IA was helpful as one aspect of multimodal pain treatment.

Bollinger, et al¹¹ (2015) showed that pain management is a crucial part of patient care for older patients with hip fractures, however using opioids can be challenging for a variety of reasons. A systematic procedure for geriatric hip fractures that includes planned perioperative IV acetaminophen has been shown to be effective in reducing hospital length of stay, managing pain and reducing opioid usage, enhancing PT participation, and raising the rate of home release. IV acetaminophen has been shown to be beneficial in other orthopedic specialties, and this study backs up its usage in the elderly hip fracture group.

Table 1. The literature include in this study

Author	Origin	Method	Sample	Result
Beloil et al, 2019⁹	France	Randomized controlled study	237 patients	Between July 2013 and November 2016, 237 patients undergoing major surgery were included in the study. The PNK group's 24-hour morphine intake [median (inter-quartile range)] was considerably lower than that of the C group [27 (11-42) mg; P<0.05] or the N group [21 (12-29) mg; P<0.05], even if the sample size was not reached. 48 hours following surgery, the results were comparable. In comparison to the C, N, and P groups, the PNK group's patients reported feeling less discomfort. There was no discernible variation in the frequency of adverse effects associated with morphine.

Takeda et al, 2019¹⁰	Japan	Randomized controlled study	97 patients	The Numerical Rating Scale score of the IA group was significantly higher at rest 24 hours after THA than that of the control group (-0.91, 95% confidence range -1.56 to -0.26, P =.006), indicating that using IAs might be beneficial for pain management. Following surgery, the IA group consumed considerably less fentanyl citrate overall over the course of 24 hours than the control group (52.07 ± 7.64 mg vs. 57.83 ± 12.44 mg, P <.001).
Bollinger et al, 2015¹¹	USA	Retrospective study	332 patients	A statistically significant difference was seen between Group 2 and Group 1 in terms of the mean length of hospital stay (4.4 vs 3.8 days), mean pain score (4.2 vs 2.8), mean narcotic consumption (41.3 vs 28.3 mg), rate of missed PT sessions (21.8% vs 10.4%), and likelihood of release home (7% vs 19%; P ≤.001). Additionally, the same characteristics were consistently and independently predicted by IV acetaminophen use (P <.01).
Connolly et al, 2020¹²	USA	Retrospective study	123 patients	During this time, 65 patients (52.8%) got acetaminophen via IV. There were no appreciable variations in the groups' baseline characteristics. After surgery, delirium struck 10 out of 65 patients who received IV acetaminophen, whereas 19 out of 58 patients who did not receive the drug suffered from delirium (15.4% versus 32.8%, P = 0.024). Additionally, on the first postoperative day after surgery, the IV acetaminophen group needed fewer IV opioid doses (0.37 versus 1.19 doses, P = 0.008), was less likely to need one-on-one monitoring (9.2% against 24.1%, P = 0.025), and spent less time in the hospital (6.37 compared 8.47 days, P = 0.037). The two groups' readmission rates and discharge policies did not significantly differ from one another.
Xiao et al, 2019¹³	China	Randomized controlled study	180 patients	141 patients in all were recruited and randomized into two groups: the control group (n = 72) and the PS group (n =

				69). After the operation, the PS group's VAS ratings at rest and during movement were considerably lower in the PS group at 4, 12, 24, 36, and 48 hours after surgery (all $P < 0.001$) as compared to the control group. Regarding all outcomes, including blood loss, postoperative blood drainage and transfusion, and the number of days required to complete straight-leg raising and off-bed exercise, there was no statistically significant difference between the PS group and the control group.
Wang et al, 2023¹⁴	China	Randomized controlled study	106 patients	A total of 106 patients were enrolled and randomly allocated to the VC-ESPB group (n = 53) and the conventional group (n = 53) between October 30, 2019, and May 1, 2023. The rate of nonsteroidal anti-inflammatory medication rescue analgesia was comparable in the VC-ESPB group and the conventional group within the first 48 hours following surgery. Both the conventional group (n = 0, 0%) and the VC-ESPB group (n = 0, 0%) did not have any treatment-related deaths. One patient in the VC-ESPB group experienced local site paralysis (n = 1, 2.0%), while another patient experienced rash (n = 1, 2.0%). There was one patient (n = 1, 2.0%) in the conventional group who had a rash before surgery. Postoperative nausea and vomiting rates were markedly reduced in the VC-ESPB group, as was the frequency of severe sequelae.

Connolly, et al¹² (2020) showed that the addition of IV acetaminophen to a multimodal pain regimen resulted in a reduction in delirium episodes. This result could have been mostly attributed to the decreased usage of painkillers just after surgery. Shorter hospital stays might result from lower delirium rates, which would also lessen the need for inpatient services for direct patient supervision.

Xiao, et al¹³ (2019) showed that in a multimodal regimen, perioperative PS administration effectively lowers surgical pain, length of hospital stay, cumulative morphine consumption, and perioperative inflammatory response without raising the risk of perioperative hemorrhage.

Wang, et al¹⁴ (2023) showed that For patients with hepatocellular carcinoma (HCC) undergoing open major hepatectomy (OMH), visualised continuous opioid-free erector spinae plane block (VC-ESPB) demonstrated noninferiority when compared to traditional opioid-based postoperative pain treatment, suggesting that full opioid-free postoperative pain

management is achievable. The OMH textbook result is improved and postoperative recovery is enhanced by the safer, more practical, and better aftereffects of VC-ESPB.

DISCUSSION

Twenty to thirty percent of surgical patients may experience chronic postsurgical pain (CPSP), which can have serious repercussions for the patient. According to the James Lind Alliance, CPSP is the eleventh most important research priority across all anesthetic disciplines. The gold standard for managing acute pain, non-opioid analgesia, may help lower CPSP via lowering acute pain or by targeting certain molecules that cause perioperative sensitization.¹⁵

For the purpose of controlling postoperative pain, non-opioid analgesics are crucial, both when used alone and in conjunction with other analgesics. These medications help lessen the risks and side effects associated with opioids while providing effective pain relief. NSAIDs, such as ibuprofen, diclofenac, and ketorolac, are often used due to their strong analgesic and anti-inflammatory properties. They stop prostaglandins from being synthesized, which causes pain and inflammation. NSAIDs are particularly beneficial for inflammatory pain, such as discomfort after abdominal or orthopedic surgery. It is advised to use caution while giving NSAIDs to people who have a history of cardiovascular disease, renal insufficiency, or gastrointestinal bleeding.¹⁶

Acetaminophen is useful for treating mild to severe postoperative pain and is often used in combination with other analgesics. It has an acceptable safety profile when taken as prescribed; nevertheless, prolonged or excessive use may cause liver damage. The word "synergism" refers to the enhanced analgesic or pain-relieving effect that comes from combining nonsteroidal anti-inflammatory drugs (NSAIDs) with paracetamol (acetaminophen) as opposed to using them alone. Their different ways of working together create a synergy that might aid in pain management.¹⁶

Local anesthetics like bupivacaine or lidocaine can be used in a number of ways to control pain following surgery. Catheters in the wound or local anesthetic injections into the surgical site are two ways to provide targeted pain control. When implementing regional anesthesia techniques such as peripheral nerve blocks or epidural analgesia, local anesthetics are utilized to block pain signals originating from specific locations. These techniques can successfully control pain and may reduce the need for opioids and other systemic analgesics.¹⁶

A multimodal strategy is required for effective postoperative pain management, which is essential for patient comfort and recovery. This involves mixing several analgesics in order to reduce risks and adverse effects. Although they are useful, opioids should only be taken sparingly because of possible side effects. Both opioids and non-opioid alternatives, such as NSAIDs and paracetamol, have their uses. Techniques for regional anesthetic, such as nerve blocks, can lessen the requirement for systemic opioids. When opioids alone are insufficient to treat neuropathic pain, adjuvant medicines may be taken into consideration. It is critical to customize treatment based on patient-specific criteria such as age, comorbidities, and surgical technique. To maintain efficient pain management and make necessary adjustments to treatment regimens, ongoing monitoring is necessary.

CONCLUSION

In summary, this systematic review contains the postoperative outcomes in patients after treated with intravein non opioid analgetics after surgery than in controls in terms of 24 hours post operative of opioid use, the pain score, hospitalization prior and the occurrence of opioid related adverse events.

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