LADUR Education Article

Issues in Pain Management

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Issues...

• Pain is..."an unpleasant sensory and emotional experience associated with actual or potential tissue damage..."

• Pain has multiple types and roles.

• This article focuses on the management of pain associated with some common chronic conditions.

Pain is a part of the human experience; everyone will experience pain at some point in his or her life. Pain has been defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage." [1]

Pain has multiple types and roles:

Protective or acute pain is a sharp, intense pain resulting from injury. It can serve as a warning of potential danger; for example, the heat from a flame warns of potential danger. Reparative pain is a dull, spreading pain that is produced in an attempt to avoid stimuli and immobilize an injured area. *Chronic* pain is pain that continues a month or more beyond the usual recovery period for an illness or injury or pain that goes on over months or years as a result of a chronic condition. It may be continuous or may fluctuate.

Neuropathic pain occurs as a result of damage to the nervous system itself. It doesn't protect or repair the body. *Somatic* pain arises from somatic structures such as bone and joints. It is usually well localized and is worsened by palpation or movement. *Visceral* pain arises from the visceral organs and is usually poorly located.

This article focuses on the management of pain associated with some common chronic conditions.

Cancer Pain

Pain is the most feared symptom for patients diagnosed with cancer,[2] affecting 9 million people worldwide.[3] As many as 1/5 of all cancer patients have pain that is inadequately relieved, despite the availability of many analgesic agents and published guidelines such as the analgesic ladder established by the World Health Organization (WHO).[2] When used appropriately, up to 90% of patients will experience pain relief.[3, 4]

Pain associated with a diagnosis of cancer can have many possible origins. It can result from tumor infiltration or pressure on pain sensitive structures, or it can result from attempts to treat the cancer, such as surgery or chemotherapy.

In 1986, the WHO published guidelines for the treatment of cancer pain. These guidelines are comprised of three steps to the management of cancer pain.

Step 1- For patients experiencing mild pain, a non-opioid analgesic should be initiated. This would include NSAIDS, acetaminophen, and aspirin.[4]

Step 2- For patients experiencing pain despite the non-opioid analgesics, or for patients experiencing moderate to severe pain, opioids such as codeine, dihyrocodeine, hydrocodone, or oxycodone should be added to the maximum dose of the non-opioid analgesic.[4]

Step 3- Patients who continue to experience pain despite adequate doses of the step 2 products, or those who are experiencing moderate to severe pain, should be started on morphine, hydromorphone, oxycodone, fentanyl, or methadone.[4]

The level of pain a patient is experiencing is assessed by written or verbal numerical rating scales. Ratings of 1-4 are usually considered to be mild, 5-6 are considered moderate, and 7-10 are considered severe.[4]

Non-opioid analgesics

Care should be used to ensure that the maximum dose of acetaminophen or the NSAIDS is not exceeded. This should also be considered when using combination products such as Lorcet®, Lortab®, Vicodin®, etc.

Product	**Usual Dosage Range**	**Maximum daily dose**
Acetaminophen	325-1000mg q4-6h	4000mg
ASA	325-650mg q4h	4000mg
Ibuprofen	200-400mg q4-6h	3200mg
Ketoprofen	25-50mg q6-8h	300mg

Naproxen	220-440mg q8-12h	660mg
Rofecoxib	50mg q24h	50mg
Celecoxib	200mg q12h	400mg

Possible side effects with NSAIDS

Gastric ulceration	Patients at greatest risk include: • Pts>65 years of age with a history of GI bleed or PUD • Pts on long term corticosteriods • Pts on anticoagulation therapy
Inhibition of platlet aggregation	Patients at greatest risk include: • Pts with cancer who have thrombocytopenia or symptomatic bleeding
Renal dysfunction	Patients at greatest risk include: • Hypervolemic patients

Opioid analgesics

The opioids used in the second step of the WHO analgesic ladder are limited to use in moderate pain due to either their fixed combination with non-opioid analgesics or dose limiting side effects. Propoxyphene is not recommended for use due to its long half-life and toxic metabolite, norpropoxyphene.[4]

The opioids used in step three of the WHO analgesic ladder should be used one agent at a time, and the dosages should be titrated to relieve the patient's complaints of pain. Morphine is the opioid of choice, and is the standard of comparison in the management of cancer pain. Oxycodone that is not part of a fixed combination with non-opioid analgesics is a good alternative agent.[4] Meperidine is not used due to its short half-life and toxic metabolite, normeperidine. Fentanyl patches are especially useful for patients with stable pain who cannot take oral medications.

Equianalgesic dosages for opioids

Step 2 Opioids	**Oral/Rectal dose (mg)**	**Parenteral dose (mg)**
Codeine	200	120
Dihydrocodeine	100-150	N/A

Hydrocodone	45	N/A
Oxycodone	20	N/A
Step 3 Opioids		
Morphine	30	10
Hydromorphone	8	4
Oxycodone	20	N/A
Methadone	20	10
Fentanyl	*	*

*see package insert for dosing table

It is important to remember that there is no ceiling dose with Step 3 opioids.[4] The regimen should be started with a dose that is appropriate for the patient's current level of pain and previous response to analgesic therapy. The dosage should be titrated upwards to a level that will alleviate the pain while minimizing side effects. A good approach is to start the patient on a regimen of a short acting opioid and titrate until the patient is comfortable. The patient can then be changed to a long acting opioid, with rescue doses of the short acting product allowed for breakthrough pain. As the patient's use of rescue doses increases, the long-acting product should be increased. The goal would be for the patient to be as comfortable as possible with a minimum of side effects and only infrequent use of rescue doses.

Points to remember:

The simplest regimen and least invasive methods should be used first.[5] Many patients can be adequately managed on oral therapy, which is not only the simplest and least invasive, but also less expensive than parenteral or transdermal therapy.[4]

Doses of long acting opioids should be scheduled around the clock, with additional rescue doses allowed for breakthrough pain.[4, 5] The same amount of medication given as the regularly scheduled dose should be allowed in rescue doses. For example, a patient taking 60mg of morphine every 12 hours should be allowed 20mg of short acting morphine every 4 hours for breakthrough pain.

For patients who cannot take oral medication, the rectal, transdermal, subcutaneous, or intravenous routes may be used.[4, 6]

Adverse Effects of Opiods

Effect	Treatment

Somnolence	Tolerance may reduce effect; persistent somnolence may require caffeine or methylphenidate.
Nausea/vomiting	Centrally acting anti-emetics such as prochlorperazine, haloperidol, or metoclopramide may be useful.
Respiratory depression	Appropriate titration will usually prevent.
Decreased GI motility resulting in constipation	Regular laxative therapy should be initiated when opioid is started.
Histamine release resulting in urticaria and pruritis	Usually diminishes over time.
Confusion or delirium	Haloperidol 0.5-1mg 2-3 times daily may be useful.
Myoclonic jerks	Clonazepam 0.25-5mg 3 times daily may be useful.

Adjuvant medications

Adjuvant medications are used to enhance the analgesia of opioids or treat certain types of pain. The drug classes most commonly used include: NSAIDS, tricyclic antidepressants, anticonvulsants, and corticosteroids.

• *NSAIDS.* NSAIDS are used in treating pain due to bone metastasis as well as other
inflammation based pains.

• *Corticosteroids.* Corticosteroids are used in nerve compression, elevated intracranial pressure,
and visceral distension.

• *Tricyclic antidepressants.* Tricyclic antidepressants are useful in the treatment of neuropathic
pain. They provide additional advantages of improving depression and insomnia.

• *Anticonvulsants.* Anticonvulsants are used for neuropathic pain, either alone or in combination
with antidepressant therapy.

Neuropathic Pain

Neuropathic pain is the result of damage to the nervous system, which causes hypersensitivity of the neurons in the spinal cord. It can be associated with a

variety of conditions, and can be grouped according to the location of the damage to the nervous system.[7]

Peripheral	Central
• Diabetic neuropathy	• HIV sensory neuropathy
• Phantom limb pain	• Multiple Sclerosis
• Post herpetic neuralgia	• Parkinson's disease
• Trigeminal neuralgia	• Post-traumatic spinal cord injury pain
• HIV sensory neuropathy	• Post-stroke pain
• Chemotherapy induced polyneuropathy	

Medications commonly used to treat neuropathic pain include anticonvulsants and antidepressants.

1st Line Therapy Have been shown to be effective in more than one randomized, controlled trial.[7]

- Gabapentin
- 5% Lidocaine patch
- Opioid analgesics
- Tricyclic antidepressants

2nd Line Therapy Reserved for use in patients who don't respond to first line therapy.[7]

- Lamotrigine
- Carbamazepine
- SSRIs – citolapram, paroxetine
- Venlafaxine
- Buproprion

Rheumatoid Arthritis

Pain in rheumatoid arthritis results from the chronic inflammation affecting diarthrodial or hingelike joints.[8] Analgesic therapy usually focuses on agents possessing both analgesic and anti-inflammatory properties, such as the NSAIDS.[9] Topical analgesics, such as capsaicin, may also be of benefit.

Osteoarthritis

Osteoarthritis is not due to inflammatory processes, but is due to the breakdown of cartilage in the joints. Pain management focuses on the analgesic properties of medications rather than anti-inflammatory properties.[9]

• Acetaminophen, in doses up to 4gm/day, is the drug of choice.[10]
• Tramadol may be used for acute exacerbations or in patients not responding to acetaminophen.[10]
• NSAIDS should be used in patients not responding to acetaminophen.
• Opioid analgesics should be used for short term management of acute exacerbations.
• Topical agents may also be of benefit.[10]

Sickle Cell Anemia

Sickle cell anemia is a disease in which the red blood cells become crescent shaped instead of the normal disc shape. As a result, they function abnormally and cause small blood clots, which give rise to recurrent painful episodes called “sickle cell pain crises”. Crisis management usually consists of hydration and analgesia. The American Pain Society has developed guidelines for the management of sickle cell crisis.[9]
• Mild to moderate pain. The patient should be started on a non-opioid analgesic, such as NSAIDS or acetaminophen. If the patient doesn’t respond, an opioid should be added.
• Moderate to severe pain. The characteristics and duration of pain should guide the choice of opioids. For pain expected to occur for several days, a sustained release product should be used, along with a short acting product for breakthrough pain.
• Severe pain. The management of severe pain should include intravenous administration, if possible. The use of patient-controlled analgesia (PCA) should be considered. Doses should be scheduled around the clock, with rescue doses available.

Common Misconceptions

In order to appropriately manage pain, healthcare professionals must be able to separate facts from commonly held myths regarding opioid use and pain management, especially in terms of addiction and dependence. It is generally understood that patients treated with opioids for chronic pain may experience physical dependence and tolerance, but rarely do they experience addiction. The American Society of Addiction Medicine (ASAM), the American Academy of Pain Medicine (AAPM), and the American Pain Society (APS) have recommended the use of the following definitions:[11]
Addiction: a primary chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Pseudoaddiction: a term used to describe patient behaviors that may occur when pain is undertreated. Pseudoaddiction can be distinguished from true addiction in that the behaviors resolve when pain is effectively treated.

Physical Dependence: a state of adaptation that often includes tolerance and is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

Tolerance: a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.

Conclusion

The recognition and treatment of pain is becoming increasingly important within the health-care industry in the United States. This is evident by the variety of agencies that have produced clinical guidelines for the treatment of various types of pain, ranging from acute pain during operative procedures to pain resulting from sickle cell disease.[12] In addition, the Joint Commission on Accreditation of Healthcare Organizations included pain management standards in its 2000-2001 standards manual.[13]

Management of pain associated with a variety of conditions must be addressed in order for the patient to be able to function in any sort of normal capacity. Drug therapy, including opioids, is often an integral part of the management of pain. Hopefully, increasing the knowledge and awareness of the members of the healthcare team will prevent anyone from suffering needlessly.

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