REVIEW ARTICLE

Post-operative Analgesia from Preemptive to Preventive Approach: Evolution and Clinical Implications

Ahmed Abodonya[1,2]

[1]Department of Surgery, College of Medicine, Prince Sattam Bin Abdulaziz University, Alkharj, Saudi Arabia, [2]Department of Anesthesia, Intensive Care, and Pain Management, Faculty of Medicine, Al-Azhar University, Cairo, Egypt

Abstract

Pain management has shifted from a reactive approach to a proactive strategy focused on prevention. This study analyzes the development, neurophysiological foundation, and clinical uses of preemptive and preventive analgesia in the perioperative setting. Regardless of advancements in analgesic approaches, post-operative pain is frequently insufficiently managed in numerous sufferers, with more than 80% experiencing moderate-to-severe discomfort and up to 50% developing chronic pain after specific procedures. The shift from preemptive analgesia (interventions before surgical incision) to preventative analgesia (interventions during the perioperative phase) signifies our improved comprehension of pain processes. This article examines pain assessment tools, technological advancements, and evidence-based methodologies for implementing efficient perioperative pain management procedures. Multimodal strategies integrating pharmacological treatments, regional anesthesia procedures, and personalized care plans demonstrated substantial enhancements in patient outcomes, such as diminished pain severity, reduced opioid usage, and a lower occurrence of chronic postsurgical pain. Future directions highlight individualized analgesic regimens, the use of artificial intelligence, and ongoing research into innovative treatment strategies to optimize pain management and improve post-operative recovery.

Key words: Post-operative analgesia, preemptive analgesia, preventive analgesia

INTRODUCTION

The revised definition of pain, adopted in 2020, states that pain is "an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage." The new definition reflects that pain is more multifaceted than just nociception.[1] Studies consistently reveal that more than eighty percent of patients have moderate to severe pain following surgical procedures. This is to be expected despite the fact that there have been considerable advancements in analgesics and modern drug delivery methods. The significance of the need for improved treatment solutions comes into focus for those concerned.[2] The high incidence of prolonged post-operative pain is particularly concerning, impacting nearly 50% of patients following thoracotomy and mastectomy surgeries.[3] Perioperative pain management has evolved considerably, transitioning from reactive treatment approaches to proactive prevention strategies. This paradigm shift demonstrates an enhanced understanding of how surgical trauma impacts the neurological system and pain perception. The conventional method of administering analgesics only after pain manifests is increasingly being replaced by advanced preventive treatments that address pain pathways before, during, and after surgical interventions.[4] A fundamental shift occurred when researchers recognized that surgical incision is not the sole trigger of central sensitization. The understanding expanded to include pre-operative noxious inputs, intraoperative stimuli, and post-operative inflammatory mediators.[4] Individual variation in post-operative pain intensity requires personalized approaches to pain management. Modern practices incorporate

Address for correspondence:
Ahmed Abodonya, Department of surgery, College of Medicine, Prince Sattam bin Abdulaziz University, Al-Kharj, Saudi Arabia.
E-mail: a.abodonya@psau.edu.sa

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telemedicine and continue post-operative monitoring to improve patient outcomes. This development has resulted in a variety of provisional pain programs and perioperative surgical places that employ multiple strategies, including education, rehabilitation, and multimodal pharmacologic and non-pharmacologic therapies.[5] Inadequate pain management is adversely affecting patient recovery and overall health outcomes. Irrespective of progress in pain management techniques, many patients still encounter insufficient relief from post-operative pain.[6] Inadequate management of post-operative pain has consequences that extend beyond the discomfort that arises immediately. Patients with suboptimal pain control often face delayed mobilization, prolonged hospital stays, and increased risk of complications.[7] Furthermore, it may result in the development of chronic pain syndromes, adversely affecting the patient's quality of life in the long term.[8]

POST-OPERATIVE PAIN MANAGEMENT: FROM REACTIVE TO PROACTIVE APPROACHES

Reactive pain management has been the standard post-operative care for years, with interventions starting after pain manifestation or patient complaints. This reactive approach has significant drawbacks that adversely affect patients. When pain escalates before treatment, higher opioid doses are needed to relieve it, resulting in a cycle of rising pharmaceutical needs.[9] This reactive model often causes considerable pain before medication, which impairs recovery by increasing anxiety, sleep disruptions, and pain control. Opioids as primary analgesics can also cause respiratory depression, nausea, and constipation, which can slow recovery and lengthen hospital stays.[7] Preventive analgesia and other proactive pain management measures improve post-operative results. Preemptive to preventive analgesia originates from a deeper understanding of post-operative pain's multifaceted causes. According to research, incisions alone do not cause central sensitization. Instead, pre-operative pain conditions, intraoperative stimuli such as tissue retraction and organ manipulation, and post-operative inflammatory responses increase pain perception and may cause long-term hyperalgesia and allodynia.[4] Although pain management has improved, many patients still have inadequate post-operative pain relief.[6] Inadequate post-operative pain management arises from a complex interaction of individual patient characteristics and systemic healthcare conditions. Epidemiological studies have identified various demographic and clinical predictors of ineffective pain management, including younger age, female gender, tobacco use, psychological comorbidities (notably depression and anxiety), sleep disorders, elevated body mass index, preexisting pain conditions, and previous analgesic use.[10] The clinical view is further complicated by chronic diseases, continuous medication, and age-related physiological changes that alter analgesic pharmacokinetics and pharmacodynamics, consequently complicating standard pain management methods.[11] In resource-limited healthcare settings, such as African healthcare systems, medication supply chain disruptions, inadequate healthcare practitioner training, and essential resource shortages make pain management difficult.[12] Besides these actual limits, procedural and communication issues, including insufficient pain assessment, clinician-patient conversation, and unrealistic pain management expectations, further hinder therapeutic results. The convergence of these factors, along with an overreliance on reactive "as-needed" analgesic protocols, inadequate treatment customization, and the neglect of evidence-based multimodal analgesic methods, worsens post-operative pain management in modern clinical practice.[13]

HISTORICAL PERSPECTIVE: FROM REACTIVE TO PROACTIVE APPROACHES

Pain therapy has developed throughout the centuries due to scientific understanding, societal attitudes, and medical practices. Magico-religious ideas affected ancient Egyptian, Sumerian, Assyrian, and Greek therapies. They used natural medications such as opium and laudanum, whereas the Hippocratic approach established contemporary palliative care with a methodical and interdisciplinary approach.[14] The Islamic era served as an essential intersection, bridging ancient Pharaonic or Greek medicine with the modern Renaissance period. With a good diagnosis, Ibn Sina began addressing the cause of pain. He differentiated between hypnotics and analgesics using medicines to induce sleep and decrease the feeling of pain.[15] The 19th century marked a crucial turning point with the development of modern pain theories, the synthesis of analgesics, and the introduction of surgical anesthesia, despite initial ethical reservations.[16] This evolution continued into the 20th century with the establishment of pain clinics and the rise of multidisciplinary teams, demonstrated by John J. Bonica's pioneering work in founding the first multidisciplinary pain clinic in 1947.[17] More recently, the recognition of pain as the "Fifth Vital Sign" has underscored its critical role in healthcare, prompting a shift from an opioid-centric model to diverse, multimodal treatment strategies.[18,19] This transition from reactive pain treatment, which was widely used in the 1960s and 1970s, often led to unsatisfactory outcomes. In the 1980s, this approach shifted to preemptive analgesia.[20] Preventive analgesia, developed in the 2000s, aimed to limit pain sensitisation throughout the entire perioperative period.[5,20,21] Currently, nonopioid multimodal analgesia is a cornerstone of modern pain care. This proven and effective technique reduces opioid use and associated complications.[22] In the current decade, research is progressively focused on tailoring preventive analgesia to meet the unique needs of individual patients to optimize long-term outcomes.[23]

NEUROPHYSIOLOGY OF PAIN AND BIOPSYCHOSOCIAL MODEL

Understanding the neurophysiology of pain is crucial for efficient perioperative pain management. Pain signal processing represents four primary components: Transduction, transmission, modulation, and perception.[24] The system initiates at peripheral nociceptive receptors located throughout the body and concludes at the cerebral somatosensory cortex. Each component offers possible avenues for therapeutic intervention to alter the pain experience.[25] Transduction occurs when nociceptors convert unpleasant impulses into electrical signals. Mechanical, chemical, and heat stimuli activate transient receptor potential and acid-sensing ion channels. Transmission occurs when signals from the injury site reach the central nervous system via Aδ and C fibers, which send nociceptive information to the spinal cord. These signals are processed in the dorsal horn's substantia gelatinosa before being sent to higher brain centers.[26] Modulation refers to the mechanisms that affect the intensity and quality of pain perception. This occurs at various levels related to the spinal cord and brain. Different neurotransmitters and intraneuronal circuits function to either enhance or attenuate pain signals. Serotonergic and enkephalinergic pathways can suppress pain transmission, yielding a natural analgesic effect.[27] Perception is the end phase, wherein the brain analyzes pain signals by synthesizing sensory and emotional elements. This extends to various brain regions, commonly termed the "pain matrix," which includes the somatosensory cortices, anterior cingulate cortex, and insular cortex.[27] Modern pain science recognizes that pain extends beyond a simple reflection of tissue damage to encompass a complex interplay of biological, psychological, and social elements. This biopsychosocial model has transformed approaches to pain management, particularly in surgical contexts. The model incorporates biological factors, such as tissue damage and nervous system sensitization; psychological factors, including anxiety, depression, and pain catastrophizing; and social factors involving cultural background and environmental stressors. By addressing all these components, healthcare providers can develop more comprehensive and effective pain treatment strategies.[28,29]

MECHANISMS OF POST-OPERATIVE PAIN

Post-operative pain refers to various interrelated processes. Peripheral nociceptors are initially activated by tissue injury, primarily through inflammatory mediators such as prostaglandins, cytokines, and chemokines.[30] Mediators such as CC chemokine ligand 17 (CCL17) and CCL22, secreted by skin-resident dendritic cells, exacerbate inflammatory and neurogenic mechanisms and activate sensory neurons through the C-C chemokine receptor 4 (CCR4) receptor, indicating a possible therapeutic target.[31] Central sensitization arises after the initial activation of nociceptors, enhancing the excitability of spinal cord and brain neurons by modifying the equilibrium of excitatory and inhibitory impulses, as regulated by brainstem circuits. Neuroinflammation, marked by the activation of glial cells in the central nervous system and the consequent release of cytokines, intensifies the process of central sensitization.[32] Furthermore, interactions among immune system cells, such as monocytes, macrophages, and T-cells, together with nociceptors, further influence pain by increasing nociceptor sensitivity and perhaps facilitating the progression from acute to chronic pain conditions.[33]

PREEMPTIVE ANALGESIA

Preemptive analgesia is the administration of pain-relieving interventions before a painful stimulus occurs, with the aim of preventing or reducing subsequent pain and analgesic requirements.[34] It is characterized by two key features: Its ability to decrease post-operative pain and analgesic consumption compared to other treatments and an effect duration that extends beyond the clinical action of the administered drug.[35] The primary goals include preventing persistent post-operative pain, reducing pain severity, and decreasing analgesic needs by interrupting the nociceptive cascade before it begins.[9] Preemptive analgesia has conflicting evidence. Several studies indicate efficacy in lowering post-operative pain and painkiller usage, particularly in specific surgical operations such as limb procedures and mastectomy.[36] Non-steroidal anti-inflammatory medications (NSAIDs), local anesthetic wound infiltration, and epidural analgesia have all demonstrated the potential in reducing pain intensity and analgesic requirements in certain circumstances when administered beforehand.[20] However, preemptive analgesia encounters certain limitations that impact its clinical efficacy. The success of the intervention differs significantly among surgical procedures, demonstrating effectiveness in limb surgeries and mastectomies, while exhibiting limited advantages in abdominal surgeries due to complex innervation patterns.[36] Research findings have been variable, with not all trials showing significant decreases in pain or analgesic usage relative to post-incisional therapy.[35] Further issues include the emergence of opioid tolerance with acute use, which may require escalated dosages and diminish analgesic effectiveness, as well as the risk of opioid-induced hyperalgesia, wherein patients exhibit heightened pain sensitivity following the cessation of the initial analgesic effect.[37] Methodological issues limit the efficacy evaluation of preemptive analgesia. Study design concerns, such as pre-operative versus post-operative comparisons, might dramatically alter outcomes and lead to premature conclusions concerning limited utility.[38,39] The substantial possibility of bias and wide drug type and dosage variability in many research studies make conclusions challenging.[40]

THE TRANSITION FROM PREEMPTIVE TO PREVENTIVE PAIN MANAGEMENT: A PARADIGM SHIFT

A significant change in perioperative pain management is the shift from preemptive to preventive analgesia. It shows a better understanding of pain etiology and the requirements for holistic surgical solutions. This action focuses on improving patient outcomes by efficiently managing all pain aspects.[21] Preemptive analgesia targets nociceptive signals before surgery, while preventative analgesia targets them during the perioperative period. This conceptual expansion was caused by significant proof that suppressing nociceptive signals in the peripheral and central nervous systems throughout surgery reduces post-operative pain intensity and analgesic needs.[4]

PREVENTIVE ANALGESIA

Preventive analgesia aims to reduce sensitization from harmful stimuli during the entire perioperative continuum rather than exclusively during the pre-incisional phase.[4] This thorough method inhibits the nociceptive cascade at various levels and intervals, significantly reducing the probability of central sensitization and resulting in pain hypersensitivity, which is a vital element in the onset of chronic pain disorders.[41]

PHARMACOLOGICAL APPROACHES TO PREVENTIVE ANALGESIA

The pharmacological basis of preventative analgesia includes multiple classes of medications with differing effectiveness profiles. Preventive opioid treatment, while providing inconsistent outcomes, may deliver slight advantages to diminishing 24-h morphine usage; however, without consistently significant decreases in early or late acute post-operative pain. In contrast, preemptive opioids given solely before incision have shown the ability to diminish both early and late acute post-operative pain in specific surgical scenarios, especially dental operations.[42] Preventive use of acetaminophen has been linked to several advantageous results, such as diminished 24-h opioid usage, lowered immediate post-operative pain levels, and a lower occurrence of post-operative vomiting.[43] Likewise, prophylactic intravenous ibuprofen administration has demonstrated potential in diminishing post-operative pain severity and opiate consumption; nevertheless, further investigation is necessary to draw conclusive findings.[44]

NMDA receptor antagonists, such as ketamine and dextromethorphan, exhibit significant preventative effects. Their analgesic advantages persist beyond their pharmacokinetic duration in circulation, indicating effective control of pain hypersensitivity mechanisms.[39] Supplementary medications such as propofol, ketamine, and alpha-2 adrenoceptor agonists have been effective in modifying emerging agitation and alleviating post-operative pain severity.[45]

MULTIMODAL APPROACHES

Multimodal analgesia is the cornerstone of preventive analgesia, entailing the deliberate integration of pharmacological drugs with diverse modes of action, constitutes the foundation of preventive pain management. This strategy improves overall pain management by concurrently addressing different pain pathways through the use of mixtures of NSAIDs, opioids, and local anesthetics, thereby reducing the need for individual medications and their related side effects.[21] The advantages of multimodal preventative analgesia are significant and diverse. Substantial decreases in opioid usage have been routinely recorded across several surgical specialties, including spinal, orthopedic, cardiac, and gynecological operations. This opioid-sparing effect directly translates to reduced risk of opioid-related complications, addiction potential, and adverse effects.[21,39,42,43,46] Multimodal preventive analgesia, as an essential element of Enhanced Recovery After Surgery protocols, significantly reduces surgical stress response, accelerates recovery, shortens hospitalization, and decreases the incidence of post-operative complications, including infections and thromboembolic events.[47,48]

NON-PHARMACOLOGICAL DIMENSIONS OF PREVENTIVE ANALGESIA

Non-pharmacological methods enhance pharmacological treatments and are essential to integrated preventative analgesia programs. Physical therapies have shown considerable analgesic effectiveness across several clinical environments.[49,50] Cognitive and behavioral treatments, such as distraction, guided imagery, hypnosis, systematic relaxation regimes, and biofeedback, provide effective supplementary methods for pain management, especially in pediatric populations and emergency care settings.[51] Complementary therapies such as acupuncture, music therapy, and reflexology have shown effectiveness in diminishing pain intensity in many clinical settings.[50]

PAIN ASSESSMENT TOOLS AND TECHNOLOGICAL ADVANCES

Effective pain management relies on accurate assessment. Pain assessment tools can be categorized as unidimensional, multidimensional, or specialized for specific populations.[52] Unidimensional instruments such as the Visual Analog Scale (VAS), Numeric Rating Scale (NRS), and Verbal Rating Scale

(VRS) are commonly utilized to assess acute pain intensity. The VAS features a horizontal line, typically 10 cm in length, with "no pain" at one extremity and "worst pain imaginable" at the opposite end. Although it is highly responsive to changes in pain intensity, it can cause challenges for patients with cognitive impairments or those in intensive care environments. The NRS allows patients to rate pain on a scale from 0 to 10, providing excellent sensitivity and high compliance due to its straightforward nature. However, it can be problematic for young children or individuals with cognitive difficulties. The VRS uses verbal descriptors such as "no pain," "mild pain," and "severe pain," rendering it accessible for patients who prefer verbal assessments. However, it is less sensitive compared to other scales.[52-56] Multidimensional tools assess sensory, emotional, and functional consequences of pain. The McGill Pain Questionnaire contains sensory, affective, and evaluative word descriptors to help patients characterize their subjective experience, along with an intensity scale and additional elements to define pain characteristics. The Brief Pain Inventory and Geriatric Pain Measure evaluate pain's impact on daily functions and are particularly valuable for chronic pain assessment and in older adults.[29,53,57,58] Specialized tools address specific populations. The Faces Pain Scale-Revised (FPS-R) and The Face, Legs, Activity, Cry, Consolability (FLACC) Scale are recommended for pediatric populations, while the Behavioral Pain Scale and Critical-Care Pain Observation Tool serve nonverbal critically ill adults by focusing on behavioral indicators of pain.[59] Conventional pain assessment tools are inherently subjective, leading to potential unreliability. Recent advances in technology provide interesting new methodologies for more objective and precise pain evaluation. Pain intensity is estimated by automated recognition systems using facial activity descriptors and physiological markers. Advanced algorithms in machine learning and AI evaluate facial expressions, physiological signs, and behavioral markers. Electrocardiography, galvanic skin response, and electromyography are increasingly used to quantify pain, with machine learning models successfully identifying pain levels.[60,61] Electronic programs and mobile applications for pain assessment and management are being integrated into clinical practice. These technologies have demonstrated considerable impacts on pain intensity, depression, and self-efficacy among chronic pain patients, especially in short- and intermediate-term evaluations. Mobile applications have proven beneficial in alleviating pain intensity and enhancing quality of life, particularly in non-clinical environments, providing a valuable complement to conventional pain management techniques.[62,63]

STRATEGIES FOR IMPLEMENTING PREVENTIVE ANALGESIA

Preventive analgesia expands the preemptive strategy to include therapies across the entire perioperative phase. Implementation approaches involve multimodal analgesia, which addresses various pain pathways through the use of numerous analgesics and procedures, including the combination of localized blocks with systemic drugs. This synergistic approach minimizes opioid-associated side effects, such as respiratory depression and gastrointestinal problems.[64,65] Tailoring treatment to individual patient needs sets up with a comprehensive pre-operative examination, covering medical history, pain thresholds, psychological condition, and risk factor evaluation to personalize the analgesic regimen. Patient-specific guidelines consider age, comorbidities, and prior opioid exposure when modifying prescription dosages for safety and effectiveness. Psychoeducational assistance with pain management expectations and anxiety alleviation can help mitigate the likelihood of chronic postsurgical pain.[66] Modifications in surgical techniques substantially enhance pain control results. Minimally invasive techniques diminish the likelihood of nerve damage and chronic pain, with laparoscopic treatments typically resulting in less persistent discomfort compared to open surgeries.[66] Successful implementation in clinical environments necessitates interdisciplinary cooperation among surgeons, anesthesiologists, nurses, and pain management specialists, accompanied by frequent team meetings and protocol evaluations. Educating patients and involving them by explaining the advantages and rationale of preventive analgesia enhances compliance and pain assessment. Ongoing assessment with recognized pain metrics facilitates immediate analgesic modifications post-surgery. Evidence-based protocols must be consistently revised to integrate the newest research findings and technological advancements.[66]

CHALLENGES AND FUTURE DIRECTIONS

Despite considerable progress, many obstacles remain in preventive analgesia. Variability in patient responses to pain therapies is a critical issue, characterized by differing pain perceptions and treatment effectiveness among individuals. The acceptance of innovative medicines, such as newer anti-inflammatory agents, cytokine-targeting biologics, and neuromodulation techniques, demonstrates potential but necessitates meticulous integration into current multimodal treatment protocols. Extensive, longitudinal research is essential to comprehensively learn about the impact of preventative analgesia on chronic post-operative pain and other enduring effects. Future directions in pain management include incorporating artificial intelligence for objective pain evaluation, formulating personalized analgesic protocols informed by genetic and phenotypic variables, improving patient monitoring through digital technologies, broadening preventive strategies for outpatient procedures, and ongoing investigation into innovative therapeutic methods.[66]

CONCLUSION

The transition from reactive to proactive pain management indicates a significant improvement in perioperative

treatment. Clinical experience and evidence-based outcomes indicate considerable advantages of modern preventive methods, including a reduction in post-operative pain intensity through multimodal techniques, a decrease in opioid consumption in surgical cases, patient satisfaction scores with preventive strategies, earlier mobilization, and a reduction in hospital stays. In addition, preventative analgesia has reduced the occurrence of chronic postsurgical pain in several surgical procedures. These improvements result in superior functional recovery outcomes, increased patient adherence to rehabilitation programs, reduced post-operative complications, and an elevated quality of life during recovery. Key elements for success involve strong interdisciplinary team collaboration, thorough patient education and engagement, frequent protocol revisions informed by outcomes data, ongoing quality improvement initiatives, and an emphasis on long-term functional outcomes rather than solely acute pain management. The advancement of our comprehension of pain mechanisms and the emergence of new technology render the field of preventive analgesia highly promising for improving patient comfort and recovery post-surgery.

CONFLICTS OF INTEREST DISCLOSURE

The author declares no known competing financial interests or personal ties that may have influenced the work presented in this paper.

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