Brief review: Perioperative management of the patient with chronic non-cancer pain

[Article de synthèse court : Prise en charge périopératoire des patients souffrant de douleur chronique non cancéreuse]

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Purpose: Both opioid and non-opioid medications are being utilized increasingly in the treatment of chronic non-cancer pain, and the number of surgical patients receiving large regular doses of opioids is ever-expanding. The perioperative pain control of these patients is often challenging, and is broadening the role of the anesthesiologist as 'perioperative physician'. These patients need to be identified before surgery to plan optimal pain control postoperatively. The purpose of this review is to provide an update on the important considerations in managing the chronic non-cancer pain patient receiving high dose opioids and other adjunctive medications/analgesics.

Source: English language articles published between June 1980 and May 2006 were identified by a computerized Medline search using keywords "chronic pain", "opioid dependent" and "perioperative". This same search strategy was repeated and updated using both Medline and Embase. All relevant publications were retrieved and their bibliographies were scanned for additional sources.

Principal findings: Although an increasingly common problem for the acute pain service, there is very little published on this topic. Key points include the concept of opioid equivalency, tolerance, the role of adjunctive medications, and the need for good communication between the surgical team, the acute pain service and the patient who is often anxious about the upcoming procedure due to previous unpleasant experiences with poor pain control in hospital.

Conclusion: Clinical care of the opioid-dependent patient in the perioperative period can be a daunting task. Education to all staff involved in this area needs to be enhanced to improve outcome and patient satisfaction.

Objectif : On traite de plus en plus les douleurs non cancéreuses avec des substances opiacées ou non opiacées et, en chirurgie, on retrouve un nombre croissant de patients prenant de fortes doses d'opiacés. Dans ce contexte, la prise en charge de la douleur représente souvent un défi et contribue au rôle grandissant de l'anesthésiologiste en « médecine périopératoire ». Ces patients doivent être identifiés avant la chirurgie pour planifier la prise en charge de la douleur en période postopératoire. L'objectif de cet article est de mettre à jour les éléments importants dans la prise en charge de la douleur non cancéreuse chez les patients qui reçoivent des doses élevées d'opiacés et d'autres médicaments/analgésiques adjuvants.

Source : Les articles publiés en langue anglaise de juin 1980 et mai 2006 ont été identifiés grâce à une recherche informatisée dans Medline avec les mots-clés « chronic pain », « opioid dependent » et « perioperative ». La même stratégie de recherche a été répétée et mise à jour avec Medline et Embase. Toutes les publications ont été retrouvées et leur liste de références a été fouillée pour repérer des documents additionnels.

Constatations principales : Même s'il s'agit d'un problème fréquent pour les services de douleur aiguë, il y a peu de publications sur ce sujet. Les thèmes principaux sont le concept d'équivalence pour les opiacés, la tolérance et le rôle des médicaments adjuvants. On retrouve aussi l'importance de la communication entre l'équipe chirurgicale, le service de douleur aiguë et le patient, qui est souvent inquiet de la chirurgie annoncée à cause d'expériences antérieures déplaisantes à l'hôpital où la prise en charge de la douleur laissait à désirer.

Conclusion : Les soins cliniques aux patients avec une dépendance aux opiacés peut constituer une tâche décourageante en période périopératoire. La formation des intervenants dans ce domaine doit être développée pour améliorer le pronostic et la satisfaction du patient.

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Funding: No financial support has been obtained in the writing of this manuscript.

Accepted for publication July 4, 2006.

Revision accepted September 5, 2006.

CHRONIC pain is a common and challenging medical problem facing our society.¹ Anesthesiologists have provided leadership in the development of the practice of pain management, with the application of nerve blocks and pharmacotherapy.² One area of growing concern for the anesthesiologist involves the perioperative assessment and management of the opioid-dependent chronic pain patient.³

In the past, many physicians were reluctant to prescribe opioids for the treatment of chronic non-cancer pain. However, a recent systematic review of the efficacy and safety of opioids in chronic non-cancer pain reveals that opioid therapy can relieve pain, improve mood and day-to-day functioning without impairing cognitive function or producing psychological dependence in many of these patients.⁴ In addition, increasing use of opioid management for chronic non-cancer pain was probably responsible for a twofold increase in opioid prescriptions in the United States between 1994 and 2001.⁵ Misunderstandings regarding the concept of physical dependence vs psychological dependence and the development of tolerance contribute to the difficulties encountered by physicians treating these patients perioperatively. Frequently these patients also have reduced physiological reserves and are therefore at increased risk for the deleterious effects of the neuroendocrine response to pain.⁶

Relieving pain perioperatively has always been a basic role of the anesthesiologist, and anesthesiologists have considerable expertise in managing acute pain. The unique features of patients with chronic pain, however, demand a very different approach in the perioperative setting. Chronic pain is almost always accompanied by anxiety and depression, which requires medication regimens that may include antidepressants, anticonvulsants, skeletal muscle relaxants and antiarrhythmic drugs, in addition to opioids.⁷ This pharmacological complexity entails significant implications for the perioperative period, specifically with respect to complex drug interactions and altered dosing schedules in the perioperative setting.

This review provides an update on the clinical aspects of opioid pharmacology including physical dependence and tolerance, and other adjuncts used in the management of chronic pain, with particular focus on pharmacological considerations for the perioperative period.

Pain classification

The International Association for the Study of Pain provides a widely accepted definition of chronic pain as 'pain without apparent biological value that has

persisted beyond the normal tissue healing time usually taken to be three months.⁸ A practice guideline for chronic pain management has been published by the American Society of Anesthesiologists (ASA), in which chronic pain is defined as 'pain of a duration or intensity that adversely affects the function or well-being of the patient'.⁹ The ASA has also published practice guidelines for acute pain management in the perioperative setting.¹⁰ However, specific recommendations for the perioperative management of chronic pain patients are absent from these guidelines.

Causes of chronic non-cancer pain (CNCP) are categorized in Table I. In some cases, there is no discernible cause, but no matter what the original etiology, chronic pain is now considered the disease. Chronic pain is generally divided into two categories which can overlap - neuropathic (central or peripheral) and nociceptive (somatic or visceral). Examples of neuropathic pain include postherpetic neuralgia and post-thoracotomy pain; chronic visceral pain may be due to inflammatory bowel disease. Chronic non-cancer pain can also result from conditions where there is ongoing nociception, such as arthritic inflammation.¹¹ Some types of CNCP have well-defined characteristics and a temporal pattern, whereas others do not. Neuropathic and myofascial CNCP may co-exist and be difficult to differentiate.¹²

Epidemiology of chronic pain

Numerous surveys have investigated the prevalence and characteristics of chronic pain in various populations. However, the exact incidence of chronic pain remains difficult to quantify.¹³⁻¹⁵ Chronic pain is recognized as one of the most common reasons why people seek medical attention,¹³ and patients with chronic pain access health care services up to five times more frequently than the rest of the population.¹⁵ Statistics from Canada's National Population Health Survey, carried out in 1994-1995, revealed a chronic pain prevalence rate of 15% in men and 20 % in women.¹⁶ A subsequent study of chronic pain in Canada found an overall pain prevalence of 27% for men and 31% for women, showing that chronic pain is common in adults, supporting a previously recognized association between chronic pain, women, and older age.¹⁷

A recent publication suggests that over two million adults suffer from neuropathic pain in the United States.¹⁸ Post-surgical neuropathic pain has long been recognized as an important cause of chronic pain. One large survey of patients attending chronic pain clinics in the United Kingdom determined that surgery was the prime contributing cause in 22.5% of cases, second only to degenerative factors.¹⁹

TABLE I Examples of chronic non-cancer pain

A	Neuropathic (central or peripheral)
-	Central (spinal cord injury, post-stroke, MS)
-	Peripheral (CRPS type I and II, peripheral neuropathy, trigeminal neuralgia, post-herpetic neuralgia, phantom limb pain, failed back syndrome)
B	Nociceptive (somatic or visceral)
-	Somatic (osteoarthritis, degenerative disc disease, myofascial pain, fibromyalgia)
-	Visceral (chronic pancreatitis, chronic PUD, IBS)

CRPS = complex regional pain syndrome; IBS = irritable bowel syndrome; MS = multiple sclerosis; PUD = peptic ulcer.

Opioid equivalency

A key concept related to the perioperative management of opioid-dependent patients is that of opioid equivalency. Determination of opioid equivalency will facilitate accurate conversion to patient-controlled analgesia (PCA) opioids or alternative oral opioid regimens when suitable in the postoperative period.

Physicians are often required to convert patients to an alternative opioid during the course of chronic pain therapy due to lack of efficacy, development of intolerable side effects, inability to use oral formulations or variable absorption of transdermal preparations. There may be additional practical considerations such as high cost or limited availability in local pharmacies. Opioid rotation is also done deliberately whenever the patient develops a high tolerance to one opioid. The concept of opioid rotation is based upon the rationale that a different opioid will act on a different opioid receptor subtype, and be metabolized differently. Whenever changes are made in opioid administration, the use of analgesic equivalency tables facilitates the selection of an opioid dose that closely approximates the needs of the patient for continuation of the same analgesic effect to avoid pain exacerbations or withdrawal symptoms. Although opioid rotation is practiced more frequently in chronic pain settings and particularly in palliative care, it also has a role in acute pain management. It may be valuable to use an alternative opioid in the first few days after surgery, as the alternative opioid may be effective in doses that are much lower than expected (based on analgesic equivalency) due to incomplete cross-tolerance.²⁰ Using the cancer pain model, the usual recommendation in switching from one opioid to another is to initiate the new opioid at 50% of the equianalgesic dose because of incomplete cross-tolerance.²¹

Following administration of the initial dose, subsequent doses are titrated to effect, based on the patient's response. The most commonly used opioids in patients with CNCP are listed in Table II. Generally,

TABLE II Opioid analgesics used in patients with moderate to severe chronic pain

<i>Opioid</i>	<i>Terminal half-life (hr)</i>	<i>Oral bioavailability %</i>	<i>Active metabolite</i>
Morphine	2–4	10–50	M6G, M3G
Meperidine	3–4	30–60	Normeperidine
Methadone	6–150	60–90	Unknown
Fentanyl	3–7	< 2	Unknown
Codeine	3–4	60–90	Morphine
Oxycodone	2–6	40–100	Oxymorphone
Hydromorphone	2–4	35–80	H3G

M6G = morphine-6-glucuronide; M3G = morphine-3-glucuronide; H3G = hydromorphone-3-glucuronide.

long acting opioids are administered using q8hr or q12hr dosage schedules with short acting opioids titrated for breakthrough pain.²¹ It is important to obtain an accurate history of the total number of milligrams of opioid taken throughout the day from both long- and short-acting medications. For example, if the patient takes slow-release morphine (MS Contin) 30 mg q8hr plus six oxycodone tablets (5 mg) per day for breakthrough, the total number of milligrams in morphine equivalents would be 150 mg (oxycodone is twice as potent as morphine). Most opioid analgesic conversion data originate from older studies not optimally designed for clinical application in dose-conversion, including single dose studies and studies that were not specifically designed for the evaluation of relative opioid potencies.²² Table III provides a guide to the basic principles using an equianalgesic chart of oral and parenteral dosing equivalents of opioid medications.²³

Tolerance, dependence, addiction and pseudo-addiction

These terms are widely misunderstood due to inadequate or non-existent exposure to addiction medicine in undergraduate and postgraduate training programs.²⁴ The American Academy of Pain Medicine, American Pain Society, and the American Society of Addiction Medicine approved the following definitions in 2001.²⁵

Tolerance

Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time. Pharmacodynamic tolerance involves adaptations that occur at both the site of the drug action, e.g., receptor, ion channel, as well as in related systems more distal to

the site of the drug action. For example, pharmacodynamic tolerance to opioids is evident at both the level of the opioid receptor in the locus coeruleus (primary) and in the dopaminergic reward pathways afferent to the site of this discrete drug action (secondary).²⁶ Development of tolerance to opioids is not necessarily a sign of addiction.

Physical dependence

Physical dependence is manifested by symptoms of withdrawal on abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist. If a patient on long-term opioids demonstrates symptoms of withdrawal, this does not necessarily infer opioid abuse.

All opioids, benzodiazepines, anticonvulsants, antidepressants and ethanol produce clinically relevant physical dependence when consumed for a prolonged period of time, which is a naturally expected physiological response. An increased sensitivity to pain may develop as a consequence of physical dependence.²⁷ Based on clinical experience, patients with continuous opioid intake of a daily *iv* morphine equivalent exceeding 30 mg for more than two to four weeks, should be considered at risk for withdrawal syndrome if adequate substitution of opioids in the perioperative period is withheld.²⁸ Abrupt cessation or rapid dose reduction resulting in decreasing blood level of the substance, and/or administration of an antagonist to the substance can produce a withdrawal syndrome that may include, but is not limited to nausea, vomiting, diaphoresis, diarrhea, abdominal cramps, seizures or even death.²⁶

Addiction

Addiction is a biopsychosocial disease with genetic, psychological, and environmental factors influencing its development and manifestations. It is characterized by the following characteristics known as the “four C’s”; impaired control over drug use, compulsive use, continued use despite harm, and craving.

Addiction to opioids in patients with chronic pain syndromes does not commonly occur among patients with no history of substance abuse.^{4,29} A recent study examined the prevalence of addiction in patients with chronic pain seen in outpatient pain specialist clinics.³⁰ Twelve percent of patients were diagnosed with ongoing psychoactive substance abuse dependence. This corresponds to prevalence estimates of alcohol and drug addiction among the general population.³¹

Pseudoaddiction is a term coined by Weissman and Haddox,³² to describe the behaviour of seeking more analgesic medication in response to under-treat-

ment of the pain syndrome. Patients develop feelings of anger and isolation which lead to acting-out behaviour. The health care team initially experiences frustration at not controlling the patient’s complaints of pain combined with fears of inducing tolerance and dependence. Over time, they will seek to avoid contact with the patient as a means of reducing the source of conflict. Both behaviours continue to occur with escalating mistrust on both sides.³² These behaviours disappear once the pain is adequately controlled. It is only possible to make this diagnosis retrospectively.

Opioid-induced hyperalgesia

Common concerns regarding the use of opioids include the potential for long-term consequences such as physical dependence, and addiction. Another complication that may be observed with the use of opioids is opioid-induced hyperalgesia (OIH). Patients receiving opioids to control their pain somewhat paradoxically may become more sensitive to pain as a direct result of opioid therapy.³³

In laboratory animals, acute and chronic exposure to opioids can result in increased pain sensitivity (i.e., OIH). In most animal studies, OIH was generally observed to peak during periods of opioid abstinence or in periods between regularly administered opioid doses.³⁴ These findings were interpreted to imply that the chronic administration of opioids leads to compensatory neurobiological changes that facilitate nociception and, thus, lead to hyperalgesia that is especially evident between opioid doses.

The mechanistic basis for OIH is unclear, but the clinical observation that only a subset of individuals is susceptible to this phenomenon strongly suggests a genetic influence. Furthermore, the observation that OIH is more common in patients with a history of opioid abuse suggests that OIH and opioid abuse may share common underlying genetic and neurobiologic mechanisms.³⁵

Non-opioid treatment of chronic pain

Adjuncts include antidepressants, anticonvulsants, local anesthetics, N-methyl-D-aspartate (NMDA) receptor antagonists, and nonsteroidal anti-inflammatory drugs (NSAIDs). Due to the challenges in conducting randomized controlled trials in this area, recommendations for the use of non-opioid medications in the management of chronic pain are based on quite variable levels of evidence. Accordingly, we assign levels of evidence according to the criteria of the Oxford Centre for Evidence-Based Medicine.³⁶

Tricyclic antidepressants (TCAs) are frequently used in chronic pain management, mostly for neuropathic

pain for which their analgesic efficacy is well documented³⁷ (Grade A). The doses used as an adjunct for pain relief usually do not exceed 75 mg·day⁻¹, significantly less than the 150 mg·day⁻¹ required for mood modification. Tricyclic antidepressants may also help normalize sleep patterns. The sleep effects of these drugs are likely to be seen at relatively low doses and within a few days of treatment initiation, whereas analgesic effects require at least three weeks of therapy.³⁸ Possible mechanisms by which TCAs produce pain relief include stabilization of nerve membranes and blocking reuptake of serotonin and noradrenaline at presynaptic membranes within central neurons involved in biologic analgesia.

In the 1970s, there were reports indicating that use of tricyclic antidepressants preoperatively resulted in arrhythmias. Therefore, it was recommended that they should be discontinued 72 hr before surgery. More recently, it was shown that the incidence of intraoperative hypotension and arrhythmias was low in patients on antidepressant therapy, whether treatment was ceased preoperatively or not. On the other hand, discontinuation of antidepressants was associated with a definite increase in the incidence of delirium, confusion and depressive symptoms³⁹ (Grade B). The risk/benefit ratio would dictate that it is preferable to continue the usual TCA dosing and the newer generation of antidepressants such as selective serotonin-reuptake inhibitors during the perioperative period.⁴⁰ (Grade C).

Anticonvulsant drugs have been shown to be effective in a variety of neuropathic pain states⁴¹ (Grade A). One of the most widely-used medications is now gabapentin, which has a low incidence of serious side effects and drug interactions. Its mechanism of action is not fully elucidated, although it is thought to act by blocking voltage-controlled calcium channels.⁴² Dirks *et al.*⁴³ showed that after a single dose of 1200 mg oral gabapentin, there is a substantial reduction in postoperative morphine consumption and movement-related pain after radical mastectomy (Grade B). Gabapentin has gained some support as an adjunct to postoperative analgesia. Recently, Seib *et al.* conducted a meta-analysis of all randomized trials that addressed gabapentin's role in acute postoperative pain control⁴⁴ (Grade B). The authors concluded that, when given preoperatively, gabapentin is effective in reducing postoperative opioid consumption in the first 24 hr after surgery and, to a lesser extent, reducing pain scores. Pregabalin, an analogue of gabapentin, has a more rapid onset of action with additional anxiolytic and sleep-enhancing properties, and is well tolerated by patients⁴⁵ (Grade B). In 2001, Hill *et al.* published

the first postoperative trial of an alpha-2 delta ligand which involved pregabalin⁴⁶ (Grade A). After oral surgery, pregabalin 300 mg provided a significantly higher pain intensity difference than placebo.⁴⁶ Topiramate, lamotrigine, and oxycarbazepine have lower degrees of evidence supporting their use in neuropathic pain. Given the incomplete efficacy of currently available non-opioid analgesics, and the identified benefits of opioid sparing, anticonvulsant medications may be useful adjuncts for postoperative analgesia⁴⁷ (Grade D). No anticonvulsant, whether administered for seizure disorders or neuropathic pain, should be discontinued abruptly, to avoid potential central nervous system hyperexcitability and rebound pain. Therefore, these medications need to be maintained throughout the perioperative period.

Tissue damage or inflammation, occurring after surgery or trauma, can activate NMDA receptors which subsequently facilitate development of peripheral hyperalgesia (greater pain than normally expected) and central sensitization ("windup") to painful stimuli. It is thought that NMDA receptors, located in the spinal cord, are involved in the development of the wind-up and central sensitization. There is evidence for NMDA receptor involvement in many types of pain such as inflammatory, postoperative, neuropathic and ischemic pain.⁴⁸ The most common NMDA receptor antagonist in clinical use is ketamine, a drug that has been used as an anesthetic agent for many years. There is growing evidence that adjunctive use of very low dose ketamine by infusion improves analgesia during the perioperative period. More recently, De Kock *et al.*⁴⁹ investigated ketamine intraoperatively to determine whether it has a postoperative anti-hyperalgesic and an analgesic effect, and to determine the preferential route of administration, either *iv* or epidural. It was concluded that a sub-anesthetic dose of *iv* ketamine is a useful adjuvant for perioperative balanced analgesia (Grade B). The systemic route, when compared to the epidural route, is the preferential method of administration. Moreover, the use of "low dose" ketamine has been described in the treatment of patients who have developed tolerance to opioids after the continuous use of morphine or fentanyl^{50,51} (Grade D). The addition of ketamine in these cases resulted in superior analgesia and reversal of opioid tolerance leading to dramatic reduction of the total daily dose of opioids. Very rarely, patients with chronic oral ketamine medication will present to the operating room. Case reports from an intensive care setting indicate that so long as analgesic doses are used, no withdrawal syndrome will develop during the perioperative period⁵² (Grade D).

Nonsteroidal anti-inflammatory agents are not sufficiently effective as sole analgesic agents after major surgery, but are best used in combination with opioid analgesics to enhance the quality of analgesia with movement⁵³ (Grade A). The use of NSAIDs results in a 20%–40% reduction in opioid requirements, and in a significant reduction in nausea, vomiting and sedation, but not other opioid-related side effects⁵⁴ (Grade B). Unlike opioids, NSAIDs do not induce tolerance and physical dependence, but may cause serious renal, gastrointestinal and coagulation abnormalities, and increase the risk of stroke or myocardial infarction.⁵⁵ Following considerable criticism over the potential risk of adverse cardiovascular events, the U.S. Food and Drug Administration (FDA) issued an advisory in April 2005 which stated that “short-term use of NSAIDs to relieve acute pain, particularly at low doses, does not appear to confer an increased risk of serious adverse cardiovascular events”.⁵⁶ Therefore, the use of NSAIDs as adjuncts for short-term use in the perioperative management of CNCP is encouraged, given the risk-benefit ratio.

The use of regional anesthesia in opioid-dependent patients

Regional anesthesia presents a particularly attractive choice for this group of patients who are at high risk for intensified postoperative pain, because near-complete analgesia can be obtained. It is essential to remember that chronic pain patients choosing to have a regional technique still require 50% of their usual daily opioid dose either intravenously or orally, to prevent opioid withdrawal symptoms.

Current evidence from the literature examining the optimal dosing of neuraxial opioids in opioid dependent patients is limited. Rapp *et al.*⁵⁷ reported superior postoperative pain control in chronic opioid dependent patients who received epidural fentanyl compared with epidural morphine (Grade D). In a case report, de Leon-Casasola *et al.*⁵⁸ documented poor analgesia with epidural morphine and bupivacaine in an opioid dependent patient. Analgesia improved when the epidural morphine was switched to the more lipid-soluble sufentanil (Grade D). The authors confirmed prospectively that epidural sufentanil is superior to epidural morphine⁵⁹ (Grade D), and speculated that sufentanil may provide superior pain control because its greater potency allowed analgesic effects to be exerted at a lower receptor occupancy.

As discussed previously, epidural administration of opioid medications, particularly of very potent lipid-soluble compound such as sufentanil and fentanyl, in combination with a local anesthetic, provides an

attractive approach for treating postoperative pain in chronically opioid dependent patients. However, opioid dependent patients treated with regional techniques for postoperative pain control must also have access to systemic opioids by the *iv* or oral route for prevention of opioid withdrawal symptoms.

Perioperative considerations of patient on methadone

Methadone is available only in oral formulations, either as liquid solution or capsules. Patients may be receiving methadone q8hr or q12hr for chronic neuropathic pain. Patients receiving methadone to treat opioid addiction generally are on a single daily dosing schedule. In either situation, patients on methadone should receive their usual dose prior to, and on the day of surgery to avoid unnecessary fluctuations of the drug concentration. An abrupt discontinuation of methadone before surgery will make it difficult to provide adequate postoperative analgesia.⁶⁰ Another important preoperative consideration is that patients receiving higher doses (> 200 mg·day⁻¹) of methadone may develop a prolonged Q-T interval, which is a risk factor for the development of Torsades de pointes. Therefore, a baseline electrocardiogram should be available for comparison⁶¹ (Grade C). When planning analgesic strategies for postoperative pain control in patients who will be fasting, physicians should convert methadone to an appropriate choice of opioid and an equianalgesic regimen to prevent opioid withdrawal⁶² (Grade C). Expert opinion on the best equianalgesic dosing schedule may be sought from a physician with a methadone-prescribing exemption.

Opioid conversion examples

To illustrate effective opioid conversion schemes, we consider two hypothetical examples. The first is preoperative conversion of sustained release morphine sulphate (MS Contin) which a patient scheduled for hip arthroplasty had been taking, in a dose of 200 mg *po* tid, for several years. In this instance, the oral MS Contin medication should be given preoperatively at the usual time. The total daily dose of morphine is 600 mg orally, which is equivalent to 200 mg *iv* morphine (Table III) or 8 mg·hr⁻¹. One should begin the basal infusion at 50% of this calculated hourly rate (4 mg·hr⁻¹), then set the PCA dose at least 50% higher than for an opioid naïve patient (1.5 mg boluses with a six-minute lock-out interval, and an hourly maximum dose of 15 mg). Alternatively, depending on patient and surgical factors, an epidural infusion may be appropriate. Standard epidural opioid and local anesthetic solutions (e.g., 0.125% bupivacaine plus fentanyl 2

TABLE III Oral and parenteral dosing equivalents of opioid medications

	Parental	Oral
Morphine	10 mg	30 mg
Codeine	100 mg	200 mg
Oxycodone	NA	15 mg
Hydromorphone	2 mg	6 mg
Methadone	1 mg	2 mg
Fentanyl	25 µg·hr ⁻¹ ·24 hr	= morphine 50 mg·24 hr
Meperidine	75 mg	300 mg

NA = not available.

µg·mL⁻¹) have been used successfully in large numbers of patients receiving opioids in high doses before surgery. Additional epidural bolus doses of local anesthetic/opioid mixtures may be given as required, while maintaining oral MS Contin will avoid withdrawal symptoms. These patients should be reassessed every six to 12 hr for adequacy of pain control (more frequently during the first few hours postoperatively).

A second conversion example involves a young adult patient with chronic abdominal pain secondary to Gardner's syndrome, for which she receives methadone 120 mg *po* q8hr. The patient presents with large bowel obstruction requiring an urgent laparotomy. This example is important to illustrate the appropriate conversion of methadone. In this case, the total daily methadone dose is 360 mg orally per day, equivalent to hydromorphone 360 mg·day⁻¹ intravenously (Table III). Begin a basal infusion at 50% of the calculated hourly rate (7.5 mg·hr⁻¹). The initial PCA dose should be at least 50% higher than for an opioid naïve patient (representing a bolus dose of hydromorphone 0.3 mg *iv* with a six-minute lock-out period and an hourly maximum of 3 mg).

In both examples, NSAIDs and anticonvulsants including gabapentin and pregabalin should be prescribed for optimal pain management in chronically opioid-consuming patients. These medications can be given either as preemptive analgesics, or in the postoperative period when oral intake is resumed.

Postoperative transition from an iv to oral opioid regimen

After surgery, the transition from an *iv* to an oral opioid regimen requires special attention in chronic opioid-consuming patients. Some patients may have their pain reduced as a result of surgery, but many patients can expect to require opioid doses similar to doses they were receiving preoperatively.

TABLE IV General perioperative anesthetic considerations for opioid-dependent patients

- 1- Identification of chronic opioid-dependence prior to surgery.
- 2- Inform the responsible anesthesiologist of the OR and the surgeon about the diagnosis of "chronic non-cancer pain patient".
- 3- Adequate preoperative assessment should include:
 - Documentation of CNCP diagnosis including site of pain and intensity.
 - Type and location of surgery.
 - Precise opioid use (dose, opioid type, route, side effects, etc.).
 - Discussion with the patient of the potential for increased postoperative pain.
 - Discussion of patient's fears and expectations related to pain management.
 - Discussion of effective management strategies after previous procedures if any.
 - Education of the patient regarding the perioperative procedures.
- 4- Calculate opioid dose requirement and modes of administration; provide anxiolytics or other adjunct medications as clinically indicated.
- 5- Plan preoperatively for postoperative analgesia before hospital discharge, and formulate primary strategy as well as suitable alternatives.
- 6- Ensure frequent postoperative visits by APS.
- 7- Arrange for a timely outpatient pain clinic follow-up visit to re-assess pain level and medications.

OR = operating room; CNCP = chronic non-cancer pain; APS = acute pain service.

No broadly accepted guidelines have been established to indicate the optimal method of converting parenteral to oral opioid regimens for these patients following the acute recovery phase. One approach that has worked well in our institution is to calculate the total PCA consumption over the last 24 to 48 hr, administer one-half to two-thirds of this dose in the form of a long-acting opioid, while allowing the remainder of the requirement to be used as a short-acting opioid as needed. The long-acting opioid provides a steady baseline drug concentration for control of pain, while the short-acting drug provides for control of breakthrough pain. It is also important to consider continuing adjunctive medications such as NSAIDs and anticonvulsants during the postoperative transition phase. Frequent assessment of the patient's pain level is essential to avoid discharging the patient with more opioid medication than the usual preoperative baseline drug regimen.

Key management points

Multidisciplinary communication

The surgeon and preadmission clinic personnel must identify chronic pain patient as high risk, alert the

acute pain service (APS), and consult preoperatively with an anesthesiologist to discuss the patient's concerns and plan a management strategy.

Preoperative assessment

The medication history must be carefully documented, including the daily dose of both long-acting and short-acting opioids (Table IV), as well as all adjunctive analgesics, anxiolytics, antidepressants and anticonvulsants. Long-acting opioids and adjuncts should be prescribed up to, and including the morning of surgery.

Multimodal analgesic strategies

In addition to the planned opioid regimen, administration of adjunctive medications including NSAIDs and anticonvulsants should be encouraged. Also consider a ketamine infusion if pain proves refractory to other measures in the postoperative period.⁶³

Anesthetic technique

Strongly consider use of regional anesthesia.

Postoperative opioid conversion

If PCA is chosen, convert the patient's daily opioid dose into morphine equivalents (Table III). Opioid equivalency tables should be readily available from the postanesthetic care unit to the APS to ensure accurate conversion. Patients receiving methadone require special attention with the conversion calculations. Calculate their hourly opioid consumption in morphine equivalents, and initiate the basal infusion at 50% of this value. Use bolus doses initially 50% greater than for an opioid-naïve patient. Reassess the patient frequently due to inter-individual variability and incomplete cross tolerance.

Pain assessment

Accept the patient's self-report of pain in addition to objective pain assessments. Patients with a past history of opioid abuse, if opioids are indicated, should receive opioids in effective doses. Ineffective analgesia may lead to anxiety, drug-seeking behaviour as well as pain.²⁰

Postoperative follow-up

Communicate with the primary physician regarding the treatment plan, and re-evaluate in the outpatient pain clinic to re-assess pain levels and medications.

Conclusion

The management of the opioid-dependent patient in the perioperative period has unquestionably improved

with a better understanding of opioid equivalency and the problems of opioid tolerance. Anesthesiologists must remain at the forefront of managing the unique perioperative considerations and analgesic requirements of this growing number of patients. Chronic pain patients receiving long-term opioid medications should be identified before surgery to provide for their optimal care throughout the perioperative period. The use of adjuvant analgesics and regional anesthetic techniques are encouraged. Future research in this domain must focus on the optimal use of NMDA antagonists such as ketamine, long-acting depot local anesthetics, and psychological screening to identify individuals at risk for persistent severe postoperative pain.

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