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LEARNING OBJECTIVES

Upon successful completion of this lesson, you should be able to:

1. define and describe the concept of acute on chronic pain
2. describe common myths around chronic pain and chronic pain sufferers
3. review the basic principles of analgesic therapy
4. describe the pathophysiology of opioid tolerance
5. provide basic guidelines for the treatment of acute on chronic pain in chronic pain patients taking opioids and in patients taking methadone
6. describe the role pharmacists can play when dealing with pain management in opioid-tolerant patients

To successfully complete the post-test for this lesson, you may need access to the *Compendium of Pharmaceuticals and Specialties (CPS).*

INSTRUCTIONS

1. After carefully reading this lesson, study each question in the post-test and select the one option you believe is the best answer. Although more than one option may be considered acceptable, only one option is the *best* answer.
2. To pass this lesson, a grade of at least 70% (14 out of 20) is required. If you pass, your CEU(s) will be recorded with the relevant provincial authority(ies). (Note: some provinces require individual pharmacists to notify them.)

ANSWERING OPTIONS

A. For immediate results, answer online at www.pharmacygateway.ca.
B. Mail or fax the printed answer card to (416) 764-3937. Your reply card will be marked and you will be advised of your results within six to eight weeks in a letter from *Pharmacy Practice*.

Acute on chronic pain—Managing acute pain in the opioid-tolerant patient

By Marianne J Nagata, BScPhm, ACPR

Imagine yourself taking chronic opioid therapy for a chronic pain condition—be it cancer, lower back pain, diabetic neuropathy or any number of other conditions. Now, imagine you are experiencing an acutely painful event like surgery. Postoperatively, you are given a standard dose of a common weak opioid analgesic. Based on your past experience, you anticipate this will be insufficient to relieve your pain and request a stronger analgesic, but are told this is what your physician ordered. You ask for more medication before the prescribed dosing interval has elapsed, as your pain is poorly controlled. Your request is received with some suspicion and you believe you have now been labelled a clock-watching drug seeker. How would you feel?

Unfortunately, this scenario is not uncommon, as many chronic pain patients suffer inadequate pain control when they experience acute pain. The causes of acute pain can stem from surgery, trauma/injury, and medical procedures.[1] Acute pain in a chronic pain patient can be thought of as "acute on chronic pain." As the recognition and treatment of chronic pain from cancer and noncancer conditions continues to evolve and improve, the number of patients on chronic opioid analgesics will rise, and the proportion of patients with superimposed acute on chronic pain will also rise.[2] Increasingly, patients with chronic nonmalignant pain are managed with opioids—a practice supported by the consensus statement and guidelines published by the Canadian Pain Society.[3] In addition, due to its unique N-methyl-D-aspartate

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(NMDA) antagonist property and its long duration of action with chronic dosing,[4] methadone's use is expanding from methadone maintenance programs to chronic pain management.[5] Patients on chronic opioids, including methadone, will display some degree of opioid tolerance. The management of acute pain in these patients poses a challenge to healthcare professionals.

Pharmacists in both community and hospital settings encounter patients with acute on chronic pain, and are in an ideal position to advocate for the patient and ensure appropriate analgesic orders. Since they interact with other healthcare professionals, such as nurses and physicians, as well as patients and their families, pharmacists have a responsibility to educate and help dispel myths about opioid use in opioid-tolerant patients.

This lesson will describe the management of acute on chronic pain in adult patients who are opioid-tolerant due to opioid therapy for chronic pain and/or methadone maintenance. The basic principles of analgesic therapy and the pathophysiology of opioid tolerance will be reviewed. As well, common myths surrounding the use of opioids in chronic pain sufferers will be discussed. Roles pharmacists can play when dealing with pain management in opioid-tolerant patients will also be addressed.

Acute versus chronic pain

Pain is described as an unpleasant sensory and emotional experience, associated with actual or potential tissue damage.[6] Although unpleasant, pain can serve a very important protective role. If we get too close to a flame, our body feels pain and this message of harm transmits to our brain. Our brain then tells our body to move further away from the flame, avoiding further injury. Chronic pain and acute post-operative pain, however, have no useful purpose and can cause significant discomfort and suffering. Both can have far-reaching effects on a person's mood, ability to sleep, eat and function, and overall quality of life.[7] In addition, poorly controlled acute pain can result in a stress response that may lead to an increased risk of thromboembolic events, immune, respiratory and cardiovascular complications, as well as neuroplastic changes in the brain that may result in the development of chronic pain. Indeed, the importance of appropriate management of acute pain extends beyond the prevention or minimization of suffering. Optimal acute pain management facilitates recovery and rehabilitation and can help prevent the development of chronic pain.[8]

Chronic pain is a medical condition that receives very little public attention. It is defined by the International Association for the Study of Pain as "pain without apparent biological value that has persisted beyond the normal tissue healing time (usually taken to be 3 months)."[9] Worldwide, its prevalence and severity are underappreciated by both society and healthcare providers. As an example, a random sample of more than 2,000 Canadian adults who were examined for chronic pain, defined as continuous or intermittent pain for at least six months, indicated a prevalence of 29%. The average duration of pain exceeded 10 years, and was more common in women and the elderly. Although the vast majority of chronic pain patients (80%) reported moderate to severe pain, fewer than 10% received a strong opioid.[10]

Chronic pain is a heterogeneous condition stemming from surgical (e.g., phantom limb pain, post-thoracotomy pain syndrome), traumatic (e.g., spinal cord injury), infectious (e.g., post-herpetic neuralgia, HIV), musculoskeletal (e.g., osteoarthritis, chronic low back pain) and other causes (e.g., cancer, fibromyalgia).[11]

Both acute and chronic pain can be classified as "nociceptive" or "neuropathic." Nociceptive pain typically results from musculoskeletal or visceral injury, or disease. Pain from skin, muscle or bone is usually characterized as aching, throbbing, stabbing, and/or a sensation of pressure. Pain emanating from internal organs tends to be described as gnawing, cramping, aching, sharp and/or stabbing sensations.[12]

Neuropathic pain is caused by lesions or physiologic changes in the nervous system and has unique qualities—burning, numbness, tingling, touch sensitivity (allodynia), hyperalgesia (exaggerated response to painful stimuli), or shooting sensations. Neuropathic pain tends to persist long after the initiating event has resolved.[12]

Traditionally pain is treated according to its mechanism and original source. Contrary to earlier thinking however, opioid analgesics are useful for both nociceptive and neuropathic pain; they reduce pain-producing signals and perception throughout the nervous system regardless of pathophysiology and have been shown to reduce pain in a number of neuropathic syndromes.[13] Equally relevant, although pain after surgery is primarily nociceptive, it is now believed there is a temporary neuropathic component to post-operative pain.[14]

Myths and labels

Patients suffering from chronic pain often also suffer at the hands of society, which can be sceptical and unsympathetic when pain and/or opioid use lasts beyond the time of tissue/injury healing. There exists a common misunderstanding that patients on long-term opioids are addicted and psychologically dependent. Three terms often misused are addiction, dependence and tolerance. While patients on long-term opioids may be physically dependent and display tolerance to the drug, they should not automatically be labelled as an "addict."

Addiction is a psychological dependence and desire to take a drug for non-pain-relieving purposes. It is characterized and defined by the presence of one or more of the "4 Cs"—impaired ***c***ontrol over drug use, ***c***ompulsive drug use, ***c***ontinued use despite harm, and ***c***raving. It has been defined as a primary, chronic, neurobiological disease, with genetic, psychosocial and environmental factors influencing its development and manifestations.[15] Some pain patients display drug-seeking behaviours, such as double doctoring and requesting early refills of their analgesics, and are therefore thought to be addicted. Referred to as ***pseudo-addiction***, this is because their current analgesics are insufficient, and once their pain is under control, they no longer display these negative behaviours.[15]

Physical dependence describes an adaptation that can occur by two weeks of opioid use.[16,17] If the opioid is abruptly stopped or its dose rapidly reduced, or if an opioid receptor antagonist like naloxone is administered, the body will experience a withdrawal reaction characterized by adrenergic hyperactivity hypertension, tachycardia, chills, piloerection, diaphoresis, nausea, vomiting, diarrhea, abdominal cramps, salivation, lacrimation,

figure 1

Stepwise approach to pain management*

STEP 3 – Severe pain
- nonopioids
- opioid for moderate to severe pain
- +/- adjuvant

STEP 2 – Moderate pain
- nonopioids
- opioid for mild to moderate pain
- +/- adjuvant

STEP 1 – Mild pain
- nonopioids
- +/- adjuvant

*Adapted from the World Health Organization Analgesic Relief Ladder for cancer pain[39]

table 1

Usual adult doses of nonopioid analgesics for acute pain[5,23,27,28,30,33-35,40-42]

Drug	Dose	Side effects	Comments
acetaminophen	650 mg q4h or 1 g q6h	• hepatotoxicity in overdose	• dose ceiling effect • maximum dose 4 g/day • reduce dose in elderly, alcoholics, liver or cardiac dysfunction, malnutrition/cachexia, concurrent isoniazid use • doses > 2 g/day may increase INR • watch for hidden sources of acetaminophen in combination products
NSAIDs e.g., naproxen	250–500 mg BID	• GI: nausea, vomiting, dyspepsia, ulceration, bleeding, perforation • renal: acute renal failure • allergy: bronchospasm, urticaria, angioedema • inhibition of platelet aggregation • sodium and water retention	• dose ceiling effect • reduce dose in elderly • avoid/caution in patients on anticoagulation and/or a history of GI bleed, IBD, renal dysfunction, hypovolemia, sodium-retaining conditions (e.g., CHF, cirrhosis), MI, CVA, IHD, NSAID allergy, bleeding disorder
coxibs e.g., celecoxib	200 mg q12h	• GI: same as NSAIDs but decreased incidence • renal: acute renal failure • sodium and water retention	• dose ceiling effect • reduce dose in elderly • avoid/caution in patients with IBD, renal dysfunction, hypovolemia, sodium-retaining conditions • avoid use in patients with a history of MI, CVA, IHD, CHF • considered safe in patients with NSAID-induced bronchospasm, but may cross-react in patients with NSAID-induced urticaria

CHF = congestive heart failure; coxib = selective cyclooxygenase-2 inhibitor; CVA = cerebrovascular accident; GI = gastrointestinal; IBD = inflammatory bowel disease; IHD = ischemic heart disease; INR = international normalized ratio; MI = myocardial infarction; NSAID = nonsteroidal anti-inflammatory drug

rhinorrhea and yawning.[2,16]

Tolerance is an adaptation that can occur within days to weeks of drug exposure, and describes a reduction in drug effects.[16] Tolerance develops to all opioid effects—analgesia, as well as side effects, albeit less so for miosis and constipation.[18] Tolerance to the opioid's analgesic effects can be mitigated by increasing the opioid dose. With the exception of codeine, there is no dose ceiling for opioids and some patients may require doses tens or even hundreds of times higher than doses used for opioid-naive patients.[19]

Pharmacists are faced with opportunities to clarify these terms. "Are these addicting?" is a common question from patients, and pharmacists can help destigmatize the chronic use of opioids by explaining the difference between ***physiological*** and ***psychological*** dependence.

Basic principles of analgesic therapy

When focusing on pain management, it is important to have an understanding of the basic principles of analgesic therapy. These are summarized below.[20-22]

1. Follow a stepwise approach to analgesia depending on pain severity (Figure 1). For mild pain (Step 1), use nonopioid analgesics (Table 1). If this is inadequate, or if the patient has moderate pain (Step 2), add a weak opioid to the nonopioid analgesic(s). If this is inadequate or the pain is severe (Step 3), add a strong opioid to the nonopioid analgesic(s). Steps 2 and 3 are examples of "multimodal analgesia," which takes advantage of using analgesics with different mechanisms of action.
2. Give medications orally whenever possible. It is convenient and minimally invasive.
3. When pain is constant or present most of the day, administer analgesics regularly and around-the-clock, not prn, to maintain an adequate level of analgesia. This method is more likely to keep pain under control and help avoid unnecessary suffering and anxiety.
4. Consider adjuvant analgesic therapy at all stages. Adjuvant analgesics are those for which the primary indication is something other than pain relief (e.g., anticonvulsants, antidepressants).
5. Ensure there is always an analgesic order for breakthrough pain.

6. Anticipate and prevent adverse effects of analgesics.
7. Treat analgesic adverse effects aggressively.

Pathophysiology of opioid tolerance

As noted, patients on chronic opioid therapy display some degree of opioid tolerance. This means they require higher opioid doses than opioid-naive patients to provide adequate analgesia.[5] Patients tolerant to one opioid will display tolerance to other opioids, but such "cross-tolerance" is incomplete. This is because each opioid acts on different opioid receptors and receptor subtypes.[23] Therefore, it is recommended that when switching opioid-tolerant patients from one opioid to another, the calculated equianalgesic dose (Table 2) of the new opioid should be reduced by 25–50%.[4]

Until recently, the reason some patients required escalating opioid doses was explained solely by opioid tolerance and desensitized opioid receptors. It is now also believed chronic opioid administration induces neuroplastic changes in pain perception in the brain, which result in increased pain sensitivity or pain intolerance. This phenomenon is called opioid-induced hyperalgesia (OIH),[24,25] and makes the opioid's analgesic effect less effective.[22] Animal and human studies and case reports suggest OIH can occur within a week.[26]

The challenge to clinicians is differentiating between opioid tolerance and OIH in the setting of decreased opioid effectiveness, as the management approaches are very different. Opioid tolerance is managed by increasing the opioid dose, whereas OIH is managed by dose reduction of the offending opioid, opioid rotation and/or the addition of adjuvant analgesics.[26]

Basic guidelines for the treatment of acute on chronic pain

Management of the patient with acute on chronic pain presents a challenge to the clinician. Guidelines for the management of acute pain in opioid-tolerant patients, largely based upon case reports, retrospective studies and expert opinion, are summarized below and should help in the care of these patients.

table 2

Equianalgesic doses of selected opioids*[,4,16,21,43]

Drug	Parenteral (mg)	Oral (mg)	IR dosing frequency**
Strong opioids			
morphine	10	30	q2–4h
hydromorphone	2	6	q2-4h
oxycodone	not available	15	q2-4h
Weak opioids			
codeine***	100	200	q2-4h
meperidine	75	300	q2-4h

*doses are approximately equianalgesic to 10 mg of parenteral morphine; **onset of analgesia occurs within 45 minutes and peaks in 1-2 hours for most IR opioids; ***dose ceiling effect seen at oral doses > 65 mg; IR = immediate release

ANALGESIC HISTORY

Obtaining an accurate analgesic history is a critical first step in the delivery of acute on chronic pain management.[18,27-30] In a nonjudgmental manner, patients should be specifically asked about their use of oral, transdermal, rectal, nasal and injectable opioid analgesics (including illicit opioids), as well as their use of nonopioid prescription and over-the-counter analgesics. If patients are on methadone, checking with their community pharmacy/methadone prescriber to verify doses and determine if there are any carry privileges is very important to ensure uninterrupted and safe methadone therapy. Pharmacists should strongly encourage all chronic pain patients to always carry a current list of their analgesics/opioids, as this information is essential for ensuring optimal pain management following acute injury/trauma or surgery.

PRE-OPERATIVE CONSIDERATIONS FOR THE PATIENT ON CHRONIC OPIOIDS

Patients should be instructed to take their regular opioid (oral or transdermal) the morning of surgery.[17,18,28,30,31] If increases in body temperature are anticipated (e.g., use of warming blankets during the operation), fentanyl patches should be removed and replaced with an equianalgesic dose of a systemic opioid, as elevations in body temperature can increase the rate of fentanyl absorption and the risk of toxicity.[18,30] Pre-operatively, an individualized peri-operative pain management plan can be devised. Since inflammatory mediators and cytokines are active well before an incision is closed, the plan should include pre-operative administration of multimodal analgesics.[17,23,28,30]

INTRA- AND POST-OPERATIVE ADJUSTMENT OF OPIOID DOSES

There exists wide interpatient variability in intra- and post-operative opioid requirements. However, opioid-tolerant patients should receive intra- and post-operative opioid doses that are initially 1.3–3 times higher than standard doses used in opioid-naive patients.[18,28,31] Opioid doses for the acute pain are adjusted based upon frequent assessments of pain and opioid side effects. In addition, post-operatively, opioid-tolerant patients must continue their regular opioid to prevent withdrawal.[28,30-32] Patients who are unable to take their regular oral opioid post-operatively need to receive an equianalgesic dose via an alternative route (e.g., parenteral).

Switching to another opioid, or opioid rotation, should be considered for patients who are unable to tolerate an increased opioid dose. When switching opioids, it is recommended the new opioid be dosed at 50–75% of the equipotent dose of the previous opioid (determined from equianalgesic dose tables) due to incomplete cross-tolerance.[4] Patients undergoing surgical procedures, expected to significantly reduce their level of pre-operative chronic pain (e.g., nerve compression by a tumour), should have their baseline pre-operative opioid dose reduced by 25–50%.[18]

Mixed opioid agonist-antagonist analgesics (e.g. pentazocine) must not be used, as they can displace the baseline opioid from the opioid receptor and precipitate

a withdrawal reaction in the opioid-tolerant patient.[22] Meperidine is not recommended for acute or chronic pain due to the potential for accumulation of the normeperidine metabolite and subsequent central nervous system (CNS) excitation (anxiety, tremor, myoclonus, seizures).[16]

MULTIMODAL ANALGESIA

Multimodal analgesia is the use of multiple analgesics that work on different pain pathways or different receptors. This practice usually combines opioids with nonopioids. The use of multimodal analgesia in the post-operative setting is well-accepted and has been shown to improve pain control and patient satisfaction, promote a quicker return of bowel function, decrease length of hospital stay and reduce the amount of acute opioid the patient requires. By being opioid dose-sparing, studies have shown a reduction of opioid-related side effects (e.g., nausea, vomiting). Unless there is a contraindication, patients should receive multimodal analgesia.[27,28,30-32]

The perioperative use of gabapentin or pregabalin is becoming more popular. These agents work by inhibiting high-voltage-activated calcium currents and treat the temporary neuropathic component (allodynia and hyperalgesia) that occurs after surgical trauma. These agents improve pain control and decrease opioid requirements. Because they may prevent or attenuate the development of opioid tolerance, their use in acute on chronic patients is highly recommended.[14]

As both opioid tolerance and hyperalgesia involve the NMDA receptor, low dose ketamine, which is a phencyclidine derivative and NMDA receptor antagonist, has been used as an adjunct to enhance analgesia and to prevent or minimize opioid tolerance. Its routine use is limited by its side effects which are primarily CNS (hallucinations) and dose related.[23,27,30,33-35]

If appropriate, regional anaesthetic agents should be utilized.[30,32] Tissue infiltration and peripheral nerve blocks using local anaesthetics and epidural/intrathecal modalities should be used if clinically indicated. Information is available in the literature on these more invasive techniques.[31] Nonpharmacological therapy (e.g., transcutaneous electrical nerve stimulation [TENS], massage) and psychological therapy (e.g., relaxation, biofeedback, psychotherapy) may also be beneficial.[27]

BREAKTHROUGH PAIN

Breakthrough pain (BTP) can be described as pain which "breaks through" or exceeds the control provided by the around-the-clock analgesic, usually an opioid. BTP is treated with a fast-acting/immediate-release analgesic, again usually an opioid, but may include other modalities. As a dosing guideline, 10% of the total daily dose of the regularly scheduled oral opioid or its equivalent, given orally q2h prn, is recommended for BTP.[13] BTP is an important element of pain management and for more information, readers are referred to a comprehensive discussion of this topic.[36]

DOSE TAPERING

As acute pain subsides, it is important to ensure there is an appropriate opioid-tapering regimen back to the previous baseline chronic opioid dose. If patients are on around-the-clock opioids, they should be educated to avoid abruptly discontinuing the additional opioid in order to prevent a withdrawal reaction. Rather, the opioid dose can be reduced by 25% every two to four days as tolerated.[28,31] Frequent assessments of pain control and withdrawal symptoms are required any time an opioid is being reduced or discontinued. An adequate supply of BTP analgesics should always be available during the opioid taper. If the patient is discharged before the end of the taper, or a slower, more prolonged taper is required, appropriate followup by a pain clinic or the family physician should be arranged.[31]

Special considerations for patients on methadone maintenance

Consider the following scenario. You overhear a nurse say her patient is requesting pain medication now, so she is going to give him his methadone 60 mg po daily. Upon reviewing his chart, you learn he underwent major surgery one day ago and has been on methadone 60 mg po daily for approximately six years for a previous heroin addiction. How will you respond?

Unfortunately, patients who suffer from an opioid addiction disorder often receive less than optimal acute pain management. Some physicians may be reluctant to prescribe opioids in this population due to fear of precipitating an addiction relapse and opioid-related side effects.[22] Opiophobia, which describes the tendency of healthcare providers to undermedicate patients with opioids, can be particularly problematic in the patient with an opioid addiction disorder.[22]

COMMON MISCONCEPTIONS

The challenge to deliver optimal pain control in this population is amplified by common misconceptions held by healthcare professionals. Misconceptions or myths include:

1. the maintenance methadone provides analgesia
2. the use of opioids for analgesia is contraindicated as they may result in addiction relapse
3. the additive effects of opioids for acute pain and methadone may cause respiratory and CNS depression
4. the patient's report of pain may be an act to obtain additional opioids.[22]

Pharmacists are in a position to educate healthcare professionals and help dispel and clarify these myths.

Refuting Myth 1: Although methadone suppresses opioid withdrawal for a prolonged period (24–48 hours), its duration of analgesia is significantly shorter (4–8 hours) after single dose administration.[4,22] However, the more significant reasons patients would derive little analgesia from methadone are opioid tolerance and OIH.[22] These patients also display cross-tolerance to the analgesic effects of other opioids, and thus require higher opioid analgesic doses to derive adequate pain control.[22] In addition, OIH may, in fact, counteract the analgesic effect of methadone and these patients may be less able to tolerate pain.[22,27]

Refuting Myth 2: Studies have shown the use of opioids for the treatment of acute pain does not increase the rate of relapse in patients being treated for opioid addiction. In fact, it is believed unrelieved pain is a stronger trigger for relapse than adequate analgesia.[22]

Refuting Myth 3: Because tolerance develops rapidly to opioid side effects, such as respiratory and CNS depression, there is no theoretical or clinical evidence of increased risk of severe opioid

toxicity.[22] However, some advocate frequent monitoring of sedation and respiratory depression when administering opioids in higher doses.[29]

Refuting Myth 4: Although it becomes more difficult to distinguish between appropriate analgesic requests and addiction when the medication has a high abuse potential, health professionals should keep in mind there may be appropriate reasons (e.g. surgery) for these patients to be requesting analgesics.[22] Equally important, the period following surgery or trauma/injury is not the appropriate time to deal with a patient's dependence condition.[28]

RECOMMENDATIONS REGARDING METHADONE THERAPY

Recommendations for treating acute pain in the patient receiving methadone for opioid dependence follow similar principles for the management of acute pain in the opioid-tolerant chronic pain patient.[22,25,27,28,30]

1. Contact the methadone prescriber and pharmacy to verify both the methadone dose and time the last dose was administered. Also, inform them of the patient's hospital admission and discharge date.
2. Continue the maintenance methadone. To prevent opioid withdrawal, it is very important the baseline methadone therapy is administered uninterrupted.[22,24,25,27,32]
3. Use analgesics for the acute event, including maximal use of nonopioids and gabapentin or pregabalin in conjunction with additional opioids for the acute pain.[22] Due to opioid tolerance and increased pain sensitivity, these patients will require higher acute opioid doses administered more frequently.[22,28] The focus should be on optimal pain control, while avoiding withdrawal reactions or overdose. As the acute painful episode subsides, the additional opioid can be tapered while the methadone is continued.

Due to fears of addiction relapse, both prescribers and patients may be hesitant to use opioids. If possible, avoid any drug to which the patient has had a past addiction problem.[25] Liaise with the patient's addiction specialist and prescribing physician if you have any concerns about new opioid prescriptions. In at least some provinces, patients must inform their methadone prescriber if they receive an opioid prescription from another physician.[37] Upon discharge, patients without methadone carry privileges may need to receive their new opioid prescription on a "daily dispense" basis.[25,37] Pharmacists who work with methadone patients should contact their provincial regulatory body for specific guidelines in their area.

Role of the pharmacist

Since length of stay in hospital after surgery has tended to become shorter, and the number of chronic pain patients is rising, pharmacists are more likely than ever to see opioid-tolerant patients and acute on chronic pain. Some important roles for pharmacists include the following:

1. Review the patient's history to determine current drug use, possible adverse drug reactions, and drug-drug and drug-disease interactions.
2. Recognize possible acute on chronic pain situations and ensure the appropriateness of specific opioids and opioid doses. For example, if a patient has been taking morphine SR 200 mg TID for chronic pain, a standard codeine-containing product is unlikely to do much for the acute pain.
3. Strongly encourage multimodal analgesia, including the addition of various nonopioid therapies and nonpharmacologic measures.
4. Advocate around-the-clock dosing.
5. Initiate patient counselling on the use of BTP medication, as well as opioid dosing, side effects, how long those side effects might last, and preventative measures (e.g., for the prevention of constipation, encourage increased fluid intake and the use of stimulant laxatives +/- stool softeners).[38]
6. Monitor patient profiles for possible over- or underadherence, which may be related to poor pain control, side effects or misconceptions. Also, ask patients how their pain is responding to therapy. Use specific questions such as the duration of efficacy per dose, adverse effects they may be experiencing (including those that suggest opioid withdrawal) and how much/how often the patient needs BTP medication.
7. Contact the physician if the patient does not have an order for BTP medication, and make sure a sufficient quantity of that medication is prescribed.
8. Help dispel myths regarding opioid use with patients, their families, and healthcare providers.

Summary

Opioid-tolerant patients include chronic pain patients on opioids, as well as patients on methadone maintenance for drug addiction. Due to the improved acceptance of the use of opioids for the treatment of chronic pain, as well as the use of methadone for the management of opioid addiction, the opioid-tolerant patient is not uncommon to pharmacists. The management of acute pain in these patients poses a unique challenge to the healthcare team. Studies have shown acute pain is poorly managed, especially in the opioid-tolerant patient. With improved knowledge and heightened awareness, pharmacists can help improve pain management, prevent withdrawal, and assist with the monitoring of analgesia in these patients. Even if an analgesic order is appropriate, patients may experience delays in obtaining relief if a high-dose opioid order is questioned by healthcare providers. As highly visible and easily accessible members of the healthcare team, pharmacists should be ready to advocate for and support the opioid-tolerant patient. pp

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Questions

To answer online, go to www.pharmacygateway.ca, CE section, CE Online, Pharmacy Practice

1 What is the estimated prevalence of chronic pain in Canada?

a) less than five per cent
b) nine per cent
c) 19%
d) 29%
e) 39%

K.H., a 53-year-old female, had left-knee replacement surgery today. She has been prescribed a typical dose of morphine via a Patient-Controlled Analgesia (PCA) pain pump (dose 1 mg; lockout interval 6 minutes; 4-hour maximum 35 mg) to self-administer when she has pain. You are asked to see her as she is pressing the PCA button every few minutes and is still experiencing severe pain. She is taking no other analgesics while in hospital.

2 Your first plan of action is to:

a) Review K.H's history, including her past medical history, medication (including analgesics) history and allergy status.
b) Inform K.H. that morphine is a strong analgesic and she can only receive it every six minutes.
c) Contact the physician to suggest changing K.H.'s morphine PCA to an equivalent dose of hydromorphone PCA.
d) Encourage nonpharmacologic measures (e.g., mental imagery, relaxation)
e) either a) or c)

3 Upon reviewing K.H.'s chart, you discover she has no known allergies, a history of osteoarthritis of her left knee and fibromyalgia. Your medication-analgesic history reveals she takes oxycodone CR 160 mg po q8h, oxycodone 20–30 mg po prn, gabapentin 400 mg po q8h and nortriptyline 100 mg po qhs. How would you respond to this new information?

a) Contact the physician to reorder K.H.'s oxycodone CR, gabapentin and nortriptyline.
b) Contact the physician to reorder only the gabapentin and nortriptyline, as K.H. is receiving opioid via the PCA.
c) Contact the physician to suggest changing K.H.'s oxycodone CR to an equivalent dose of morphine SR.
d) None of the above

4 Should K.H.'s morphine PCA dose be increased?

a) yes
b) no

5 The physician's new orders for K.H. include acetaminophen and celecoxib around-the-clock and an increase in gabapentin for a few days. K.H. wonders if all the additional pain medication means she is becoming "immune" to her usual narcotic. How would you respond to K.H.?

a) Explain that because K.H. now has a new pain on top of her chronic pain, she temporarily requires more narcotic than usual.
b) Tell K.H. that the non-narcotic medications she's been given work differently than her narcotics and are meant to add to her pain relief as well as help reduce the amount of morphine she needs.
c) Reassure K.H. that while a person's body can become used to a certain dose of narcotic, there is no real maximum for the drug she is using, so the dose can always be increased.
d) Both a) and b)
e) All of the above

6 Opioid tolerance can develop within as little as one week of regular opioid use.

a) true
b) false

7 Multimodal analgesia is the use of:

a) anxiolytics to help control pain
b) endogenous compounds to help alleviate pain
c) multiple analgesics that work on different pain pathways or receptors
d) agents targeted to prevent opioid side effects
e) both c) and d)

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Acute on chronic pain—Managing acute pain in the opioid-tolerant patient

8 Side effects of opioids include:
a) respiratory depression, diarrhea
b) nausea, vomiting, miosis
c) urinary retention, hypertension
d) pruritus, liver toxicity

A.C., a 52-year-old male with a history of heroin addiction, has been on methadone 70 mg po daily for two years. He is otherwise healthy, but had surgery earlier today for a fractured ankle. After his surgery, he is discharged to his home and comes into your pharmacy demanding and argumentative.

9 A.C. shows you his prescription for acetaminophen/codeine 30 mg 1–2 tablets every four hours if needed and tells you he needs something stronger as his pain is "20 out of 10." What is the most appropriate response to A.C.'s concern?
a) Tell A.C. that all ankle fracture patients receive prescriptions for, and do well on acetaminophen/codeine 30 mg.
b) Reassure A.C. that his methadone will help relieve his pain.
c) Since he is on methadone, recommend to the physician that A.C. be allowed to take up to three acetaminophen/codeine 30 mg tablets at each dose.
d) Suggest A.C.'s physician add a short course of around-the-clock acetaminophen, an NSAID or coxib, and gabapentin, plus change acetaminophen/codeine 30 mg to morphine around-the-clock and q2h prn for a few days.

10 A.C's physician prescribes a strong opioid around-the-clock and prn for breakthrough pain. Two days later, the home-care nurse says A.C. "really likes his new drug. He uses a lot of breakthrough doses in addition to his around-the-clock doses, for what he says is still moderate pain. I think he is getting addicted to it." How would you respond to the nurse?
a) Explain that A.C. is opioid-tolerant because of the methadone. As such, he requires more frequent and higher opioid doses for pain than opioid-naive patients.
b) Explain that A.C. has developed OIH from the new drug so he requires significantly higher opioid doses for pain.
c) Tell the nurse she is probably right. A.C.'s use of strong narcotics should be limited as he has had an addiction problem to opioids in the past.
d) Both a) and b)
e) None of the above

11 Optimal post-operative pain management begins intra-operatively.
a) true b) false

12 Are coxibs safe to use in a patient with a history of ASA/NSAID-induced asthma?
a) yes b) no

13 Which of the following help explain why chronic opioid users require higher opioid doses when treating an episode of acute pain?
a) tolerance
b) psychological dependence
c) pseudoaddiction
d) physical dependence
e) both a) and d)

14 Select the best answer to the following statement. Ketamine has become an agent of interest in treating acute pain in chronic opioid users because of:
a) its psychotomimetic effects
b) its long duration of action
c) its NMDA receptor antagonist property and beneficial effect on opioid tolerance
d) its action as an anaesthetic agent
e) its NSAID properties that improve pain control

15 For acute pain present most of the day, how should an opioid be dosed?
a) Use a short-acting opioid on a prn basis.
b) Use a long-acting/sustained-release opioid on a prn basis.
c) Use an opioid on an around-the-clock basis.
d) Either b) or c)

16 Which of the following analgesics display a dose ceiling effect?
a) acetaminophen
b) diclofenac
c) hydromorphone
d) a) and b)
e) all of the above

17 Which symptom(s) can a chronic pain patient on opioids for analgesia experience if they abruptly stop their opioids?
a) dry mouth and constipation
b) lacrimation, diaphoresis, diarrhea
c) decreased blood pressure
d) decreased analgesia
e) b) and d)

18 A physician calls and asks for your help calculating the equianalgesic dose of hydromorphone SR for a patient whose pain has been well-controlled on morphine SR 100 mg q12h for several months. Taking into account incomplete cross-tolerance, which of the following would you suggest the physician prescribe?
a) either hydromorphone SR 6 mg or 9 mg po q12h
b) either hydromorphone SR 10 mg or 15 mg po q12h
c) either hydromorphone SR 12 mg or 15 mg po q12h
d) either hydromorphone SR 18 mg or 21 mg po q12h
e) hydromorphone SR 20 mg po q12h

19 If morphine SR 60 mg po q12h was ordered for a patient, what would be a suitable order for breakthrough pain?
a) morphine 10–15 mg po q2h prn
b) codeine 30–60 mg po q2–4h prn
c) morphine 30 mg po q4h prn
d) codeine 100 mg po q2h prn

20 What are some examples of how pharmacists can help improve the management of acute on chronic pain?
a) Make sure a patient's chronic pain opioid is continued when an opioid for acute pain is ordered.
b) Contact the prescriber if a patient is taking multiple anti-inflammatory analgesics.
c) Ask patients on opioids specifically about constipation, as tolerance to this side effect is less likely to occur.
d) Both a) and b)
e) All of the above

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THIS MONTH
Acute on chronic pain—Managing acute pain in the opioid-tolerant patient

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All lessons are reviewed by a minimum of six pharmacists for accuracy, currency and relevance to current pharmacy practice.

This lesson is valid until February 14, 2011. Information about managing acute pain in the opioid-tolerant patient may change over the course of this time. Readers are responsible for determining the most current aspects of this topic.

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