Treatment of Cancer Pain

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Summary and Key Points

1. Chronic cancer pain is usually managed with multimodal analgesia, the combination of opioids, Cyclooxygenase (COX) inhibitors, anticonvulsants, and/or antidepressants.
2. Opioids are excellent analgesics but are associated with significant toxicity. Ventilatory depression may be life-threatening, particularly in opioid-naïve subjects or those receiving concurrent benzodiazepines. Constipation is nearly universal and warrants pre-emptive therapy when opioids are initiated.
3. COX inhibitors are also excellent analgesics. Gastrointestinal (GI) ulceration, and decreased platelet function are significant adverse effects of the nonselective and selective COX-1 inhibitors, but not the selective COX-2 inhibitors, which are associated with an increased risk of myocardial infarction.
4. Anticonvulsants and/or antidepressants may be particularly useful in neuropathic pain.
5. Glucocorticoids may relieve pain, either by decreasing swelling or by an adjuvant effect.
6. Combination therapy with two or more classes of medications may decrease the doses of each required to achieve adequate pain relief.
7. Radiation therapy is very effective local treatment for certain types of cancer pain, particularly bone pain, compression of nerves and Glissen's capsule pain.
8. Blocking neural transmission by injection of local anesthetics or neurolytics can respectively, relieve pain temporarily or long-term (months).
9. Transcutaneous electrical nerve stimulators (TENS) units may be used as local therapy.
10. Physical therapy or physical measures such as heat, cold or bracing, may relieve some pain.
11. Cognitive behavioral therapy may make pain more bearable.
12. Complementary or alternative therapies have a role for some patients.
13. Pain is a part of the course of the disease for greater than half of cancer patients, roughly in proportion to stage of disease. But uncontrolled pain is the greatest fear of most patients and their families.
14. Epidural or intrathecal administration of opioids, local anesthetics, and other agents can give relief in the setting of intractable pain or intolerable side effects of systemic opioids.

Introduction

Pain is one of the first concerns most cancer patients express when newly diagnosed or meeting a new physician. They are concerned about how much pain they presently have, how much pain they are likely to experience, and their physicians' commitment to treating cancer pain. The reality is that many cancer patients will never experience pain during their course and for those that do, the great majority can be well-managed with the tools described in this chapter. It is incumbent on every physician to understand the mechanisms of cancer pain and the fundamentals of treating it.

Cancer pain may be somatic (e.g., a pathological fracture of a long bone with a metastasis), visceral (e.g., a locally metastatic intra-abdominal tumor or neuropathic (e.g., spinal nerve root compression from a vertebral metastasis). It is important to attempt to identify the mechanism of cancer pain because neuropathic pain responds poorly to opioids and COX inhibitors.

There are four primary classes of analgesics given systemically to treat cancer pain:

- opioids
- COX inhibitors
- anticonvulsants
- antidepressants

Different medications may be injected locally to block neural transmission to relieve pain, either temporarily (e.g., local anesthetics) or long-term (e.g., absolute ethanol).

Analgesics may be administered for systemic effect by several different routes. The best route depends on the clinical situation. It is important to remember that time to maximal effect varies depending on the agent and on the route of administration. Most commonly, the oral route is used. If the oral route is not available (due to inability to swallow, loss of consciousness or other reasons), or if more rapid onset is desired, intramuscular injection (IM), buccal or sublingual or transanal (PA) routes may be used. If even more rapid onset of action is required, intravenous administration (IV) is used. Epidural or intrathecal administration of opioids, local anesthetics, and other agents can give relief in the setting of intractable pain or intolerable side effects of systemic opioids. Finally, fentanyl is available as a transdermal patch for long acting use.

Opioids

Opioids are used for many conditions. The opioids used in cancer pain are full agonists at the μ-opioid receptor. The mechanisms of analgesia involve modulating the transmission of pain impulses in the spinal cord and altering the perception of pain in the brain. Unlike local anesthetics that may render an area numb and insensate, opioids do not prevent the perception of pain but permit the patient to feel it as less noxious.

In addition to analgesia, opioid agonists produce other characteristic dose-dependent effects:

- ventilatory depression
- sedation
- miosis (pupillary constriction)
- constipation (by decreasing GI propulsive muscle activity and increasing GI sphincter activity)

Tolerance develops when opioids are administered for chronic pain. This effect is manifested as a decrease in the duration and the intensity of the analgesic effect following a dose and requires increasing the opioid dose as the duration of therapy increases. Along with tolerance is the development of physical dependence, defined as the occurrence of a stereotypical withdrawal syndrome when drug administration is stopped abruptly or an antagonist is administered. It is important to differentiate tolerance and physical dependence from substance use disorder (formerly called addiction). While it is typical for persons with substance dependence who use opioids to develop tolerance and physical dependence, it is actually quite uncommon that persons appropriately prescribed opioids for pain develop new substance use disorder.[1]

A recent study, based on the newly-released DSM-5 criteria for opioid-use disorder, revealed that the lifetime risk of moderate or severe opioid-use disorder among patients using opioids long-term for chronic (non-cancer) pain was only 13%.[2] There is a significant genetic component to the risk of developing opioid use disorder. Persons with impulsivity and novelty-seeking behavior types that may be in part genetically determined are at higher risk. Additional risk factors include those related to family, peer, and environmental factors.

Several screening instruments are available to assess risk of substance use disorder. These include the Opioid Risk Tool (ORT), the Diagnosis, Intractability, Risk and Efficacy Inventory (DIRE), the Screener and Opioid Assessment for Patients with Pain (SOAPP), and the NIH-National Institute on Drug Abuse has a chart of Evidence-Based Screening Tools for Adults & Adolescents. One small study found that a semi-structured clinical interview combined with SOAPP were most effective at predicting risk at baseline in a group of patients who were discontinued from opioid medication for drug related issues.[3]

Patients have often undertreated their pain with opioids because of the severity of the associated constipation. The new peripheral opioid antagonists, methylnaltrexone and naloxegol, are opioid receptor antagonists that do not penetrate the central nervous system. As a result, they do not interfere with the analgesic properties of opioids. However, by blocking the effects of opioids on the gut, they treat or prevent opioid-induced constipation. These novel agents are useful when the traditional daily laxative regimen is ineffective.

The primary difference between the opioids is their kinetics of onset and duration. The most common opioids are discussed below and summarized in Table 1.

Table 1. Dose, Time to Peak Effect, and Duration of Analgesia for Opioid Agonists

Opioid	Dose (mg)[a]	Peak (min)	Duration (h)
Morphine (IV*)	10	>30	3-4
Morphine (PO**)	40	60-120	3-6
Codeine (PO)	60[b]	60-120	3-6
Oxycodone (PO)	20	60-120	3-6
Hydromorphone (PO)	6	60-120	3-6
Methadone (PO)	10	120-180	(see text)[c]
Fentanyl (transbuccal)	0.15	35-45	4-5

[a]Approximately equianalgesic dose

[b] See paragraph below on codeine.

[c]The initial dose of methadone lasts about 3-6 h. As steady-state is approached after several days of therapy, a duration of 12-24 h can be expected.

Morphine

Morphine is the prototypical opioid to which all others are compared. It has a relatively slow onset, even after injection, and long duration. It has relatively low oral bioavailability (about 25%), and one of its metabolites, morphine-6-glucuronide, is active. Morphine is unique in that it commonly causes histamine release, an anaphylactoid reaction that may be manifested as flushing or itching. This is not an allergic reaction and in fact true allergy to morphine is unknown. Morphine is available both as an immediate release medication and as long-acting, sustained-release formulations.

Codeine

Codeine is a prodrug that requires conversion to morphine via CYP2D6. As mentioned in the footnote to Table 1, there is great interindividual heterogeneity in the expression of this isozyme. There is significant interindividual variability of the CYP2D6 phenotype with specific drug metabolism depending on the genotypic variation of the allele. About 10% of persons of western European descent lack CYP2D6 function and do not obtain analgesia from codeine, while some persons of middle-eastern descent have extra copies of CYP2D6 and may experience opioid toxicity from the usual doses of codeine. This property can cause significant risk to some patients with their first-ever dose of codeine, particularly children.

Codeine is most commonly taken as a fixed-dose preparation that also contains acetaminophen. All acetaminophen-containing opioid products should be avoided in chronic pain patients because as the opioid dose is increased, a toxic dose of acetaminophen (> 4 g/d) is likely to be achieved. Persons with underlying liver disease or who drink ethanol may suffer liver damage at a lower daily dose of acetaminophen.

Oxycodone

Oxycodone has higher oral bioavailability than morphine and a more rapid onset. It is available alone or in combination with acetaminophen. Alone it is available as a conventional (i.e., immediate-release) formulation as well as a long-acting sustained-release preparation.

Hydromorphone

Hydromorphone is about sevenfold more potent than morphine-based IV dosing, about thirteenfold more potent than morphine-based PO dosing, and it does not cause histamine release as is sometimes seen with IV morphine.

Methadone

Methadone is inherently long-acting and does not require a sustained-release formulation to be effective in once- or twice-daily dosing. It therefore takes days to reach steady-state and dosing changes should generally not be made more often than weekly. It is an excellent choice for patients with chronic pain and is inexpensive compared to other opioids. Methadone has also been associated with greater risk of a specific cardiac arrhythmia (torsades de pointes) that may prove fatal. Because methadone is also an antagonist at NMDA receptors, it is more effective against neuropathic pain than other opioids.

Fentanyl

Fentanyl is a highly potent, lipophilic opioid that is commonly used by IV route during anesthesia or for noxious procedures. It has both very rapid onset and offset by the IV route, however it has low oral bioavailability. It is commonly used in chronic pain, both as a patch and as a buccal tablet. The fentanyl patch is designed to be applied every three days and it is prescribed as the amount of fentanyl absorbed in mcg/hr. In general, it should only be used in persons tolerant to opioids. The fentanyl buccal tablet releases the drug for absorption directly through the buccal mucosa resulting in a rapid onset of effect. It is commonly used for breakthrough

Prodrug– A compound, which requires metabolism within the patient to become active.

pain in patients also using a fentanyl patch or some other long-acting opioid preparation.

A person with severe cancer pain is generally given a long-acting medication to be taken on schedule as prescribed by their physician (by the clock), and in addition given a rapid-onset, short-duration medication as needed for breakthrough pain (the occurrence of a short-lived but intense increase in pain above and beyond the background of chronic pain, often brought on by a specific activity).

It is helpful for patients to keep a log of their breakthrough medication usage and a rating of pain severity when the medication was taken. This information can be used to adjust the long-acting medication dosage, and may reveal that the patient is developing tolerance to the long-acting medication. The patient may then need an increase in dose and/or a decrease in dosing interval of the long-acting medication. Switching to a different opioid ("opioid rotation") may restore, fully or partially, the analgesic effect.

Severe or intractable cancer pain often results in very high doses of opioids used, for example a daily oral morphine total of 400 mg or more (or the equianalgsic amount of a similar agent.) At these doses, patients often have intolerable somnolence and sedation that can be reduced with the addition of a psychostimulant, such as methylphenidate. In addition, patients taking such high doses can develop neuro-excitatory side effects due to dose-dependent agonism of the N-methyl-D-aspartate (NMDA) receptor leading to myoclonus, allodynia (abnormal painful sensation to usual stimuli), and hyperalgesia (heightened pain sensation despite opioid use). Neuroexcitatory side effects call for a reduction in total opioid use, or rotation to a different opioid.

An additional strategy for intolerable opioid side effects or ineffective pain relief is to deliver analgesic agents to the spinal cord and nerve roots by an epidural or intrathecal catheter connected to a temporary or implantable pump. Drug delivery can be regionalized to certain segments of the neuraxis and a combination of agents can be effective such as opioids, local anesthetics, and both sympathetic and para-sympathetic agents. Neuraxial medication delivery can allow much lower overall doses, reducing systemic side effects; there are unique complications of these interventions including infection and neurologic deficits.

A person with cancer pain is also often given other medications to potentiate the opioid effect and/or decrease the needed dose of opioid. These medication classes are discussed below and this approach is called multimodal analgesia.

COX Inhibitors

Cox Inhibitor medications inhibit the isozymes of cyclooxygenase (COX) that catalyze the biosynthesis of prostaglandins. These agents were previously (and still in common parlance) erroneously called NonSteroidal Anti-Inflammatory Drugs, or NSAIDs. The desirable properties of many "NSAID's" are due to profound antinociceptive, and not primarily anti-inflammatory, effects (most notably ketorolac), but the anti-inflammatory effect may potentiate analgesia as well.

There are two isozymes of COX, COX-1 and COX-2. COX-1 is a constitutive enzyme; its most important roles include the mediation of pain, stimulation of platelet adhesion, maintenance of renal blood flow, and protection of the GI mucosa. COX-1 inhibition has an anti-nociceptive effect. COX-2 is an inducible enzyme whose most important roles include the mediation of inflammation and the synthesis of an important endogenous vasodilator and anticoagulant (prostacyclin, or PGI_2). COX-2 inhibitors have anti-inflammatory effects. Some COX inhibitors are more specific for COX-1 or COX-2 while others are nonspecific (Table 2). The degree of inhibition of COX-1 is associated with the propensity for causing GI ulceration. Long term (greater than 12 months) use of COX-2 inhibitors is associated with an increased risk of cardiac ischemia and death.

Table 2. Characteristics of COX Inhibitors

Drug	Dosing Interval	COX Inhibition
Aspirin	4 h	1 > 2
Acetaminophen	4 h‡	1 = 2‡
Celecoxib	12 h	2 > 1
Diclofenac	24 h*	2 > 1
Diflunisal	12 h	1 = 2
Etodolac	24 h*	2 > 1
Ibuprofen	6 h	1 = 2
Indomethacin	8 h*	1 >>2§
Ketorolac	6 – 8 h†	1 >> 2
Naproxen	12 h	1 ≥ 2

*Duration of the extended-release formulation
†6 h for IV administration, 8 h for intramuscular (IM) administration
‡At usual clinical concentrations, COX is inhibited only about 50%. Also, a metabolite of acetaminophen, *N*-acetyl-*p*-benzoquinone imine (NAPQI), is a hepatotoxin, which should limit total daily dose.
§Has additional immunosuppressive actions beyond COX inhibition

In cancer patients it is important to remember that acetaminophen is hepatotoxic in doses above about 4 g/d, and much less in children and patients with liver compromise due to tumor involvement, cachexia and malnutrition, cirrhosis, or history of alcohol use.

Anticonvulsants

While these medications do not typically act as analgesics in persons with nociceptive or inflammatory pain, they often relieve neuropathic pain and may potentiate opioid-induced analgesia. The most common anticonvulsants used for these purposes are gabapentin, pregabalin, and carbamazepine.

Table 3. Characteristics of Anticonvulsants

Drug	Dosing Interval
Carbamazepine	12 h*
Gabapentin	8 h
Pregabalin	8 h

*Duration of the extended-release formulation

Carbamazepine has two important adverse effects that require careful attention: toxicity from elevated levels can lead to encephalopathy and ataxia, and rarely, carbamazepine can cause dangerous agranulocytosis.

Antidepressants

Antidepressants in the tricyclic class may also be used to treat neuropathic pain or to potentiate opioid effects. The most common antidepressant used in this way is amitriptyline. It is usually given once daily at bedtime. For patients with glaucoma or those unable to tolerate the side effects of amitriptyline, consider other tricyclics such as desipramine or nortriptyline that have fewer anticholinergic side-effects, or one of the newer serotonin-norepinephrine reuptake inhibitors such as duloxetine or venlafaxine.

Glucocorticoids

Dexamethasone is used to treat or prevent edema, which sometimes will immediately relieve pain from nerve compression or intracranial pressure, by reducing vascular permeability, and inhibiting prostaglandin synthesis, decreasing inflammation. There is some direct reduction in inflammatory pain from the anti-inflammatory effect of these steroids.

Dexamethasone and prednisone also have an important adjuvant function to other pain medications (as well as nausea medications), particularly for bone pain, neuropathic pain and visceral pain.[4]

Bone Stabilizing Agents

Bone stabilizing agents such as bisphosphonates and denosumab are routinely used to prevent/postpone skeletal related events such as pathologic fractures in patients with known bone metastases, especially in breast cancer, thereby preventing the development of pain.[5] High dose bisphosphonates have been shown to relieve bone pain in some patients with bony metastatic breast cancer.[6]

Principles of Medication Pain Management

Use of COX inhibitor medications prior to starting opioid therapy may decrease the opioid dose required to achieve adequate pain relief. In addition, use of two or more classes of medications will often decrease the total dose required of each medication. But the use of fixed dose tablets such as Tylenol #3® (acetaminophen + codeine) or Percocet® (acetaminophen + oxycodone) can be dangerous in cancer patients because patients will often attempt to achieve better pain control by self-

escalating their doses to the point of acetaminophen toxicity. It is much safer to prescribe the two agents separately, and inform patients and caregivers how to increase both, and what the safe limit of each drug is. In general codeine should be avoided for cancer pain because of individual differences in activity of the enzyme, CYP2D6, which metabolizes it into its active metabolite, morphine.

The World Health Organization (WHO) has published a "three-step ladder" approach to pain management, which suggests that pain management should start with non-opioid medication, with or without adjuvant medications, stepping up to "mild opioids" with or without adjuvants, including non-opioid analgesics, and finally a strong opioid, supplemented by the same adjuvant medications as Step 2. It is available here:

http://www.who.int/cancer/palliative/painladder/en/

For children, the WHO has modified this to a two-step ladder, starting with a non-opioid analgesic, and progressing to the addition of morphine or other strong opioid, but this is controversial.[7] Pediatric pain management is even more complicated than adult care. Here is a useful chart summarizing pediatric pain management principles:

https://www.compassionandsupport.org/pdfs/professionals/pain/pain_pediatric_guide.pdf

Pain management must be individualized for each patient and is not static. For example, opioids can cause unpleasant symptoms some of which are patient specific, and rotating to a different opioid may relieve those symptoms. Constipation is an opioid class effect, and must be managed prospectively with careful bowel regimens for every patient. Patients metabolize agents at different rates, and this may require variation from textbook scheduling. Escalating doses of strong opioids can actually exacerbate pain, referred to as opioid-induced hyperalgesia. Opioid-induced hyperalgesia may respond to rotation to another opioid or decreasing the dose of the original medication.[8]

Very severe pain unresponsive to normal management is called pain crisis; it is a medical emergency and requires the presence of a physician experienced in management of this crisis in constant attendance until a primary diagnosis is made and treatment initiated (e.g., pathological fracture, spinal cord compression or deep venous thrombosis), and/or pain relief is achieved.[9]

Pain Relief from Radiation Therapy

The mechanism of action of pain relief from radiation therapy has not been studied in depth, although it clearly works. Therefore, this section is based on speculation, and is intended to provide opportunities for research.

Bone pain response varies from virtually immediately to very gradually, sometimes as much as two months after treatment. The almost instantaneous relief is probably due to a well-accepted anti-inflammatory effect; white cells are readily killed by low dose radiation. This effect used to be used regularly for pain of osteoarthritis, and clinical experience suggests that it was effective immediately in many patients. Patients' pain sometimes responds a bit more gradually, over a few days to weeks, well before any radiographically visible bone healing or even visible change in tumor. This may be due to subtle tumor shrinkage, or an ill-defined hormonal response. Finally, pain may be relieved over six weeks- three months; this is consistent with bone healing after tumor cell death and resorption. Radiotherapy is a very effective therapy; one study demonstrated two-thirds of patients had pain relief and one-fourth were off opioids entirely.[10]

A second, older study of 255 bone lesions in 205 patients with bone metastasis found complete pain relief in 62% and partial relief in an additional 14%. Prostate cancer metastases were most likely to respond; breast cancer lesions slightly less and nonsmall cell lung cancer lesions least likely to achieve complete pain relief. Complete relief and higher dose also lead to more durable response.[11]

Bone seeking radiopharmaceuticals have been used for decades to treat pain from widely metastatic osteoblastic malignancy, most often prostate cancer. They work by seeking osteoblasts and any lesion that is evident on bone scan is likely to take up the isotope. Most of these agents have emitted beta particle, such as strontium-89 and samarium-153.[12] Recently, radium-223, an alpha emitter, has been used, with randomized clinical trial evidence that it can also extend life expectancy.[13]

It seems most likely that tumor shrinkage due to tumor cell kill is the mechanism of action for relief of pain due to nerve compression, Glisson's capsule distension[14] and obstruction of hollow visci.[15]

Interventional Radiology

Regional nerve blocks are usually done under radiologic guidance, usually ultrasonic or fluoroscopic, although they can be done as a dentist does, by detailed understanding of the neuroanatomy.

Local anesthetics can be used to temporarily block nerve transmission, either to prevent acute pain, or to treat a regional chronic pain syndrome. For example, long acting local anesthetic injected into an operative site before thoracotomy, in combination with adequate postoperative pain management, will often prevent the development of post thoracotomy pain, a severe chronic pain issue after chest surgery. Lumbar, brachial and celiac plexus blocks are effective means of treating regional pain.

Table 4. Characteristics of Local Anesthetics

Drug	Duration*
Lidocaine	2-4 h
Bupivacaine	12-24 h

*Using epinephrine-containing solution. Duration will be at the longer end of the range with plexus block, and at the shorter end of the range with peripheral nerve block.

If a local or regional block has been effective in relieving longstanding regional pain, consideration may be given to injection of a neurolytic agent to permanently ablate the nerve or ganglion transmitting the pain. Neurolytic ablation of the celiac plexus is particularly useful in treating the severe pain of inoperable pancreatic cancer. The two neurolytic agents used are 6% phenol and absolute (100%) ethanol. Phenol is a local anesthetic with a very prolonged (i.e., months) duration. While ethanol is more likely than phenol to result in permanent destruction of the nerve, its injection is initially quite painful, and requires the prior injection of a short-acting local anesthetic (e.g., lidocaine) or that the alcohol injection is made with the patient under general anesthesia (as is commonly done with ultrasound-guided endoscopic celiac plexus ablation). Injecting a 1:1 mixture of absolute alcohol and 1% lidocaine may reduce the pain of injection during celiac block.

Pain from vertebral compression fractures may be treated with one of two forms of intervention, vertebroplasty, injection of medical cement into the damaged bone, or kyphoplasty, using a balloon to create a space in the bone which can then be filled with cement.

Surgery

Fractures at multiple adjacent vertebral levels may be treated with external fixation. Similarly, pathologic fractures of long bones will usually need surgical fixation to treat the pain of the fracture, followed by radiation therapy to prevent tumor progression and further fracture.

Surgery may be also performed to relieve obstruction of hollow visci, but limited data on efficacy is available, and randomized controlled trials would be very difficult to perform.[16] A limited number of other painful lesions may be most readily palliated with surgical resection.

Topical Agents

Some types of cancer pain involving the skin or relatively superficial structures (ribs, muscles, joints) can be treated by the local application of three agents as follows. For intact skin, lidocaine can be applied as a gel or cream with a relatively short duration of relief (10-30 minutes). A slow release lidocaine patch can provide up to 20 hours of relief for pain with a relatively superficial source. A mixture of lidocaine and prilocaine in a cream (EMLA) is commonly used in pediatric cancer patients before lumbar punctures and bone marrow aspiration biopsies to numb the skin, in combination with sedation.

Subcutaneous tissues express opioid receptors, and topical morphine can be an effective salve for painful cancer-related wounds, particularly the inflammatory skin involvement typical seen in some breast cancers. Finally ketorolac gel is a product often used for osteoarthritic joint pain; it can be effective on intact skin for bone, muscle, and joint pain with reduced systemic side effects and pill burden.

Non-Medical Treatments for Pain

There are multiple types of non-medical treatments for pain that are available for patients. Patients are encouraged to talk with their health care providers when using these treatments. This section is not intended to be comprehensive; for more information, the American Cancer society has a list of non-medical treatments at: http://www.cancer.org/treatment/treatmentsandsideeffects/physicalsideeffects/pain/non-medical-treatments-for-cancer-pain.

Transcutaneous Electrical Nerve Stimulation (TENS)

TENS treatment is said to be useful in the management of cancer pain, but a recent Cochrane review found the data for the use of this device to be equivocal. One study found some relief of bone pain on movement; another was negative.[17]

Physical Therapy

Many patients will benefit from physical therapy, massage therapy and heat or cold therapy to treat regional areas of pain.

Acupuncture or Acupressure

Acupuncture or acupressure will relieve pain in some patients. It requires a trained, licensed acupuncturist to administer the acupuncture, but patients and caregivers can be trained to do acupressure, sometimes with a BB glued or taped to the critical spot.

Psychotherapy

Cognitive and behavioral therapy, meditation and mindfulness training will either relieve pain or make it more bearable for some patients.

Alternative and Complementary Therapies

Finally, complementary and alternative therapies may play a role in making patients feel better (see chapter).

Conclusion

Although pain is by no means part of the course of the disease for all cancer patients, it can be one of the greatest fears of newly diagnosed cancer patients and their families[18]. It is important to remember that modalities beyond medications are available, and that fatigue, depression and emotional/spiritual distress may exacerbate the experience of pain, requiring different or additional management. This chapter is focused on physical pain; existential pain, depression (whether reactive or longstanding) and spiritual pain are just as real but are largely beyond the scope of this chapter.

Patients need to be aware that the goal may be to make pain bearable, rather than complete freedom from pain, especially if they wish to minimize side effects of pain medications. The use of the term “painkiller” should be discouraged for that reason.

Management of pain in the cancer patient is complex, but every physician must have an understanding of the basics and be prepared to help with management and with reassuring patients that pain relief modalities will remain available to them throughout their experience of the disease.

Thought Questions

1. A 64 year old woman has been treated for metastatic breast cancer for the last three years. At the current time she has metastases in many bones, including ribs, spine, and both femurs. Plain films of the femurs do not suggest that she is at significant risk for fracture. However, she is having increasing pain in her back and chest wall. She was given oxycodone, but finds that she has persistent pain even after taking 10 mg every four hours. She has noted no drowsiness or constipation since starting oxycodone. In addition to discussing changes in anti-cancer therapy with her at her next visit, what changes to her pain treatment could you consider?

   Your answer:

Expert Answer

2. Monday morning, a 60 year old man arrives at the oncology clinic from his primary care physician with a painful ulcer on the base of his tongue, complaining of pain he describes as 10 on the 0 to 10 pain scale, worse at times, especially when the pain wakens him from sleep. Friday afternoon, he was given a prescription for hydrocodone/acetaminophen 5/325, and is taking 2 tablets every 3 to 4 hours, or 4 to 5 times per day, with some relief. He has a history of Hepatitis C, is currently smoking 2 packs per day, and describes past heavy alcohol use and current sobriety. What adjustments should be made to his analgesic regimen?

   Your answer:

Expert Answer

3. A 57 year old man has been diagnosed with metastatic lung cancer. He describes severe back pain and has involvement of his vertebrae by metastases. He receives radiation to these areas but continues to have pain. When you meet with him for the first time you learn that he is divorced and lives by himself. No one has come with him to your appointment. He has adult children in the area that he sees a few times a year. He had been employed as an accountant, but has had to cut back his work because of his illness. He has a prescription for morphine (15 mg tablets) which he uses very rarely, because "I don't want to become addicted". In addition to suggesting treatment of his lung cancer, what other advice can you give him for pain control?

   Your answer:

Expert Answer

4. Why is the use of the term “painkiller” unfortunate?

   Your answer:

Expert Answer

Glossary

μ-opioid receptor– The most important opioid receptor family for pain control

Analgesics- Drugs used to provide pain relief

Buccal- Relating to the cheek

Cochrane review– Cochrane Reviews are internationally recognized systemic reviews considered to be the highest standard in evidence-based health care and health policy. http://community.cochrane.org/cochrane-reviews

Nociceptive pain– Pain from irritation of specialized nerve endings called nociceptors, which is seen in burns, for example.

Neuropathic pain– Pain due to a malfunction from nerve injury– diabetic neuropathy for example

Prodrug– A compound, which requires metabolism within the patient to become active.

Torsades de pointes- A form of ventricular tachycardia, often seen with prolonged QT interval, in which the QRS complex has variable form, with the peaks pointing up and down, causing decreased blood pressure and sometimes syncope or near syncope.

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