Perioperative Pain Management in Patients on Opioid Replacement Therapy: An Integrative Review

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Background

Pain is something that affects a significant number of people all over the world, whether it be acute or chronic. This unpleasant sensation is conveyed to the brain by sensory neurons and can be the result of actual or potential tissue damage. Pain can stem from several causes such as an injury, illness, a psychological disorder, or it may occur without an identifiable cause. Lifestyle conditions, such as smoking, obesity, stress, anxiety, and health co-morbidities can influence pain as well.[1]

Despite the lack of compelling evidence to support long-term efficacy in the treatment of opioid abuse, opioids are one of the most common classes of medications prescribed in the United States.[2] As such, the significant increase in prescription and illicit opioid abuse since the nineties has led to a surge in patients recovering from addiction and now maintained on opioid replacement therapy (ORT).[3] Due to this rapid growth in ORT, there has been a strong interest in utilization of opioid agonists such as methadone, and partial agonists such as buprenorphine, which have been increasingly utilized to treat severe chronic pain and to prevent withdrawal symptoms in those who have an addiction to opiates.[2] The growth of this patient population has presented anesthesia providers with a challenge. Specifically, these medications interfere with the usual effect of opioids anesthesia providers use to deliver anesthesia and treat acute pain.[3] Understanding the pharmacodynamics of the individual ORT medications prescribed is critical in terms of using the best practices to control pain in the perioperative setting. Additionally, it is imperative to communicate with all members of the healthcare team and to have a plan for managing acute perioperative pain.

Introduction

The aim of this project was to conduct an integrative review of the literature in order to identify best practice guidelines for managing pain perioperatively in the patient population receiving ORT. More specifically, guidelines for patients who have a history of narcotic dependence, whether it be prescription drugs, such as oxycodone, or illicit drugs, such as heroin, and are currently receiving methadone, buprenorphine, or naltrexone therapy will be addressed. The overall goal when delivering anesthesia for this subset of patients is to provide pain control during their surgical experience while simultaneously trying to prevent further dependence and escalation in opioid dosages. This integrative review will include anesthetic management of patients receiving specific ORT medications in order to improve pain scores, decrease narcotic usage postoperatively, and decrease the length of hospital stay. In addition to drug specific considerations and recommendations, this review provides overall recommendations for managing ORT patients in the preoperative, intraoperative, and postoperative phases in a multimodal fashion.

Method

The design used an integrative review of the literature focused on managing patients receiving methadone, buprenorphine, and naltrexone during the perioperative period. The literature was searched with multiple databases including PubMed and MEDLINE to find all relevant articles that pertained to the perioperative use of methadone, buprenorphine, and naltrexone. Key words used in the literature search were, “perioperative”, “buprenorphine”, “methadone”, “naltrexone”, “opioid replacement therapy”, “opioid agonist therapy”, and “pain management”. Of the approximate 80 articles published between the years 2000-2016 initially found, 37 were selected based on their relevance to the topic and chosen themes: perioperative

guidelines for methadone, buprenorphine, and naltrexone usage along with pain management techniques for patients on opioid replacement therapy.

Problem

About 500,000 to 1 million Americans are thought to be opioid dependent and in a methadone maintenance program in the United States.[4] In a recent study done to examine opioid agonist therapy use in Medicare patients, it was concluded that the Medicare population has one of the highest and fastest growing incidences of chronic opioid use. With more than 6 of every 1,000 patients diagnosed, this includes about 300,000 out of 55 million patients. Of that population, about 81,000 Medicare patients are on buprenorphine therapy for their opioid dependence.[5] Even in pregnant women, opioid abuse has increased from 1.19 to 5.63 per 1,000 hospital births per year. Many of these women are now being placed on methadone during their first trimester in attempting to decrease the use of opioids in this population and fetal complications.[2] With this data, the number of patients with chronic or illicit opioid use has increased, and so has the number of patients on ORT.[3]

These patients can be a challenge for anesthesia providers when arriving for surgery. Many providers have misconceptions with this patient population, which leads to inadequate treatment of pain with opioid and non-opioid based techniques. Acute pain management is imperative for increasing patient satisfaction, improving health care cost, and reducing postoperative complications.[2] Understanding too the pharmacodynamics of the individual ORT prescribed is critical in terms of using the best practices to control pain in the perioperative setting. Additionally, it is imperative to communicate with all members of the healthcare team and to have a plan for managing acute postoperative pain.

Findings

Opioid Receptors and Opioid Replacement Drugs The individual ORTs prescribed have variable effects on specific opioid receptors. Several receptors have been identified: mu, kappa, sigma, and delta. These receptors can be found in the brain, spinal cord, and the periphery. An agonist acting on the mu receptor will produce supraspinal analgesia, which causes an inhibitory response acting on pain pathways. It will also cause euphoria and a reduction in ventilatory drive. Kappa receptor stimulation produces spinal analgesia, which is an activation of presynaptic receptors, further decreasing calcium influx and release of neurotransmitters involved with nociception. Sedation and miosis are the ultimate effects of kappa receptor activation. The delta receptor has multiple roles, including responding to enkephalins, modulation of mu receptors, and promotion of spinal analgesia.[6] Opioid replacement therapy interacts with these receptors in order to create similar exogenous results with less euphoric effects.

Methadone (Dolophine) was developed in 1947 during World War II in response to a shortage of morphine.[3] It is a synthetic mu receptor agonist that in present day is most often used for managing chronic pain and opioid addiction.[7] The S-isomer is an agonist of the mu and delta receptors whereas the R-isomer is an antagonist of the N-methyl-D-aspartate (NMDA) receptor, which further increases analgesic effects.[2,7] As a result, methadone inhibits pain pathways, decreasing the awareness and response to discomfort.[8] By strongly binding and occupying mu receptors, it lessens withdrawal symptoms, reduces opioid cravings, and will diminish the euphoric effects of other illicit opioids, if used.[8,9]

Methadone is highly protein bound and has active metabolites which are renally cleared.[2] As a result, it has a relatively long and variable pharmacologic half-life of 8 to 60 hours with

analgesic effects lasting up to 24 hours, but usually between 4 to 8 hours. It is associated with less euphoria and does not mimic the effects of typical opioids. Due to this, there is less potential for abuse. However, a notable drawback to methadone use is the tendency to promote the development of hyperalgesia or pain intolerance over time due to upregulation of pronociceptive pathways. Since it has pharmacological unpredictability, it is possible methadone will adversely interact with other medications, which further complicates managing this population. Additionally, methadone is known for its' propensity to cause QT prolongation. Providers need to take caution when co-administering other medications that cause QT prolongation, such as ondansetron.[3]

Buprenorphine is an opioid agonist-antagonist also used as an oral preparation for the control of chronic pain and opioid addiction. It functions as a partial agonist at the mu and delta receptors, and as a competitive antagonist at the kappa receptor.[10] As a partial mu agonist, it has less potential for life-threatening respiratory depression. As a potent kappa antagonist, it will display less dysphoria effects compared to methadone and can potentially be better tolerated.[11] It also has a "ceiling effect", which means after a certain point, increasing the dose will not provide any additional benefits.[12] When clinicians started prescribing buprenorphine in the 1980s, they noticed that patients typically did not receive any analgesic benefit from the addition of other opioids.[3] The frequent inability of other opioids to provide additional analgesia is secondary to buprenorphine's high affinity to the mu and kappa-receptors, which is 1000-fold higher than morphine.[3,12,13] Buprenorphine slowly dissociates from its receptors which accounts for its long half-life of 37 hours.[2]

Buprenorphine is much like methadone in the sense addicts do not experience a sense of euphoria when other opioids are used concurrently, which helps discourage illicit drug use.

Buprenorphine can be manufactured as a buprenorphine-only product (Subutex) or as a combination product with naloxone (Suboxone) which are both administered sublingually.[3] The naloxone component is added as an antagonist to block opioid receptors and to deter IV abuse and prevent potentially fatal overdose.[2]

Naltrexone is a long-acting oral opioid antagonist with a high affinity to mu receptors.[14] It functions to prevent and reverse effects that mu opioid agonists produce and has been shown to reduce the desire for opioid drugs.[3,15] The half-life is about 4 hours, but the extended-release formulation can produce significant plasma levels for up to 30 days.[3] Naltrexone has been shown to reduce symptoms in chronic conditions such as multiple sclerosis, fibromyalgia, Crohn's disease, and complex regional pain syndrome.[16] Long term use of the drug has been shown to produce upregulation of opioid receptors. When treating acute pain and stopping naltrexone, an amplified response to opioid agonists may result. [17]

Preoperative Management

The first step in developing and planning an anesthetic technique is to communicate with the patient and obtain a comprehensive health history. If the patient has a history of opioid abuse, establishing rapport helps them to open up and display honesty about any recent drug use.[2] It is vital to create a nonjudgmental environment in order to ask questions about history of drug use, drug use frequency, and any other pertinent questions. The patient will more likely be forthright about prior or ongoing drug use if it is understood this information will be utilized in an effort to achieve more effective perioperative pain management. A urinary drug screen may be indicated if ongoing drug use is suspected but not divulged by the patient.[2]

Once the specific ORT has been identified, a perioperative pain management plan can be developed. The next step is to ensure the ORT has been administered appropriately. Each drug has specific recommendations developed to best ensure pain control.

Methadone Managing a patient in the operating room who is receiving methadone for ORT presents many challenges. The daily dose of methadone should be administered and continued through the perioperative period.[2,7] Instructions to take the usual dose the morning of surgery should be given in the pre-anesthesia clinic.[7] If the morning dose is not taken, an equivalent dose of morphine or hydromorphone can be given orally or IV.[18] Converting methadone doses to morphine (or equivalent) can be achieved by utilizing expert guidelines such as the Royal Perth Methadone Conversion Protocol. This protocol accounts for the typical finding that patients on higher doses of methadone require higher ratios of morphine. The recommended conversion ratio of methadone to morphine ranges from as low as 1:3 for patients on lower doses of methadone to as much as 1:20 for patients on high doses of methadone.[19] The correct dose of ORT methadone should be verified with the patient and prescribing physician, if possible.[2,7] If postoperative oral methadone is not feasible, IV dosing can be utilized. The usual ratio for conversion from oral to IV is 2:1, although patients may require a higher ratio of 1:1.[2]

The anesthesia provider must communicate a history of opioid abuse will not prevent the administration of pain medications.[7] A common misconception is the maintenance dose of methadone provides adequate perioperative analgesia. Due to the analgesic effect being shorter than the pharmacological effect and the tendency toward hyperalgesia, a comprehensive pain regimen must be in place for the perioperative period.[10]

In a double-blind study done by Doverty, Somogyi, White, et al., it was found that patients taking maintenance methadone therapy were cross-tolerant to the analgesic effects of

morphine, and when pain relief was achieved, it did not last as long as expected. This may explain why ORT patients may necessitate higher and more frequent dosing of analgesics in order to achieve pain relief.[20] This underscores the need for a comprehensive perioperative pain management plan tailored to each patient. It is generally agreed that opioids along with non-opioid based techniques should be employed to help manage these patients perioperatively.[3] This multimodal approach will be discussed further on.

Buprenorphine Given buprenorphine's unique pharmacologic properties, specifically its' high affinity for opioid receptors, long half-life, and tendency to block effects of other opioids, it can be very problematic in the perioperative setting. For the surgical patient receiving buprenorphine, there are a few options available that the literature suggests. The particular option used for a given patient should be based on the anticipated duration of pain, treatment, and response to the chosen option.[9]

Option 1 is to continue the buprenorphine maintenance therapy during the perioperative period, maximize the use of nonopioid analgesics, and treat acute pain with opioid analgesics.[2,5,21] Significantly higher doses of opioid analgesics may be needed in order to provide adequate comfort because of competition with buprenorphine at the mu receptors. Weak opioids, such as codeine and hydrocodone, are not usually given as they are unlikely to have any effect.[2] Highly potent opioids, such as sufentanil, are much more likely to be beneficial. The daily dose of buprenorphine may be divided and administered every 6 to 8 hours in order to fully utilize the analgesic properties of the drug, although this is usually only beneficial in low-dose therapy.[2,3] This first option is recommended for patients whose procedure will involve mild to moderate pain.[2,7,21]

Option 2, and the most preferred for anticipated moderate to severe postoperative pain, is to discontinue buprenorphine altogether. Ideally, it will be tapered over a 2-3 week period and totally discontinued as of 72 hours prior to the procedure. As withdrawal may be inevitable, it is recommended to consider starting methadone 30-40 mg per day.[2,3,7] If withdrawal symptoms still occur, methadone may be increased by 5-10 mg per day.[2] Stopping buprenorphine will eradicate the partial blockade at the mu receptor caused by the partial agonist actions. The patient will then be buprenorphine free for the procedure, allowing for better pain management perioperatively. Further surgical pain is controlled with nonopioid analgesia, including regional anesthetic techniques, along with IV opioids for acute pain management.[2,7] Postoperatively, the patient may be discharged home on pure agonist opioids with the plan to begin an induction protocol for buprenorphine at home. Alternatively, buprenorphine can be resumed in the hospital once opioid agonists are no longer administered.[2,7] Situations such as these require a multidisciplinary approach involving a pain specialist.

When weighing options for perioperative pain control in buprenorphine maintenance, each individual patient's unique circumstances should be considered, along with provider experience. There is limited clinical experience with this population and current recommendations are based on case reports and clinician practice preferences.[2] In a summary statement by Kornfeld and Mandredi, "the use of full agonist opioids for patients stabilized on buprenorphine may be problematic because of the tight binding at the mu receptor, leading to a partial opioid blockade and reduced analgesia, and that postoperative care in the opioid-dependent patient has special risks, requiring careful monitoring for respiratory depression as well as adequate pain control."[22] That being said, clinical experience may help the clinician

decide how best to prepare patients on buprenorphine.[2] All sources agree on utilizing opioid and non-opioid analgesic techniques regardless of the management option selected.

Naltrexone Naltrexone does not need to be discontinued in the perioperative setting if the patient is to undergo a minor procedure and nonopioid techniques can be utilized. For a major surgery where opioids will be needed, naltrexone should be stopped 24 to 72 hours prior.[17,23] The amount of opioid needed may be increased if a serum level of naltrexone remains at the time of surgery.[23] Alternatively the receptor upregulation effect may reduce the opioid required to achieve pain control. As such, the provider must be mindful of respiratory depression with larger dosages of narcotics.[23]

Multimodal Pain Therapy

The next step in the development of an anesthetic plan is to select a pain management regimen. Unfortunately, additional research needs to be conducted in order to make a specified recommendation.[24] In the research available, multimodal therapy is emphasized. Multimodal therapy is a means for treating pain through two or more differing mechanisms of action.

Heit and Gourlay suggest if time allows, a consultation with a pain specialist should be scheduled beforehand in order to discuss postoperative pain treatment.[25] Patient education is necessary in order to relieve anxiety and to discuss concerns related to pain control.[18] There is no recommended universal pain regiment, but each plan should be individualized in regard to the patient, their pain level, and the procedure planned.[25] Several articles reference multimodal analgesic therapy highlighting the use of regional anesthesia whenever possible.[7,18,26,27] Systemic nonopioid analgesics should be utilized as well. These include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, gabapentin or pregabalin, ketamine, and lidocaine.[7,18,26] Acute

pain can also be treated with opioids during the intraoperative setting, but larger doses may be needed.[2,3]

Ideally, this multimodal approach to pain control includes IV opioids, IV or oral acetaminophen, gabapentinoids, alpha-2 agonists, NSAIDs, ketamine, and regional analgesia, including subcutaneous infiltration.[27] This paper will not discuss other adjuncts discussed in the literature such as magnesium, lidocaine infusions, or glucocorticoids.

Acetaminophen is an antipyretic and analgesic which has minimal anti-inflammatory properties, but has few side effects compared to traditional opioids.[28] It is usually given orally, but IV acetaminophen (Ofirmev) has become more commonly used in recent years. It has an onset of about 5-10 minutes when given IV and is usually administered as a 100 mL solution over 15 minutes.[28,29] A meta-analysis found that adding IV or oral acetaminophen to morphine following major surgery led to a statistically significant reduction in morphine use.[30] Unless contraindicated, IV acetaminophen can be considered as a principal analgesic in a multimodal regimen to provide basal pain relief via administration in a scheduled fashion, utilizing opioids on an as needed basis for breakthrough pain. It is preferred in the perioperative setting due to the peak analgesic activity at about 1 hour following administration and the 6 hour duration of action. The most common IV dosing for adults is 1000 mg every 6 hours, not to exceed 4000 mg in 24 hours. Scheduled acetaminophen can decrease the amount of opioid required for pain relief while also improving overall pain control.[31] Combining acetaminophen, whether oral or IV, with NSAIDs in a multimodal approach has been shown to help with pain control and should be considered in pain management.[32]

Gabapentinoids, such as gabapentin and pregabalin, act on presynaptic calcium channels and inhibit neuronal influx of calcium, resulting in a reduction of excitatory neurotransmitters

(glutamate and substance P). This neurotransmitter reduction decreases neuronal excitability after tissue or nerve damage. Gabapentinoids can contribute to the multimodal approach by reducing postoperative pain and preventing opioid tolerance.[33] Both medications have been shown to reduce opioid requirements after minor and major surgical procedures and are most effective when administered during the preoperative phase 1 to 2 hours before incision. Optimal dosing has not been concluded, but it is shown that higher doses can be more effective. This class of drugs is encouraged in the population with high opioid tolerance.[34]

Alpha$_2$ adrenergic agonists act on receptors located presynaptically and postsynaptically in the central and peripheral nervous system. When presynaptic receptors are activated, a negative feedback loop is initiated, which inhibits the release of norepinephrine. Stimulation of postsynaptic receptors in the central nervous system prevents sympathetic nervous system activation. Clonidine and dexmedetomidine are two well-known drugs in this class.[33] Although not used often, a preoperative dose of 150-200 mg of clonidine has been shown to improve hemodynamic stability, reduce postoperative opioid use, and decrease anxiety.[35,36] Postoperative use of clonidine has not shown to be effective. A dexmedetomidine bolus of 1 mcg/kg IV before regional anesthesia has shown to reduce anxiety, sympathoadrenal responses, and intraoperative opioid requirements.[37] A recent review concluded that both medications were associated with a decrease in pain intensity, opioid consumption, and postoperative nausea.[38]

NSAIDs are another means of pain relief supported in the literature. They inhibit prostaglandin synthesis and achieve pain relief by acting on COX-1 and 2 receptors with analgesic, antipyretic, and anti-inflammatory properties.[30] Utilizing celecoxib 200-400 mg 30 minutes to 1 hour before surgery has shown a reduction in Visual Analog Scale pain scores compared to those who received a placebo.[31,34] In another randomized, double-blind trial, 800

mg of ibuprofen given every 6 hours reduced morphine consumption by 22% and was generally well tolerated.[32] The Practice Guidelines that have been developed by the American Society of Anesthesiologists recommends the use of NSAIDs around-the-clock as part of the multimodal pain regimen, unless contraindicated.[34]

Intraoperative

There are several interventions during the intraoperative time period that have shown to be beneficial in a multimodal pain management regimen. One such intervention that is recommended is maintaining a consistent dosing schedule of NSAIDs. Ketorolac is the most widely used, and can be given IV 30-60 minutes prior to the end of surgery, if not contraindicted.[39] This nonselective medication has been shown to reduce opioid consumption by up to 45%, lowering opioid-related side effects.[40]

Ketamine has gained the attention of many clinicians as part of the multimodal approach toward treating acute pain. It acts on the N-methyl-D-aspartate (NMDA) receptor in the central and peripheral nervous systems, and non-competitively blocks the NMDA receptors. Ketamine has analgesic and antihyperalgesic properties so it is a useful adjunct in the management of perioperative pain.[33] IV ketamine infusions have been associated with decreased postoperative opioid use compared to placebo infusions, and a few studies showed a reduction in pain scores. Ketamine administration in the pre, intra, and postoperative time periods with widely varying doses has been studied. There has not been enough evidence to determine the optimal time and dose, but it is suggested a preoperative bolus of 0.5 mg/kg followed with an infusion of 10 mcg/kg/min intraoperatively, with or without a postoperatively infusion, is helpful. Ketamine is especially suggested for use in the highly opioid-tolerant patient population. Clinicians who administer it should be familiar with the adverse effects, such as hallucinations. It is also

recommended that ketamine infusions be discontinued 60 minutes before the end of surgery in order to prevent prolonged emergence.[34]

The use of peripheral and neuraxial anesthesia with local anesthetic is advocated for multimodal pain management due to its effectiveness in postoperative pain control.[34] These techniques help to "inhibit the neural conduction from the surgical site to the spinal cord and decrease spinal cord sensitization".[28] The use of peripheral regional anesthesia can be done on a multitude of procedures, especially in orthopedic cases. A single-injection or continuous infusion may be utilized, but it is recommended that a continuous infusion be administered if postoperative pain is more likely to be prolonged due to the limited duration of action with a single-shot technique.[34] Peripheral techniques may have several advantages over systemic opioids, such as a decrease in the opioid-related side effects, while still providing superior pain control.[28]

Neuraxial analgesia is highly recommended for major thoracic, abdominal, hip and lower extremity procedures, especially in patients with a pertinent cardiac or pulmonary history. Epidural and spinal analgesia are associated with a reduction in postoperative pain scores and opioid use in a multitude of procedures. There are many benefits to neuraxial techniques, such as a decreased risk of postoperative mortality, venous thromboembolism, myocardial infarction, pneumonia, and ileus. A potential benefit of epidural compared to spinal analgesia is that an epidural technique can be used as a continuous infusion of local anesthetic or as patient-controlled epidural analgesia (PCEA).[34]

The use of subcutaneous infiltration of long-acting local anesthetic at the surgical site has also been studied in many surgical procedures, including total knee replacements, cesarean

sections, laparotomies, and hemorrhoid surgery. Some studies have found a benefit while others find no benefit to infiltration of local anesthetics.[34]

Postoperative

Most of the pain control techniques discussed are implemented before the postoperative phase begins, but may be continued during the patient's hospital stay. A postoperative patient-controlled analgesia (PCA) pump provides for a useful option for pain control. Utilizing this in the post-anesthesia care unit (PACU) will help with inadequate doses of medication and breakthrough pain. Due to the high opioid dose requirements sometimes necessary, heart rate, respiratory rate, airway patency, and pupil dilation should be closely monitored to prevent complications in recovery. It is necessary to continue baseline chronic pain opioids and all pain adjuncts that have been utilized during the preoperative and intraoperative periods.[18]

Summary

Patients who are receiving long-term ORT are presenting to the operating room with increasing frequency for both elective and emergent surgical procedures. Patients receiving these medications require special care and consideration, distinguishing them from patients requiring typical opioid agonists. The complexity of perioperative pain management in conjunction with ORT requires collaboration and a multidisciplinary approach. Each patient should be made aware their history of narcotic usage does not preclude adequate perioperative pain management, which is often not achieved without a structured approach. A tailored plan should be developed specific to each individual patient in order to address their particular form of ORT as well as managing their perioperative pain. Methadone should always be continued through the day of surgery and during the postoperative phase. Depending on the particular patient and surgical scenario, buprenorphine may be continued, stopped altogether, or transitioned to methadone.

Similarly, naltrexone may either be continued or stopped, depending upon the surgical intervention and anticipated pain control requirements.

In all cases, a multimodal approach to pain management is crucial. Multimodal approaches include – but are not limited to – IV opioids for acute pain, acetaminophen, gabapentinoids, alpha-2 agonists, NSAIDs, ketamine, and regional analgesia. These multimodal agents should be initiated during the preoperative phase and continued throughout the hospital stay. Continued communication with the patient, surgeon, pain specialist, and treating physician is imperative for best treatment outcomes. The recovery team should be made aware of all techniques used for pain management and assessments should be done at timely intervals.

Discharge planning should be initiated at an early phase due to the potential complexity of managing ongoing pain and transitioning safely back to a stable ORT regimen. This is especially important in the case of re-initiating patients on buprenorphine maintenance given the risk of precipitating withdrawal from opioid prescribed in the post-operative phase. Again, a collaborative approach involving a pain specialist is often necessary. If the patient is returning home while requiring opioids, it is recommended the patient be provided specific education and instructions on tapering and transitioning opioids after discharge from the hospital.[34]

Conclusion

Chronic pain and substance abuse are a pervasive problem throughout the world. Management of opioid addiction via ORT is increasingly common and presents unique challenges to the anesthesia provider. An understanding of the basic pharmacology of various medications used for ORT, such as methadone, buprenorphine, and naltrexone, is critical in order to safely provide satisfactory analgesia in the perioperative setting. To do so, the provider must take each individual's specific situation into special consideration and approach each case in a

collaborative fashion. Multimodal therapies are essential and are increasingly being utilized and expanded upon. Further development of new multimodal therapies is an area of active interest. With ongoing awareness and pursuit of further modalities, anesthesia providers will be able to manage patients on ORT with increasing confidence and success.

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