Advanced Oncology Certified Nurse Practitioner

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Making Cancer History®

Introduction

- Pain is one of the most feared and prevalent symptoms associated with cancer and cancer treatments.
- Pain can severely affect the quality of life of patients with cancer; therefore, pain must be managed to reduce physical and emotional distress (Mesgarpour et al., 2014).
- The European Society for Medical Oncology (ESMO) reported that more than 80% of patients with advanced metastatic disease will experience pain (Ripamonti, Santini, Maranzano, Berti, & Roila, 2012).

Introduction continued

- Cancer pain can be caused by the infiltration of a tumor or injury to nerves, bone, or soft tissue because of chemotherapy, radiation therapy, surgery, or radiation-induced vascular occlusion (McMenamin, 2011; Portenoy, 2011).
- In 1996, the World Health Organization (WHO) estimated that about one-third of patients receiving cancer treatments and 60%–90% of patients with metastatic disease experience moderate to severe pain (WHO, 1996).
- Unfortunately, the epidemiology of cancer pain has remained consistent over the past 20 years; numerous studies continued to report that cancer pain remains undertreated (Miaskowski, 2010a).

Definitions and Incidence

- The concept of pain is complex, varying by individual and culture.
- The International Association for the Study of Pain (2011) defines pain as an unpleasant sensory and emotional experience related to actual or potential tissue damage.
- Pain can be **acute or chronic**. **Acute pain** is shorter, limited in duration, has an identifiable cause, and functions to warn and protect from tissue damage. It may be caused by diagnostic procedures, treatment, or surgical interventions. In most clinical situations, acute pain will improve over time.
- **Chronic pain** continues well past the expected recovery time following injury to the body. Chronic pain generally continues for over one to six months or reoccurs at various intervals. It can occur from sites of metastatic disease but may also develop because of preexisting conditions (such as diabetic peripheral neuropathy, osteoarthritis, and lower back pain) (Miaskowski, 2010a).
- Cancer pain may be acute, chronic, or both, as both types can occur simultaneously depending on the disease state, diagnostic procedure, or treatment.

Definitions and Incidence

- Pain can be described as nociceptive when caused by ongoing tissue injury.
- The two types of nociceptive pain include somatic and visceral pain.
- Neuropathic pain is another type caused by abnormal somatosensory processing in the peripheral or central nervous system (Dworkin et al., 2010).
- It is important to recognize that patients with cancer may have one or a combination of the three mechanisms of pain (Bennett et al., 2012). For these reasons, oncology practitioners must accurately assess, treat, and evaluate patients experiencing pain.

Definitions and Incidence

- Controlled-release opioids are prescribed for patients with cancer experiencing persistent moderate to severe chronic pain. Controlled-release opioids are administered around the clock and on a fixed schedule.
- Extended-release or long-acting medications include oxycodone, methadone, oxymorphone, hydromorphone, and transdermal fentanyl and buprenorphine.

Definitions and Incidence

- ***Breakthrough pain*** is defined as transitory pain that occurs in the setting of adequately controlled pain by an opioid regimen. Breakthrough pain may be somatic, visceral, neuropathic, or a combination.
- Breakthrough pain medication is also known as “rescue” medication.
- Short-acting opioids are used to control breakthrough pain and include oxycodone, morphine, hydromorphone, and oxymorphone (NCCN, 2015a).
- Breakthrough pain can occur without stimulus or as a result of certain activities or biologic events and is associated with decreased quality of life and increased cost and hospitalizations (Wengström et al., 2014).

Definitions and Incidence

Optimal pain management requires an understanding of

- addiction
- physical dependence
- and tolerance

Definitions and Incidence

- **Addiction** is a disease with strong genetic, psychosocial, and environmental influences.
- Opioid addiction is uncommon among patients with cancer (Anghelescu, Ehrentraut, & Faughnan, 2013).
- The American Society for Pain Management Nursing defines *addiction* as a chronic, relapsing, treatable disease of the brain characterized by craving, dysfunctional behaviors, and an inability to control impulses regarding consumption of a substance with compulsive use despite harmful consequences (Oliver et al., 2012).
- **Pseudoaddiction** occurs because of inadequate pain management and is often interpreted as drug seeking (Anghelescu et al., 2013; Bell & Salmon, 2009). Pseudoaddictive behaviors are pain-relief–seeking behaviors that occur when a patient's pain is unrelieved, and healthcare clinicians view the patient's request for more pain medication as addictive behavior. This is more likely to happen when the patient is undermedicated, requiring an adjustment in the current pain management strategy (Anghelescu et al., 2013).

Definitions and Incidence

- **Opioid dependence**
- involves physical symptoms, including tolerance of opioid medication and symptoms of withdrawal when the opioids are withheld (Garland, Froeliger, Zeidan, Partin, & Howard, 2013).
- This is an anticipated response to ongoing opioid therapy and should not be confused with addiction. Physical dependence may occur within a few days, although it varies among patients.
- Physical dependence may be seen as a withdrawal syndrome if the drug is abruptly stopped, if the dose is rapidly reduced, or if an antagonist is administered.
- Withdrawal symptoms can be avoided by tapering the narcotic over some time (Anghelescu et al., 2013).

Definitions and Incidence

- **Tolerance**
- The need to increase the dosage of drug or the frequency of use to achieve the same level of pain relief and results from chronic administration (Garland et al., 2013).
- When tolerance occurs, the frequency of dosing should be increased, or another opioid could be prescribed.

Etiology and Pathology

- Nociceptors are specialized receptors (sensory neurons) located throughout the body (skin, viscera, and musculoskeletal tissues) that respond to painful stimuli. When either mechanical or chemical stimuli activate nociceptors, nociceptive information is sent along A-delta and C fibers to the brain, and the individual then experiences somatic and/or visceral pain.
- A-beta fibers convey non-nociceptive information (caused by damage to the nervous system), and when the brain receives them, neuropathic pain results (Fornasari, 2012).
- A-delta fibers are tiny, thinly myelinated fibers activated by stimuli such as pinpricks.
- C fibers are thin and unmyelinated and are activated by tissue damage. Tissue damage causes C fibers to release chemical metabolites called *transducers*, such as epinephrine, prostaglandins, leukotrienes, serotonin, and substance P, that sensitize the area of damage (causing inflammation) and activate nociceptors, thus causing pain.

Etiology and Pathology

- A-beta axons are larger, more heavily myelinated, and activated by light touch, transmitting information much more rapidly than the A-delta or C fibers.
- Pain information enters the spinal cord via the dorsal root synapse, and transmission is mediated by excitatory amino acids, mainly glutamate but also aspartate, substance P, and calcitonin gene-related peptide.
- The pain information then crosses to the spinothalamic tracts and is transmitted to the thalamus and cortex. From there, the sensory cortex, frontal lobe, and reticular formation process the information, resulting in pain perception (Fornasari, 2012; Walker, 2010).
- Opioid receptors are located on ascending and descending pain pathways and will produce the analgesic effects of opioid pharmaceuticals. More opioid receptors are located in certain parts of the brain and spinal cord.

Etiology and Pathology

- Understanding of the neurotransmitters involved in pain transmission has led researchers to explore targeted strategies for cancer pain management (Chou et al., 2009).
- Strategies include blocking pain at the periphery (as with nonsteroidal anti-inflammatory drugs [NSAIDs] and anesthetics), activating inhibitory processes in the spinal cord and brain (as with opioid treatments), and interfering with the perception of pain (as with relaxation therapy).

Etiology and Pathology

- Somatic pain originates from skin, bone, muscle, blood vessels, subcutaneous and connective tissue.
- Patients may describe somatic pain as dull, constant, or aching. Bone metastases or postsurgical incision pain are examples of somatic pain in oncology.
- Approximately one-third of all cancer pain is somatic (Miaskowski, 2010a).

Etiology and Pathology

- The etiology of visceral pain may be caused by organ obstruction (e.g., bowel, pancreatic duct, ureteral) or injury to another pain-sensitive visceral structure such as the pleura, hepatic capsule, or peritoneum.
- It is important to determine the etiology of visceral pain and establish whether it is due to compression, infiltration, or distension of viscera when considering management strategies. This type of pain occurs in patients with gastrointestinal and gynecologic malignancies (McMenamin, 2011).
- It is usually poorly localized in nature and may be described as deep, squeezing, cramping, splitting, or pressure-like. Visceral pain can occur when metastasis to an organ occurs.
- It is often referred to as areas away from the actual disease site. Causes include the tumor or injury from chemotherapy, radiation therapy, or surgery.

Etiology and Pathology

- **Neuropathic pain** is poorly localized and may be described as sharp, shooting, hot or burning, electric shock-like, or “painfully numb.” If localized, it usually occurs at the injury site, and this area may be hypersensitive to other stimuli.
- Neuropathic pain may be delayed in onset, occurring days to years after the nerve-damaging event. Several causes of neuropathic pain syndromes exist. Neoplastic invasion to the spinal cord, nerve roots, plexuses, or peripheral nerves is a common cause.
- Surgical procedures such as radical neck dissection, thoracotomy, and limb amputation are another reason for the development of neuropathic pain syndromes.
- Chemotherapy toxicity from agents such as taxanes and cisplatin is also known to cause neuropathic pain. Infection also can be considered when patients report neuropathic pain symptoms (Miaskowski, 2010a).
- The prevalence of neuropathic pain is estimated to occur in 18%–21% of patients with cancer (Bennett et al., 2012). It is interesting that when mixed pain is reported, neuropathic pain was reported more frequently and estimated to occur 19%–39% of the time (Bennett et al., 2012).

Etiology and Pathology

- Several pain syndromes commonly appear in patients with cancer (see Table 10-1). A cancer pain syndrome is described as a constellation of meaningful signs and symptoms in a patient with cancer (Portenoy, 2011).
- Approximately 75% of patients with cancer with chronic pain have nociceptive or neuropathic pain that is directly related to the individual malignancy (Portenoy, 2011).
- Patients often experience mixed types of pain. For example, patients with bone metastasis (somatic pain) also may experience a component of neuropathic pain. Other causes of chronic pain occur as a result of antineoplastic treatment unrelated to the disease (Bennett et al., 2012).
- Bone metastasis is a pain syndrome that is one of the most prevalent causes of chronic cancer pain (Falk & Dickenson, 2014).

Etiology and Pathology

- Bone metastasis may be caused by direct tumor invasion, damage to adjacent structures, or a secondary pathologic fracture. The pain is often described as severe and localized. The exact mechanism of action is unknown, but it is known that normal bone remodeling is disrupted during this process. (Monczewski, 2013; Portenoy, 2011).
- The most common sites of metastasis include the spine, pelvis, hip, femur, and skull. APNs need to monitor for specific complications of bone metastasis, which include cord compression, fracture, and hypercalcemia.

Etiology and Pathology

- Many pain syndromes are treatment-related, such as chemotherapy-induced peripheral neuropathy caused by an agent or combination of agents such as vincristine, platinum compounds, and taxanes (Ferrier, Pereira, Busserolles, Authier, & Balayssac, 2013). Even years after radiation therapy, patients may experience the onset of pain from neural damage.
- The etiology of breakthrough pain in patients with cancer is not always clear (Greco et al., 2011). It can occur spontaneously or be precipitated by an activity such as walking, turning, or standing.
- Breakthrough pain may also result from “end-of-dose failure” caused by declining analgesic levels—that is, pain occurring before the next scheduled dose of pain medication.

Etiology and Pathology

- Leptomeningeal metastasis is another example of a pain syndrome.
- Any solid or hematologic malignancy can cause this, but it is more common in breast and lung cancer, as well as lymphoma and leukemia (Le Rhun, Taillibert, & Chamberlain, 2013).
- Patients may report headache and back pain, which seizures, cognitive impairment, or neuropathy, may accompany.

Risk Factors

- Many factors potentially increase the risk of cancer pain.
- Advanced, The location.
- Studies show that psychosocial factors, such as depression, anxiety, and feelings of isolation, influence pain reports (Ripamonti et al.,2012).
- Patients with inadequate acute pain management during treatment are more likely to have subsequent chronic pain (Burton, Fanciullo, Beasley, & Fisch, 2007; Burton, Fine, & Passik, 2012).

Risk Factors

- Factors also exist that increase the risk of inadequate pain management.
- These include age (older than 70 or younger than 3 years old), female sex, cognitive impairment, a history of substance abuse, and minority races (McMenamin, 2011; Walker, 2010).
- Minority populations; A study conducted by Fisch et al. (2012) reported that minority patients were twice as likely to experience uncontrolled pain when compared to nonminority patients.

Signs and Symptoms

Acute	Chronic	Neuropathic
• Autonomic signs* – Diaphoresis – Elevated blood pressure – Pallor – Tachycardia	• Autonomic signs absent • Constipation • Decreased appetite • Decreased libido • Depression • Fatigue • Insomnia • Social withdrawal	• Allodynia • Dysesthesias • Hyperalgesia • Hyperesthesia • Hyperpathia • May follow neural pathway

Figure 10-1. Clinical Signs and Symptoms of Pain

* Autonomic signs are not sensitive in differentiating pain from other sources of distress. Absence of autonomic signs does not indicate absence of pain.

Note. Based on information from Kendall et al., 2013; Miaskowski, 2010a; National Comprehensive Cancer Network, 2015a; Portenoy, 2011; Ripamonti et al., 2012.

Many **assessment tools exist**, with various strengths and weaknesses. Generally, the baseline assessment is more comprehensive, whereas ongoing reassessment tools are more succinct.
Table 10-2 lists standard cancer pain assessment tools. Using validated pain assessment tools may improve pain intervention outcomes (Tracy & Morrison, 2013).

Table 10-2. Pain Assessment Tools

Tool	Description	Advantages/Disadvantages
Numeric Rating Scale (McCaffery & Pasero, 1999)	0–10 scale where 0 = no pain and 10 = worst pain imaginable	Rapid, good for assessment of intervention efficacy
Breakthrough Pain Questionnaire (Portenoy et al., 1999)	Structured interview	Designed to characterize breakthrough pain
Checklist of Nonverbal Pain Indicators (Feldt, 2000)	Six-item checklist rated by observer where 0 = behavior not observed and 1 = behavior observed	For patients who are cognitively impaired or otherwise unable to verbally rate pain presence or intensity
Edmonton Symptom Assessment Scale (Bruera et al., 1991)	Nine-item visual analog scale for symptoms in patients receiving palliative care	Gives a numeric score; higher scores reflect greater severity of patient condition; easy to perform
Memorial Symptom Assessment Scale (Fishman et al., 1987)	Assesses 32 symptoms in three dimensions: intensity, frequency, and distress	Broader range of information, more time consuming; two abbreviated forms available that assess 32 or 14 symptoms in one dimension; valid in patients with or without cancer
Wong-Baker FACES Pain Rating Scale (Wong & Baker, 1988)	Six faces that vary from smiling (0 and no pain) to crying (10 and worst pain)	Recommended for people age 3 or older; useful in patients with language barriers
McGill Pain Questionnaire (MPQ) (Melzack, 1987)	Three major classes of word descriptors—sensory, affective, and evaluative—used by patients to describe subjective pain experience; also has intensity scale	Qualitative and quantitative information; originally developed for nonmalignant pain, but valid in cancer populations as well
Multidimensional Affect and Pain Survey (Knotkova et al., 2006)	101 descriptors rated by patients as to closeness to their own feelings, emotions, and experiences	Similar to MPQ; takes no more than 15 minutes to complete; assesses somatosensory and emotional experiences and feelings of well-being
Brief Pain Inventory (Cleeland & Ryan, 1994; Tittle et al., 2003)	Measures pain by severity and interference with function	Developed for use in patients with cancer; validated across cultures and various languages; validated in surgical patients with cancer and chronic nonmalignant pain; time intensive

A comprehensive pain **assessment** includes four important components.

- 1. Obtaining a detailed history of pain.
- 2. Psychosocial assessment.
- 3. Examining the site of pain and determining the physical impact.
- 4. Diagnostic evaluation of the pain, the potential pain syndromes, and the effect on the patient's quality of life and overall function are determined (Miaskowski, 2010a; NCCN, 2015a; Tracy & Morrison, 2013).

Assessment

- Breakthrough pain assessment should be performed, and breakthrough pain's location, intensity, and timing should be determined.
- Temporal patterns, precipitating or exacerbating factors, relieving factors, and response to interventions.
- The number of pain episodes per day should be documented. The relationship of breakthrough pain to the overall clinical status (Greco et al., 2011; NCCN, 2015a).
- Rating pain is often subjective. Pain assessment tools or rating scales can be an effective way of quantifying and qualifying pain symptoms.

Assessment

- Reassessment is performed following any intervention
- Assessing intervention side effects, adverse events, and effects on quality of life (Apolone et al., 2009; Miaskowski, 2010a).
- A pain management diary may help assess treatment strategies' efficacy. This may enhance patients' awareness of pain and its contributing factors and give them an increased sense of control over pain.
- The patient report will guide the physical examination.

Assessment

- The differential diagnosis of pain may be related to its etiology and pathophysiology.
- Pain may result from a nonmalignant issue, such as peripheral neuropathy caused by diabetes, osteoarthritis, or chronic fatigue syndrome.
- Clinicians should consider the patient's medical history when assessing and treating cancer pain, although the distinction is often unclear (Portenoy, 2011).
- Potential specific cancer pain syndromes, such as post-thoracotomy pain syndrome, and potential oncologic emergencies, such as spinal cord compression or hypercalcemia, should be considered in the differential.

Treatment of Cancer Pain

- An individualized, multidisciplinary, and multimodal pain management approach and should include physical, mental, psychological, cultural, and social factors (Miaskowski, 2010a; Ripamonti et al., 2012).
- An essential component of successful pain management is the oncology advanced practitioner's ability to work with the patient and the patient's caregivers and communicate the treatment plan.
- Treatment interventions are initiated based on the assessment, and treatment plans are evaluated frequently (Miaskowski, 2010a).
- Clinicians should initiate pain treatment promptly while awaiting a workup to determine the specific etiology of the pain (Portenoy, 2011).
- Interventions include pharmacologic and nonpharmacologic strategies to control pain.

Pharmacologic Treatment

- Initial pharmacologic intervention is based on the patient's report of pain severity.
- Pain rated 1–4 using the NRS is considered mild and may require nonopioid interventions. Moderate pain is usually described as 5 or 6, whereas severe pain is rated 7–10. Severe pain is considered a pain emergency requiring immediate interventions (Miaskowski, 2010a).
- Pharmacologic interventions include nonopioids, opioids, and co-analgesics. The most appropriate medication is based on the cause and severity of pain. NCCN (2015a),
- ESMO (Ripamonti et al., 2012) and the American guidelines provide evidence-based information to reduce variation in the clinical management of cancer pain and improve patient outcomes.
- A crucial concept for cancer pain management based on the WHO (1996) three-step analgesic ladder. This is because pain assessment is subjective and individualized, and treatment is based on the patient's pain intensity, comorbidities, and current medications (McMenamin, 2011; NCCN, 2015a).

Nonopioid Treatment

- Following a comprehensive pain assessment, if the patient has a pain intensity of 1–3, a nonopioid analgesic agent such as an NSAID or acetaminophen may be administered, or a short-acting opioid can be considered(NCCN, 2015a). Commonly used NSAIDs in the management of cancer pain include aspirin, ibuprofen, naproxen, and Celebrex.
- NSAIDs have a ceiling effect and do not produce tolerance, dependence, or addiction. Common side effects associated with NSAIDs include dyspepsia, gastrointestinal bleeding, and renal insufficiency (McMenamin, 2011; Portenoy, 2011).
- Acetaminophen appears to have fewer side effects. Daily acetaminophen dosing of greater than 4 g is not recommended because of the increased risk of hepatic toxicity that can occur, which is more likely in alcoholic individuals and those with liver disease (Miaskowski, 2010a).
- NSAIDs are used cautiously in patients at risk for gastrointestinal or renal toxicities. If two different NSAIDs are prescribed without successful control of pain, another strategy should be considered.

Opioid analgesics

- Opioids are the principal analgesics to treat moderate to severe pain based on the WHO analgesic ladder (WHO, 1996). Opioids bind with mu-opioid receptors within and outside the central nervous system (Miaskowski, 2010a).
- Morphine continues to be the opioid of choice for the management of moderate to severe cancer pain. Although no controlled trials have demonstrated its superiority over other agents, it is readily available, is relatively inexpensive, and has multiple routes of administration (McMenamin, 2011).
- Before an opioid is prescribed, nurses, providers, and pharmacists should have an understanding of the medication's mechanism of action, common starting doses, equivalence to other opioids, duration of effect, half-life, available routes, and associated adverse effects.
- Initial opioid titration for opioid-naïve patients is done at a slower pace than in opioid-tolerant patients (NCCN, 2015a).

Opioid analgesics

- Opioids that are prescribed for chronic pain should be administered regularly.
- As previously discussed, long-acting pain medication or extended-release opioids provide a consistent release of analgesia. An oral or transdermal route of administration is preferred.
- Extended-release or long-acting pain medications (e.g., morphine, oxycodone, fentanyl patch) should be given along with medication that is administered for breakthrough pain.
- When long-acting opioids do not adequately control pain, a short-acting or breakthrough medication should be prescribed. Breakthrough pain medication may be needed at the end of the extended-release medication schedule or with increased activity during the day.
- Breakthrough pain medications include morphine, oxycodone, and hydromorphone. Other rapid-onset opioids include fentanyl transmucosal or fentanyl buccal tablets (McMenamin, 2011; Miaskowski, 2010a; NCCN, 2015a).

Table 10-3. Opioid Classification and Dosing

Opioid Class	Class Effects	Agents
Pure opioid agonists	Increasing dose increases effectiveness but with no ceiling effect. Will not reverse or decrease effects of other pure opioid agonists if given together Caution with impaired breathing, bronchial asthma, increased intracranial pressure, or liver failure	Morphine • Opioid of choice for cancer pain • Standard of comparison for opioids • IV • Oral – Immediate release – Extended release Hydromorphone • Synthetic opioid with short half-life • Useful in those intolerant of morphine • More potent than morphine • Peak effect slightly more rapid than morphine but with slightly shorter duration of action • May cause less nausea and hallucinations than morphine • IV • Oral Oxycodone • Synthetic opioid, better oral absorption than morphine • May cause less nausea and hallucinations than morphine but more constipation • No parenteral route, oral only

(Continued on next page)

Note. Based on information from Coyle & Layman-Goldstein, 2007; Fallon, 2013; McMenamin, 2011; Miaskowski, 2010a; National Comprehensive Cancer Network, 2015a; Ripamonti et al., 2012; Vallejo et al., 2011.

Table 10-3. Opioid Classification and Dosing *(Continued)*

Opioid Class	Class Effects	Agents
Pure opioid agonists *(cont.)*		Fentanyl • Opioid with short half-life • Much more rapid onset of action but effect of shorter duration • Transdermal and transmucosal routes • May be less constipating than morphine • When given transdermally, the drug is stored in subcutaneous fat, and serum concentration may take several hours to decline. • IV • Transdermal • Transmucosal Methadone • Excellent oral and rectal absorption, long duration of action, low cost, and no known active metabolites • Used in severe pain situations such as neuropathic pain • Accumulates with repetitive dosing • After a few days, the interval of administration can be increased while maintaining analgesic effects. • For use by experienced prescribers • Careful titration and follow-up • IV • Oral Oxymorphone • Short half-life and more potent than morphine and an active metabolite of oxycodone • IV • Oral – Immediate release – Extended release Hydrocodone • Considered a weaker opioid than oxycodone agents • Often used in antitussive agents Propoxyphene • Not often used in treating cancer pain
Partial agonists	Less effect at the opioid receptor than full agonists	Buprenorphine • This class of opioids is not recommended for the treatment of cancer pain. • Ceiling effects • May precipitate withdrawal in patients on pure opioid

Opioid analgesics

- **Morphine** is a potent analgesic with a strong affinity for the mu receptor in the brain and spinal cord. IV morphine is three times more potent than oral morphine and often is considered the first-line treatment for cancer pain.
- As with most opioids, morphine is metabolized by the liver. Morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G) are two metabolites of morphine that have been identified. M6G is twice as potent as morphine and is excreted by the kidneys. Although M3G does not bind to opioid receptors, it may be responsible for some of the toxicities associated with morphine.
- Morphine is available as an IV and oral medication (McMenamin, 2011). Oral medication is available as extended-release or immediate-acting medications. Morphine also is available for rectal, intraspinal, epidural, or subarachnoid administration (McMenamin, 2011; NCCN, 2015a).

Opioid analgesics

- **Hydromorphone** is a semisynthetic morphine analog. It is five to eight times more potent than morphine. IV hydromorphone is five times more potent than oral hydromorphone (McMenamin, 2011). The metabolite, hydromorphone-3-glucuronide, is excreted by the kidney and has been identified to cause neuroexcitation at higher doses. Hydromorphone can be administered in IV, oral, rectal, and spinal formulations (McMenamin, 2011; Walker, 2010).

- **Oxycodone** is a semisynthetic opioid derived from morphine. It is available as an oral medication as an extended-release or immediate-release formulation. The active metabolite of oxycodone is oxymorphone is a very potent analgesic.

Opioid analgesics

- **Fentanyl** is a potent lipophilic opioid that is 75–100 times more potent than morphine (McMenamin, 2011). Fentanyl is poorly absorbed in the gastrointestinal tract but well absorbed via the buccal mucosa, skin, and blood-brain barrier.
- Fentanyl patches are commonly used to control cancer pain and are recommended for opioid-tolerant patients currently on stable opioid medications.
- The absorption of transdermal fentanyl can be altered if patients are diaphoretic, febrile, or dehydrated. Transmucosal fentanyl citrate and fentanyl buccal tablets are rapid-onset opioid preparations that require enrollment into the risk evaluation and mitigation strategies program (McMenamin, 2011; Miaskowski, 2010a; NCCN, 2015a).

Opioid analgesics

- **Methadone** is a potent mu-opioid and should be prescribed by providers with experience and understanding of methadone's unique pharmacologic characteristics.
- Methadone is metabolized by the P450 cytochrome system, and a large portion is excreted in the feces. Plasma methadone concentrations increase slowly (up to one week); therefore, titration should occur slowly. The steady state of methadone is achieved after four to five half-lives (Aiello-Laws et al., 2009; Miaskowski, 2010a; NCCN, 2015a).

Opioid analgesics

- Partial agonists (e.g., buprenorphine) have little use in cancer pain because of their ceiling effects and their ability to precipitate withdrawal syndrome in patients on pure agonist agents (NCCN, 2015a).
- Patients receiving mixed agonist-antagonist agents (e.g., butorphanol, nalbuphine, pentazocine) may have more side effects, such as agitation, dysphoria, and confusion, than with pure opioid agonists.
- These agents are not recommended for cancer pain treatment.

Opioid Management

- If the patient's pain intensity is rated 4 or greater, a short-acting opioid is ordered and titrated for adequate analgesic effect (NCCN, 2015a).
- Adjuvant analgesics are given as indicated by assessment and response to initial opioid treatment.
- A pain reassessment is completed within 24 hours of treatment initiation. Upon reassessment, if the patient's pain is rated 1–3, conversion to a sustained-release agent is recommended; If pain continues to be rated 1–3, the patient may be assessed weekly until comfortable and then at each healthcare visit.
- However, if, upon reassessment, the patient's pain intensity is 4 or greater, opioid titration should continue.

Opioid Management

- Short-acting opioids have a peak effect at 60 minutes if given orally and 15 minutes if given intravenously.
- Generally, when clinicians are prescribing opioids, the dose is increased by 25% for pain intensity of 1–3; 25%–50% for pain intensity of 4–6; and 50%–100% for pain intensity of 7–10 (NCCN, 2015a).
- For the example: a patient is currently taking opioids but now reports pain rated at 8, and the total 24-hour dose (including the breakthrough doses) is calculated. The new scheduled dose is determined by the previous 24-hour dose and increased by 50%. The breakthrough dose is calculated at 10%–20% of this new 24-hour dose and is given every hour as needed.
- The most appropriate dose for any patient with cancer pain is whatever dose it takes to relieve the individual's pain.

Opioid Management

- **Breakthrough pain** is anticipated in patients with cancer, and medication should be available as needed to control pain.
- Consideration of the etiology is critical (Greco et al., 2011). If the breakthrough pain is of neuropathic etiology, it may be beneficial to add an antidepressant, anticonvulsant, or other neuropathic agent.
- If the etiology is bone-related, an NSAID or corticosteroid might be helpful.
- Pretreatment for events that cause pain should be considered (NCCN, 2015a).
- For breakthrough pain caused by end-of-dose failure, increasing the dosage or frequency of the regular analgesic can improve pain control.
- Treatment for breakthrough pain should have a rapid onset and short half-life. Adjustments in regularly scheduled analgesic dosing are considered if frequent episodes of breakthrough pain are reported (NCCN, 2015a; Portenoy, 2011).
- The rescue dose should reflect the amount of the regularly scheduled medication. Usually, this dose is 10%–20% of the daily opioid dose and may be given every hour as needed (Ripamonti et al., 2012); however, this can vary significantly among patients (NCCN, 2015a). Titration of the dose to patient response is necessary to manage pain adequately and to balance untoward side effects.

Opioid Management

- When adequate pain control is not achieved or if patients are experiencing intolerable opioid side effects, opioid rotation may be considered.
- **Opioid rotation** is defined as substituting one opioid with another using equianalgesic ratios. In one study, opioid rotation was conducted in 31% of outpatients with cancer, with a 65% success rate (Reddy et al., 2013). When converting or rotating from one opioid to another, the first step is to determine the amount of the current opioid taken in 24 hours. When switching to any opioid (other than methadone or transdermal fentanyl), clinicians use the equianalgesic chart to calculate the new opioid dose.
- If the pain is controlled, the dose of the new medication should be reduced by 25%–50% to allow for incomplete cross-tolerance between the two opioids. If the previous dose was ineffective, the new medication could be prescribed at 100%–125% of the equianalgesic dose (Fine & Portenoy, 2009; NCCN, 2015a; Ripamonti et al., 2012).
- If switching to methadone, the dose should be 75%–90% lower than the calculated equianalgesic dose. When changing from an opioid to a transdermal patch, clinicians should obtain the package insert for accurate information regarding the titration procedure (Fine & Portenoy, 2009; NCCN, 2015a).

Management of Treatment Side Effects

- Pharmacologic intervention for pain, particularly opioids, may produce a variety of side effects, many occurring as a result of the effects on the gastrointestinal system.
- The most common side effects of opioids are constipation, cognitive impairment, sedation, somnolence, nausea and vomiting, reduced libido, and delirium. Constipation, the one side effect that does not improve with routine opioid use, is best treated prophylactically. Initiation of a bowel regimen including a stimulant laxative such as polyethylene glycol, senna, bisacodyl, and a stool softener (docusate) and titrated to effect is critical when patients are started on opioid therapy (McMenamin, 2011; Mesgarpour et al., 2014; NCCN, 2015a)

Management of Treatment Side Effects

- Respiratory depression is one of the most feared toxicities of opioids.
- It occurs when there is decreased sensitivity of the medulla to rising carbon dioxide levels that normally create spontaneous respirations. Respiratory depression usually is not an issue for patients with cancer who are prescribed opioids for chronic pain.
- Patients with pulmonary conditions may be at risk for developing opioid-related respiratory depression. If respiratory depression occurs, it can be managed with naloxone (0.4 mg in 10 ml of normal saline); 0.5 ml every two minutes to avoid abrupt withdrawal symptoms and severe pain as well as seizures (Miaskowski, 2010a; NCCN, 2015a).
- Methylphenidate, dextroamphetamine, or modafinil (Provigil) may be appropriate for the treatment of persistent opioid-induced sedation (Portenoy, 2011). Research suggests that psychomotor and cognitive functioning usually is not affected after stable doses of opioids are attained. Gaertner et al. (2006) found that the use of long-term (at least four weeks) controlled-release oxycodone did not prohibit driving, but they emphasized that individual assessment is vital. Patients should be educated about the potential risks of driving after taking pain medication.

Coanalgesics

- Coanalgesics often are used in conjunction with opioids or NSAIDs to treat neuropathic pain.
- Coanalgesic medications include antidepressants, anticonvulsants, corticosteroids, and topical agents such as capsaicin or local anesthetics (Fallon, 2013). Coanalgesics or adjuvant analgesics are medications that have pain-relieving properties in specific clinical situations; however, the primary indications of coanalgesics are not for the treatment of pain.
- Common analgesic medications include tricyclic antidepressants (such as nortriptyline), and anticonvulsant drugs. The Neuropathic Pain Special Interest Group of the International Association for the Study of Pain developed evidence-based guidelines for treating neuropathic pain (Dworkin et al., 2010). Tricyclic antidepressants (nortriptyline or venlafaxine), calcium channel ligands (gabapentin or pregabalin), and topical lidocaine were recommended as first-line treatment interventions (Dworkin et al., 2010).
- Anticonvulsants often are used for pain related to peripheral neuropathy. Tricyclic antidepressants are effective and inexpensive medications used to treat neuropathic pain; however, patients should be monitored for cardiotoxicity, urinary retention, orthostatic hypotension, constipation, and drowsiness. Secondary amine tricyclic antidepressants such as nortriptyline are preferred over tertiary amine tricyclic antidepressants (e.g., amitriptyline) because they are better tolerated.
- Coanalgesics medications such as anticonvulsants and antidepressants should be increased slowly to avoid toxicities (Aiello-Laws et al., 2009; NCCN, 2015a). Treatment of metastatic bone pain requires not only NSAIDs and opioids but also bisphosphonate therapy, which currently is accepted to provide moderate analgesic effects (Gralow et al., 2013; NCCN, 2015a).
- Local treatments such as external beam radiation therapy, radiofrequency ablation, and surgical interventions (e.g., bone stabilization procedures) also may be used.

Interventional Strategies

- Although opioids are the foundation of pain management, it is estimated that 10%–20% of patients with cancer may require a combination of treatment interventions (Hanks et al., 2001; Mercadante, 2014).
- In this clinical situation, alternative methods of pain control should be considered. Interventional therapies are considered for a variety of reasons. Interventional strategies may be regarded as if adequate oral pain management has produced intolerable side effects or if pain is more likely to be controlled with a nerve block, as in the case of a block for uncontrolled pancreatic pain.
- Interventional approaches may include nerve blocks (temporary or permanent), neurostimulation, neuraxial analgesic infusion, neuroablation, and surgical intervention (McMenamin, 2011; NCCN, 2015a; Walker, 2010). Neuroablative procedures such as brachial plexus or cordotomy may be considered for well-localized pain syndromes. Neurostimulation procedures such as transcutaneous electrical nerve stimulation (TENS) modulate the transmission of pain stimulus, thereby relieving pain (Walker, 2010).
- Surgical interventions such as a vertebroplasty or kyphoplasty also may be considered. Vertebroplasty involves the injection of orthopedic cement into fractured vertebrae. Kyphoplasty is a procedure that consists of inserting a vertebral catheter and then the inflation of a “balloon” tamp to restore the height of the vertebrae before injecting orthopedic cement.
- Other surgeries for pain management might include amputation, tumor debulking, organ excision, or skeletal fixation (McMenamin, 2011).

Nonpharmacologic Treatment

- Nonpharmacologic or integrative interventions often are used in conjunction with pharmacologic approaches for cancer-related pain.
- Cognitive and physical interventions enhance a patient's ability to control pain (NCCN, 2015a).
- Cognitive interventions include imagery/hypnosis, distraction, relaxation, graded task assignments, cognitive behavioral training, or active coping training.
- Examples of physical nonpharmacologic interventions include physical therapy, energy conservation, massage, application of heat or ice, TENS, acupuncture, ultrasonic stimulation, bed, bath, and walking supports (NCCN, 2015a; Running & Turnbeaugh, 2011).
- Integrative therapy: Massage, TENS, ultrasonic stimulation, and other modalities may also be appropriate to manage pain (NCCN, 2015a; Walker, 2010). Heat or cold applications may be beneficial in certain types of pain, particularly postsurgical pain (NCCN, 2015a). Patients must be warned about the potential for burns, especially if neuropathy or other disorders are present that would disrupt their perception of pain or temperature.

Nonpharmacologic Treatment

- Psychiatric symptoms, including anxiety and depression, in patients with cancer pain should first be considered to be a result of uncontrolled pain and then reassessed after pain is controlled.
- Patients with pain that interferes with their daily activities express more anxiety, which compounds intolerance of daily activities (Running & Turnbeaugh, 2011).
- Psychosocial support is vital, and patients and families should understand that emotional reactions to pain are normal and should be treated as part of the pain management plan (NCCN, 2015a).
- Reinforcing positive coping skills, enhancing personal control, and focusing on optimal quality of life are all part of psychosocial support to patients and families or support systems.

Complementary and Alternative Treatments

- The treatment of pain with complementary or alternative medicine (CAM) is an evidence-based science.
- In a study reported by Templeton et al. (2013) of 342 patients with early-stage breast cancer, nearly half (46%) used at least one CAM treatment.
- Complementary and alternative methods used included vitamins (38%), teas (29%), homeopathy (19%), herbal medicine (19%), and mistletoe (16%).
- In a recent study, Ndao et al. (2013) reported that CAM therapies are used by 31%–84% of children with cancer, both within and outside of clinical trials.
- A wide variety of CAM pain interventions exist, including yoga, Qigong, Reiki, Shiatsu, hypnosis, imagery, massage, nutrition, meditation, acupuncture, acupressure, aromatherapy, magnet therapy, mind-body medicine, reflexology, spiritual cures, therapeutic touch, and traditional Chinese medicine (Running & Turnbeaugh, 2011).
- Patients with cancer use CAM for many reasons, but a common one is unrelieved pain (Running &Seright, 2012).
- Cognitive behavioral interventions, such as keeping a pain diary or a journal about thoughts and emotions surrounding the pain experience, may promote feelings of control over the pain (NCCN, 2015a; Running & Turnbeaugh, 2011). Perceived control over pain is an influential aspect of pain response (Templeton et al., 2013). Behavioral interventions examine behaviors that influence the pain experience. Examples of behavioral interventions include Biofeedback, hypnosis, music and art therapy, distraction training, systematic desensitization, and relaxation therapy.
- Evidence suggests that cognitive behavioral interventions effectively provide immediate but not long-term pain relief (Running & Turnbeaugh, 2011). Randomized controlled clinical trials are needed to evaluate CAM interventions in the management of cancer pain.

Treatment of Patients With Substance Abuse

- Treatment of cancer pain in people with a history of substance abuse is an issue that oncology APNs should be prepared to encounter.
- While maintaining respect for the potential for abuse of controlled substances such as opioid analgesics, one must understand that these medications are the most effective way to treat cancer pain. Patients with a known substance abuse history often are undermedicated (McMenamin, 2011; Modesto-Lowe, Girard, & Chaplin, 2012).
- Several organizations U.S. Drug Enforcement Administration, have issued a joint statement titled *Promoting Pain Relief and Preventing Abuse of Pain Medications: A Critical Balancing Act* (U.S. Drug Enforcement Administration, 2002). This statement reinforces the need to prevent abuse of prescription pain medications while still ensuring availability for those who need them. The American Society for Pain Management Nursing stated that patients with addictive disease and cancer pain have the right to be treated with dignity, respect, and the same quality of pain management (Oliver et al., 2012). The management of pain in patients with addictive disease requires a nonjudgmental approach and assumes that patients' self-reports are true. Higher doses may be necessary because patients may have developed a tolerance to some medications or increased sensitivity to pain because of drug use.
- A pain contract that includes precise, written patient expectations and responsibilities with nonnegotiable limits will help to deter aberrant behavior. A pain contract clearly outlines patient and clinician responsibilities, patient expectations, and consequences of aberrant behavior and sets clear, nonnegotiable limits. Patients should be monitored with periodic pill counts and drug screens.
- Careful documentation of pain etiology, assessment, education, prescription, management, and follow-up will protect clinicians while providing the rationale for proper management (McMenamin, 2011; NCCN, 2015a; Oliver et al., 2012).ns (including ONS and the American Cancer Society).

Patient and Family Education

- A vital part of pain management plans is patient and family education. Lack of knowledge and incorrect beliefs about pain are barriers to optimal pain relief (Vallerand, Musto, & Polomano, 2011; Wengström et al., 2013).
- Research shows improvements in cancer pain when patients and families are taught about their pain and its management (Vallerand et al., 2011).
- Individualized education may reduce the disparity in cancer pain management among minorities (Vallerand, Pieper, Crawley, Nordstrom, & Dinardo, 2013).

Evaluation of Outcomes

- Following reassessment of cancer pain after therapeutic intervention, if pain control appears to be inadequate, oncology APNs should assess patients for factors that impede pain relief.
- Successful outcomes of pain interventions include not only a decrease in pain intensity but also an increase in functional abilities and improved quality of life. Reassessment should include patients' continued ability to obtain and afford medications or treatment (NCCN, 2015a).
- Documentation of outcomes is essential for continuity of care and legal obligations. Compliance with the therapeutic regimen and follow-up must also be documented

- Stoicism
- Fear of addiction
- Language barriers
- Healthcare staff turnover
- Desire to be a "good patient"
- Poor access to pain specialists
- Cost of medications/procedures
- Patients' lack of support people
- Misconceptions about cancer pain
- Lack of national policies on pain relief
- Healthcare providers' resistance to change
- Lack of consistent use of assessment tools
- Low expectations that pain can be relieved
- Inadequate dosing of pharmacologic agents
- Fear of side effects of pharmacologic agents
- Legal concerns on part of healthcare providers
- Inadequate time on part of healthcare providers
- Incomplete effectiveness of some interventions
- Inadequate reimbursement for healthcare providers
- Inadequate knowledge about cancer pain etiology and control
- Organizational factors (e.g., increasing paperwork, documentation)
- Varying rules and regulations on controlled substances state to state
- Nurses' or support people's reluctance to administer opioids
- Inadequate knowledge about cultural variations regarding pain responses
- Unmanaged negative psychosocial factors (such as depression and anxiety)
- Reluctance to report pain because of fear that pain stems from progressive or recurrent disease
- Shortages of healthcare providers, particularly those specializing in cancer pain management
- Poor recognition of importance of pain control or low priority of pain control in optimal cancer treatment and care
- Disagreement between patient and support system or patient and provider on presence and severity of pain
- Fear of tolerance (i.e., that cancer pain will worsen toward death and interventions will then be ineffective)
- Poor communication (e.g., between healthcare provider and patient; provider and provider; provider and support systems; patient and support systems)

Figure 10-4. Barriers to Optimal Cancer Pain Management

Note. Based on information from Miaskowski, 2010a; National Comprehensive Cancer Network, 2015a; Portenoy, 2011; Ripamonti et al., 2012.

Evaluation of Outcomes

- Ongoing quality improvement is vital to improve the quality of cancer pain management and evaluate evidence-based practice (Vallerand et al., 2011).
- Continuing education of physicians, nurses, and ancillary staff improves the quality of pain management (Walker, 2010). Ideally, all practice settings should have a formal process for evaluating and improving cancer pain management (NCCN, 2015a).
- All healthcare providers must follow evidence-based standards of care.
- When patients transition from one healthcare setting to another (such as hospital to home), care must be taken to maintain optimal pain management.

Evaluation of Outcomes

- Oncology nurses play a vital role in assessing and managing pain in patients with cancer.
- It is essential that advanced oncology practitioners assess pain consistently and manipulate treatment plans to optimize patients' quality of life.
- It is essential to educate patients and families about medication titration, which is critical to achieving quality pain control.

Questions?

Thank you!

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