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Research Progress on Multimodal Analgesia for Preventing Postoperative Pain Following Extraction of Impacted Mandibular Third Molars

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ABSTRACT

Pain, as a common complication after the extraction of impacted mandibular third molars, significantly affects patients' physiological functions, social activities, and psychological well-being. Given that traditional analgesic methods are often accompanied by numerous side effects, multimodal analgesia strategies have emerged and gained widespread advocacy. This strategy involves precise pain assessment and the combined use of multiple analgesic drugs with different mechanisms of action, along with non-pharmacological treatments, aiming to achieve optimal pain relief while minimizing adverse reactions. This article reviews the pain assessment methods, non-pharmacological treatments, and pharmacological regimens within the multimodal analgesia strategy, with the goal of providing scientific evidence and practical guidance for pain management in patients undergoing impacted mandibular third molar extraction.

KEYWORDS

Painmanagement; Pain assessment; Pharmacological treatment; Non-pharmacological treatment

1. INTRODUCTION

Alleviating and managing postoperative pain is one of the fundamental responsibilities of healthcare professionals. Despite continuous preventive measures, a significant proportion of patients still face challenges with postoperative pain. Studies show that 7.5% of patients experience severe pain during recovery, while up to 19.8% report severe pain within the first 24 hours post-surgery, meaning one in five patients endures intense pain on the day of surgery [1, 2]. This is an issue requiring close attention.

Patients often experience various complications during the recovery period after the extraction of impacted mandibular third molars [3]. Pain is the most common complication, typically lasting from several hours to over ten days [4]. It is not only a major concern for patients but also profoundly impacts their physiological, social, and psychological well-being, posing significant challenges for clinicians [5]. Post-extraction pain arises from multiple causes, including intraoperative tissue damage-induced inflammation and local swelling, postoperative wound infection, dry socket, and nerve injury. Although adhering to surgical principles—such as adequate patient preparation, aseptic techniques, effective hemostasis, controlled force, thorough debridement, and meticulous handling of bone and soft tissues—can reduce the incidence and severity of complications, pain remains a frequent issue. Currently, pain management after impacted molar extraction has become a key focus of research.

To prevent postoperative infection and pain complications following third molar extraction, clinicians commonly recommend oral, intramuscular, or intravenous antibiotics and analgesics [6, 7].

Acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), and opioids are the primary medications used for postoperative pain management [8]. However, these drugs often come with significant side effects, particularly opioids, which carry high risks of misuse, abuse, and addiction, warranting heightened vigilance [9]. A study analyzing over 500,000 dental patient records from 2011 to 2015 found that 29% of opioid prescriptions exceeded the recommended morphine equivalent for acute pain management, and more than half exceeded the suggested duration of use [10]. To mitigate the side effects of traditional postoperative analgesics, the concept of "multimodal analgesia" has been widely advocated [11]. This approach involves combining analgesics with different mechanisms of action or adopting diverse analgesic measures to target various stages of pain perception and transmission [12], aiming for synergistic effects to achieve optimal pain relief while minimizing adverse reactions. This strategy systematically encompasses comprehensive pain assessment, pharmacological regimens, and non-pharmacological therapies [5, 13]. This article reviews domestic and international research progress on multimodal analgesia for postoperative pain prevention from three perspectives—pain assessment, pharmacological treatment, and non-pharmacological therapies—to provide scientific references for pain management in patients undergoing impacted mandibular third molar extraction.

2. PAIN ASSESSMENT

Currently, due to the lack of objective biochemical markers, pain assessment primarily relies on patients' subjective reports, with diversified scales serving as key tools for measuring postoperative pain intensity [14]. Among the various assessment tools, the Visual Analog Scale (VAS) and Numerical Rating Scale (NRS) are the most widely used methods for postoperative pain evaluation. Additionally, emerging tools like the Verbal Rating Scale (VRS) and Facial Pain Scale (FPS) offer richer and more nuanced options for pain assessment.

2.1. VAS

VAS is the most prevalent pain assessment tool [15]. It consists of a 100-mm horizontal line with "no pain" and "worst pain imaginable" at either end. Patients mark their pain level on the line, enabling quantitative assessment. The scale is widely recognized for its simplicity, reliability, validity, and practicality, ensuring feasibility and patient acceptance [16]. In recent years, VAS has also been used to assess pain intensity after impacted mandibular third molar extraction, further validating its applicability in this field [17]. Notably, VAS evaluates not only pain intensity but also incorporates other sensory and emotional factors, providing a more comprehensive assessment. Moreover, VAS correlates with age, reflecting differences in pain perception across age groups. As a multidimensional tool, VAS combines quantitative precision with qualitative richness. It requires patients to visualize their pain, enhancing sensitivity and multidimensionality, while millimeter-based scoring improves accuracy [18]. Variants of VAS include designs with graded points along the line or the use of numbers and emojis for modernized assessment [19], making it more contemporary and user-friendly for patients of all ages and literacy levels.

2.2. NRS

NRS typically uses a 0–10 scale for real-time pain assessment, where 0 represents "no pain" and 10 signifies "worst pain imaginable.[20]" Studies show a high correlation between NRS and VAS, but NRS demonstrates better compliance and higher completion rates [14,21]. Weiyu Ye et al. [22] found that patients preferred NRS over VAS, reporting a better user experience. However, NRS currently relies on integer-based scoring, limiting its precision and sensitivity compared to VAS [14].

2.3. VRS and FPS

The pain assessment system also includes the Verbal Rating Scale (VRS) and Facial Pain Scale (FPS). VRS quantifies pain based on patients' self-reports using predefined descriptive terms ranging from "no pain" to "severe pain." Its key advantage is intuitiveness, requiring no numerical or graphical interpretation, making it suitable for patients of all ages, cultural backgrounds, and cognitive abilities [23]. FPS presents a series of facial expressions, from smiling (no pain) to crying (extreme pain), guiding patients to select the symbol that best reflects their current pain level. However, recent studies suggest that VRS and FPS may partially reflect anxiety rather than pure pain intensity, influenced by personal beliefs, and are less precise than VAS and NRS [24]. Nevertheless, these scales are more suitable for elderly, pediatric, and cognitively impaired patients due to their high acceptability.

3. NON-PHARMACOLOGICAL TREATMENTS

In multimodal analgesia, non-pharmacological methods are diverse and increasingly integral to pain management due to their minimal side effects and sustained efficacy.

3.1. Physical Therapy

3.1.1. Cryotherapy

In postoperative management of impacted mandibular third molar extraction, non-pharmacological therapies like cryotherapy and heat therapy play critical roles in reducing complications and alleviating pain. Cryotherapy reduces local tissue blood flow, controlling inflammatory exudation and swelling, thereby diminishing peripheral nerve stimulation and pain perception. This method is simple, requiring only ice packs for home use, and is particularly effective for acute postoperative pain [25–27]. Additionally, cryotherapy has been found to alleviate anxiety and depression in some patients, improving postoperative outcomes [28].

Alternative cryotherapy applications have been explored for pain and complication management after impacted mandibular third molar extraction. Sneha Patil [29] and Xianghuai Zheng [30] used kinesiology tape with comparable efficacy to cryotherapy. Both studies demonstrated that kinesiology tape effectively managed pain and prevented complications. The tape's micro-convolutions enhance fascial and tissue fluid movement, improving local circulation and reducing edema. Its scattered adhesive design promotes lymphatic drainage, further alleviating swelling and pain.

Beyond local cryotherapy, intraoperative irrigation water temperature has been studied for postoperative complication prevention. One study compared 4°C and 25°C saline irrigation during bilateral impacted mandibular third molar extraction, finding that cold irrigation (4°C) had more significant benefits than traditional ice packs. The cold solution directly acts on surgical areas (muscles, bones, and soft tissues), yielding deeper effects [31].

3.1.2. Massage Therapy

Selye's stress theory explains the systemic physiological response induced by massage, regulated by the hypothalamus, leading to global enhancement or inhibition of central nervous system excitability. Specifically, hand massage applications can modulate the neural matrix (brain regions processing pain perception) [32]. In traditional Chinese medicine, massage is a professional technique applying pressure to specific acupoints to unblock meridians, harmonize qi and blood, and promote overall health. Studies show that massaging Neiguan (PC6) and Hegu (LI4) acupoints activates endogenous analgesia, increasing opioid peptide release and pain relief. It also boosts endorphin secretion, reduces spinal dorsal horn neuron excitability, and raises pain tolerance thresholds [33–35]. Foreign researchers have applied acupoint massage clinically, such as using Hegu (LI4) massage to reduce

pain during pediatric venipuncture [36]. Given its non-invasive nature, further exploration of acupoint massage during impacted mandibular third molar extraction holds promise.

3.2. Photobiomodulation Therapy

Photobiomodulation (PBM) therapy, a form of light therapy, uses specific wavelengths to penetrate skin and act on mitochondrial function in damaged or diseased tissues. This non-thermal, non-ionizing treatment employs red and near-infrared light (600–1000 nm) [37], also called low-level laser therapy (LLLT). As an adjunct, PBM reduces inflammatory cytokines and pain-related neuropeptides, promoting wound healing, inflammation reduction, and analgesia [38], while enhancing certain analgesics' efficacy [39]. Ehsan Momeni et al. [40] studied 25 patients undergoing mandibular third molar extraction, applying 940-nm diode laser intraorally post-surgery. VAS assessments showed lower pain in the laser group over seven days, confirming PBM's pain-relieving effects.

PBM's role in cellular metabolism is well-documented, with increased ATP production aiding neuronal membrane repair and pain signal reduction [41]. It also enhances vascular perfusion, facilitating lymphatic drainage and explaining its efficacy in reducing pain and edema post-surgery [41, 42].

However, optimal PBM parameters (duration, wavelength, energy) remain debated, requiring further research [43, 44].

3.3. Music Therapy

Music modulates brain regions involved in emotional regulation [45] and the dopamine system, increasing endorphin release [46, 47]. This inhibits neurotransmitter hyperactivity, activating pain suppression mechanisms [48, 49].

Pedro Christian Aravena et al. [50] found music intervention reduced anxiety, pain, and cortisol levels post-surgery. Feng Yuezhuan [51] et al. reported that relaxing music (<40 dB) during extraction significantly lowered pain at 30 minutes post-op ($P < 0.05$), with reduced anxiety and stress responses.

As a non-invasive, patient-friendly adjunct, music therapy is highly effective in dental settings, alleviating anxiety, improving pain perception [52], and potentially shortening procedure times.

3.4. Virtual Reality (VR) Technology

VR creates immersive, computer-generated environments that engage multiple sensory resources (visual, auditory, tactile) to distract from pain, per Wickens' [53] multiple-resource theory . As VR matures, anesthesiologists and pain specialists consider it a novel non-pharmacological option for multimodal analgesia [54].

Hoffman et al. [55] demonstrated VR's pain-reducing effects in burn patients during physical therapy. Sarig-Bahat et al. [56] showed a single VR session (e.g., swatting virtual flies) improved cervical mobility and neck pain. Xiong Xiaoju et al. [33] used VR pre-extraction to distract patients, significantly reducing intraoperative pain and anxiety.

However, VR pain management remains nascent. Variations in device quality, session duration, and patient heterogeneity may affect outcomes. Some studies used low-fidelity, non-immersive VR with insignificant results [57, 58], highlighting the need for further optimization.

3.5. Aromatherapy

Aromatherapy involves inhaling essential oil vapors, which convert to chemical signals affecting the central nervous system. Scents like marjoram, neroli, and ylang-ylang calm the parasympathetic

nervous system, while lavender balances autonomic function. These blends reduce stress, stabilize anxiety, and lower pain sensitivity perioperatively [59].

Essential oils rapidly enter circulation, ensuring quick onset and metabolism for safety and patient acceptance [60]. However, research on aromatherapy for post-extraction pain is limited, with mechanisms, oil selection, and timing requiring further study.

4. PHARMACOLOGICAL TREATMENT

Nociceptive pain transmission involves five stages: 1. Peripheral mechanical, thermal, or chemical stimuli are transduced into action potentials via nociceptors. 2. These signals travel to spinal cord synapses. 3. Signals transfer from primary to secondary neurons. 4. Pain information is modulated by neurons and glial cells in the brain and spinal cord. 5. Signals reach the somatosensory cortex, interpreted as pain, potentially with central sensitization or hyperalgesia [61–63].

Preemptive analgesia works by administering analgesics pre-injury to reduce inflammatory mediators and block pain signals [64]. Multimodal analgesia combines drugs targeting different receptors in nociceptive and neuropathic pathways to alleviate acute pain, surgical stress, and related mechanisms [65].

Common analgesics include NSAIDs (blocking pain signals), local anesthetics (slowing conduction), and opioids (modulating pain thresholds). Combining these enhances efficacy while minimizing side effects (especially opioids), the core goal of multimodal analgesia [11, 66]. Studies have explored various combinations. Others tested personalized opioid regimens to reduce dosage and addiction risk, supplementing with rescue analgesics [67].

For outpatient third molar extraction, ibuprofen or loxoprofen are typically recommended, though dosages are sometimes unspecified. Motov et al. [68] noted that NSAID doses often exceed analgesic ceilings, increasing side effects without added benefit. Here, multimodal analgesia shines—combining drugs improves outcomes. Soo-Ho Kim et al. [11] used sequential multimodal dosing (pre-op NSAIDs/opioids + acetaminophen, post-op other analgesics) to reduce pain and side effects. However, tramadol + dexketoprofen increased drowsiness, headache, dizziness, and nausea [69], underscoring the need for further optimization of opioid ratios and adverse effect mitigation.

Currently, no consensus exists on multimodal regimens for impacted molar extraction, warranting deeper research into combinations, dosages, and ratios.

5. SUMMARY AND OUTLOOK

Multimodal analgesia holds great promise for post-extraction pain management. Achieving this requires precise pain assessment, rational drug selection, and integration of non-pharmacological therapies for comprehensive perioperative and postoperative pain control.

Future directions include:

(1) Technological innovation for more precise and efficient analgesia.

(2) Advances in pharmacotherapy, introducing novel analgesics.

(3) Personalized pain management tailored to individual differences.

(4) Remote monitoring and follow-up for timely adjustments.

(5) Multidisciplinary collaboration to elevate pain management standards.

These efforts aim to enhance patient comfort, reduce postoperative pain incidence and severity, and promote faster recovery.

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