

Use of multimodal anesthesia in the treatment of postoperative pain

Uso da anestesia multimodal no tratamento da dor pós-operatória

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ABSTRACT

BACKGROUND AND OBJECTIVES: Hippocrates already said 2400 years ago: “relieving pain is a divine work”. Postoperative pain is an important symptom, because it affects the patient’s recovery and because of the risk of pain chronicity. And as a treatment option, there is multimodal analgesia, mentioned in several studies as the best approach, although opioid therapy is still the main treatment for pain after surgical interventions. The objective of this study was to describe the use of multimodal anesthesia in the treatment of pain, especially in the postoperative period.

CONTENTS: A literature review was performed on studies that explained multimodal analgesia, its components, and which analyzed therapeutic drug options. The theme was approached from a consultation of articles published in LILACS, Scielo, Medline and Pubmed, in English and Portuguese, between the years 2012 and 2022. The keywords used for research were: “multimodal analgesia”, “multimodal anesthesia”, “surgical procedures” “postoperative”. In the results, examples of drugs that are part of multimodal analgesia in different procedures were listed.

CONCLUSION: In this way, multimodal anesthesia has demonstrated its benefits for the treatment of postoperative pain in various surgical procedures. However, further studies are needed so that this modality can be used more widely.

Keywords: Multimodal anesthesia, Pain, Postoperative, Treatment.

RESUMO

JUSTIFICATIVA E OBJETIVOS: Hipócrates já dizia há 2400 anos: “aliviar a dor é uma obra divina”. A dor pós-operatória é um sintoma importante por causar repercussões na recuperação do paciente e devido ao risco de cronicidade da dor. Como opção de tratamento, tem-se a analgesia multimodal, sendo mencionada em diversos estudos como a melhor conduta, embora a terapia com opioides ainda seja o principal tratamento para a dor após intervenções cirúrgicas. O objetivo deste estudo foi descrever o uso da anestesia multimodal no tratamento da dor, em especial no pós-operatório.

CONTEÚDO: Foi realizada uma revisão de literatura sobre estudos que explicitaram a analgesia multimodal e seus componentes, ou que analisaram opções terapêuticas de fármacos. O tema foi abordado a partir de uma consulta de artigos publicados nas bases LILACS, Scielo, Medline e Pubmed, na língua inglesa e em português, entre os anos de 2012 e 2022. As palavras-chaves utilizadas para pesquisa foram: “”, “”, “” e “”. Nos resultados, foram listados exemplos de fármacos que fazem parte da analgesia multimodal em diferentes procedimentos.

CONCLUSÃO: Nesse sentido, a anestesia multimodal demonstrou seus benefícios para o tratamento da dor no pós-operatório em vários procedimentos cirúrgicos. Contudo, são necessários novos estudos a fim de que esta modalidade seja utilizada de forma mais abrangente.

Descritores: Anestesia multimodal, Dor, Pós-operatório, Tratamento.

INTRODUCTION

According to the International Association for the Study of Pain, pain is defined as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage”. Pain is considered one of the main causes of human suffering, resulting in disability, which affects quality of life¹.

Acute pain is caused by the activation of nociceptors, chemical mediators and inflammation, which help to prevent tissue damage. In the acute pain scenario, pain can be classified as nociceptive, inflammatory and neuropathic. Nociceptive pain is the result of the activation of high-frequency peripheral sensory neurons by strong noxious stimuli, which can be mechanical, chemical or thermal. Inflammatory pain arises from the response to tissue inflammation, resulting in the release of sensitizing inflammatory mediators, which reduce the threshold of the nociceptors present in the inflamed tissue. Neuropathic pain is caused by damage to nerves or the sensory transmission system of the spinal cord or the brain².

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HIGHLIGHTS

- This article describes the components of multimodal anesthesia and shows its effectiveness through combined analgesia procedures.
- This article discusses the multimodal theory and the importance of the rational use of opioids.

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Pain is one of the effects of most surgical procedures. In the post-operative period, if not properly controlled, it can become chronic pain, which can interfere with sleep and physical activity, and have a negative impact on the patient's well-being. Proper pain control is important to prevent complications such as acute myocardial infarction, arrhythmia, paralytic ileus, poor wound healing and respiratory failure³.

The management of postoperative pain with a single analgesic (unimodal approach) has been shown to be unfeasible, possibly due to the involvement of multiple mechanisms. The timing of analgesic intervention after surgical stimulation has been investigated because the administration of analgesics reduced pain to a certain extent, but had insufficient long-term benefits and did not reduce hypersensitivity, which can lead to its chronicity⁴.

In this sense, multimodal analgesia acts in different ways and at different sites in the nervous system, with the aim of relieving pain through pharmacological or non-pharmacological resources. Pharmacological treatments include the traditional use of local anesthetics, non-steroidal anti-inflammatory drugs (NSAIDs), opioids and non-traditional drugs such as anticonvulsants, alpha-2-adrenergic agonists and N-methyl D-aspartate (NMDA) receptor antagonists. Non-pharmacological interventions include cognitive-behavioral therapy, transcutaneous electrical nerve stimulation (TENS), among others⁵.

The use of multimodal analgesia has been shown to be more effective, reducing the use of opioids and adverse effects compared to the use of a single modality⁶. Continued exposure to opioids reduces their analgesic effects, so patients end up needing increasingly higher doses, increasing the risk of addiction, overdose and respiratory depression, which can lead to death⁷. Opioids have been used for many years with the intention of reducing the need for hypnotic agents and ensuring effective analgesia⁸. However, this category of drugs has several adverse effects, such as nausea, vomiting, constipation and urinary retention; as well as other limitations, such as less effectiveness against pain if the patient is moving, delayed postoperative rehabilitation and paradoxical hyperalgesia. In addition, opioids can cause acute and chronic pain, and it is possible to immunomodulate the body, which has an impact on infectious and cancerous diseases, and also raises doubts about whether opioids can cause neurotoxicity⁹. Studies show that many patients who were initially prescribed opioids to treat acute pain, including post-operative pain, went on to purchase substances on the black market, abusing the drugs. Thus, prescriptions were incriminated in the perioperative period and in the treatment of chronic pain. All these reasons explain the reduction in opioid administration in the postoperative period, as well as during anesthesia in general⁹.

The study of pain phenomena is becoming increasingly important, as the proper management of patients is still a challenge. The fact that subjective assessments are prone to errors and results with low clinical accuracy can affect the approach to pain and the patient's quality of life¹.

Thus, multimodal analgesia, or balanced analgesia, has emerged to adequately control postoperative pain through the ad-

ditive and synergistic effects of various low-dose analgesics and peripheral blockade techniques, reducing their adverse effects. Thus, the present study's objective was to describe the benefits of multimodal analgesia in the treatment of postoperative pain, aiming to describe the most commonly used drugs.

CONTENTS

This study is a literature review on multimodal anesthesia in the treatment of postoperative pain. To this end, an initial search was carried out in the Descriptors in Health Science (DeCS) database, made available by the Regional Library of Medicine (BIREME), using the following keywords: "adult and multimodal", "surgical procedures" and "postoperative". The following databases were then screened: LILACS, Scielo and Pubmed. Also included were articles found in the virtual library of the Brazilian Society of Anesthesiology website, deemed relevant by the authors of this study.

The criteria for the inclusion of articles were: randomized controlled clinical trials and case reports that addressed the use of multimodal anesthesia and the postoperative management of adult patients undergoing surgical procedures and their postoperative period, based on a consultation of articles published in English and Portuguese between 2012 and 2022. To check that the articles met the inclusion criteria, the titles of the studies were first analyzed; those that were approved went on to read the abstracts and, finally, a selection was made based on reading the articles available in full.

This research excluded case studies or studies with fewer than 10 patients, studies that evaluated other cases related to pain in non-adult patients, as well as studies that did not prove the benefit of multimodal anesthesia and only addressed the use of opioids.

A descriptive analysis of the data presented in the selected articles was carried out, which was essential for formulating the discussion in this review. The data was collected and presented for each study analyzed, with the drugs and doses used depending on the type of surgery.

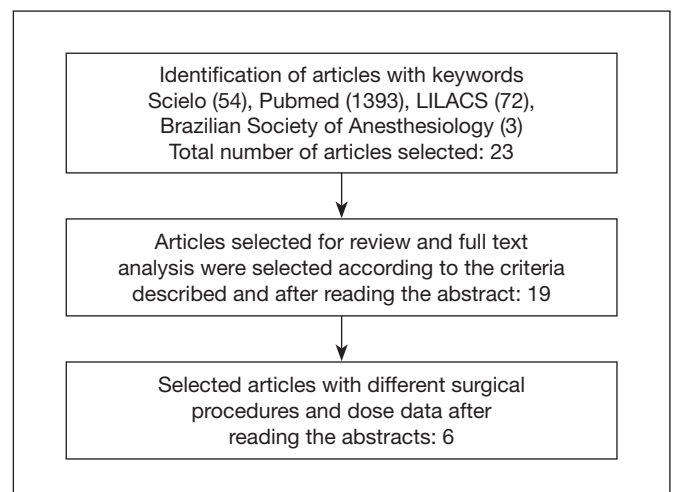


Figure 1. Selection of the articles used in this literature review

RESULTS

Protocol-optimized anesthesia

In 2001, the Enhanced Recovery After Surgery (ERAS) was created, a term used to define the guidelines of the Society for Optimized Recovery After Surgery. The protocol encompasses 23 items, describing pre-, intra- and post-operative care, with recommendations formed after a review of the evidence by groups of specialists¹⁰. The basic elements of the protocol are described in table 1.

Table 1. Basic elements of the Enhanced Recovery After Surgery (ERAS) guidelines

ERAS protocol basics
Pre-admission
Pre-operative guidance, assessment and optimization
Active care
Carry out antibiotic prophylaxis, thromboprophylaxis, prevent nausea and vomiting, maintain normothermia
Factors that reduce surgical trauma damage
Avoid bowel preparation, do not insert nasogastric tubes, perform minimally invasive surgery, use short-acting anesthetic agents, use thoracic epidural anesthesia in open procedures, avoid the use of drains, remove the urinary catheter early.
Elements to reduce ileus
Avoid water overload, perform minimally invasive surgery, use non-opioid analgesia, use anti-inflammatory drugs and regional anesthesia
Elements to optimize metabolic response
Avoid prolonged fasting, use carbohydrate solutions, promote early re-feeding
Auditing results
Verify adherence to protocols and check results.

The ERAS guidelines provide an evidence-based, multimodal approach to surgical care and to improving outcomes after major surgery. The main principles of enhanced recovery consider reducing disruption and the surgical stress response, which

leads to better recovery, reduced complication rates and shorter hospital stays¹¹.

According to ERAS, well-controlled pain, called the “fifth vital sign”, is widely recognized as an important metric for successful surgery and patient recovery. Postoperative pain is often underestimated and undertreated, with long-term sequelae. This makes pain control an important quality, a goal for individual, institutional and social improvement¹¹.

Based on ERAS, the multimodal educational protocol called Acceleration of Total Postoperative Recovery (ACERTO) was created to reduce the time needed for patients’ postoperative recovery (figure 2)¹⁰.

In order for these protocols to be put to good use, improving patient recovery, it is important for a multidisciplinary team, made up of surgeons, anesthesiologists, nursing staff and care teams, to work together. These protocols were created with the aim of aiding patients’ post-operative recovery, and need to be applied individually in each hospital. However, the use of these protocols is of great value, and new protocols should be created.

Multimodal anesthesia components

As already described, multimodal analgesia involves the use of several simultaneous pain control mechanisms that act synergistically to increase the analgesic effect and reduce the dosages of any single agent to minimize the risk of side effects, using the necessary dosages and thus reducing the risk of opioid side effects, which are common and cause delays in recovery. There are many pathways and mediators involved in nociception and targeting various mechanisms can increase the effectiveness of analgesics when using a combination of systemic and regional anesthesia¹¹. Analgesia includes pharmacological and non-pharmacological interventions, as exemplified in table 2⁵.

Related to systemic analgesia, multimodal anesthesia in ERAS setting involves the use of combinations of non-steroidal anti-inflammatory drugs (NSAIDs), paracetamol, anticonvulsant

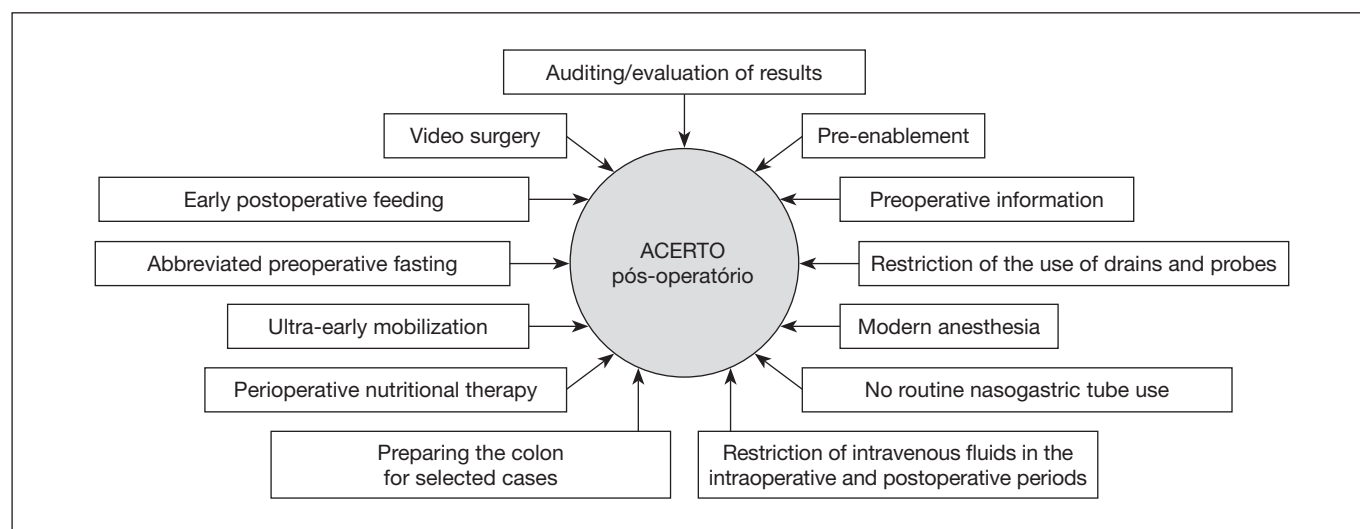


Figure 2. Main conducts addressed in the ACERTO project

Source: adapted and translated from www.periop.com.br

Table 2. Analgesia: pharmacological and non-pharmacological interventions. Adapted⁵

Pharmacological
Traditional Local anesthetics, Acetaminophen, Non-steroidal anti-inflammatory drugs, Opioids
Non-traditional Anticonvulsants, N-methyl-D-aspartate (NMDA) receptor antagonists, alpha-2 adrenergic agonists, antidepressants, analgesics
Non-pharmacological
Those with degrees of evidence of efficacy include: transcutaneous electrical nerve stimulation, cognitive-behavioral therapies (relaxation methods, hypnosis), acupuncture, heat therapy, massage, cold therapy and shock therapy.

Table 3. Components of systemic analgesia. Adapted¹¹

<p>Non-steroidal anti-inflammatory drugs Blocking the enzymatic action of cyclooxygenase (COX-1 and COX-2 inhibitor), reduce the synthesis of prostaglandins, reducing peripheral nociception, edema and symptoms associated with tissue damage. Examples: aspirin, ibuprofen, diclofenac, parecoxib and celecoxib. They are recommended in the post-operative period and are effective in the multimodal opioid-sparing regimen for acute pain control; recommended by the ERAS Society.</p> <p>Acetaminophen (paracetamol) Its mechanism of action is not fully understood. It is also recommended by the ERAS Society guidelines, containing a regular regimen of 15 mg/kg to 1 g, 4 times a day, orally or intravenously. It is well tolerated, but is hepatotoxic in high doses.</p> <p>Opioids ERAS recommends the use of short-acting opioids (fentanyl and alfentanil) and ultra-short-acting opioids (remifentanyl via infusion), if necessary, intraoperatively. Morphine is more likely to cause adverse effects, such as respiratory depression and nausea during recovery. Some opioids have been used as adjuvants in local anesthesia in field block, as well as in transverse abdominal plane (TAP) block and in low doses in spinal or epidural anesthesia. For post-operative pain control, if possible, it is recommended to avoid their use; opioids should be used as a last resort.</p> <p>N-Methyl D-Aspartate receptor antagonists It includes ketamine, memantine and magnesium sulphate. Ketamine modulates nociception by non-competitive binding and allosteric inhibition of the NMDA channel excitatory glutamate receptor site. At anesthetic doses, ketamine can produce a dissociative state, but at lower doses it produces analgesic effects, reduces postoperative pain and the use of opioids. However, its routine use is not recommended in ERAS; it is used predominantly in patients with cardiovascular instability.</p> <p>Gabapentin and pregabalin These drugs reduce the need for opioids, but there is not enough evidence to guarantee their inclusion and recommendation in ERAS so far. Analogues of gamma-aminobutyric acid (GABA) not only interact with voltage-dependent calcium channels, but also with NMDA receptors and protein kinase C.</p> <p>Local anesthetics Used for subcutaneous infiltration and regional anesthesia. There is growing evidence of the use of local anesthetics systematically via the venous route. IV lidocaine is highlighted by the ERAS Society, with benefits including analgesia, anti-hyperanalgesia and anti-inflammatory properties. However, caution should be exercised with and infusion doses to avoid toxicity.</p>

agents and calcium channel blockers, drugs that target different pain receptors and peripheral and central pain transmission pathways¹¹.

Systemic analgesia is supplemented by the use of injections or infusions of local anesthetics around specific peripheral nerves or the nerve plexus, in the tissue at the incision site, in the joint spaces, peritoneal spaces, tissue planes, and in the epidural or subarachnoid route. Local anesthetics are used, such as lidocaine and bupivacaine, in varying concentrations and volumes, with the aim of reducing or blocking nerve transmission. Although sensory transmission is the target, the motor and autonomic nervous systems can be affected, depending on the dose, and autonomic blockade can induce an increase in analgesic properties¹¹.

In thoracic epidural analgesia and spinal anesthesia, there is an infusion of local anesthetic via the mid-thoracic epidural and subarachnoid, recommended for open colorectal surgery, open radical cystectomy and open general gynecological surgery. However, the recommendation to use thoracic epidural anesthesia (TEA) for laparoscopic surgery is weaker, as well as for bariatric surgery, due to the higher complication rates reported in this population. Transverse abdominal plane blocks and continuous wound infiltration are included in the ERAS guidelines, particularly for open abdominal surgery and in cases where TEA is not used. Intraoperative aerosol administration of intraperitoneal local anesthetic is not currently recommended¹¹.

Rational use of opioids

For post-operative pain control, if possible, the ERAS Society recommends avoiding the use of opioids, which should be used as a last resort. The response to opioid use can vary greatly between patients, depending on the metabolism and elimination of the drug. Susceptibility to adverse effects also varies between patients, which include nausea, intestinal ileus, constipation, urinary retention, hypotension, respiratory depression, confusion, hallucinations and tolerance. For these reasons, multimodal analgesia aims to avoid or reduce opioid consumption by introducing other synergistic systemic agents and by using regional or neuroaxial blocks. If pain is not controlled by another method, post-operative opioids can be administered, with the dose being individualized and not standardized¹¹.

Multimodal anesthesia theory and its agents

The body's nociceptive system consists of nociceptors, ascending nociceptive pathways and descending nociceptive pathways. Cell bodies arise in the dorsal horn of the spinal cord and send one axonal process to the periphery and another to the spinal cord or brainstem. The ascending lives transmit stimuli from the periphery to the spinal cord and then to the brainstem (medulla and midbrain), amygdala, thalamus and primary and secondary sensory cortices (figure 3)¹².

Because there are different neurotransmitters and mediating neural synapses in the ascending and descending pathways, there are also several targets on which antinociceptive agents can act to interrupt the processing of nociceptive information. The simultaneous targeting of multiple targets in the nociceptive system is

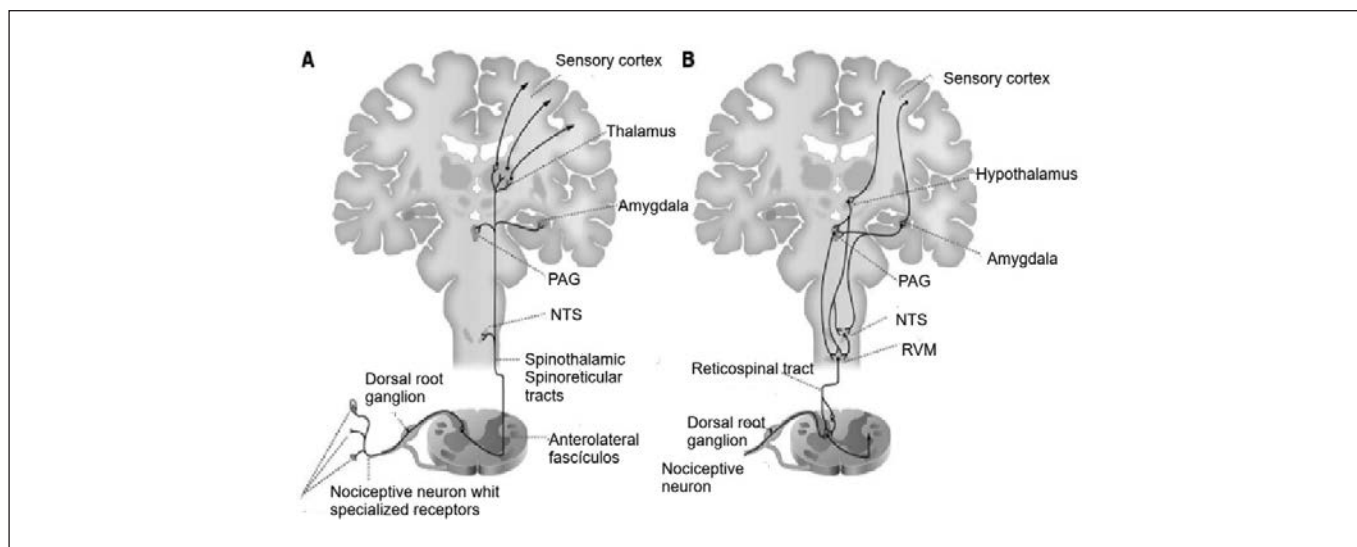


Figure 3. Ascending and descending nociception pathways. Adapted¹²

A - Nociceptive signals enter the spinal cord through nociceptive neurons that have specialized sensory receptors found in the tissue and in cell bodies found in the dorsal root ganglia. These neurons make synapses in the dorsal horn of the spinal cord, in primary projection neurons that travel in the anterolateral fascicle, through the spinal reticular tract and the spinal-thalamic tract, to the thalamus. Projections from the thalamus continue to the primary sensory cortex. B - The descending pathways begin in the sensory cortex and project to the hypothalamus and amygdala. The projections carried in the spinal reticular tract modulate the nociceptive information received by synapses on inputs to nociceptive neurons at the level of the dorsal horn.

the key concept behind the development of a multimodal strategy for nociceptive control and, therefore, multimodal general anesthetics. Nociceptive pathways have strong connections with excitatory pathways, which is why the administration of antinociceptive agents decreases excitation.

For each of the main behavioral states of general anesthesia, this strategy defines drugs that are administered to explicitly maintain that state and those that implicitly contribute to maintaining that state. For example: remifentanyl is administered explicitly to maintain antinociception, but its sedative effects implicitly contribute to unconsciousness. The main characteristics of this strategy are: making the control of nociception a primary objective in the choice of anesthetics used for maintenance, using combinations of mechanically distinct agents; taking advantage of the fact that each anesthetic has an explicit and an implicit effect in the choice of pharmacological combinations, especially the effect of antinociceptive agents on unconsciousness; making multimodal pain control a fundamental objective in the postoperative period¹².

To maintain antinociception during general anesthesia, several antinociceptive agents can be used simultaneously, including opioids. The use of several antinociceptive agents in addition to an opioid creates the opioid-sparing effect of these agents. Each agent targets a different component of the nociceptive system so that together they can suppress nociceptive transmission more completely. Hypnotic agents reduce the ability to perceive pain and thus implicitly contribute to antinociception¹².

During general anesthesia, unconsciousness is mainly maintained by the use of a single titratable agent, such as propofol or sevoflurane. Antinociceptive agents contribute profoundly to unconsciousness by interrupting nociceptive-induced excitation. As each of the antinociceptive agents decreases arousal, their

combination significantly reduces the hypnotic dose needed to maintain unconsciousness. Amnesia is maintained by ensuring unconsciousness because a patient who is truly unconscious, and not simply insensitive, is also amnesic¹².

A single muscle relaxant (nicotinic anticholinergic agent) can be used to maintain immobility. GABAergic hypnotic agents contribute to muscle relaxation by blocking γ motor neurons at the level of the spinal cord. Magnesium, administered as part of an antinociceptive regimen, also significantly increases muscle relaxation. In this case, the dose of muscle relaxant should be reduced accordingly¹².

MULTIMODAL ANESTHESIA

From a review of articles, data was collected to describe the benefits of multimodal anesthesia in several surgeries and procedures. In a study of 40 patients undergoing laparoscopic bariatric surgery, the use of ketamine (0.1-0.3 mg/kg/h), lidocaine (1-1.5 mg/kg/h), magnesium sulphate (30 mg/kg, after induction) and clonidine (1 mcg/kg/h, after induction) was observed, as well as adjuvants such as NSAIDs and dipyron, if the patients had no contraindications. The patients underwent balanced general anesthesia, using an inhaled anesthetic (isoflurane or sevoflurane) with 1 MAC, associated with remifentanyl in a continuous infusion pump (BIC) 0.04-0.25 mcg/kg/min). All patients used neuromuscular blockers and adequate decurarization. The anesthetic maneuvers were satisfactory, with the possibility of sparing opioids (used at around 0.5-0.7 mg/kg), maintaining good postoperative analgesia¹⁰.

A randomized controlled study included 120 patients scheduled for laparoscopic cholecystectomy and divided into 3 groups. One group received lidocaine at 1 mg/kg and continuous intravenous

Table 4. Evidence of multimodal anesthesia

Authors	Types of surgery	Drugs	Dosages
Rodrigues and Palotti ¹⁰	Bariatric surgery	Ketamine	0,1-0.3 mg/kg/h
		Lidocaine	1-1.5 mg/kg/h
		Magnesium sulphate	30 mg/kg, after induction
		Clonidine	1 µg/kg/h, after induction
Toleska et al. ¹³	Laparoscopic cholecystectomy	Ketamine	0.5 mg/kg
		Magnesium sulphate	Continuous infusion of 1.5 gr/kg
		Lidocaine	1 mg/kg and continuous infusion with lidocaine 2 mg/kg/h
Schoenbrunner, Joshi and Janis ¹⁴	Cosmetic plastic surgery	Paracetamol	1000 mg every 6 hours for up to 7 days after surgery
		Ibuprofen	600-800 mg every 8 hours for up to 7 days after surgery
		Ketorolac IV (meloxicam)	15-30 mg intraoperatively
		Gabapentin (pregabalin)	300-600 mg every 8 hours
		Cyclobenzaprine (tizanidine)	2-4 mg up to a maximum dose of 36 mg in 24 hours
		Oxycodone (hydrododone)	5 mg for breakthrough pain
Dong et al. ¹⁵	Laparoscopic radical hysterectomy for malignancies	Flurbiprofen axetil	50 mg intravenously for preventive analgesia
		Ropivacaine	0.5% was administered for local incision infiltration
		Flurbiprofen axetil	100 mg intravenously after surgery
De Jong and Shysh ¹⁶	Lower limb amputation	Bupivacaine 0.125-0.25%	Continuous infusion of 1 to 14 ml/H, up to 4 to 5 days postoperatively
		Paracetamol	4000 mg/day for 3 to 5 days
		Gabapentin	100 mg
		NMDA antagonists (ketamine)	0.1 to 0.2 mg/kg/h for 24 to 72 hours for acute pain
		Amitriptyline	25 mg
Forkin et al. ¹⁷	Caesarean section	Ketochorate	30 mg IV in post-anesthetic recovery room
		Acetaminophen + ketorolac	975 mg post-op + 30 mg IV
		Acetaminophen + ketorolac	975 mg post-op + 15 mg V every 6 h administered together (first dose 6 h after the post-op recovery room)
		Acetaminophen + naproxen	975 mg every 8 h + 500 mg naproxen every 8 h (administered together)
Singer et al. ¹⁸	Polytrauma	Acetaminophen	975 mg orally every 8 hours
		Ibuprofen	600 mg orally three times a day with meals
		Ketorolac	Injection 15 mg IV every 6 hours
		Gabapentin	300 mg orally every 8 hours
		Gabapentin	5% transdermal patch 1-3 patches daily

infusion with lidocaine at 2 mg/kg/h, a second group received ketamine at 0.5 mg/kg and the third group received continuous intravenous infusion of magnesium sulfate at 1.5 g/kg. Patients in the lidocaine group had the highest postoperative pain scores at rest and when coughing, and the ketamine group had the lowest pain scores. Rescue analgesia was given more to the lidocaine group and less to the magnesium group. The magnesium group received the highest dose of fentanyl during surgery and the lowest dose was received by the lidocaine group patients¹³. In plastic surgery, the option of multimodal anesthesia is based on giving local or regional analgesia preoperatively or intraoperatively at the maximum dosage necessary, using paracetamol and NSAIDs intraoperatively and continuing postoperatively, as well as gabapentin. Cyclobenzaprine and oxidone are indicated for the post-operative period. These drugs have shown lower opioid consumption and better analgesia, which has been confirmed by

the evidence-based approach to multimodal pain treatment in these types of procedures¹⁴.

A study was designed to investigate the effect of multimodal analgesia on gynecological cancer patients after radical resection. The study included 98 patients with cervical cancer who underwent laparoscopic radical resection in a hospital. In this sense, 47 patients in the research group (RG) received multimodal analgesia and 51 in the control group (CG) received conventional postoperative analgesia. This study proved that multimodal analgesia is safe and effective for patients with gynecological neoplasms after laparoscopic radical resection. This procedure can speed up recovery from the disease and improve quality of life, which is worthy of clinical application. However, there are still some shortcomings, such as short trial time, failure to investigate long-term follow-up and a small number of trials¹⁵.

Lower limb amputations are commonly performed on senior individuals with significant comorbidities. These procedures can cause pain after amputation with an incompletely understood pathophysiological mechanism. Despite these problems, implementing a strategy using a multimodal analgesia protocol allows for pain control at these multiple levels and complex pathways¹⁶.

The Enhanced Recovery After Caesarean (ERAC) protocol aims to reduce maternal morbidity and aid recovery. Multimodal analgesia is an important element of the ERAC protocol, but there is no consensus on the timing of drug administration. One study compared maternal pain outcomes after scheduled caesarean section. Intraoperatively, all patients received spinal anesthesia with 12.5-15 mg of bupivacaine, mixed with 150-200 µg of preservative-free morphine and 15-20 µg of fentanyl. At the end of the surgery, the patients were transferred to the post-anesthetic recovery room (PACU) and then to the mother-baby unit. Patients in ERAC 1 (alternating administration group) received 30 mg of ketorolac intravenously on arrival at PACU. Three hours later, these patients received 975 mg of acetaminophen orally, followed three hours later by 15 mg of ketorolac intravenously (with this fixed interval continuing for 24 hours). On postoperative day 2, the patients received paracetamol 975 mg every 8 hours and naproxen sodium 500 mg every 12 hours. Patients in ERAC 2 (combined administration group) received acetaminophen 975 mg orally and ketorolac 30 mg intravenously on arrival at PACU. Six hours later, the patients received 975 mg of acetaminophen orally with 15 mg of ketorolac intravenously in combination every 6 hours. On the second postoperative day, the patients received 975 mg of combined paracetamol and 500 mg of naproxen sodium orally every 8 hours. The modified non-opioid analgesic regimen involving combined administration (ERAC 2) alternating administration (ERAC 1) of multimodal analgesia resulted in a decrease in total postoperative opioid use. Total postoperative opioid use in ERAC 2 group was also significantly reduced compared to the Pre-ERAC group¹⁷.

The implementation of multimodal analgesia in the context of polytrauma was effective and reduced opioid consumption, both inpatient and outpatient. With the implementation of the multimodal analgesia protocol, one study noted an increase in gabapentin consumption. Further studies should be carried out on trauma patients, as well as elective patients, to determine whether these multimodal analgesia protocols reduce the conversion of acute pain to chronic pain¹⁸.

CONCLUSION

Multimodal analgesia can include several pharmacological components, which involve simultaneous pain control mechanisms that work together to increase the anesthetic effect and reduce the dosage of opioids. In this way, this type of analgesia manages to provide patients with fewer painful stimuli in the post-operative period, reducing hospitalization

and recovery times, as well as reducing the onset of chronic pain.

Standardized care pathways, such as enhanced recovery programs after surgery, promise to improve perioperative outcomes. In this sense, multimodal analgesic regimens are an essential component of enhanced recovery programs after surgery, potentially reducing complications and improving recovery. Although multimodal analgesia is recommended by the American Society of Regional Anesthesia and Pain Medicine, perioperative opioid administration remains the dominant component of most postoperative pain management plans.

In this sense, it is important for all healthcare professionals to be aware of the various analgesic options and interventions available in order to implement an aggressive pain management plan that better promotes recovery and rehabilitation. Ideally, multimodal analgesia protocols should be created by presenting a compilation of commonly used agents that have been shown to be effective. Thus, further research is needed to develop insight into additional approaches and the creation of specific multimodal analgesia protocols targeting several surgical procedures.

AUTHORS' CONTRIBUTIONS

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Data Collection, Conceptualization, Research, Writing - Preparation of the Original

Danila Malheiros Souza

Supervision

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