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Opioid Free Anesthesia – Benefits and Risks

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1 Summary

The discussion surrounding the use of opioids in anaesthesia is complex and raising questions about potential risks and alternatives. Although opioids are well known for their benefits in pain management, they are increasingly being criticised for their side effects, as well as the risk of addiction and misuse. In this context, the concept of opioid-free anaesthesia, which aims to avoid the use of opioids during anaesthesia, is gaining importance. New anaesthesiological concepts for opioid-free anaesthesia and enhanced recovery after surgery focus on alternative approaches to pain management based on co-analgesics such as dexmedetomidine, lidocaine, ketamine, nonsteroidal anti-inflammatory drugs and regional anaesthesia techniques. These approaches may help to avoid opioid-related complications and improve perioperative outcomes. In particular, opioid-free anaesthesia could be beneficial for patient groups with sleep apnoea, postoperative nausea and vomiting, increased risk of addiction, or chronic cancer pain. However, despite the potential of these approaches, research is needed to assess the practicality and long-term impact of opioid-free anaesthesia on perioperative outcomes. The decision to use opioids in anaesthesia should be based on a multimodal approach and careful evaluation of both benefits and risks.

2 Keywords

Anaesthesia, opioid-free anaesthesia, opioids, opioid crisis, multimodal analgesia, PONV, ERAS, onco-anaesthesia, regional anaesthesia, risks, benefits, pain management.

3 List of abbreviations

Abbreviation	Definition
PONV	Postoperative nausea and vomiting
OFA	Opioid-free anaesthesia
TIVA	Total intravenous anaesthesia
NSAIDs	Nonsteroidal anti-inflammatory drugs
OSAS	Obstructive sleep apnoea syndrome
ERAS	Enhanced recovery after surgery

IVRA	Intravenous regional anaesthesia
GABA	Gamma-aminobutyric acid
NMDA	N-methyl-D-aspartate

4 Introduction

At a time when the opioid crisis and its consequences are coming to the fore, the question of alternative approaches to pain management in anaesthesia is becoming increasingly important. [1] Standard peri- and postoperative pain management involves the use of opioids. However, opioids have clinically relevant side effects such as respiratory depression, increased risk of addiction, postoperative nausea and vomiting, which have raised concerns. [2, 3, 4] This problem draws attention to the rational use of opioids and alternative treatment methods. In this context, the concept of opioid-free anaesthesia has emerged. This is a promising area that can reduce unwanted risks and side effects while still providing effective pain relief. [2]

Opioid-free anaesthesia is growing in popularity worldwide as its multimodal approach improves postoperative analgesia. [5] It is based on the avoidance of intraoperative opioids and combines various drugs and techniques to provide high-quality, opioid-free anaesthesia. Regional anaesthesia techniques and multimodal analgesia play a crucial role in reducing the need for opioids and increasing patient satisfaction. [6, 7]

This narrative review aims to analyse the concept of opioid-free anaesthesia and assess the benefits and risks. The focus will be on the definition of opioid-free anaesthesia, the drugs, the application areas, and the potential risks and benefits. Furthermore, the advantages and disadvantages of opioid-free anaesthesia in the perioperative and postoperative periods will be analysed, taking into account the pharmacology of opioids and the associated risks. The aim is to develop a comprehensive understanding of this promising approach in modern anaesthesia and to optimise pain management.

5 Literature search strategy

A comprehensive electronic search for English-language publications was conducted using literature databases such as PubMed, Google Scholar and leading anaesthesia journals. Case reports, reviews, clinical trials, meta-analysis and guidelines are included on the topic of opioid-free anaesthesia. The selection of articles was restricted to English-language publications.

Search terms included "general anaesthesia", "opioids", "opioid crisis", "physiology of pain", "opioid-free anaesthesia", “ERAS”, “onco-anaesthesia”, "nonopioid medication" and "regional anaesthesia".

6 Background Information

6.1 Term of anaesthesia

The word "anaesthesia" comes from ancient Greek. It describes the loss of feelings and sensations and translates as 'numbness' or 'without sensation'. [8] Anaesthesia is an essential part of medicine, allowing diagnostic procedures, surgery and operations to be performed without the sensation of pain. General anaesthesia aims to create a reversible state of consciousness, which is achieved through a tailored combination of hypnosis, muscle relaxation and analgesia. This triad not only eliminates pain during surgery, it also provides amnesia. This is achieved by switching off the reflexes of the autonomic nervous system while maintaining physiological stability. In this way, a safe environment is created for the patient during surgery under general anaesthesia. [9, 10]

6.2 Opioid crisis

The opioid crisis is one of the most pressing public health crises of our time, particularly in the United States. Several factors initially caused it, one of them is the increase in the number of opioid prescriptions. With the availability of synthetic opioids such as fentanyl, this epidemic has evolved into a complex crisis. Social and economic changes, as well as the limited availability of effective analgesics and treatment options for opioid dependence, are contributing factors. Although the number of opioid prescriptions is decreasing, the number of opioid-related deaths continues to rise. Unlike illegal substances, opioids cannot be banned. When used correctly, opioids have a potent analgesic effect. This makes regulation and control complex. [1, 11] The situation is further complicated by the difference between the legal pharmaceutical form of fentanyl for human use and the highly potent veterinary analogues. [1]

During the initial wave, the crisis primarily resulted from people misusing opioids and becoming addicted to prescription opioid painkillers. Later, semisynthetic derivatives of morphine, such as heroin, were added to the mix. [11, 12] Illegal synthetic opioids were then increasingly used in the third wave. [11] Combinations of other drugs, such as xylazine and

fentanyl, are causing an increasing number of deaths as well. Xylazine-contaminated fentanyl is also known as "tranq-dope". Xylazine is an alpha-2 adrenergic receptor agonist that is commonly used as a sedative in veterinary practice. This medication is not approved for humans. Fentanyl and xylazine synergistically interact, which can result in life-threatening situations and significantly increases lethality. [13]

Overall, the causes of the opioid crisis are complex, but pain relief is the key to this crisis. As opioids are often an essential part of the postoperative recovery process, special care should be taken when prescribing opioids for postoperative discharge management. The risk of relapse to unrestricted opioid use is highest in this setting. [14]

6.3 Physiology of Pain

Pain is a physiological defence mechanism of the body. It is a warning of impending damage. Pain can be categorised in a number of different ways, which allows a more differentiated view and treatment. Somatic pain impacts the external structures of the body, such as muscles, bones and joints, often results in a sharp or stabbing sensation. Visceral pain comes from the internal organs and can be described as pressing, cramping or diffuse. Neuropathic pain is caused by dysfunction or damage to the nervous system and can be described as burning, tingling or electrifying. Central neuropathic pain involves the central nervous system. Referred pain occurs at a site that may not be the origin of the pain. Based on aetiology, pain can be divided into three areas. Direct damage or injury to tissue causes nociceptive pain, while nerve damage or dysfunction in the nervous system causes neuropathic pain. The third area is nociplastic pain, which occurs when the nervous system becomes hypersensitive, and pain signals are amplified or altered without apparent tissue damage. [15]

Pain involves complex signal transduction pathways. Nociceptors are an important part of these signalling pathways. Different chemicals such as potassium, prostaglandins, bradykinin and histamine activate nociceptors in different tissues. Nociceptors are sensory neurons that are activated when tissue is damaged. They can discriminate between noxious and innocuous stimuli. They transmit thermal, mechanical and chemical stimuli via Aδ and C fibres. Aδ fibres transmit a painful stimulus very quickly, whereas C fibres transmit a painful stimulus more slowly. This is why an intense, localised pain is felt first, followed by a non-specific, dull pain after an injury. [15] The distinction between acute and chronic pain is essential. Acute pain is an event that occurs suddenly and may be necessary for the organism to survive. Chronic pain is prolonged and can lead to improper conductance. [12, 16]

The ascending pain pathway begins with nociceptors detecting painful stimuli and then transmuting them to the brain through first, second and third-order neurons. This transmission includes transducing, transmitting, modulating and finally perceiving pain. Descending pain pathways are modulatory circuits that originate in the midbrain. They inhibit ascending nociceptive information in the spinal cord. Neurons from the periaqueductal grey area activate serotonergic neurons in the raphe magnus nucleus, which release noradrenaline and serotonin. These substances activate small opioidergic interneurons in the spinal cord, which cause the release of endogenous opioids and thus reduce the painful input. In addition, exogenous opioids such as morphine can have a similar effect. They inhibit pain transmission in the spinal cord and descending modulatory pain pathways. [12, 15]

6.4 Stages of anaesthesia

In 1937, Dr. Arthur Guedel developed a scheme that clearly defined the different stages of anaesthesia, with increasing depth from stages one to four. This was a milestone in anaesthesiology practice, as anaesthetic dosage was often imprecise and the depth of anaesthesia was assessed solely by clinical observation. Guedel's classification is still used in modern anaesthesia, which underlines the importance of his work in this field. [17]

6.4.1 Stages of anaesthesia according to Guedel's classification

Analgesia and disorientation are achieved in the first stage of anaesthesia, the induction phase. The patient's state of consciousness changes to a state of sedation. Patients may initially be talkative but become quieter as they are sedated. Respiration remains regular initially but then gradually becomes slower. This stage marks the transition from a painless state without memory loss to a painless state with amnesia. Complete loss of consciousness ends the first stage. [9, 17]

Disinhibition and delirium accompanied by uncontrolled movements, hypertension and tachycardia occur in the second stage of anaesthesia. An indicator of the onset of this stage is the loss of the ciliary reflex. It is extremely important to avoid airway manipulation at this stage, because of the increased risk of laryngospasm. Therefore, any manipulation of the endotracheal tube and suctioning of the airway should be avoided. This stage should be kept as short as possible and the transition to general anaesthesia should be quick. [16]

Surgical anaesthesia is defined as the third stage and is divided into four levels. In the first level, the patient still breathes regularly and spontaneously. The pupils are constricted and the gaze is

centred. The second level is characterised by intermittent apnoea. Laryngeal and corneal reflexes may be lost. This may result in increased lacrimation. In the third level, the pupillary light reflex is lost and the muscles are completely relaxed. Especially, the muscles in the intercostal spaces and the abdomen become increasingly relaxed. In the fourth level, the diaphragm is paralysed and breathing becomes irregular, even apnoeic. Overall, the third stage is the most ideal for most operations. [16]

Stage four only occurs if too much anaesthetic is given relative to the surgical stimulus, causing an overdose. At this stage, it is essential to provide respiratory and cardiovascular support. Otherwise, the consequences can be fatal. Worsening depression of the brain and medulla may eventually lead to respiratory arrest. Vasodilatation in the peripheral circulation and a reduction in the pumping function of the heart lead to increased hypotension with weak pulses. [16]

Today, general anaesthesia can be divided into 3 phases: Induction, maintenance and recovery. In the induction phase, the patient is brought from a state of wakefulness to anaesthesia. The second stage is called maintenance. Inhaled volatile agents or continuous intravenous infusions can be used to maintain anaesthesia. Several factors determine the choice of technique. These include the type of surgery and the characteristics of the patient. Emergence and recovery are the final stages of anaesthesia. At the end of anaesthesia, maintenance drugs are discontinued. Pain relief and antiemetics are given before awakening. Extubation is usually performed after oropharyngeal suctioning but in some cases, may be performed when the patient is under anaesthesia to avoid complications. The patient's vital signs will be observed in the recovery room and any complications will be treated there immediately. [9]

6.4.2 Anaesthesia Methods

The choice of anaesthetic is crucial and is made on an individual basis based on several factors, including the patient's individual risk of postoperative nausea and vomiting (PONV). In general, volatile anaesthetics such as sevoflurane, isoflurane or desflurane can be used to maintain anaesthesia. Combining different anaesthetics, including mixing intravenous anaesthetics such as propofol with volatile anaesthetics, is possible. Anaesthetics can be administered continuously through an intravenous infusion or via a vaporiser that disperses the anaesthetic as a gas for the patient to inhale. For patients who are at increased risk of PONV, a total intravenous anaesthesia (TIVA) is often the preferred choice. This method has the advantage of avoiding the use of anaesthetic gases, which can trigger nausea and vomiting. Each method has its own advantages and disadvantages, which must be considered in relation to the

individual needs of the patient and the requirements of the surgical procedure. [9] In this way, it is possible to tailor the anaesthesia to the needs of the patient and the requirements of the surgical procedure. [9, 18]

7 Opioids

7.1 Origin of opium

The word 'opium' is a derivation of the Greek word 'opos', meaning 'juice'. It refers to the milky juice extracted from the immature capsules of the opium poppy (*Papaver somniferum*). Drying the juice produces a raw material from which opium is extracted by autoxidation. The entire process of the production and extraction of opium has remained the same for more than 2,000 years. [19, 20]

7.2 Classification of opioids

Opioids are generally classified into three main groups: natural opioids (opiates), such as morphine, papaverine, codeine and thebaine. Semisynthetic opioids (morphine derivatives) are produced by altering the structure of the morphine molecule (heroin, hydromorphone) and fully synthetic opioids (fentanyl, methadone and pethidine). [12]

These fully synthetic opioids can be further subdivided into several subgroups, including morphine-, diphenyl- or methadone-derivatives, benzomorphans and phenylpiperidine. [12] The body has the ability to produce its own opioids. These opioid peptides bind specifically to the opioid receptors. Endogenous opioids are produced in the neurons of the central nervous system, the peripheral nervous system and the autonomic nervous system. They can also be produced in primary neurons, lymphocytes and macrophages in response to inflammation or tissue trauma. The endogenous opioids enkephalins, dynorphins and endorphins are formed from the three precursors. In comparison, exogenous opioids have pharmacological significance. They are used for medicinal purposes and drug abuse. [12, 21, 22]

7.3 Opioid receptors

Opioid receptors are divided into three main categories, the δ-, κ- and μ-opioid receptors. They are located in different regions of the brain, spinal cord and nerve plexuses of the gut and bladder. Their action is mediated by inhibitory G-proteins, but they are differentially sensitive

to a variety of ligands. Enkephalins, dynorphins and endorphins are endogenous opioids formed from the precursors proenkephalin, proopiomelanocortin and prodynorphin. They are receptor ligands for these opioids. These are peptides that reduce the excitability of cells by binding to the receptors. Opiates and semisynthetic opioids are exogenous opioids. They are semisynthetic or fully synthetic compounds. They differ in their affinity for different types of receptors and especially in their clinical kinematics. [21, 22, 23]

Ligands at opioid receptors are classified into agonists or antagonists depending on the strength of their binding to specific receptors and their own potency. Agonists are further subdivided into pure agonists and partial agonists. Pure agonists have a high level of intrinsic activity with a high affinity at the μ-opioid receptors. At the same time, they have low activity at the κ-opioid receptor. Partial agonists bind to the μ-opioid receptor with a higher affinity than pure agonists but have a lower level of intrinsic activity. There is also a group of mixed agonist-antagonists. These have a heterogeneous spectrum of activity and, therefore, have different intrinsic activity for different receptor types. This means that they act differently depending on the receptor type. They can be agonistic, partially agonistic or antagonistic. Pure antagonists are a very important group. They block the action of other molecules or drugs. Two main antagonists, naloxone and naltrexone, are commonly used for opioids. Naloxone is a short-acting antagonist with a duration of action of about 1 to 2 hours. It is used to reverse opioid-induced effects, particularly in cases of overdose, which can lead to respiratory depression or loss of consciousness. Naltrexone is a long-acting antagonist with a duration of action of more than 24 hours. It is used to treat opioid dependence because it blocks the effects of opioids and can prevent relapse. Both antagonists act on opioid receptors in the body and block the effects of opioids. It is important to note that naloxone and naltrexone antagonise almost all opioid receptors equally, which means that they can almost completely block the effects of opioids on the receptors. They are, therefore, not considered to be opioids per se. Their primary use is in opioid overdose and intoxication. They act competitively at the receptors and have no intrinsic activity. [12, 21, 22]

7.4 Opioid pharmacokinetics

Opioid pharmacokinetics and pharmacodynamics may change throughout the day. The duration of analgesia, for example, with intrathecal sufentanil may vary over the day. Through the peripheral mechanism, opioids can also provide analgesia outside the central nervous system. By inducing immune cells to enter the site of inflammation, they release endogenous opioid-like substances that act on opioid receptors on primary sensory neurons. [12] The plasma half-

lives of different opioids are also very different. In the case of short-acting opioids such as hydromorphone or morphine, the peak effect of a dose change occurs very quickly. With methadone and other long-acting opioids, it takes longer for the peak effect to occur after a dose change. Active metabolites may lead to a longer plasma half-life. [23]

In general, all opioids cross the placenta. This means that if they are administered during labour, they can cause respiratory depression in the newborn. Furthermore, chronic maternal opioid abuse can lead to physical dependence in the fetus and cause withdrawal symptoms that can be life-threatening. [21, 22]

7.5 Pharmacological actions of opioids

Opioids act as analgesics through the stimulation of opioid receptors, which are probably the most important molecules in the antinociceptive system. Genetic and environmental factors influence the effects and side effects of opioids. [12]

The neurophysiological effects of opioids in humans include, in addition to the desired analgesic effect, a euphoric and, hence, anxiolytic mood alteration, usually without loss of consciousness. This pain relief is selective and does not have an effect on other sensations. [12, 21, 22] Opioids have a mild inhibitory effect on the cough centre and can, therefore, also be used in the treatment of cough. By stimulating the parasympathetic nervous system, they induce miosis and by increasing the tone of the smooth muscles of the gastrointestinal tract, they inhibit motility, which can lead to severe constipation. In the case of diarrhoea, opioids can be used as antidiarrhoeal agents. This can be both a desirable and an unwanted effect. [21, 22] There are gender differences in the effects of opioids. Women can have a higher morphine effect but also a slower effect. [12]

However, there are also undesirable side effects associated with opioids. The euphoric effects of opioids increase the risk of developing physical and psychological dependence. At the same time, they also have a sedative effect. [21, 22] The repeated administration of opioids can lead to the development of tolerance, so higher and higher doses are needed to achieve the same level of pain relief. [21, 22, 24] By stimulating the chemoreceptors in the area postrema, the drugs can cause nausea and vomiting. Depending on the dose, there may also be an inhibition of the respiratory centre. At worst, spasms of the ureter or the bladder may occur, leading to the retention of urine. Opioids can also cause adverse symptoms such as itching and vasodilation. In the worst case, they induce bronchoconstriction due to increased histamine release from mast

cells. [12, 21, 22]

7.6 Acute risks of opioids in perioperative and postoperative settings

The use of opioids in the perioperative period has the potential to cause adverse effects. These include nausea and constipation. Respiratory complications, such as opioid-induced respiratory depression, can lead to brain damage or even brain death. When this happens, it is usually in the first 24 hours after surgery. [25] The incidence of respiratory depression varies according to the type of opioid, the route of administration and the type of monitoring used. [26] The use of opioids in the postoperative area harbours risks for patients with concomitant illnesses. The continued use of opioids in patients with mental health conditions such as anxiety or depression, as well as substance abuse disorders such as alcohol and tobacco use, is correlated with these. Patients who were issued an opioid prescription 30 days prior to surgery have a higher risk of continuing to use opioids after surgery. Due to the fact that a significant proportion of opioid-naive patients undergoing surgery and potentially becoming long-term opioid users, anaesthetists should minimise opioids during the perioperative period. By identifying patients at high risk for opioid abuse or opioid dependence in the perioperative outpatient setting, a plan can be developed to minimise the patient's exposure to opioids in and out of the hospital. [27]

The basic building blocks of a balanced anaesthetic are immobility and analgesia combined with unconsciousness and amnesia. During surgery, nociceptive stimuli are constantly being sent. [28] Because of their ability to block these ascending nociceptive stimuli while maintaining haemodynamic stability, synthetic opioids have been widely used in the anaesthetic field. They provide adequate analgesia and reduce the need for the use of hypnotic drugs. [2]

During anaesthesia, nociception can occur in the absence of pain. It is, therefore, essential to make a distinction between pain and nociception. Pain is the conscious perception of a stimulus that is potentially harmful to the body. Nociception is the stimulation of the pain receptors. [29] Regulation of the nervous system's autonomic response to nociception is necessary in intraoperative analgesia. Although opioids are commonly used in anaesthesia, they are not generally irreplaceable. Suppression of nociceptive pathways can be achieved by many different methods and routes. Opioids need not be used exclusively for this purpose. [2]

8 Concept of opioid-free anaesthesia

Opioid-free anaesthesia (OFA) is a method in which no medication containing opioids is used

during the course of a surgical procedure. This includes the systemic, neuraxial and intracavitary use of opioids. The aim of OFA is the provision of adequate and effective analgesia, the avoidance of adverse effects of opioids and the reduction of postoperative complications. [2] Multimodal anaesthesia is a good approach. It involves the use of nonopioid drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs). Regional anaesthetic techniques, such as plexus blocks and selective blocks, can also help to avoid the use of opioids and provide a good level of analgesia. [30] The integration of multimodal, non-opioid-based analgesia means that perioperative opioids are no longer routinely required as standard analgesia in an integrated multimodal therapy. [5]

8.1 Indication for opioid-free anaesthesia

The indications for OFA are diverse, encompassing different patient groups. On the one hand, opioid-free strategies are used in order to achieve a more rapid recovery after surgery. [6] However, there are certain groups of patients who may also benefit from this strategy. In particular, people who are severely obese and have undergone gastric bypass surgery may benefit from OFA, as they are at an increased risk of developing postoperative respiratory problems. [4] Patients with underlying obesity often suffer from obstructive sleep apnoea syndrome (OSAS). In bariatric surgery, the prevention of respiratory depression is of particular importance. Reduced cardiac contractility and respiratory depression should be avoided. In addition, opioids are known to be associated with PONV. Their use should, therefore, be reduced in these patient groups and avoided if possible. Urinary retention and constipation are also reduced postoperatively. [3, 4]

Patients with chronic pain syndromes who are already on long-term opioid medication may also benefit from OFA, as they may have developed an increased tolerance to opioids. They also have a higher risk of experiencing more severe pain after surgery. [24, 31] Other patient groups that may benefit from OFA include immunocompromised patients and oncology patients. The advantage here is that opioids are known to have immunomodulatory effects, which may not be suitable for immunocompromised patients. People with inflammatory conditions such as rheumatoid arthritis may also benefit from OFA, as the use of opioids can be associated with worsening inflammation. [2, 3]

In summary, OFA is a promising option for a wide range of patients, particularly those at increased risk of opioid-related adverse events or those for whom conventional opioid-based

anaesthesia is less effective or contraindicated. However, it is important that the decision to use OFA is always individualised, taking into account the specific needs and risk factors of each patient. [3, 31]

8.2 Contraindication of opioid-free anaesthesia

Although there are many advantages to the concept of OFA, there are certain groups of patients for whom this method is contra-indicated. The drugs used in OFA can have an effect on the sympathetic nervous system and cause hypotension and bradycardia. Special care should be taken in patients with arrhythmias, especially severe bradycardia. Conditions such as hypovolemic shock or polytrauma represent an unstable haemodynamic situation and require careful consideration before using OFA. Similarly, patients with autonomic disorders such as autonomic neuropathy or diabetes and those with cerebrovascular diseases such as stroke or transient ischaemic attack should be carefully assessed. [31]

In the absence of sufficient epidemiological studies on the use of OFA, contraindications can initially be derived from the known contraindications of the drugs used. It is, therefore, important to assess each patient's situation individually and carefully weigh up the risks and benefits in order to minimise potential risks and achieve optimal treatment outcomes. [3, 31]

8.3 Enhanced recovery after surgery

The implementation of pathways following the enhanced recovery after surgery (ERAS) protocol, which includes the reduction or avoidance of at least long-acting opioids as an essential part of its guidelines, has driven the broader use of OFA. Initially, the ERAS concept was applied to the speciality of general surgery. In recent years, the concept has been increasingly applied to other specialities, such as urology. [32]

The multimodal approach to pain relief is based on combining neuraxial anaesthesia, peripheral nerve blocks and nonopioid medications. ERAS relies on minimally invasive surgery and early mobilisation. This allows for faster recovery and reduces the side effects of opioids. Minimising the use of opioids without compromising pain control or recovery is a crucial goal of ERAS protocols. This approach also reduces the length of hospital stay. The result is greater patient satisfaction. [6]

ERAS has a number of essential components. It is important to provide counselling to patients before surgery in order to ensure the best course of treatment. Detailed explanations and advice

can help to reduce anxiety and potential complications for the patient. Therefore, preoperative counselling is crucial for successful surgery and recovery. Improving comorbidities is also an important and fundamental component. In the case of cardiopulmonary risk factors, an internal medical assessment should also be carried out to improve comorbidities before and after surgery. Another cornerstone of the ERAS protocol is the avoidance of smoking and alcohol consumption in the four weeks prior to surgery and the avoidance of traditional preoperative bowel preparation. Instead, a low-carbohydrate solution is administered shortly before surgery to reduce thirst and insulin resistance. The choice of surgical technique is also important. Minimally invasive procedures and appropriate intraoperative fluid management may be part of the ERAS protocol to reduce the likelihood of postoperative complications. Early mobilisation after surgery is another essential element. It is important to mobilise patients immediately after surgery in order to minimise the risk of complications and speed up recovery. The ERAS protocol aims to resume oral nutrition as early as possible, for example, by removing the feeding tube. It is also important to avoid opioid analgesics perioperatively to prevent bowel damage. Instead, nonopioid analgesics are preferred. The use of pain catheters may provide adequate pain control. [32] Many hospitals have an acute pain management team in place. This team is made up of anaesthetists who look after patients after an operation to ensure the best possible pain control. Pain management is also tailored to the patient's individual needs. [6] Overall, ERAS protocols are based on multimodal and tailored analgesic regimens that include paracetamol, NSAIDs and gabapentinoids. Regional anaesthesia techniques and a multidisciplinary approach, which requires close cooperation between all the professionals involved, are also important as the fundamental building block. [32, 33]

The aim is to successfully integrate multimodal analgesia and patient care to improve postoperative outcomes. However, there are no precise guidelines for prescribing pain medication at discharge. [6, 30]

8.4 Pharmacologic strategy of opioid-free anaesthesia

The pharmacological strategy consists of combining different drugs. The basis of multimodal pain management are nonsteroidal anti-inflammatory drugs and paracetamol. This is supplemented by infusion therapy with a variety of different drugs. These include steroids, gabapentinoids, dexmedetomidine, lidocaine, ketamine and magnesium infusions, which are often used as analgesic adjuncts. [28, 33, 34] β-blockers are used to support haemodynamic stability. [35]

8.4.1 Pharmacologic agents

Nonsteroidal anti-inflammatory drugs

NSAIDs are used for the relief of inflammation, postoperative pain or chronic pain. They can be used for both short-term and chronic pain. They can also be used as an adjunct to solid painkillers. [21, 33, 36] These include ibuprofen, diclofenac, naproxen, indomethacin and ketorolac. A comparison of pain relief and functional recovery in patients with acute soft tissue injuries showed that there were no differences in functional recovery at one week. The analgesic effect was also similar between NSAIDs and paracetamol or opioids. [36] Ketorolac and diclofenac are among the most commonly used NSAIDs in anaesthetic practice. [33]

The combination of paracetamol and diclofenac gave slightly better pain relief than either paracetamol, indomethacin or diclofenac alone. However, more adverse effects were reported by patients who had taken opioids. Intravenous ketorolac is a common treatment in the early postoperative period. This has also been shown to be effective in paediatric patients who have undergone surgery. NSAIDs have been shown to be as effective as opioids or paracetamol in relieving acute renal colic pain. While COX-2 inhibitors are alternatives to NSAIDs with reduced gastrointestinal side effects, they increase the risk of adverse cardiovascular events similar to NSAIDs. Recent clinical trials suggest that both NSAIDs and COX-2 inhibitors carry some risk for cardiovascular events. [36] Although there are concerns about gastrointestinal bleeding, platelet dysfunction and kidney damage with NSAIDs, the risk is low in patients with normal kidney function. [33, 36]

Paracetamol (Acetaminophen)

Paracetamol has been used for many years to relieve pain. Intravenous paracetamol has shown positive results in several types of surgery. Patients with bowel cancer who were given paracetamol showed a reduction in medication use, a shorter hospital stay and better pain control. They also experienced a faster recovery of bowel function, resulting in a lower rate of postoperative ileus. Patients undergoing cholecystectomy had a shorter length of stay in the hospital and, therefore, lower costs. They also required lower doses of morphine equivalent per day and were less likely to experience respiratory depression. [36] The time of administration of paracetamol is important. [33] In particular, intravenous paracetamol before or during surgery can reduce the incidence of PONV. [33, 36] Paracetamol also has an antipyretic effect.

[21]

However, there are concerns about a possible increased risk of neurodevelopmental problems with long-term use, especially during pregnancy, and liver toxicity in combination with alcohol. [36]

Steroids

Steroids are a group of drugs with anti-inflammatory properties. In the anaesthetic setting, steroids can be used to reduce inflammation and control pain after an operation. [34] Dexamethasone is an inexpensive synthetic steroid with high glucocorticoid activity. It has traditionally been used to control PONV. It has also shown promising results in the improvement of postoperative pain and the reduction of the length of stay in the hospital. Perioperative dexamethasone can lead to reduced pain sensations, a reduction in opioid consumption and, therefore, a shorter stay in the recovery room. Despite its benefits, there are also potential side effects such as hyperglycaemia, infection and impaired wound healing. [33]

Gabapentinoids

Gabapentinoids, such as gabapentin and pregabalin, are drugs initially developed for the treatment of epilepsy. They can also use for pain relief. Gabapentin and pregabalin are structural analogues of gamma-aminobutyric acid (GABA). [33, 36] They inhibit the development of hyperalgesia and central sensitisation. [33] Gabapentin has been used successfully to treat several neuropathic pain conditions. It was initially approved as an anticonvulsant. It blocks voltage-gated calcium channels and modulates nociceptive transmission by reducing calcium influx. In addition to painful diabetic neuropathy and post-herpetic neuralgia, gabapentin is effective in several other neuropathic pain conditions. These include multiple sclerosis, cancer and spinal cord injury. The dose should be increased slowly to keep side effects such as dizziness to a minimum. Gabapentin may also be used in combination with other medications to improve pain control. A multimodal drug therapy allows better pain control with lower doses of each drug involved. [36]

While gabapentin is approved for the treatment of chronic neuropathic pain, the clinical effects of pregabalin are variable. [33] Pregabalin is another anticonvulsant, which also blocks calcium channels. Its mechanism of action is similar to that of gabapentin. There are significant drug interactions with benzodiazepines or GABA, as pregabalin has no activity at these receptors.

Pregabalin has been used successfully in neuropathic pain conditions. It is particularly effective in painful diabetic neuropathy and post-herpetic neuralgia. It has a rapid onset of action and can also improve sleep problems. It is possible to experience side effects such as dizziness, but these are usually mild to moderate. [36]

Pregabalin can significantly reduce postoperative opioid consumption but not pain intensity. In contrast, gabapentin has shown promising results in reducing pain and opioid consumption in the postoperative period. It is often given as a single dose before surgery but can lead to postoperative sedation. [33]

Dexmedetomidine

Dexmedetomidine is an α2-adrenoceptor agonist used to sedate and relieve pain. [33, 37] It is used in a variety of clinical scenarios, including premedication, sedation in the intensive care unit, procedural sedation, local and regional anaesthesia procedures and postoperative analgesia. The use of dexmedetomidine has been shown to result in a significant reduction in postoperative pain and opioid consumption without compromising haemodynamic stability. [37]

Due to its sedative, anxiolytic, analgesic and sympatholytic properties, dexmedetomidine is used as premedication. It reduces oxygen consumption intra- and postoperatively, which leads to reduced stress on the cardiovascular system. [37]

In the treatment of high blood pressure, especially during heart surgery, dexmedetomidine also has a beneficial effect. It reduces the oxygen consumption of the heart and may reduce the development of myocardial ischaemia. In neurosurgery, dexmedetomidine stabilises the haemodynamics of the brain and prevents a sudden increase in intracranial pressure. [37]

Dexmedetomidine is used in the intensive care unit to sedate initially intubated and mechanically ventilated patients. It has been shown to be effective in maintaining sedation for up to 24 hours. It provides improved sedation in mechanically ventilated postoperative patients by reducing oxygen requirements while maintaining a high partial pressure of oxygen. [37]

Dexmedetomidine has also proved effective for procedural sedation in non-intubated patients. It has been used safely for several procedures, including transesophageal echocardiogram, colonoscopy and vitreoretinal surgery. [37]

Dexmedetomidine is also an effective adjunct to local and regional anaesthesia. It improves the

postoperative analgesia and prolongs the duration of the sensory and motor blockade induced by the local anaesthetic agents. It can also be used in intravenous regional anaesthesia (IVRA) and improves the quality of anaesthesia without causing side effects. [37]

However, especially at higher plasma concentrations, side effects such as bradycardia and hypotension are common. Dosage adjustments are necessary, especially in elderly patients, to account for potential sedative effects. [33] It has proven to be a versatile and effective drug with a high degree of safety and efficacy. [37]

Lidocaine-Infusion

Sodium channel blockers such as lidocaine are important in the treatment of neuropathic pain. They can suppress the abnormal excitation of nerve fibres without interfering with normal nerve conduction. [36]

Lidocaine infusions are commonly used for perioperative pain control. They can reduce the need for opioids and decrease PONV. Lidocaine also has anti-inflammatory properties and can improve postoperative recovery. However, its antinociceptive effect is multifactorial. Intravenous lidocaine infusion has become increasingly important in managing postoperative pain and improving surgical recovery. In addition to pain relief, positive effects on gastrointestinal motility, shortening of hospital stay, postoperative nausea and opioid consumption have been observed. Therefore, lidocaine infusion may be a helpful component of postoperative pain management protocols to improve recovery. [38]

For chronic pain conditions that are difficult to treat, lidocaine can be used as a therapeutic agent. These include neurological conditions such as neurogenic facial pain, stroke and myofascial pain. However, the limited duration of action of lidocaine limits its use. [36]

In addition, topical lidocaine patches and gels provide local pain relief for patients with neuropathic pain, such as painful diabetic neuropathy and post-herpetic neuralgia. The lidocaine patch has been shown to be an effective component of multimodal drug therapy. It is used with other medications to achieve a synergistic effect and improve pain control. [36, 38]

Ketamine-Infusion

Ketamine is analgesic, amnestic and psychotomimetic. [33, 39] These effects are explained by the blockade of the N-methyl-D-aspartate receptor **(**NMDA receptor) by non-competitive inhibition of glutamate binding. Ketamine also interacts with other neurotransmitter receptors,

such as nicotinic receptors, muscarinic receptors, cholinergic receptors and opioid receptors. It also interacts with voltage-gated sodium and L-type calcium channels, which can lead to mild local anaesthetic effects and cerebral vasodilation. [33] Ketamine has been used successfully in a variety of surgical procedures to reduce pain and minimise opioid use. The risk of side effects is minimal. It can be effective as an intraoperative bolus alone or in combination with a postoperative infusion over a period of 24 to 72 hours. [39]

The strengths of both drugs are exploited in the combination of ketamine and dexmedetomidine. A low dose of this combination provides effective pain relief, moderate sedation and haemodynamic stability without the risk of postoperative hallucinations. It also reduces the risk of postoperative sore throat. This expands the options for OFA. [34]

Magnesium

Magnesium is often used as an antiarrhythmic agent and to inhibit premature labour. It also has analgesic properties as an NMDA receptor antagonist and calcium channel blocker. [40] Intravenous administration of magnesium as an adjunct can reduce postoperative opioid use and pain without significant toxicity. Magnesium also improves haemodynamic stability during surgery. There is a reduction in heart rate variability, which may be due to its antinociceptive effects, although this has not been clearly established. [33] These effects could reduce opioid-associated side effects such as nausea, vomiting, respiratory depression, gastrointestinal distress, postoperative hyperalgesia, addiction and pruritus by reducing the use of opioids during and after surgery. [33, 40] The use of magnesium infusions may be associated with a significant reduction in opioid use without compromising haemodynamic stability. [34, 40] In addition, magnesium may provide a greater degree of haemodynamic stability compared to remifentanil. [40]

β-Blocker

In order to maintain stable blood flow during surgery, it was recommended to use β-blockers during the perioperative period. [35] Administration of esmolol during anaesthesia has been shown to reduce the need for inhaled anaesthetics and fentanyl during surgery, haemodynamic responses and morphine consumption in the first three days postoperatively. Although data on the use of β-blockers in the context of OFA are limited, studies have shown savings in the use of intra- and postoperative opioids and a reduction in PONV. However, it is important to consider the potential side effects of perioperative β-blocker use, such as an increased risk of

stroke. [35, 41]

8.5 Onco-anaesthesia

There are several factors in the perioperative period that may promote tumour progression. [42] In general, it is not easy to avoid opioid-related harm in the treatment of severe chronic cancer pain. The patient's physical condition plays a significant role in the treatment of cancer patients. [43] Concomitant symptoms such as malnutrition can influence the pharmacokinetics of medication. [3]

Adequate pain management is fundamental in oncology because pain can have an immunosuppressive effect. Surgery is always stressful for the body. During surgery, transforming growth factor beta is released, which plays an important role in establishing blood supply to tumours and cell proliferation. At the same time, there is an increase in vascular endothelial growth factor, which promotes the formation of new blood vessels and, thus, tumour growth. In contrast, levels of tumour-related anti-angiogenic factors such as angiostatin and endostatin are reduced, which helps to inhibit the development of new blood vessels and slow tumour growth. Even if a tumour is completely removed by surgery, there is still a risk that tumour cells will spread or that released tumour cells will circulate. In the worst case, this can lead to metastasis and recurrence. [42] The immune system can be affected by surgery, anaesthesia and opioid analgesics. Ultimately, each part of this process can affect cancer prognosis. [3] This affects the functions of various cells. Volatile compounds can inhibit natural killer cell function and lymphocyte antigen activity. This has been confirmed in animal studies. This effect suggests explicitly that anaesthesia has the ability to impair the immune system and thus effectively target tumour cells. Volatile anaesthetics can also stimulate hypoxia-inducible factors in tumour cells. This makes the tumour cells more resistant and allows them to multiply more quickly. Tumour-promoting and cell-protective processes can now be activated in the remaining tumour cells. This increases the likelihood of tumour recurrence. [42]

It is possible that avoiding opioid analgesics may improve cancer prognosis. However, there still needs to be conclusive prospective data. [3] Regional anaesthesia is an excellent solution to this problem. Stress-related reactions to surgery and pain are reduced and adequate analgesia is achieved. The need for opioids can be minimised or eliminated. In vitro studies have shown that amide local anaesthetics have a cytotoxic effect, which may prove helpful in preventing cancer recurrence. [42] Studies on the perioperative use of epidural analgesia and its effect on the recurrence of cancer suggest a possible link with improved survival rates. [44] Local

anaesthesia is, therefore, an optimal option in oncological anaesthesia and may improve the prevention of cancer recurrence and metastases. [42, 44]

8.6 Regional anaesthesia

Regional anaesthesia is the infiltration of a nerve with an anaesthetic. Regional anaesthesia has many advantages over general anaesthesia, including the avoidance of airway manipulation, lower drug doses and faster recovery times. It also allows for a significant reduction in postoperative pain and an early start to physiotherapy. [32, 45] The decision to use a regional anaesthetic depends on a number of factors. These include the type of procedure, the individual characteristics of the patient and the preferences of the anaesthetist. Indications include avoiding the side effects of general anaesthesia, such as respiratory depression. In addition, regional anaesthesia is often used for postoperative pain control and can also be used to treat certain chronic pain conditions. [45]

Neuraxial anaesthesia aims to numb specific areas of the body by injecting local anaesthetics near the spinal cord. This can be either a spinal anaesthetic, where the drug is injected directly into the cerebrospinal fluid space around the spinal cord, or an epidural anaesthetic, where the drug is injected into the epidural space outside the spinal cord. [45] Neuraxial anaesthesia, including spinal anaesthesia, is often used below the neck as the sole method of anaesthesia or in combination with general anaesthesia. It is beneficial for lower abdominal, pelvic and leg surgery. When the anaesthetic is applied, it is essential to tell the patient that their movements will be restricted until the block wears off. Spinal anaesthesia is best for short procedures that do not affect breathing. Possible complications of nerve blocks depend on the type of block used. [46]

Epidural anaesthesia is mainly used for childbirth and surgery on the chest, abdomen or spine. It can also be used for pain management during or after surgery. Patients at higher risk of postoperative complications have often benefited from epidural anaesthesia. Epidural patient-controlled analgesia can provide better pain relief and fewer complications in abdominal surgery than intravenous patient-controlled analgesia. In addition, epidural anaesthesia can reduce postoperative delirium in patients undergoing general anaesthesia and may improve cancer survival. [44] For most patients, epidural anaesthesia is considered relatively safe, although alternative methods of anaesthesia may be more appropriate for specific individuals. Absolute contraindications include patient refusal, local infection at the site of injection, increased intracranial pressure and traumatic injury to the spinal cord. Relative

contraindications may be problems with position maintenance for epidural placement in patients with haemodynamic instability, obstructive cardiomyopathy, untreated coagulopathies and therapeutic anticoagulation, thrombocytopenia and anatomical abnormalities of the spine. [44]

Peripheral nerve blocks are used to numb specific peripheral nerves to reduce pain in a specific area of the body. This technique can be beneficial for controlling pain after surgery in the extremities. [32, 45, 46] There are no established guidelines for the use of peripheral nerve blocks. However, the general logic behind them is to use it when other conservative measures fail or to avoid the side effects and complications of general anaesthesia and oral medications. [46] Peripheral nerve blocks may be a safe alternative for patients at risk of respiratory depression during general anaesthesia, whether due to respiratory disease, OSAS or other respiratory problems. [3, 46] It is also indicated when patients do not respond to or are unable to tolerate conventional oral analgesics. [24, 46] If a patient wishes to avoid systemic medication, this is also an indication. Peripheral nerve blocks are contraindicated in patients with coagulopathy, antithrombotic use, active infection at the site of injection or pre-existing neurological deficit along the block distribution. [46]

IVRA, also known as a Bier block, involves injecting a local anaesthetic into a limb to give a regional anaesthetic. This technique is often the choice for minor procedures on the arms or legs. The advantage of IVRA is that it can be carried out without the need for special equipment. [44] This makes IVRA a cheaper and simpler option for specific procedures. [47] One of the main limitations is that it does not provide residual analgesia. This means that the patient will continue to feel pain after the procedure and this will need to be managed either with systemic medication or another local analgesic procedure. This can make postoperative pain control difficult. [45] Although the risk of local anaesthesia toxicity is highly sporadic, therapeutic intervention should remain possible. [47, 48]

Overall, regional anaesthesia is an effective alternative to general anaesthesia and, in many cases, can provide better pain control and faster recovery for patients. [32, 45] In general, peripheral regional anaesthesia techniques should be preferred to neuraxial techniques due to fewer serious complications, depending on the location of the procedure. The use of local, preperitoneal or prefascial, wound catheters is also becoming increasingly popular. [7]

8.6.1 Side effects and risks of regional anaesthesia

It is clear that regional anaesthesia has many advantages. However, as with any medical

procedure, there are also risks that need to be carefully considered. [48] On the one hand, absolute contraindications to the use of regional anaesthesia include patient refusal and allergy to local anaesthetics. On the other hand, relative contraindications include active infection at the injection site, coagulopathies, pre-existing neurological deficits and inability to cooperate. It is essential to consider these contraindications carefully to minimise potential risks and ensure patient safety during the anaesthetic procedure. [45, 46]

Although serious side effects of neuraxial anaesthesia are rare, they can have serious consequences. The incidence of neurological complications due to central neuraxial blockade is estimated to be between 1/1,000 and 1/1,000,000. The possible causes of these complications include adverse physiological reactions, drug toxicity and mechanical injury due to the placement of the needle or catheter. [49]

There are several risks to consider, particularly with neuraxial and regional nerve blocks. One potential problem is the formation of epidural or spinal haematomas at the injection site. [46, 49] This is a complication that can occur with any regional anaesthetic. [48] It can lead to long-term neurological damage and is often caused by traumatic needle or catheter insertion. [49] These risks can be minimised by identifying different patient factors. For example, drugs such as low-molecular-weight heparin can increase the risk of bleeding and techniques with a lower risk of bleeding. [48, 49]

Sudden back and leg pain, numbness, weakness, bladder and bowel problems are typical symptoms of an epidural or spinal haematoma. If there is any suspicion of a haematoma, immediate neurological imaging and consultation will be necessary. [49]

Block failure is another possible risk. If the required level of anaesthesia is not achieved, rebound pain will occur. When the anaesthetic wears off, pain may suddenly increase. These events can reduce the benefits of regional anaesthesia if appropriate measures are not taken to minimise the risks. The use of continuous nerve catheters can reduce these risks and improve the effectiveness of the anaesthetic. In addition to these risks, there is the possibility of long-term neurological damage associated with regional anaesthesia. The epidemiological triangle provides a method for classifying this risk by considering the interaction between the host, the pathogen and the environment. By considering risk factors in patients, the likelihood of neurological injury can be reduced. Risk factors include pre-existing conditions, anatomical characteristics or the use of less risky application techniques. Finally, there is a risk of local anaesthetic system toxicity, where excessive anaesthetic concentration in the bloodstream can

lead to cardiovascular collapse. Early detection and treatment of this toxicity is crucial to minimize harm to the patient and ensure optimal treatment outcomes. [47,48]

The individual complications of regional anaesthesia are of significant importance to anaesthesia practice. They have the potential to influence the course of a procedure significantly. From post-puncture headaches to epidural abscesses, these complications can be diverse and require a thorough understanding and appropriate management strategies. Postdural puncture headache is one of the most common complications of neuraxial blockade. [49] They can be caused by various procedures such as spinal anaesthesia, lumbar puncture or catheter migration. In post-lumbar puncture headache, there is a leakage of cerebrospinal fluid due to a defect in the dura mater. This leads to a decrease in cerebrospinal fluid volume and pressure. Symptoms are typically bilateral and may extend from the forehead to the shoulders, accompanied by neck stiffness and back pain. Treatment can be conservative, including bed rest, hydration and analgesics or invasive. [49, 50] The current gold standard is still treatment with an epidural blood patch. [50]

A common side effect of neuraxial anaesthesia is back pain. Although it is common, neuraxial anaesthesia may not be the sole trigger for its occurrence. Localised disc trauma or overstretching of the associated ligaments as a result of paraspinal muscle relaxation may be the cause. [49] Back pain after a spinal or epidural anaesthetic is usually mild and goes away with time. However, if there is a history of back pain, there is an increased risk of persistent discomfort after anaesthesia. It is interesting to note that the intensity of back pain is not greater after a neuraxial anaesthetic. [51] Treatment usually includes NSAIDs and warm or cold compresses. [49] To prevent back pain after epidural anaesthesia, an anti-inflammatory drug can be added to the local anaesthetic for skin infiltration prior to neuraxial injection. [51]

Back pain should also be taken into account as an indicator of a severe complication. A serious but very rare complication of a neuraxial block is an epidural abscess. Diagnosis is often challenging as symptoms may not appear until days to months after the block. The classic triad of back pain, fever and neurological deficit may not occur. Treatment usually involves surgical abscess drainage and long-term antimicrobial therapy to ensure full recovery. Close monitoring and coordinated multidisciplinary management are essential for successful treatment. [49]

Inadvertent intrathecal administration of local anaesthetics during epidural or caudal anaesthesia can lead to a severe complication of total spinal anaesthesia. [49, 52] It is characterised by sudden onset of haemodynamic instability, respiratory distress, dyspnoea and

sharp Glasgow Coma Scale decline. [52]

Preventive measures such as careful aspiration, test dosing and gradual medication administration can help avoid this complication. Treatment includes placement in the Trendelenburg position to increase venous return, administration of fluids and inotropic support to increase blood pressure. It may also be necessary to perform endotracheal intubation for ventilatory support. Sedation during intubation and mechanical ventilation is usually minimal. Pupil dilatation may occur with very high doses of local anaesthetic but will normalise as the anaesthetic effect wears off. [49]

Another complication that can occur after a dural puncture is meningitis. There is also a risk of infection of the subarachnoid space. Bacteria can enter the central nervous system in several ways. They can come from outside through contaminated equipment, drugs and unsterile work or from inside through a bacterial source already present in the patient. Symptoms, including fever, headache, back pain, vomiting and lethargy, can occur hours to days after anaesthesia. The diagnosis is made by a lumbar puncture in which the cerebrospinal fluid is analysed for cloudiness, an increase in white blood cells, protein and a low concentration of glucose. Treatment consists of early administration of antibiotics before the causative organism is known. The use of steroids may be recommended in some cases, particularly for out-of-hospital meningitis. [49]

The use of neuraxial blocks remains controversial despite their long-standing use. While neuraxial anaesthetic techniques offer significant advantages depending on patient factors and settings, complications arise from a combination of the block itself and patient-specific conditions. Although complications are rare, their importance is increasing as perioperative safety improves. Proper patient selection and technique application are critical to minimising risks. Deviations from the recommendations may be acceptable at the discretion of the anaesthesiologist. Consensus statements aim to promote safe and high-quality patient care but cannot guarantee specific outcomes and are subject to revision as knowledge develops. Evidence suggests that risks traditionally associated with neuraxial anaesthesia in patients with certain medical conditions may not be as common as once thought, potentially challenging the absolute contraindication of neuraxial anaesthesia in these populations. However, further prospective studies are needed to draw definitive conclusions about safety. [49]

9 Conclusion

The increasing prevalence of opioid dependence and misuse has led to increased interest in alternative approaches to perioperative pain management. OFA and analgesia represent a significant paradigm shift aimed at minimising the risks associated with opioid use while providing adequate pain control. These approaches focus on avoiding opioid-related side effects such as respiratory depression, nausea, vomiting, constipation and cognitive impairment. At the same time, they offer targeted pain control through alternative strategies such as regional anaesthesia and the use of nonopioid analgesics. However, regional anaesthesia requires careful patient selection and consideration of contraindications to ensure safety and efficacy. By tailoring the choice of regional anaesthesia technique to individual patient characteristics and surgical requirements, healthcare providers can optimise patient outcomes and improve perioperative care.

The decision to use OFA is particularly relevant for patients with certain risk factors, such as obstructive sleep apnoea, chronic pain or pre-existing opioid dependence, where the use of opioids may increase the risk of complications. By incorporating regional anaesthetic techniques such as nerve blocks or epidural analgesia, the need for systemic opioid administration can be reduced, which may contribute to improved postoperative recovery and a faster return to normal function.

In addition, OFA is becoming increasingly important in conjunction with the principles of ERAS. These multimodal treatment approaches aim to minimise perioperative stress and accelerate recovery. The use of OFA techniques within ERAS can further improve postoperative outcomes and reduce the length of hospital stay.

In conclusion, the opioid-sparing approach offers a nuanced solution to the challenges posed by opioid dependence and misuse in perioperative pain management. Rather than outright prohibition, it advocates for a judicious and thoughtful utilisation of opioids, taking into account individual patient characteristics and surgical needs. Through the tailored use of regional anaesthesia techniques, healthcare providers have the opportunity to optimise patient outcomes and elevate the standard of perioperative care. This approach represents a promising paradigm shift, balancing the need for adequate pain control with the imperative to mitigate opioid-related risks and underscores the importance of personalised, patient-centred healthcare practices.

Although the benefits of OFA are promising, some questions remain. In particular, more

research is needed into the potential adverse interactions between the drugs used and adequate monitoring of pain control. More significant, multi-centre, randomised controlled trials are needed to clarify the long-term advantages and disadvantages of OFA and to assess its effectiveness compared with established opioid-based strategies. Until then, the decision to use OFA should be based on careful consideration of individual patient needs and clinical circumstances. Despite the promising results to date, further evidence-based studies are needed to fully demonstrate the benefits of OFA and establish its use as an alternative to conventional opioid-based anaesthesia.

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