

Combining Multi-Modal Anesthesia with the ERAS Concept: Current Status and Prospects of Non-Opioid Anesthesia

CHEN Lei ZHANG Yunwang ZENG Yi

Anesthesia Department, People's Hospital of Xishuangbanna Dai Autonomous Prefecture, Yunnan 666100

Summary

Enhanced Recovery after Surgery (ERAS) anesthesia management focuses on providing optimal surgical conditions during the perioperative period by minimizing pain, ensuring the patient's safety, optimizing the management of comorbidities, modulating stress responses, reducing surgical noxious stimuli, and decreasing the occurrence of adverse reactions and complications to enhance the quality of recovery. Under the guidance of the ERAS concept, Non-Opioid-Based Anesthesia (OFA) has gradually emerged as a multidimensional alternative, effectively replacing traditional opioid-centric anesthesia methods. OFA, while minimizing patient pain and stress, also reduces adverse reactions, facilitating early mobilization and ambulation, thereby contributing to accelerated postoperative recovery. This shift aims to achieve more personalized anesthesia management, considering individual patient differences and surgical characteristics, to provide a safer and more effective surgical experience. By adhering to the ERAS principles and incorporating OFA, anesthesiologists can better balance intraoperative anesthesia effects with the overall recovery needs of patients, creating a more favorable perioperative environment for the surgical team. Research and practice in this direction will offer more effective methods to enhance patient recovery levels and surgical outcomes.

Keywords: Enhanced Recovery after Surgery; Non-Opioid-Based Anesthesia; Adverse Reactions to Opioid Medications

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I. Introduction

The goal of Enhanced Recovery after Surgery (ERAS) is to manage the pathophysiological changes during the perioperative period through a multimodal, multidisciplinary approach^[1]. One key principle involves implementing multimodal analgesia techniques at various stages of the perioperative period to reduce the use of opioid medications and achieve optimal analgesic effects^[2]. Adverse reactions that may arise from opioid medications can negatively impact the implementation of the ERAS concept, hindering early patient recovery. Therefore, under the influence of the ERAS concept, an increasing number of scholars advocate for the adoption of non-opioid-based anesthesia. Although the safety and feasibility of Non-Opioid-Based Anesthesia (OFA) have been demonstrated in various surgical fields, there is still a need for more research and in-depth exploration due to relatively limited experimental data. Potential unknown side effects and/or complications associated with OFA may exist, warranting further investigation. This article will provide a comprehensive review of the current progress in the application of OFA.

1. The Concept Of OFA

OFA primarily involves the use of a range of drugs, including NMDA receptor antagonists (such as ketamine, magnesium sulfate), sodium channel blockers (local anesthetics), anti-inflammatory agents (including non-steroidal anti-inflammatory drugs and dexamethasone), and α -2 receptor agonists (such as dexmedetomidine, clonidine), among other non-opioid medications. These drugs are combined with various anesthesia techniques, including spinal anesthesia, nerve blocks, and local anesthesia at the incision site^[3, 4]. The goal is to achieve patient sedation and analgesia during the surgical procedure, ensuring the patient remains unresponsive to stimuli while maintaining stability of the sympathetic nervous system and postoperative analgesic effects.

2. Adverse Effects Of Opioids

The analgesic effects of opioid medications primarily occur through binding to specific receptors in the central nervous system. This binding can inhibit the activity of calcium channels while activating potassium channels, thereby relieving the body's perception of pain and achieving a reduction in the patient's surgical stress

response. Despite continuous improvements in opioid medications, they still come with a range of adverse reactions, including drug tolerance, respiratory depression, muscle rigidity, itching, shivering, nausea, vomiting, urinary retention, addiction, and opioid-induced hyperalgesia, among others [5, 6]. These reactions may potentially delay patient recovery and even cause harm. In recent years, the use of perioperative opioid medications has sparked controversy regarding their association with cancer recurrence and metastasis [7-9].

3. Clinical Benefits Of OFA

Research results indicate that the application of OFA is primarily limited to perioperative patients known to have specific risks associated with opioid use, such as malnutrition, vomiting, severe postoperative nausea, morbid obesity, and those undergoing detoxification treatment [10]. As OFA has shown favorable outcomes in areas such as weight loss surgery, breast surgery, upper gastrointestinal surgery, and orthopedic surgery [11-14], interest in its research has grown. Currently, OFA is being increasingly utilized in a variety of surgeries, particularly in pain management, where its advantages over traditional opioid anesthesia are becoming evident. Several studies suggest that OFA can achieve comparable effects to opioid medications in postoperative pain control while reducing opioid-related adverse reactions. This opens up new avenues for providing safer and more effective anesthesia management during the perioperative period. However, despite the potential advantages demonstrated by OFA in this field, its application in different types of surgeries and patient populations still requires further in-depth research to clarify its safety and feasibility.

3.1 Thoracic Surgery Applications

Due to the advancements in minimally invasive techniques, a considerable body of research suggests that intrathoracic non-intubated video-assisted thoracic surgery (NIVATS), preserving spontaneous breathing, has been successfully applied in clinical practice and has yielded positive outcomes [15-17]. This approach provides a new option for elderly patients with pre-existing high-risk factors or contraindications, especially those with severe pulmonary diseases who cannot tolerate traditional double-lumen endotracheal tube anesthesia. It effectively protects patients' pulmonary function and contributes to early postoperative recovery and rehabilitation [18]. However, these patients are significantly affected by the side effects of opioid medications. Research results indicate that combining paravertebral block [19] and sevoflurane inhalation anesthesia [16] separately applied in NIVATS resulted in satisfactory outcomes, promoting rapid postoperative recovery and potentially reducing hospitalization costs while increasing patient turnover. Meanwhile, with the development and application of ultrasound technology, numerous studies suggest that ultrasound-guided paravertebral block, thoracic paravertebral block, and intercostal nerve block under OFA are safe and effective, contributing to the reduction of postoperative adverse reactions [20].

3.2 Abdominal Surgery Applications

Laparoscopic surgery has become a primary method in surgical procedures due to its advantages of minimal trauma, reduced patient stimulation, and shorter recovery time. Although laparoscopic surgery generally alleviates pain compared to open surgery, approximately 20%-40% of patients still experience moderate to severe postoperative pain [21]. Postoperative pain not only stimulates the sympathetic nervous system, triggering a series of stress reactions [22], but it may also affect neuroendocrine function, leading to changes in postoperative mental and psychological states and internal environment instability.

Studies in gynecologic laparoscopic surgery, represented by non-opioid medications such as dexmedetomidine and ketamine, have demonstrated that OFA techniques show analgesic effects comparable to traditional methods, with good anesthesia stability during surgery and a low incidence of postoperative nausea and vomiting (PONV) [23]. Therefore, these OFA techniques can serve as alternative anesthesia in gynecologic laparoscopic surgery under the ERAS program. Despite the possibility of prolonging awakening and orientation recovery time, OFA techniques have almost no adverse effects on anesthesia and recovery quality. Initial research suggests that they may even improve postoperative sleep quality [24, 25]. In a study by Xiao Xingpeng and colleagues [26] on elective laparoscopic surgeries, such as hysterectomy for uterine fibroids or ovarian cyst removal, in patients with a history of bronchial asthma, it was found that non-opioid analgesic general anesthesia combined with epidural anesthesia not only performed well in achieving satisfactory anesthesia but also effectively reduced airway pressure after intubation. Additionally, this anesthesia approach showed a trend of reduced asthma incidence during surgery in patients with a history of asthma.

3.3 Breast Surgery Applications

Breast lump excision surgery is common in young women. Patients in this category typically have no history of opioid use or smoking, yet they become a high-risk group for postoperative nausea and vomiting (PONV). In the past, traditional opioid-based anesthesia methods resulted in up to 50% of patients experiencing nausea and vomiting after surgery [27]. Research suggests that a non-opioid-based anesthesia regimen, composed

of dexmedetomidine, ketamine, and lidocaine, can replace traditional opioid-based anesthesia, especially for short procedures like breast lump excision surgery^[28]. This non-opioid anesthesia not only provides equivalent postoperative analgesia but also demonstrates superiority in reducing intraoperative hemodynamic fluctuations and postoperative PONV. In breast cosmetic surgery, such as breast augmentation or reduction, there is a tendency for severe PONV. However, using acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) can reduce the need for opioid medications postoperatively to nearly zero^[29]. Therefore, for breast surgery, OFA is an attractive and effective choice.

3.4 Application of esophageal cancer surgery

Esophageal cancer surgery involves significant trauma, and the overall dosage of anesthetic drugs required is higher compared to other surgeries. However, with the increase in the dosage of anesthetic drugs, the risk of postoperative anesthesia-related complications also rises, with complications induced by opioid medications being the most common [30]. In a study by Shi Pinghai and colleagues^[31], it was noted that applying a non-opioid-based anesthesia approach to esophageal cancer surgery can effectively reduce extubation time and post-anesthesia care unit (PACU) stay, while maintaining hemodynamic stability and decreasing the occurrence of complications. This anesthesia approach aims to ensure the safety of anesthesia and facilitate the smooth progress of surgery.

3.5 Outpatient Surgery Applications

Anesthetic recovery is crucial for outpatient surgery, as it can accelerate patients' normal activities and rehabilitation. Research by Guo Yunhe et al. [32] indicates that outpatient gynecological laparoscopic examinations using [non-opioid-based intravenous general anesthesia] can not only improve the quality of life in the 24 hours postoperatively, extend postoperative analgesia duration, but also reduce the incidence of postoperative nausea and vomiting. It is noteworthy that this anesthesia method can also reduce the demand for propofol without delaying extubation time. This is of significant importance for outpatient procedures.

3.6 Day Surgery Applications

With the rapid development in the field of surgery, the majority of hospitals have begun to carry out [day surgery], including treatments for pneumothorax, pulmonary nodules, hyperhidrosis, and gallbladder conditions. These treatments have evolved from traditional open-chest surgeries to minimally invasive procedures performed through laparoscopy^[33, 34]. In their research, Li Min and colleagues found that [intravenous anesthesia with a combination of propofol, dexmedetomidine, and lidocaine without opioids] can replace traditional opioid-based general anesthesia, particularly suitable for short-duration day surgeries such as laparoscopic cholecystectomy. This anesthesia method demonstrates more advantages in postoperative pain management and reducing postoperative nausea and vomiting (PONV), providing a safer and more effective option for day surgery^[35]. Therefore, OFA is expected to be more widely promoted in day surgeries.

3.7 Application Of Tonsil Surgery In Children

Tonsillectomy is a common surgical procedure in pediatric patients. Children undergoing tonsillectomy often suffer from sleep-disordered breathing or obstructive sleep apnea, making them more susceptible to upper airway suppression^[36]. Additionally, the risk of laryngospasm and airway swelling may exacerbate the respiratory depressant effects of opioid medications^[37]. Some foreign scholars, in retrospective cohort studies, have found that effective and safe treatment can be achieved in pediatric patients undergoing adenotonsillectomy or tonsillectomy (grades I-II) through intraoperative and postoperative analgesia protocols without opioids^[38]. This suggests that in these surgeries, employing anesthesia and analgesia protocols without opioids may be more advantageous for patient safety and recovery.

3.8 Application Of Surgery In Elderly Patients

China, like many other countries worldwide, is grappling with the challenge of an aging population. With the increasing number of surgeries performed on elderly individuals, the risk of adverse events during surgery significantly rises due to factors such as aging, comorbidities (simultaneous presence of two or more chronic diseases), and physical frailty. Therefore, addressing how to reduce anesthesia risks, minimize complications, and maintain postoperative organ function in the perioperative period for the elderly has become a focal point in the pursuit of rapid recovery^[39]. Research by Zhang Xiaoying and colleagues suggests that applying opioid-free anesthesia in elderly patients undergoing laparoscopic radical resection for colorectal cancer is feasible and beneficial for patients. This anesthesia method not only provides satisfactory analgesic effects during the surgery but also maintains hemodynamic stability during extubation, significantly reducing the incidence of postoperative delirium and postoperative nausea and vomiting (PONV)^[40]. Another study by Liu Xinze and colleagues indicates that in elderly patients, the use of opioid-free anesthesia can safely and

effectively manage anesthesia and analgesia for laparoscopic decortication of renal cysts. Compared to general anesthesia methods, the opioid-free anesthesia group effectively reduces the occurrence of complications such as nausea, vomiting, hypoxemia, and dizziness caused by opioid medications. This suggests that for elderly patients, opioid-free anesthesia and analgesia protocols may be a safer and more effective choice ^[41].

3.9 Applications In Spine Surgery

Due to changes in work and lifestyle, spinal disorders caused by poor posture resulting from a lack of exercise and excessive use of electronic devices have become a "epidemic" in offices ^[42]. Degenerative changes in the cervical and lumbar intervertebral discs are common diseases, and their incidence has been gradually increasing in recent years ^[43]. In a study, Wang Yuxia found that the application of opioid-free anesthesia in unilateral double-channel endoscopic surgery for spinal disorders is safe and feasible. Furthermore, opioid-free anesthesia demonstrated certain advantages in postoperative pain management, reducing postoperative nausea and vomiting, and shortening extubation time. This suggests that in the surgical treatment of spinal disorders, using opioid-free anesthesia may be a safe and effective choice.

4. OFA's Existing Shortcomings And Development Direction

Despite the initial enthusiasm for OFA, current data indicates that the proposed technique is not reliable in clinical practice. Foreign scholars have reported several drawbacks of OFA, including the following points: 1. For non-obese lung cancer VATS (Video-Assisted Thoracoscopic Surgery) patients, OFA treatment seems feasible in managing intraoperative pain reactions. However, compared to opioid anesthesia, OFA results in deeper sedation levels and significantly elevated blood glucose levels ^[45]. 2. Perioperative use of lidocaine combined with dexmedetomidine effectively reduces early nausea, PONV, and 24-hour total PONV in patients undergoing laparoscopic hysterectomy. However, during the PACU stay, it increases the incidence of bradycardia, dry mouth, and excessive sedation ^[46]. 3. Research from Bergamo, Italy, suggests that despite the significant interest in OFA, there is a lack of dedicated randomized controlled trials for cancer patients. To date, there is a knowledge gap, and the ability of OFA to improve cancer surgery outcomes remains unconfirmed. The long-term impact on specific oncological outcomes is far from elucidated. 4. Massoth et al.'s study indicates that their balanced OFA strategy did not reduce PONV, postoperative pain, or morphine requirements after gynecologic laparoscopic surgery ^[47]. 5. Beloeil et al. point out that balanced OFA can lead to hypoxemia, severe bradycardia, delayed extubation, and increased PACU stay ^[48]. These research findings suggest that, despite some advantages in certain aspects, OFA may bring about adverse reactions and uncertainties in other aspects. Further research and practical experience are needed to comprehensively assess its applicability in different surgical and patient populations. While OFA receives support in various surgeries, there are still several pressing issues to address: 1. Despite the increasing literature on OFA, consensus in its application is challenging. 2. Many anesthesiologists remain accustomed to opioid drugs, posing difficulties in changing their mindset toward OFA. 3. The optimal dosage and combination of non-opioid alternative drugs need to be determined. Searching for the most effective OFA approach in terms of efficacy and cost and identifying which patients and surgical types are most suitable for OFA ^[49]. In conclusion, although OFA seems to be a safe anesthesia method with early positive results, further research and efforts are required in this emerging field. We hope that this new anesthesia approach can overcome the limitations of opioid drugs and improve surgical outcomes for patients.

5. Summary

Under the guidance of the ERAS (Enhanced Recovery After Surgery) philosophy, the new concept of OFA (Opioid-Free Anesthesia) has the potential to replace traditional opioid-based analgesia-centric anesthesia methods, bringing positive impacts from various aspects. The purpose of this transformation is to minimize patient pain and surgical stress, while reducing adverse reactions, encouraging early mobility, and facilitating the early recovery process postoperatively. However, OFA still has some shortcomings that require collaborative efforts from anesthesia professionals to address. In the future, the development of OFA will bring more possibilities and innovative ideas to clinical anesthesia. Overcoming current challenges through continuous research and practice will provide more effective methods for improving patient recovery and surgical outcomes. Therefore, a thorough understanding of OFA, comprehensive evaluation, and close collaboration among professionals will be crucial in advancing this novel anesthesia approach.

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