



Optimizing perioperative analgesia for the complex pain patient: medical and interventional strategies

L'optimisation de l'analgésie périopératoire du patient avec douleurs complexes: stratégies médicales et interventionnelles

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Abstract

Purpose *The purpose of this article is to review the literature and to highlight current practice regarding the management of the chronic pain patient presenting for surgery.*

Principal findings *It can be difficult to achieve adequate postoperative analgesia in patients who present for surgery with preexisting chronic pain. Such complex pain patients require a care plan that involves preoperative, intraoperative, and postoperative considerations. Preoperatively, it is important to identify these patients' specific concerns, to address anxiety, to review expectations of care, and to consider premedication. Intraoperatively, it is important to consider local anesthetic regional anesthesia techniques and to supplement as necessary with pharmaceutical agents, e.g., ketamine, dexamethasone, ketorolac, and opioids. Postoperatively, it is important to continue multimodal analgesia techniques. It is vital to maintain a healthy therapeutic alliance with the patient and with allied health professionals. Nonspecific treatment effects can bolster efforts to achieve adequate analgesia.*

Conclusion *Successful management of the complex pain patient requires knowledge of the art and science of perioperative medicine.*

Résumé

Objectif *L'objectif de cet article est de passer en revue la littérature et de souligner la pratique actuelle concernant la prise en charge du patient souffrant de douleur chronique et se présentant pour une chirurgie.*

Constatations principales *Il peut être difficile de réaliser une analgésie postopératoire adaptée chez les patients se présentant pour une chirurgie mais souffrant de douleur chronique préexistante. Ces patients avec douleurs complexes ont besoin d'un plan de soins qui tient compte de considérations pré-, per- et postopératoires. En période préopératoire, il est important d'identifier les préoccupations spécifiques de ces patients, de tenir compte de leur anxiété, de passer en revue leurs attentes en matière de soins et d'envisager une prémédication. En période peropératoire, il est important d'envisager des techniques d'anesthésie régionale utilisant des anesthésiques locaux et de les compléter, au besoin, avec des agents pharmaceutiques tels que la kétamine, la dexaméthasone, le kétorolac et les opioïdes, par exemple. En période postopératoire, il est important de poursuivre les techniques d'analgésie multimodales. Il est essentiel de maintenir une alliance thérapeutique saine aussi bien avec les patients qu'avec le personnel paramédical. Des effets non spécifiques d'un traitement peuvent soutenir les efforts pour obtenir une analgésie adaptée.*

Conclusion *La prise en charge réussie du patient avec douleurs complexes nécessite des connaissances concernant l'art et la science de la médecine périopératoire.*

As to diseases, make a habit of two things – to help, or at least to do no harm.

It is more important to know what sort of person has a disease than to know what sort of disease a patient has.

Hippocrates

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Introduction and scope of the problem

Pain control after surgery continues to be a major problem. It can be challenging in patients presenting from a major joint, thoracic, or open abdominal surgery. Patients presenting with anxiety, pain catastrophizing, and high levels of pain will be at increased risk of experiencing significant postoperative pain.¹ Therefore, it is not surprising that only one in four surgical patients receives adequate relief of acute pain.²

To further complicate matters, it is estimated that at least one in five Canadians suffers from chronic pain, with the majority of individuals indicating moderate to severe pain.³ Results of a Scottish survey of patients with chronic pain showed that 8% of individuals had neuropathic pain, most often reported as being severe.⁴ In Canada, fibromyalgia syndrome (FMS) is reported to occur in 2–3% of individuals,⁵ and results of another Canadian survey showed that 22% of FMS patients were also suffering from depression.⁶ Indeed, a concurrent mood disorder, such as major depression, is commonly present in chronic pain patients. In the treatment of chronic pain, practitioners often prescribe multiple analgesics, such as sustained release opioids, anticonvulsants, antidepressants, and nonsteroidal anti-inflammatories.⁷ These medications carry risks of side effects and possible drug interactions that need to be monitored in the postoperative setting. Further, patients with chronic pain tend to be more sensitive to painful conditions. They may experience a flare of their underlying pain disorder and may be more physically deconditioned, thus making it more challenging to treat them postoperatively.^{8,9} Chronic pain patients may be frustrated with the medical system, experience dysfunction in their personal life, and be irritable and sleep deprived.

Thus, individuals with chronic pain who undergo surgery can be classified as having complex pain. Fortunately, anesthesiologists can use their knowledge and skill to implement strategies to optimize perioperative pain control for patients who present with acute or chronic pain, although it may require added time and resources to do so. Anesthesiologists can guide complex pain patients through the preoperative, intraoperative, and postoperative phases. The focus of this review is to help the perioperative clinician utilize medical and interventional approaches to treat the complex pain patient with an emphasis on the management of patients with opioid tolerance, neuropathic pain, and fibromyalgia.

Preoperative phase: general principles

It is ideal for surgeons to refer patients with preexisting pain problems to an anesthesiologist for preoperative evaluation well ahead of their scheduled surgery. Vickers *et al.* have highlighted characteristics of pain patients that can provide a guide for surgical referral.¹⁰

1. Previous difficulty with adequate postoperative pain management
2. On long-term opioid therapy
3. At risk for neuropathic pain, including patients who will sustain nerve damage during surgery, e.g., thoracotomy or amputation.
4. Have a chronic pain syndrome
5. Have significant anxiety over postoperative pain

Patients seen in our preadmission clinic who are thought to be a potential challenge are flagged by the acute pain service (APS). On the date of the procedure, the APS communicates with the anesthesiologist and coordinates strategies for pain control.

A pharmacist is available in our preadmission clinic to help ensure accuracy of analgesic names and doses and possible drug interactions as well as to confirm which pharmacy the patient is utilizing. This information may help avoid errors in drug administration, especially when dealing with polypharmacy. Previous perioperative records may be reviewed in order to avoid pitfalls or to replicate good experiences.

Further information should be obtained about a complex pain patient's pharmacotherapy. If an analgesic is being used, is it effective? Has the patient tried a higher dose? If yes, what was the response or side effect? What other pain medication has a patient tried, and why was it stopped? Patients may report an inadequate response from a certain analgesic, but this may have been due to inadequacy in dosing or duration of usage; therefore, it may be reasonable to restart such a medication postoperatively. This principle often applies to anticonvulsants and antidepressants.

It is useful to record details about the underlying pain, such as location, intensity, quality, and relieving factors, e.g., response to physical modalities like heat or cold. Preoperative neurologic deficits or neuropathic conditions, such as allodynia and hyperalgesia, should be recorded, especially if regional anesthesia or topical analgesia techniques are being considered. Allodynia is pain due to a stimulus that does not normally evoke discomfort, e.g., a light touch. Hyperalgesia is a heightened response to a painful stimulus.

Recording all this information about a chronic pain patient preoperatively helps to achieve patient-centered care. Chronic pain patients who have no individualization in their perioperative analgesia care plan may feel frustrated, isolated, angry, or anxious. These are medicalized patients who have often seen multiple providers in different disciplines. They have firm beliefs about their chronic pain and expect perioperative health care workers to comprehend the nature of their condition. Recognition of chronic pain is often the first step in establishing trust in the physician-patient relationship, and

it will assist in alleviating any anxiety patients may have about their upcoming surgery. Conversely, the chronic pain patient should not be given falsely elevated hopes of minimal postoperative pain, as elevated expectations can collapse rather dramatically. Regardless of the etiology, high levels of psychological distress are likely to lead to high levels of postoperative pain and lower levels of postoperative functioning,¹¹ and they may also increase the likelihood of chronic postsurgical pain.¹²

Whenever possible, multimodal analgesia is initiated one to two hours prior to surgery with the administration of agents such as acetaminophen 1,000 mg and a cyclooxygenase-2 selective agent (e.g., celecoxib 400 mg) or an anti-inflammatory that the patient knows to be effective. Patients should also be informed of the benefits of regional anesthesia techniques for certain types of surgery, with or without general anesthesia. A gabapentinoid should be prescribed for patients with neuropathic pain or for those at high risk of neuropathic pain developing postoperatively. Gabapentin at a dose of 600 mg is commonly used,¹³ with a range of 300–1,200 mg found in the literature.¹⁴ An alternative is pregabalin 150 mg (with a range of 100–300 mg preoperatively), although it is more costly.¹⁵ If anxiety is observed preoperatively, a dose of lorazepam may be ordered. Oral clonidine^{16,17} may provide sedation, anxiolysis, and some improvement in analgesia without any respiratory depression, but its use is limited by the possibility of hypotension and bradycardia.

Preoperative considerations: opioid tolerance

Patients taking more than the equivalent of 72 mg of oral morphine per day ($1 \text{ mg}\cdot\text{hr}^{-1}$ morphine *iv*) for more than one month can be considered to have opioid tolerance.¹⁸ Most patients on long-term opioid therapy can be managed with < 200 mg per day of oral morphine equivalents.¹⁹ Patients on high doses of opioid present a challenge postoperatively since they are less responsive to exogenous opioids and may develop opioid-induced hyperalgesia (OIH).²⁰ The opioid-tolerant patient should be forewarned that it might be necessary to rotate their opioid to another one postoperatively due to the benefits of incomplete cross-tolerance. It is therefore important to document if the patient has experienced adverse effects with other opioids. The prescribing clinician may taper high doses of sustained-release opioids as much as possible preoperatively (in order to improve the odds of opioid responsiveness postoperatively), but there is no firm evidence to support this as routine practice.²¹

Patients on long-term opioid therapy should take their usual opioid as a premedication before surgery in order to maintain baseline levels of opioid and to prevent a postoperative reduction in opioid analgesic serum levels

(opioid debt) along with opioid withdrawal symptoms. Patients using a transdermal fentanyl patch may continue to use it, but the patch should be placed away from any area of intraoperative concern or away from where a heating blanket may be applied intraoperatively, since heat can significantly increase the amount of absorbed fentanyl. For major operations, it may be advisable to rotate the fentanyl transdermal patch to another sustained-release opioid.²²

Patients using methadone should have a baseline electrocardiogram to rule out any QT interval prolongation. If they are using methadone for pain or addiction, the prescribing clinician should be notified of the impending surgery, the possible need to adjust the dosing, and the need to schedule follow-up appointments following discharge. If methadone is being prescribed once a day, it will benefit pain control measures for a period of only six to eight hours.²³ In some cases, it may be possible to adjust the methadone from a once daily dose used for addiction maintenance to a three times daily dosing schedule that would benefit pain control; however, this requires collaboration with the original doctor who prescribed the methadone and with a chronic pain specialist familiar with methadone. In Canada, a federal exemption is required for prescribing methadone for hospitalized patients, and the pharmacist can be proactive in facilitating this arrangement.

Preoperative considerations: neuropathic pain

Opioids are considered third-line not first-line agents for patients experiencing chronic neuropathic pain. Thus, every attempt should be made to manage these patients with gabapentinoids, tricyclic antidepressants, and/or serotonin noradrenaline reuptake inhibitor (SNRI) medications. If the patient is a candidate for a gabapentinoid, it is ordered as a preoperative dose, and the patient should be informed of the benefits and common side effects. If the patient is already using non-gabapentinoid anticonvulsants, it may be important to order hepatorenal function and hematology tests as necessary.⁷

Preoperative phase: fibromyalgia

Recent Canadian guidelines have been published regarding the diagnosis and management of fibromyalgia.⁵ The patient with fibromyalgia will often exhibit associated anxiety, depression, and numerous somatic symptoms, including nonrestorative sleep, fatigue, morning stiffness, irritable bowels, and pelvic pain. Spending extra time with a fibromyalgia patient in order to document associated symptoms may help direct the APS and nursing care postoperatively. Patients have often tried a gabapentinoid, a

SNRI (duloxetine), or other antidepressant medication, and if they have not, they may wish to do so prior to elective surgery in order to treat and stabilize their condition. Indeed, it may be reasonable to administer a preoperative dose of gabapentinoid or anxiolytic.

Intraoperative phase: principles of management

The most helpful strategy for the intraoperative care of chronic pain patients involves the use of ketamine. Ketamine infusions should be administered for patients with opioid tolerance, neuropathic pain, poorly controlled pain (including fibromyalgia),²⁴ or for patients at risk of developing chronic postsurgical pain. Intraoperative administration of ketamine can facilitate control of postoperative pain exceeding five elimination half-lives of the drug.²² Patients should be forewarned of the small chance of postoperative psychotomimetic effects and can be given a perioperative dose of benzodiazepine. The precise dose and administration technique varies between studies, but a common regime is to administer an intravenous bolus of 0.25–0.5 mg·kg⁻¹ after induction of anesthesia, to continue with a low-dose infusion of 0.25 mg·kg⁻¹·hr⁻¹ for moderately painful procedures, and to administer an infusion of 0.5 mg·kg⁻¹·hr⁻¹ for severely painful procedures.²² These regimes usually consist of stopping the infusion or intermittent doses half an hour prior to tracheal extubation. Low-dose ketamine infusions may be continued postoperatively in some centres; however, at our institution, it is only allowed in the postanesthesia care unit and intensive care units.

In a recent meta-analysis, an intravenous dose of magnesium has been shown to reduce opioid consumption to some extent for up to 24 hr postoperatively (mean reduction 7.6 mg; 95% confidence interval -9.5 to -5.8; $P < 0.00001$).²⁵ No significant side effects, other than bradycardia, were observed at a dose of 40–50 mg·kg⁻¹ intraoperatively, commonly administered over a period of 15 min. There is a possibility of sedation and augmentation of neuromuscular blockade with the use of magnesium. It should be emphasized that magnesium deficiency occurs in 7–11% of hospitalized patients, and magnesium administration can reduce hyperexcitability of the central nervous system, augment *N*-methyl-D-aspartate (NMDA)-receptor antagonism, and reduce the incidence of nausea and shivering.²⁶

All patients with complex pain should be considered for a single dose of dexamethasone at induction of anesthesia or as a premedication as it takes one to two hours to be effective. In their recent meta-analysis of 5,769 patients, Waldron *et al.* found beneficial effects of dexamethasone in reducing postoperative pain for up to 24 hr with no adverse effects other than elevated blood sugar levels (mean

0.39 mmol·L⁻¹) at 24 hr.²⁷ The authors acknowledged that the reduction in pain may be statistically significant but may not be as clinically relevant. One recommendation is to use an 8-mg dose, although the optimal dose and timing of administration are not as clear for pain control as they are for reducing postoperative nausea and vomiting.^{28,29} An additional benefit of dexamethasone includes less fatigue in the days after surgery.³⁰

For patients considered candidates for a parenteral nonsteroidal anti-inflammatory drug (NSAID), ketorolac is often utilized intraoperatively. In an editorial by White *et al.*, they indicated that “Both intravenous and intramuscular doses of ketorolac are safe and effective in the vast majority of elective surgical patients when administered as an analgesic adjuvant during the perioperative period.”³¹ This editorial also indicated that a dose of ketorolac 30 mg may be administered intravenously and that numerous studies have shown ketorolac to improve analgesia perioperatively despite a meta-analysis indicating that a 60-mg dose is superior.³¹

In terms of intraoperative opioid management, a preoperative hourly opioid dose should be determined, and this equivalent amount should be administered intravenously during the operative phase to prevent any opioid debt. The added amount of opioid required to treat acute or chronic pain is variable and may be 30–100% over preoperative doses.³² One strategy to determine the correct amount of opioid that a patient requires is to have the patient breathe spontaneously at the end of the anesthetic, reduce the MAC levels of volatile anesthetic, and titrate administration of the opioid that will be used postoperatively (commonly hydromorphone). Administration of opioids prior to tracheal extubation should be continued until a breathing frequency of 12–14 breaths·min⁻¹ is obtained along with a slight miosis in pupillary size.³²

A lidocaine intravenous infusion is advocated for patients undergoing abdominal surgeries without an epidural catheter.^{33,34} At some centres, this infusion of lidocaine may continue into the postoperative phase for up to 24 hr.³⁵ A common dosing schedule is to use a 1.5 mg·kg⁻¹ loading dose followed by 1.5 mg·kg⁻¹·hr⁻¹ throughout the operative period.²⁶ It has not shown any benefit for somatic pain and may or may not show any benefit for neuropathic pain.^{36,37}

Intraoperative phase: interventional techniques

The principle of care for a complex pain patient requires that a local anesthetic technique should be employed when it can be employed.^{9,38,39} Specific operative procedures may have specific evidence-based management algorithms that can be found in the literature or as part of the PROSPECT group’s review of current evidence at

<http://www.postoppain.org>. Peripheral nerve plexus catheters are encouraged for complex pain patients undergoing extremity surgery, as the duration of postoperative analgesia can be extended beyond the maximum of 24 hr seen with most single-shot nerve blocks.

Epidural placement is often promoted for complex pain patients undergoing thoracic, open abdomen, or bilateral lower extremity procedures, especially in patients with a background of poorly managed preoperative pain or those with a history of sleep apnea. For patients having abdominal surgery who are not candidates for epidural placement, transversus abdominis plane blocks³⁵ may be performed or consideration may be given to intravenous lidocaine perioperatively.

Chronic pain patients may need more sedation than others for nerve blocks, both during the procedure and afterwards, especially if they continue to display high levels of anxiety about pain developing perioperatively. Some complex pain patients will request a general anesthetic or may not be candidates for any regional anesthesia technique. In these patients, it may be helpful to have the surgeon provide local anesthesia infiltration prior to tracheal extubation or place a wound catheter to deliver local anesthetics for a day or two postoperatively.

Postoperative phase: medical management

All patients with acute or chronic pain should be informed of the role of the APS, if such a service is available. It is the responsibility of the APS to manage patients with a multimodal or balanced analgesia approach.⁴⁰ This may include opioid-sparing techniques with the use of around-the-clock acetaminophen and anti-inflammatories at the maximal dose possible. Local anesthesia techniques are integral to any multimodal analgesia regime for the complex pain patient with added consideration given to single-dose dexamethasone, gabapentinoids,⁴¹ ketamine,⁴² and possibly magnesium.²⁶ Intravenous lidocaine infusions for up to 24 hr are recommended for patients having open abdominal surgery but not considered candidates for an epidural.^{33,34,43}

A newer drug that can reduce postoperative morphine consumption is dexmedetomidine, a selective centrally acting α_2 agonist.^{43,44} It has properties of sedation, anxiolysis, sympatholysis, and analgesia but no respiratory depression. Results of a recent meta-analysis indicated that dexmedetomidine (like clonidine) could reduce morphine consumption up to 24 hr after surgery with a modest reduction in pain scores.¹⁷ The magnitude of effect places it between acetaminophen and NSAIDs. Further studies are required to determine the best dosing and administration technique as well as to elucidate potential risks beyond

sedation and bradycardia.¹⁶ This agent is expensive, and its use is restricted to the intensive care unit at our centre.

Whenever feasible, patients are encouraged to take an active role in their postoperative pain management. As such, we utilize patient-controlled regional anesthesia, patient-controlled analgesia (PCA)-intravenous, PCA-oral,⁴⁵ or patient-controlled epidural analgesia. With each of these modalities, it is important that the patient-controlled delivery system actually works to deliver an improvement in analgesia.

Behavioural and cognitive techniques⁶ can be useful to reduce pain catastrophizing and alleviate fear and anxiety. Pain catastrophizing can be defined as the tendency to magnify the threat value of pain and to feel helpless within the context of pain.¹² When fear of movement is present postoperatively, there can be a significantly poorer outcome in terms of worsened pain, disability, and physical health.⁴⁶ Techniques such as hypnosis, deep breathing, reframing, guided-imagery, progressive relaxation, distraction, music therapy,³⁸ or spirituality (e.g., prayer) are considered. Physical modalities, such as cold compresses, heat, massage, transcutaneous electrical stimulation, acupressure, or acupuncture, can be utilized in some individuals, especially in the experienced chronic pain patient.

A review of the patient's expectations should be addressed, since patient education can lead to an acceptance of realistic goals of treatment and result in improved outcomes in chronic pain management.^{6,47} A discussion with nurses and surgical staff can improve their understanding of the unique characteristics of the patient, remove any misconceptions surrounding acute or chronic pain, and help enlist their support for treatment strategies. The pain management concerns and treatment plan should be clearly documented in the patient's chart, as multiple providers may be caring for the patient. Ideally, the continuity of care should be provided by a single pain management practitioner, but this is not often possible. For some difficult complex pain cases, it is helpful to organize a periodic team meeting with a senior nurse, surgeon, pharmacist, physiotherapist, and family representative. It may help to shift the model of care to ensure the complex pain patient is actively involved in a model of shared decision-making that tailors interventions according to the patient's unique needs.^{21,48}

Postoperative phase: interventional techniques

Continuous perineural techniques offer the potential benefits of ongoing analgesia, reduced opioid requirements, and reduced adverse effects,³⁸ although continuous wound infiltration can also be helpful.⁴⁹ The chronic pain patient should be forewarned that there might be a significant increase in pain when the regional anesthesia technique is

withdrawn or wears off. Multimodal analgesia techniques, including adjustment of opioid dosing, should be in place to help the transition away from regional anesthesia. At some point, it may be helpful to taper or withhold the epidural or peripheral plexus catheter infusion and observe the patient's ability to manage with systemic analgesia techniques. Once adequate analgesia is observed, the peripheral plexus catheter or epidural should be removed. A bolus dose is sometimes delivered prior to removal of the catheter, especially in cases where motor or sensory block is not detrimental.

In complex patients with multiple sites of pain, it may be necessary to combine a regional analgesia technique with systemic administration of opioid. For example, patients having lower extremity operations may have an epidural catheter placed and receive postoperative patient-controlled epidural analgesia with local anesthesia and opioid. Then again, if the patient has chronic pain beyond what is covered by the epidural, additional intravenous intermittent opioid dosing may be necessary. There is a risk of respiratory depression with combinations of neuraxial and systemic opioids, and nurses should monitor patients closely. In patients with opioid tolerance, it may be helpful to consider increasing the amount of epidural opioid infused or rotating the opioid.³² The use of low-molecular-weight heparin has reduced the frequency of epidural placement, and a shift toward peripheral blocks has resulted.⁴⁹

A chronic pain consultant may be able to assist with some cases of complex pain. For example, in the patient with troublesome myofascial trigger points, it may be useful to inject the trigger points with 2% lidocaine in a dose of 1-2 mL per site with a 25G or 27G needle and then to have a therapist assist the patient in stretching the affected muscle group. In order to avoid pneumothorax, ultrasound guidance can be used if the trigger point is thoracic in location. The chronic pain patient who presents for surgery with low back pain or sciatica may benefit from an epidural steroid injection or other interventional spine block, but this should be done with input from a chronic pain specialist and discussion with the surgeon. Before any intervention, patients should provide informed consent after being presented with an evidence-based review of the risks, benefits, and alternatives.

Postoperative phase: opioid tolerance

The patient and their family members should be informed of the dangers of simply escalating the doses of opioid being administered, including constipation, ileus, respiratory depression, or opioid-induced sleep apnea.⁵⁰ Opioid tolerance can often be overcome by increasing the

amount of opioid administered, but it may be useful to explain the concept of OIH as pain can be made worse with escalations in the dose of an opioid.

If opioid-tolerant patients are not able to ingest their usual doses of oral opioid, an equivalent intravenous infusion may be initiated. This infusion may need to be increased by 30-50% over baseline preoperative levels, but this increase is variable, and therefore it is advisable to recheck the patient every couple of hours in the initial postoperative period until a steady state is achieved. For example, if a PCA device is being used and the number of requested doses/received doses is greater than three, then the background infusion can be increased by 20% and reassessed.²² Another technique in opioid-tolerant patients on intravenous PCA is to convert one to two PCA boluses per hour as the basal opioid infusion.¹⁸ To convert someone back to oral opioids, the basal infusion can be discontinued and half of the hourly intravenous opioid consumption can be ordered as a sustained-release opioid.²⁰ The other half of the hourly requirements can be provided by immediate-release oral opioids dosed every two hours as needed or by continuing the PCA device for another 24 hr to reassess efficacy of the conversion. If opioid doses are increased in the postoperative period, there must be a clinician designated to taper the oral sustained-release opioid as the acute component of the pain resolves.

If regional anesthesia techniques help control the pain, a 50% reduction in baseline opioid administration is advisable as greater reductions carry the risk of opioid withdrawal. If opioid withdrawal symptoms occur and further administration of opioid is not wanted, then oral clonidine can be administered.

If a patient is on high-dose opioids and experiencing significant pain despite multimodal analgesia techniques, it is often useful to initiate an opioid rotation. An opioid equivalency table can be consulted (see Canadian Guidelines for The Effective Use of Opioids at <http://nationalpaincentre.mcmaster.ca/opioid>), and the dose of the new sustained-release opioid should be reduced by 25-50% of the dose indicated on the equivalency table. If the patient still requires high doses of immediate-release opioid, the dose of the sustained-release component can be increased with daily readjustment.

For patients on methadone for pain control, it may be practical to increase the dosage if the pain is expected to remain increased for a long period of time, but it should be adjusted only with the advice of a chronic pain specialist. This is due to a possible overdosage occurring days after a dose escalation as a result of a long half-life in some individuals. One option is to leave the methadone dose unchanged and to utilize other opioids as necessary, tapering them whenever possible. General surgeons will often permit oral dosing of methadone as it is readily

absorbed and, as an example, requires only half an hour of clamping a nasogastric tube. If it is necessary to stop the oral methadone, then a dose of 1:1 with morphine *iv* can be used to prevent withdrawal.²³ For example, if a patient were using 24 mg of methadone per day, a minimum of 1 mg·hr⁻¹ of morphine *iv* would be necessary to prevent withdrawal. Given the high degree of variability in cross-tolerance, it is not necessary to exceed a background infusion of 3 mg·hr⁻¹ morphine *iv* in the first 24 hr when stopping methadone. Furthermore, a PCA device can be used to help bridge any deficit and mitigate any possibility of withdrawal. In patients on methadone, close observation is necessary, and concerns need to be discussed with nurses and the pharmacist over the possibility of perioperative drug interactions and the risk of using other drugs that cause QT prolongation, e.g., ondansetron. For intractable chronic pain, methadone is sometimes prescribed by chronic pain specialists as part of an opioid rotation as it has alpha-adrenergic agonist and NMDA receptor antagonist properties³² that can reverse opioid tolerance and also serve to treat neuropathic pain.

Postoperative phase: neuropathic pain

First-line agents in patients who develop neuropathic pain are the anticonvulsant gabapentinoids and tricyclic antidepressants.⁵¹ It may be useful to start or increase both of these agents if the patient develops neuropathic pain. For gabapentin, one strategy is to increase the daily dose by 300 mg and then make further increases of 300 mg every one to three days as tolerated, with an aim of reaching at least 600 mg three times a day. The dose of pregabalin may be increased by 25 mg three times a day, and such increases may be furthered every three days⁵² with an aim of reaching at least 300 mg·day⁻¹. The problem with aggressively adjusting the dose of gabapentinoid is the likelihood of dizziness, sedation, ataxia, and falls occurring. The usual maximal dose of gabapentin is 3,600 mg·day⁻¹, whereas the usual maximal dose for pregabalin is 600 mg·day⁻¹. Carbamazepine is still the drug of choice for trigeminal neuralgia, otherwise, it is seldom recommended.⁵³

In terms of tricyclic antidepressants (TCAs) for neuropathic pain, it is important to realize that there is no difference in the effectiveness of amitriptyline compared with other TCAs and that it may take two weeks for the TCA to reach peak effect. To reduce cognitive and anticholinergic side effects, it can be useful to utilize nortriptyline as it may have the least cardiac adverse effects.⁵⁴ Sedative properties of doxepin can be useful. If daytime doses of a TCA are needed, then desipramine may be helpful. The initial dose for any TCA is 10-25 mg at bedtime. Dose adjustments are typically made at three-day

intervals by 10-25 mg as tolerated, with the average dose of amitriptyline being 75 mg·day⁻¹.⁵²

Another class of agents useful for neuropathic pain are SNRI medications such as duloxetine. Duloxetine is United States Food and Drug Administration (FDA) and Health Canada approved for diabetic neuropathy, fibromyalgia, and chronic low back pain, and it is also approved for chronic musculoskeletal pain in the United States. It is dosed at 30 mg·day⁻¹ at night, with an increase to 60 mg·day⁻¹ after one week (commonly increased thereafter to 90 mg·day⁻¹). It is contraindicated in severe states of hepatorenal disease or in those with narrow angle glaucoma. Venlafaxine is the older SNRI that can be used, but it is effective only at doses of 150-225 mg·day⁻¹ with an initial starting dose of 37.5 mg once a day and increases of 75 mg each week of the sustained-release preparation. Venlafaxine is often limited by gastrointestinal side effects and occasional elevations in blood pressure. Awareness of the potential for serotonin syndrome is necessary when administering an SNRI and other agents such as tramadol or TCAs. It may be useful to combine a SNRI medication with a gabapentinoid.

For patients with allodynia, it is useful to consider topical agents, such as topical lidocaine, which is available in the United States as a transdermal patch and is FDA approved for postherpetic neuralgia. These 10 × 14 cm patches can be cut to approximate the size of the painful area, and up to three patches can be applied for 12 hr on and then 12 hr off. There is minimal systemic absorption (2-3%).⁵⁵ In Canada, pharmacists can obtain 5-10% lidocaine gel or cream, and it can be applied three or four times a day to areas of allodynia with or without a transparent occlusive dressing.

Tramadol is considered a second or third-line agent for mild to moderate neuropathic pain, and other opioids are often utilized in the acute neuropathic pain setting. Tapentadol is an opioid recently released in Canada and is available as an immediate-release and sustained-release preparation. It also has a noradrenaline reuptake inhibitor effect and thus may be helpful to consider as part of an opioid rotation especially if it has not previously been used by the patient.^{44,56} Fourth-line agents for neuropathic pain include cannabinoids,⁵⁷ methadone, and non-gabapentinoid anticonvulsants.⁵³

Postoperative phase: fibromyalgia

Fibromyalgia patients can be difficult to treat due to a heightened sensitivity to pain stimuli, a reduced descending inhibition of pain, and a reduced analgesic response to exogenous opioids.^{24,58} Multimodal analgesia techniques are useful when dealing with the patient with fibromyalgia due their reduced responsiveness to opioids. For mild to

moderate pain intensity, tramadol may be helpful due to its property of being a weak mu-receptor agonist with weak tricyclic-like antidepressant properties.

If the patient is taking gabapentin or pregabalin, the doses should be increased if possible. In terms of sleep disruption and pain management, a dose of amitriptyline 10-25 mg may be helpful. If muscle spasm is present, cyclobenzaprine may be useful since it has been used for treating some fibromyalgia patients. A dose of 5 mg is initiated as a trial and then increased to 10 mg up to three times a day; patients should be warned of sedation and falls.

In Canada, patients may not be able to afford some medications, such as pregabalin, tramadol, or duloxetine, and thus a review of cost considerations may be appropriate prior to discharge.

Postoperative phase: communication

It is known that substantial nonspecific or placebo treatment effects occur in pain medicine when patients have faith and a good working relationship with their enthusiastic and trustworthy health care provider.⁵⁹ Patients are more likely to perceive inadequate care when only their medical needs are addressed and not their emotional needs. Further, if only the negative aspects of a treatment are emphasized, it has been shown that a nocebo effect can occur whereby the negative expectations significantly increase the odds of a negative outcome.⁶⁰ A caring attitude can be shown and maximal nonspecific treatment effects can be obtained if the following points are adhered to with each patient interaction:⁵⁹

1. Engage the patient: good body posture and eye contact, understand concerns.
2. Empathize: actively listen, reflect and acknowledge issues presented, use humour when appropriate.
3. Educate: set realistic expectations, assess patient knowledge of medical issues.
4. Enlist: provide options, seek agreement, and welcome input into the plan.
5. End: summarize the encounter, review and indicate next steps, follow through.

Summary

It may not always be possible to reduce a complex pain patient's pain score postoperatively even with multimodal analgesia techniques. Nevertheless, a comprehensive and evidence-based perioperative plan to manage the pain may improve patient satisfaction and reduce opioid-related adverse effects. Established guidelines can help to

summarize the current state of knowledge and act as a template for perioperative pain control.^{49,61,62}

A patient-centred care model in which the patient participates in the decision-making process can be helpful. It takes time and attention to detail when dealing with chronic pain patients as frequent reassessment or adjustment of pain control measures is often required. Input and collaboration with other health care providers, such as pharmacy and physiotherapy, may be necessary on an ongoing basis.

In summary, anesthesiologists dealing with complex pain patients need to utilize both the art and the science inherent in perioperative medicine. In order to bolster patient satisfaction with any proposed treatment, it is helpful to establish a healthy therapeutic alliance with the patient that extends from the preoperative to the postoperative phases of care. In doing so, the anesthesiologist is able to look beyond the needle and emerge as a successful physician-healer.⁶³

Key points

- Optimal care of a complex pain patient starts with the preoperative phase. Complex pain patients are given the opportunity to share their unique concerns. Patients should have accurate documentation about their pain medication and history. They should be educated about pain management, have realistic expectations, and be given premedication.
- For intraoperative and postoperative complex pain management, it is imperative to implement multimodal analgesia. Local anesthesia techniques are recommended to reduce opioid requirements and improve postoperative pain. Ketamine should be considered. Single-dose dexamethasone may be beneficial as well as maximal doses of acetaminophen and anti-inflammatories.
- For patients with opioid tolerance, it is helpful to consider either a judicious dose escalation or opioid rotation.
- For patients with neuropathic pain or fibromyalgia, there should be optimal doses of a gabapentinoid administered. Addition of a tricyclic antidepressant or duloxetine can be helpful for ongoing pain.
- It is helpful to employ nonspecific treatment effects when dealing with complex pain patients. Every perioperative encounter should reinforce a healthy physician-patient relationship. Complex pain patients are encouraged to be active participants in their care.

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