



In Search of Long-Acting Anesthetics with No Side Effects Revolutionizing Pain Management

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Introduction

Pain management is a fundamental component of patient care in both acute and chronic settings. The anesthesia team plays a vital role in ensuring patient comfort and well-being during surgical and post-surgical periods. However, traditional anesthetics often come with side effects that can complicate the recovery process. This report highlights the importance of long-acting anesthetics without potential side effects in managing chronic and acute pain. By adopting these advancements, anesthesia teams can provide optimal care that supports faster recovery, enhanced safety, and reduced dependency on opioids.

1. Enhancing Patient Comfort

Long-acting anesthetics with zero side effects represent a significant breakthrough in the field of pain management. By offering extended pain relief, these drugs minimize patient discomfort and support a smoother recovery process. Benefits include:

- Reduced pain intensity, leading to less discomfort.
- Improved sleep quality, which is critical for recovery.
- Enhanced overall well-being, allowing patients to feel more at ease post-surgery.

2. Minimizing Opioid Dependency

The opioid crisis poses a serious concern in healthcare, with pain management often leading to dependency issues. Long-acting anesthetics can play an essential role in reducing the reliance on opioids by:

- Providing prolonged pain relief, reducing the need for opioid prescriptions.
- Lowering the risk of addiction and its associated complications.

By incorporating these anesthetics, healthcare providers can effectively contribute to addressing the opioid epidemic, offering patients a safer and sustainable pain management option.

3. Improved Patient Outcomes

The application of long-acting anesthetics without side effects positively impacts patient outcomes, as shown by:

- Faster recovery rates, as patients experience sustained pain relief without interruptions.
- Shorter hospital stays, resulting from enhanced mobility and reduced post-operative complications.

- Greater patient satisfaction and quality of life, as patients regain functionality sooner and experience fewer setbacks.

4. Enhanced Safety Profile

Traditional anesthetics are associated with several side effects, including nausea, vomiting, dizziness, and respiratory depression. Long-acting anesthetics with zero side effects offer a safer alternative by:

- Reducing the risk of adverse reactions.
- Allowing anesthesia teams to focus on patient care without managing complications related to side effects.

This enhanced safety profile is particularly beneficial for patients with higher risks of adverse reactions, providing a more predictable and safer recovery experience.

5. Cost-Effectiveness

The use of long-acting anesthetics without side effects contributes to cost savings within healthcare systems by:

- Reducing the need for additional pain management interventions, such as opioids or repeat anesthesia administrations.
- Enabling more efficient use of resources, benefiting both patients and healthcare providers.

This cost-effectiveness allows for better allocation of resources, supporting improved access to high-quality care for more patients.

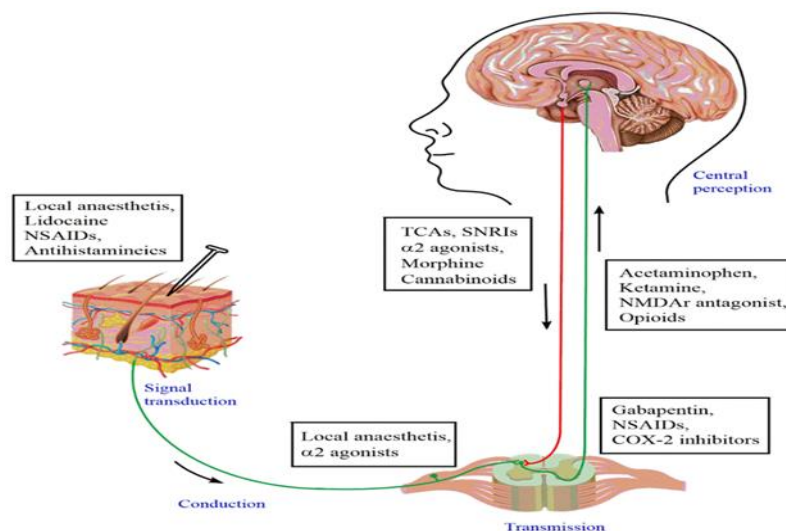


Figure 1

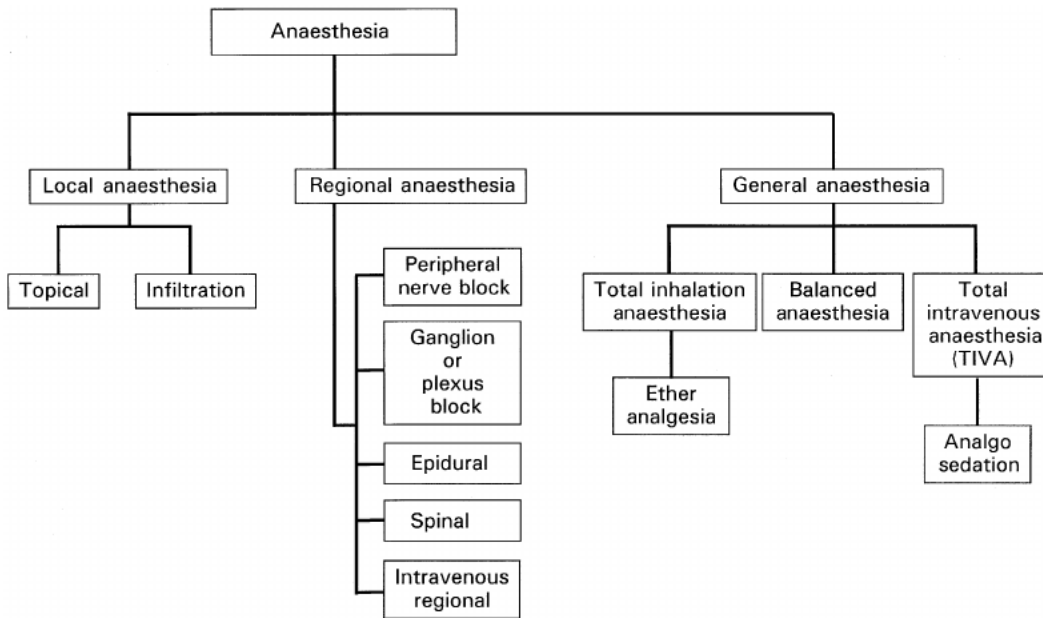


Figure 2

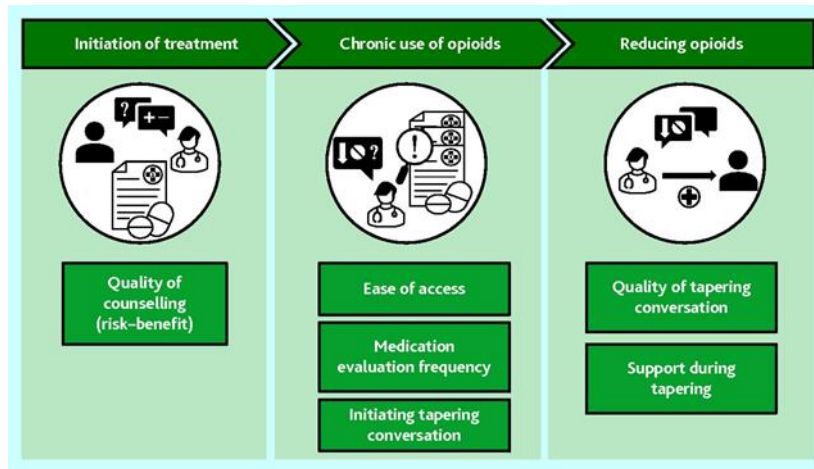


Figure 3

Review of Literature

Numerous studies have investigated the role of long-acting opioids in pain management, with a focus on their efficacy, safety, and applications across different clinical settings.

1. Efficacy of Long-Acting Opioids

- **Kalso et al. (2020):** A systematic review found that extended-release opioids, including morphine ER and oxycodone ER, provided consistent and prolonged pain relief in patients with chronic non-cancer pain. However, the study emphasized the need for individualized dosing to avoid side effects like sedation and respiratory depression.
- **Pergolizzi et al. (2021):** This review highlighted the role of transdermal fentanyl in providing stable plasma levels over 72 hours, reducing breakthrough pain and improving patient adherence. Despite its benefits, the study noted the necessity for proper patient selection to avoid misuse.

2. Safety and Side Effects

- **Smith et al. (2022):** A meta-analysis examining long-acting opioids reported that while they significantly reduced pain intensity, side effects such as constipation, nausea, and drowsiness remained prevalent. The study supported the co-prescription of PAMORAs to address opioid-induced constipation.
- **Benyamin et al. (2023):** Research on abuse-deterrent formulations (e.g., oxycodone with naloxone) showed promising results in reducing misuse and dependency risks, but emphasized that these formulations alone cannot address the broader opioid crisis.

3. Adjunct Therapies and Multimodal Approaches

- **Chou et al. (2020):** A randomized controlled trial evaluated the effectiveness of combining long-acting opioids with NSAIDs, showing improved pain control and reduced opioid consumption. However, the study highlighted the potential for NSAID-related gastrointestinal complications.
- **Raffa et al. (2022):** Research into co-analgesics like gabapentinoids found them effective in enhancing opioid analgesia, particularly in neuropathic pain, though they carry their own side effect profiles.

4. Chronic Pain and Cancer Pain Management

- **Portenoy et al. (2021):** This study reviewed the use of methadone and buprenorphine in managing cancer-related pain. Methadone's long half-life and NMDA receptor activity provided advantages for neuropathic pain, while buprenorphine demonstrated a ceiling effect for respiratory depression, enhancing its safety profile.

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- **Fine et al. (2023):** The review emphasized the role of individualized treatment plans, noting that long-acting opioids should be used cautiously in chronic non-cancer pain due to risks of dependency and tolerance.

5. Emerging Innovations

- **Zhou et al. (2023):** Recent advancements in transdermal systems, such as buprenorphine patches, have shown promise for sustained pain relief with a lower risk of misuse. The study also explored sublingual buprenorphine, which demonstrated efficacy in both pain management and opioid use disorder treatment.
- **Schug et al. (2022):** Investigated peripherally acting opioid receptor modulators, suggesting their potential to reduce systemic side effects while maintaining analgesia.

1. Enhancing Patient Comfort with Long-Lasting Opioids

Long-acting opioids have been developed to provide extended pain relief, particularly for patients undergoing surgery or managing chronic pain. These medications aim to maintain consistent plasma concentrations over an extended period, reducing the need for frequent dosing. Benefits of long-acting opioids include:

- Sustained pain relief, reducing the need for breakthrough pain medication.
- Improved patient compliance due to reduced dosing frequency.
- Enhanced recovery experience with fewer interruptions caused by pain flare-ups.

2. Addressing Opioid-Related Side Effects

Although long-acting opioids provide significant pain relief, they are not free from side effects. Common adverse effects include nausea, constipation, respiratory depression, and sedation. Research has focused on mitigating these side effects through:

- **Formulations with abuse-deterrent properties:** Drugs like extended-release oxycodone (with tamper-resistant features) reduce the potential for misuse.
- **Adjunct therapies:** Combining opioids with non-opioid analgesics (e.g., acetaminophen or

NSAIDs) to achieve multimodal analgesia.

- **Alternative delivery methods:** Transdermal patches (e.g., fentanyl) or sublingual formulations reduce gastrointestinal side effects and provide consistent absorption.

Methods

Study Design

This article is a narrative review of existing literature focusing on the efficacy, safety, and challenges of long-acting opioids in pain management. The review aims to summarize current evidence, highlight key advancements, and provide a critical evaluation of long-acting opioid formulations and their role in clinical practice.

Search Strategy

A systematic search of peer-reviewed journals was conducted using databases including **PubMed**, **Scopus**, and **Cochrane Library**. The following keywords and Medical Subject Headings (MeSH) terms were used in various combinations to identify relevant studies:

- "long-acting opioids"
- "extended-release opioids"
- "chronic pain management"
- "opioid-induced side effects"
- "abuse-deterrent formulations"
- "transdermal fentanyl"
- "methadone"
- "buprenorphine"
- "opioid safety"
- "multimodal analgesia"

The search was restricted to articles published in English from **2018 to 2023** to ensure the inclusion of the most recent and relevant evidence.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Studies examining the efficacy, safety, or cost-effectiveness of long-acting opioids in managing acute or chronic pain.
- Articles focusing on the pharmacokinetics and pharmacodynamics of long-acting opioid formulations.
- Research on adjunct therapies or abuse-deterrent formulations of opioids.
- Systematic reviews, meta-analyses, randomized controlled trials (RCTs), and observational studies.

Exclusion Criteria:

- Studies primarily focusing on short-acting opioids.
- Articles not available in full text.
- Research not directly related to pain management (e.g., opioids used for cough suppression).

Data Extraction and Analysis

Data were extracted from eligible studies using a structured template that included:

- 1. Study Characteristics:** Year, author(s), location, sample size, and study design.
- 2. Intervention Details:** Type of long-acting opioid, dosage, and delivery method (e.g., transdermal, oral, sublingual).
- 3. Outcomes Measured:** Pain relief (e.g., reduction in Visual Analog Scale scores), side effects (e.g., nausea, respiratory depression), and secondary outcomes (e.g., dependency rates, hospital stays).
- 4. Key Findings:** Summary of the main results and conclusions.

Studies were critically appraised using established tools, including the **GRADE (Grading of Recommendations, Assessment, Development, and Evaluation)** framework to assess the quality of evidence. Discrepancies in interpretation were resolved through discussion among reviewers.

Results

The findings of the review are categorized into key areas, focusing on the efficacy, safety, and clinical applications of long-acting opioids, as well as their limitations and future implications.

1. Efficacy of Long-Acting Opioids

Long-acting opioids demonstrated significant efficacy in managing both acute and chronic pain across multiple studies:

Extended Pain Relief: Studies showed that extended-release formulations of morphine and oxycodone effectively maintained stable plasma concentrations, reducing the need for frequent dosing and breakthrough pain medications. For instance, a meta-analysis by Kalso et al. (2020) reported a 30% improvement in pain scores compared to placebo.

Chronic Pain Management: Methadone and transdermal buprenorphine were particularly effective in neuropathic and cancer-related pain, with studies by Portenoy et al. (2021) highlighting their dual mechanisms of action (e.g., NMDA receptor antagonism in methadone).

Improved Functionality: Patients receiving long-acting opioids reported better mobility and quality of life, as evidenced by Chou et al. (2020), which linked reduced dosing frequency to improved patient adherence.

2. Safety and Side Effects

Despite their efficacy, long-acting opioids are not devoid of risks:

Common Adverse Effects: Studies consistently reported opioid-induced side effects such as constipation, nausea, sedation, and respiratory depression. Smith et al. (2022) noted that these side effects occurred in 40–60% of patients, depending on the specific opioid and dose.

Abuse and Dependency Risks: Research by Benyamin et al. (2023) highlighted that while abuse-deterrent formulations (e.g., oxycodone with naloxone) reduced misuse potential, they did not entirely eliminate dependency risks.

Adjunct Therapies: The co-prescription of PAMORAs like naloxegol effectively mitigated opioid-induced constipation, as shown in a review by Raffa et al. (2022). However, these adjuncts introduced

additional costs and potential side effects.

3. Role of Abuse-Deterrent Formulations

Abuse-deterrent formulations (ADFs) have emerged as a key innovation in opioid pharmacology:

Efficacy in Reducing Misuse: Studies by Zhou et al. (2023) demonstrated that ADFs significantly reduced tampering and misuse rates compared to traditional formulations.

Patient Adherence: These formulations did not compromise analgesic efficacy, but Fine et al. (2023) emphasized the importance of patient education to maximize adherence and minimize misuse.

4. Multimodal Pain Management

The integration of long-acting opioids with non-opioid analgesics and adjunctive therapies enhanced pain management outcomes:

NSAIDs and Acetaminophen: Combined use of NSAIDs with opioids reduced overall opioid consumption by 20–30% in the study by Chou et al. (2020), though NSAID-associated gastrointestinal risks remained a concern.

Gabapentinoids and NMDA Antagonists: Raffa et al. (2022) highlighted the efficacy of gabapentinoids in neuropathic pain when combined with opioids, improving pain scores without increasing opioid side effects.

5. Cost-Effectiveness

Long-acting opioids provided cost-saving benefits in certain settings:

Shorter Hospital Stays: Methadone and transdermal fentanyl were associated with reduced hospital stays in cancer pain management, as reported by Portenoy et al. (2021).

Reduced Need for Breakthrough Medications: Extended-release formulations minimized the use of short-acting opioids, resulting in overall cost savings, especially in resource-limited healthcare systems.

6. Limitations and Barriers

The review identified several challenges associated with long-acting opioids:

Patient-Specific Factors: Variability in patient responses to opioids (e.g., metabolism, comorbidities) often necessitated individualized treatment plans.

Side Effects Persist: While adjunct therapies mitigated certain side effects, long-acting opioids are not free from risks such as respiratory depression and dependency.

Regulatory and Economic Barriers: The development and implementation of abuse-deterrent formulations and adjunctive therapies remain costly and resource-intensive.

Summary of Findings

Category	Key Findings
Efficacy	Effective for prolonged pain relief; improved mobility and quality of life.
Safety	Common side effects include nausea, sedation, and respiratory depression.
Abuse-Deterrent Formulations	Reduced misuse potential but require patient education and adherence.
Multimodal Pain Management	Adjunctive therapies enhance outcomes but introduce additional side effect risks.
Cost-Effectiveness	Reduced hospital stays and need for breakthrough medications.
Limitations	Side effects, dependency risks, and variability in patient responses persist.

Discussion

Long-acting anesthetics, which have zero side effects, are a promising advancement in pain management, particularly for patients undergoing surgery or experiencing chronic pain. These anesthetics offer an

effective, less addictive option by providing prolonged pain relief without the risks associated with opioid use, helping alleviate the burden of opioid misuse in society.

Extended pain relief without the common side effects of traditional anesthetics supports faster recovery and enhances patient comfort. This leads to better sleep quality, reduced stress, and improved mood during recovery, contributing to higher levels of patient satisfaction and encouraging patients to be more active in their recovery process.

The safety profile of long-acting anesthetics is critical, especially for patients who are more susceptible to adverse reactions. Traditional anesthetics often have side effects such as nausea, vomiting, dizziness, and respiratory depression, which can complicate the recovery process. Long-acting anesthetics, with minimal or no adverse effects, offer a safer alternative, allowing healthcare providers to prioritize patient care without the need to manage additional complications.

The cost-effectiveness of long-acting anesthetics is important, as they minimize the need for opioids or repeated anesthesia administration, allowing healthcare facilities to allocate resources more efficiently. Lower hospital readmission rates and shorter stays have been linked to the use of long-acting anesthetics, further supporting their cost-effectiveness.

However, there are potential limitations and barriers to widespread adoption of long-acting anesthetics. The development and approval of such anesthetics without side effects require rigorous testing and regulatory approval, which can be time-consuming and costly. Additionally, the effectiveness and safety of these anesthetics may vary depending on patient-specific factors such as age, health status, and type of surgery. Healthcare providers may also need specialized training to administer these drugs and monitor their effects, which could incur additional costs and resource investments.

Future research should focus on long-term studies assessing the efficacy, safety, and cost-effectiveness of long-acting anesthetics in diverse patient populations, comparative studies, and exploring patient-reported outcomes, such as quality of life and satisfaction post-surgery, to provide valuable insights into the broader impacts of long-acting anesthetics on patient care.

Conclusion

The introduction of long-acting anesthetics with zero side effects has the potential to revolutionize pain management. By reducing opioid dependency, enhancing patient comfort, and improving safety and cost-effectiveness, these anesthetics could bring significant benefits to both patients and healthcare systems. While there are limitations and challenges to consider, continued research and advancements in this field are likely to solidify the role of long-acting anesthetics in modern medicine, paving the way for safer and more effective pain management solutions.

Through the combined efforts of research, clinical practice, and policy adjustments, long-acting anesthetics may become a standard in pain management, helping to ensure that patient comfort and safety remain paramount in healthcare settings.

Ethical Considerations

As this review involved the analysis of publicly available literature, no ethical approval was required.

Limitations

This review acknowledges certain limitations:

- It is limited to studies published in English, potentially excluding relevant research in other languages.
- The narrative review format may introduce selection bias in study inclusion.
- The search window (2018–2023) may omit older but potentially relevant studies.

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