

Special Issues in Pain Management

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The prevalence of chronic pain in the adult population ranges from 2% to 40%, with a median point prevalence of 15% (Manchikanti, 2006). Pain affects more than 50% of older persons living in a community setting and more than 80% of nursing home residents. Persistent pain is widely prevalent in veterans with serious illnesses and is often underdiagnosed and ineffectively managed. Pain limits functional status and can result in diminished quality of life, sleep disturbances, social isolation, depression, and increased healthcare costs and resource utilization.

Timely and effective assessment and judicious management of pain in veterans will help in alleviating their suffering, while maintaining and augmenting quality of life.

TERMS COMMONLY USED WHEN DESCRIBING PHYSICAL PAIN

- **Nociceptive pain** is the perception of nociceptive input, usually due to tissue damage (e.g., postoperative pain). Nociceptive pain is further subdivided into somatic and visceral pain. **Somatic pain** is pain arising from injury to body tissues. It is well localized but variable in description and experience. **Visceral pain** is pain arising from the viscera mediated by stretch receptors. It is poorly localized, deep, dull, and cramping (e.g., pain associated with appendicitis, hepatic cancer metastasis, bowel ischemia).
- **Neuropathic pain** is pain initiated or caused by a primary lesion or dysfunction in the nervous system.
- **Central pain** is pain initiated or caused by a primary lesion or dysfunction in the central nervous system (e.g. post-stroke pain, phantom limb pain).
- **Wind-up pain** is the slow temporal summation of pain mediated by C fibers of repetitive noxious stimulation at a rate less than one stimulus per 3 seconds. It may cause the person to experience a gradual increase in the perceived magnitude of pain.

PAIN ASSESSMENT

Pain presentation in veterans may be skewed due to a variety of factors including the culture of stoicism and battlemind as well as due to co-morbid conditions like depression, Posttraumatic Stress Disorder (PTSD), and recreational substance usage. A thorough assessment is necessary to formulate a plan to successfully treat persistent pain. The International Association for the Study of Pain (IASP) has developed taxonomy for the classification of pain that identifies five axes as below and these are a helpful framework in assessing pain.

- **Axis I: Anatomic regions:** Ask patient to point out specific areas in the body where they have pain.
- **Axis II: Organ systems:** Identify possible organs that may be involved. It is important to remember areas of referred pain, e.g. diaphragmatic pain to shoulder.
- **Axis III: Temporal characteristics, pattern of occurrence:** Assess the time the pain occurs, and exacerbating and relieving factors.
- **Axis IV: Intensity, time since onset of pain:** Some older adults may be able to use numbers (scale of 0 to 10) to describe intensity while other may prefer words (mild, moderate and severe).
- **Axis V: Etiology:** Underlying etiology of pain should be identified and reversible problems should be corrected.

Pain assessment should include an exploration of effects of pain on functional status, sleep, libido, emotional and social well-being. Scales such as the McGill Pain Questionnaire and the Pain Disability Scale measure pain in a variety of domains, including the intensity, location, and affect. Although time-intensive, scales measuring multiple domains can provide a wealth of information about the patient's unique experience of pain. It is also prudent to concurrently screen for PTSD and depression. When patients are unable or unwilling to cooperate with time-intensive pain assessments, simple scales like the Numeric Rating Scale and the Faces Pain Scale are effective. The patient is asked to rate his or her pain by assigning a numerical value (with 0 indicating no pain and 10 representing the worst pain imaginable), or a facial expression corresponding to the pain.

The persistent pain experience in veterans is often influenced by certain unique factors that are common in veterans. Military service exposes men and women in service to specific training and common life experiences and stressors that shape their thinking, behaviors, and experiences. Three types of

stress are common in Americans who serve in the armed services and these may influence how they experience and interpret disease-related pain.

- a. **Life threat:** This is a prevalent issue in combat veterans and prisoners of war.
- b. **Loss of colleagues and friends, loss of relationships and loss of limbs in the line of duty:** The loss of functionality often seen with persistent pain and the losses inherent in the chronic and serious illness process may remind veterans of past losses when they were on service, when their friends and “buddies” died in front of their eyes, or even in their arms, in combat. Loss of limbs and shrapnel injuries may trigger unusual pain syndromes like phantom pain and other neuropathic pain syndromes.
- c. **Inner conflict:** During active duty, men and women in service may be forced to carry out actions that may be in conflict with their fundamental values and beliefs. For example, they may have to kill enemy soldiers or may inadvertently harm civilians and women and children in the line of duty. This may be at odds with their personal values of being compassionate or not hurting others. Also, the presence of ongoing challenging circumstances during a tour of duty may take a toll on their physical and emotional health. These experiences will skew how they experience and interpret pain due to serious illness. For example, a veteran who killed an enemy soldier in the line of duty may feel tremendous guilt and moral distress as she or he is now wrestling with a life-limiting illness and doing a life review as a part of the dying process. Depending on their spiritual and religious beliefs, they may have worries about life after death and if and how that may be influenced by their past actions in the line of duty.

THE VETERAN CULTURE, BATTLEMIND TRAINING, AND STOICISM

Culture consists of the beliefs, behaviors, objects, and other characteristics common to the members of a particular group; in this case, members of the armed forces. Battlemind is defined as a soldier’s inner strength to face fear and adversity during combat, with courage. It is the will to persevere and win. When on a tour of duty, a person is expected to be strong and fully operational at all times. There is a strong stigma associated with any show of weakness. They cannot back away from the warfront. They are expected to meet challenges head on, and maintain mental toughness during times of adversity and challenge. For example, the United States Navy Sea Air and Land (SEAL)

personnel often quote the phrase, “the only easy day was yesterday.” This battlemind mindset, which comes from the ongoing rigorous training they receive when on active duty, often becomes an integral part of who they are. When faced with physical threats due to serious illness, veterans often work hard to meet the illness-related challenges with courage and stoicism. Data show that veterans, as a cultural group, are at a higher risk for PTSD, depression, and substance abuse. The cluster of these experiences will likely influence how pain is experienced and interpreted. In a recent study (Tan, Teo, Anderson, and Jensen, 2011) of pain and coping conducted on a group of 109 veterans with chronic pain, researchers studied nine specific pain-related adaptive and maladaptive coping and belief domains: guarding, exercise/stretch, resting, catastrophizing, control, disability, harm, medication, and pacing. Each of the nine pain-related coping responses and beliefs were classified as adaptive (exercise/stretch, control, and pacing) or maladaptive (guarding, resting, catastrophizing, disability, harm, and medication). The study results showed that maladaptive coping and beliefs play a more powerful role than adaptive coping and beliefs in predicting pain interference and depression and that adaptive responses may be more important than maladaptive responses in predicting reported pain intensity.

Posttraumatic Stress Disorder (PTSD) and pain in veterans

An estimated 25% (Breslau, Davis, Andreski, and Peterson, 1991) who have been exposed to trauma go on to develop Posttraumatic Stress Disorder (PTSD) during their lifetime. PTSD is also more common in war veterans with an estimated prevalence of about 30% in Vietnam veterans, about 10% of the Gulf War (Desert Storm) veterans, about 6% to 11% of the Afghanistan war veterans, and about 12% to 20% of the Iraq war veterans (Boscarino, 2008). Hispanic veterans are said to exhibit higher risk of developing PTSD than veterans of other racial/ethnic backgrounds. Possible mediators of the effects of Hispanic ethnicity on vulnerability to PTSD are identified, including psychosocial factors (racial/ethnic discrimination and alienation) and sociocultural influences (stoicism and normalization of stress alexithymia and fatalism). PTSD is associated with chronic pain syndromes. PTSD is also associated with poor coping skills and can thus amplify the distress or lead to refractory pain and non-pain symptoms. Many seriously ill patients suffer from symptoms like pain, dyspnea, nausea, fatigue and many others and these could be exacerbated by PTSD. A key fact in terms of how PTSD influences the pain experience is that trauma-related memory can be triggered by somatosensory triggers.

For example, cancer pain may trigger repeated flashbacks for a PTSD patient who was tortured in a concentration camp when he was a prisoner of war. Additionally, avoidance symptoms are central to the diagnosis of PTSD; these patients tend to cope by avoiding or ignoring problems (Amir et al., 1997; Bryant and Harvey, 1995). In some cases, patients may use maladaptive coping strategies like alcohol or recreational drugs to cope with pain that may be a manifestation of a serious illness like cancer or coronary arterial disease. This may cause a delay in the diagnosis of the underlying illness and result in increased mortality and morbidity in these patients.

The interaction between PTSD and pain

When PTSD patients start experiencing pain as a part of their serious illness process, the following issues need to be considered.

- a. Patients with even remote history of recreational opioid usage often have high tolerance to opioids and will likely need higher doses of opioids to control their illness-related pain. These patients are also more prone to refractory pain syndromes and require skilled palliative care services. Due to their past experiences with recreational drugs, they may be very knowledgeable about opioids and may tend to self-manage their medications and not adhere entirely to the regimens prescribed.
- b. Some patients may exhibit “pseudoaddictive behavior” due to poorly controlled pain. “Pseudoaddiction” is a phenomenon that occurs when a patient who is suffering with a legitimate chronic pain condition is undertreated with pain medication (Weissman, 2006). The situation arises when the clinician is reluctant to provide enough medication to assure adequate symptom relief for a patient who requires a higher dose of long-acting (basal) pain medication. This can provoke a series of “conditioned behaviors” focused on acquisition of the controlled drug that can appear to indicate aberrant addictive-type behaviors. To note, some patients may even revert back to taking street drugs to supplement their inadequate pain medications and this causes tremendous angst in patients and their families as they slip back into dysfunctional old patterns of behavior. For example, the patient may become furtive and avoidant and family members may start policing his or her activities. As all parties are aware that the patient is seriously ill, they may feel significant guilt. Patients also feel intense preparatory grief in addition to being at risk for depression (Periyakoil, 2012). In pseudoaddiction, the behaviors tend to disappear when an adequate amount of the drug

is prescribed. It behooves clinicians to carefully consider what opioids to use in these patients. Methadone is an effective choice for basal pain control. Newer drugs like suboxone are also effective when there are compelling concerns about abuse.

- c. The need for pain medications and the dependence on clinicians for care plan management may undermine the patient's sense of control and thereby create a sense of hostility or non-compliance in the patient and undermine the therapeutic relationship. Frank and ongoing discussions are vitally important in engaging the patient in an ongoing manner.

Prescription drug abuse: Non-medical use of prescription drugs is the second most prevalent category of drug abuse, after marijuana. The risk for abuse or dependence was highest for prescribed psychoactive drugs (Chassen et al., 2001). The most commonly abused opioid class of drugs (Manchikanti, 2006) include oxycodone (Percodan, Percocet, Roxicet, Tylox, OxyContin), hydrocodone (Vicodin, Vicoprofen, Lorcet, Lortab), hydromorphone, methadone, morphine (Astramorph, Duramorph, MS Contin, Roxanol), and codeine. Data from Department of Health and Human Services (DHHS, 2002, 2004, 2006) and Substance Abuse and Mental Health Services Administration (SAMHSA, 2004) show that while opioids are by far the most abused drugs, other controlled substances such as benzodiazepines, sedative hypnotics, and central nervous system stimulants, though described as having less potential for abuse, are also of major concern as they appear to be widely used for non-medical purposes as well. Substance abuse often coexists with PTSD (Chilcoat and Breslau, 1998; Deykin and Buka, 1997; Jacobsen, Southwick, and Kosten, 2001; Saxon et al., 2001) with PTSD patients being at more than a fourfold risk for misuse and dependence. Data suggest that drug abuse or dependence in persons with PTSD might be caused by efforts to self-medicate. It is very important to routinely screen all patients for PTSD before prescribing opioids. If they screen positive for PTSD, they should be immediately referred to a mental health professional for further evaluation. In veterans with mental health issues, analgesic regimens should ideally be charted with ongoing input from the patient, their primary family member(s), the primary care provider and mental health professional. Constant education about appropriate adherence to opioid regimen is vital to minimize misuse, abuse, diversion, or concurrent recreational drug use.

TREATMENT

Approaches to persistent pain treatment

All patients should be educated about their persistent pain, the underlying causes, and how best to track its location, intensity, and how to take medications properly. They should be encouraged to use non-pharmacological modalities and exercise regularly. They should be educated about availability of support groups and other VA services based on their specific needs (PTSD support groups, Alcoholics Anonymous, Narcotics Anonymous). Family members of veterans should be educated as well about the patient's illness condition. The more we are able to empower veterans and families to take a central role in their illness management, the better will be their outcomes.

Nonpharmacologic therapy

Recognizing the common overlap of depression, anxiety, and PTSD should prompt early consultation with mental health professionals. Psychological interventions and cognitive-behavioral therapy (CBT) are also important tools for treatment of persistent pain as they help patients cope with the stresses that accompany persistent pain. In CBT, patients are asked to track their pain and record the thoughts that are associated with the pain experience to identify maladaptive coping strategies, including misuse of prescription medications, alcohol, or recreational substance use. By conscientiously replacing these maladaptive strategies with positive coping strategies, patients can increase control over pain-related experiences and thereby over the pain. When possible, family members and caregivers should be included in the care planning and even in the therapy.

The importance of exercise cannot be overstated. Exercise (to the extent the patient can tolerate it) will maintain functional status, boost mood, and promote a sense of independence and control. For patients who are unable to tolerate weight-bearing exercises due to osteoarthritis, metastatic bone disease, etc., pool therapy (which is available in many VA facilities) should be offered. For patients with advanced illness who are bed-bound, gentle passive range of motion exercises and massage therapy are effective. The goals of therapy should be determined after discussion with the veteran (or the surrogate decision maker in cognitively-impaired patients). Such goals may include optimizing quality of life, improving functional status, minimizing dependence on prescription medications, and maintaining abstinence from nicotine, alcohol, or recreational drugs.

An interdisciplinary team approach to treatment may be strongly recommended for patients with complex pain. Including occupational therapists, physical therapists, massage therapists, mental health experts and the chaplain should be considered on a case-by-case basis. Incorporating complementary and alternative modalities such as hypnosis, aromatherapy, biofeedback, music, and pet therapy are especially valuable as they have minimal to no side effects.

Pharmacologic therapy

When starting pharmacologic therapy, nonsystemic therapies should be tried first. For example, patients that primarily have knee pain might respond to intra-articular corticosteroid injections. Topical preparations such as capsaicin or diclofenac gel or lidocaine patches might be effective. If these local therapies are ineffective, systemic therapy should be instituted and the patient should be educated to ensure understanding of the need to take medications as prescribed. The pain ladder from the World Health Organization (WHO) offers a globally-accepted approach towards analgesic management. Using relatively innocuous medications like acetaminophen for many mild to moderate pain syndromes, particularly osteoarthritic pain, is recommended as first-line therapy. The maximum adult dose is 4gm/day and in an older adult population the recommendation is to adhere to a maximum dosage of 3gm /d. For patients at risk of liver dysfunction, particularly those who have a history of alcohol intake, the dosage should be decreased by 50%, or acetaminophen should be avoided. Acetaminophen administration frequency should be based on the patient's renal function. For patients with a Keratinize clearance of 10-50 mL/minute it can be dosed every six hours and for patients with a Keratinize clearance of <10 mL/minute it should be given every eight hours. Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) are effective for chronic inflammatory pain and are used after acetaminophen has been tried and proven to be ineffective. NSAID side effects include renal dysfunction, GI bleeding, platelet dysfunction, and fluid retention; due to these significant adverse effects, they are better limited for short-term use, especially in older adults (O'Neil, Hanlon, and Marcum, 2012). Patients with history of ulcer disease or complication, those who are on dual antiplatelet therapy, or are on an NSAID with concomitant anticoagulant therapy are at high risk for GI toxicity (2008 American College of Cardiology Foundation/American College of Gastroenterology (ACG)/American Heart Association guidelines). Additional risk factors for NSAID GI toxicity include age ≥ 60

years, corticosteroid use, dyspepsia or GERD symptoms. Topical NSAIDs appear to be safe and effective in the short term, but longer-term studies are lacking.

Moderate to severe pain or pain that requires chronic treatment often requires opioid medications for sufficient relief, though the evidence base supporting the role of long-term opioids in persistent non-cancer pain is sparse. Common adverse events included constipation (median frequency of occurrence = 30%), nausea (28%), dizziness (22%), and prompted opioid discontinuation in 25% of cases. Careful and ongoing monitoring for benefits and side effects and tailoring therapy to the individual patient's response to the therapeutic regimen are keys to successful treatment.

In general, continuous and persistent pain due to a serious illness should be treated with long-acting or sustained-release formulations after opioid requirements have been estimated by an initial trial of a short-acting agent. Breakthrough pain is to be treated with rapidly acting medications with short half-lives. A typical patient requires approximately 5% to 15% of the total daily dose offered approximately every 4 hours orally for breakthrough pain. The drug dose and dosing intervals should be varied based on the patient's liver and kidney function. Tolerance develops fairly rapidly to other adverse events of opioids, such as respiratory depression and sedation; constipation usually accompanies opioid use as the opioids bind to the mu receptors found in the gut and slow down peristalsis. In fact, the most common adverse event of opioid treatment is constipation, and tolerance to constipation does not occur. Experts recommend starting therapy with a stimulant laxative (such as senna) concurrently with the opioid unless the patient has signs or symptoms of bowel obstruction. Respiratory depression is the most serious potential adverse effect associated with opioid use, but tolerance to this effect develops quickly. Older adults with a history of lung dysfunction are at particular risk when opioid dosages are increased too rapidly or when a benzodiazepine is prescribed concomitantly. It is important to educate patients about the risks of increased falls and instruct them not to drive or operate heavy equipment when opioids are started or the dosage changed. (Please see Tables 1 and 2 for further resources on principles of using opioids in persistent pain management.)

Adjuvant medications can be used effectively solely or in combination with opioids for treating patients with neuropathic pain or mixed pain syndromes. Tricyclic antidepressants (TCAs) are effective in the treatment of post-herpetic neuralgia and diabetic neuropathy. Clinical depression in patients with

persistent pain requires treatment to achieve optimal analgesia and quality of life and selective serotonin re-uptake inhibitors (SSRIs) are the first-line class of drugs. Duloxetine, an inhibitor of norepinephrine and serotonin uptake, is approved both as an antidepressant and for the treatment of pain from diabetic neuropathy and may offer a more favorable adverse-event profile than the TCAs.

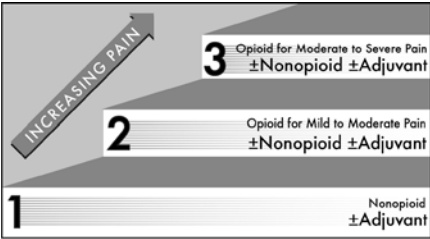
Adverse effects of opioids in some veterans with PTSD

PTSD patients use dissociation to cope with their resurgent traumatic memories. Some terminally-ill patients who are on narcotic analgesics or sedative hypnotics for palliation of their disease-related symptoms are unable to dissociate from their trauma-related memories which now seep through into their conscious mind. Thus, the opioids and benzodiazepines can precipitate distressing flashbacks and nightmares in these patients. In such cases, some patients who find the intrusive symptoms extremely distressing refuse to take opioid pain medication even in the face of severe pain due to the terminal illness; they prefer to endure the physical pain due to the terminal illness over dealing with the PTSD-related emotional pain that may be precipitated by the mind-altering property of the opioids and psychotropic medications. This may be distressing to the family and to the healthcare team as they have to witness the patient's physical pain but are unable to palliate it with opioids. However, it is critical in these situations to empower the patient and respect their decision to forego opioids and other psychotropic medications and palliate their symptoms using non-pharmacological therapeutic modalities like support groups, trauma-focused group therapy (Schnurr et al., 2003), massage therapy, music therapy, and relaxation therapy. Specific modalities like eye movement desensitization and reprocessing (Taylor, 2003) are more feasible for palliative care patients with an anticipated life-span of months to years.

In conclusion, careful and thorough assessment of pain in all seriously ill veterans requires a comprehensive approach that includes bio-psycho-socio-spiritual aspects and also carefully considers the culture of veterans and how that may affect their perception and interpretation of their pain. Effective management of pain will prevent erosion and conserve and augment (Periyakoil, 2012) dignity for all seriously ill veterans.

How to institute opioid therapy (Table 1)

When dosing opioids for a patient with chronic severe pain remember the following:

by mouth	(When giving pain medications, the oral route is always preferred over other routes like transdermal, intravenous or sub-cutaneous routes)
by the clock	(Chronic basal pain is usually best treated with scheduled long acting pain medications, with short acting pain medications on an as-needed basis for incidental or break through pain)
by the ladder	 <p>Pain Ladder from the World Health Organization</p>

Opioid Equivalency Table (Table 2)

<i>Drug</i>	<i>Oral/Rectal Route</i>	<i>Parenteral Route</i>	<i>Conversion Ratio to Oral Morphine</i>	<i>Equianalgesic Dose of Oral Morphine</i>
Morphine sulfate	30mg Oral morphine	10mg of parenteral morphine	Parenteral morphine is 3 times as potent as oral morphine	30mg Oral morphine
Oxycodone	20mg of oral oxycodone	N/A	Oral Oxycodone is roughly 1.5 times more potent than oral morphine	30mg Oral morphine
Hydrocodone	20mg of oral hydrocodone	N/A	Oral hydrocodone is roughly 1.5 times more potent than oral morphine	30mg Oral morphine
Hydromorphone	7mg of oral hydromorphone	1.5mg of parenteral hydromorphone	Oral hydromorphone is about 4-7 times as potent as oral morphine Parenteral hydromorphone is 20 times as potent as oral morphine	30mg Oral morphine
Fentanyl	N/A	15 micrograms/hr	Transdermal fentanyl is approximately 80 times as potent as morphine (This is based on studies converting from Morphine to fentanyl. Currently, there are no empirical studies converting fentanyl to morphine).	30mg Oral morphine
Meperidine Meperidine is not a recommended drug in a palliative care setting and is to be avoided. If a patient with chronic pain is on meperidine, convert patient to an equianalgesic dose of one of the other opioids listed in this table.	300mg of oral meperidine	75mg of parenteral meperidine	Oral Morphine is about 10 times more potent than oral meperidine and about twice more potent as parenteral meperidine (mg for mg)	30mg Oral morphine

Created by VJ Periyakoil, MD for Stanford eCampus curriculum:
http://endoflife.stanford.edu/M11_pain_control/equivalency_table.html

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