



Pain Relief at the End-of-life: *A clinical guide*

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Significant pain is present in the majority of patients dying of chronic diseases such as cancer, diabetes, heart and lung disease.



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Abstract

Pain at the end-of-life is usually treatable, but most dying patients are under-treated and die in unnecessary pain. This brief overview will serve to describe the problem of pain at the end-of-life, define the relevant ethical, medical, scientific, and societal issues, and present an optimal pain management plan for this vulnerable and important population. The most important factor is for physicians to make pain control a matter of paramount importance in the care of dying patients.

Introduction

Pain is a universal aspect of life. It is necessary and adaptive. It is, however, a form of suffering that can detract from the duration and quality of human life. In one of the miracles of modern medicine, pharmacologic and non-pharmacologic tools allow physicians to relieve pain and decrease suffering.

It is disturbing that most pain sufferers are still inadequately treated.¹ In foreign countries, the medicines may not be available.² In the United States, barriers include regulatory

burdens, cost, myths about pain and pain medicines, and ignorance.

Significant pain is present in the majority of patients dying of chronic diseases such as cancer, diabetes, heart and lung disease.³ Optimal end-of-life care in dying patients entails relief of suffering and aggressive treatment of painful symptoms. Pain at the end-of-life is usually treatable, but most patients are under-treated.⁴

This brief overview will serve to describe the problem of pain at the end-of-life, define the relevant ethical, medical, scientific and societal issues, and present an optimal pain management plan for the dying patient. Clinicians with a basic understanding of these principles should be able to prevent most or all pain in their dying patients.

The Problem

Pain, one form of suffering, is common at the end-of-life, and is usually accompanied by other symptoms, including dyspnea, nausea, confusion, anxiety, and depression.⁵ Pain is the predominant symptom and the most feared form of suffering.⁶ Pain at the end-of-life is protean and complicated. No two patients have identical pain pathophysiology or

psychosocial pain context. There is an ethical obligation in medicine and nursing to relieve suffering, especially pain. It is imperative that physicians and other health professionals, as well as society in general, improve and optimize pain management especially at the end-of-life.

Definitions

Several definitions will serve to help clarify and codify the terms used in this article:

- ♦ *Pain* – an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.⁷

- ♦ *Suffering* – a complex negative emotional and cognitive state characterized by perceived threat to the integrity of the self, perceived helplessness in the face of that threat, and exhaustion of psychosocial and personal resources for coping with that threat.⁸

- ♦ *Breakthrough pain* – sudden increases in the base level of pain or different but recurring pains.⁹

- ♦ *End-of-life* – the point in a life-limiting chronic illness when further curative or disease-modifying therapy is ineffective or overly burdensome and when symptom management only is most appropriate.

- ♦ *Opioid* – (also called opiates) a class of medications that share the property of analgesia mediated by binding to a class of receptors in the nervous system called opioid receptors.

- ♦ *Analgesic* – a medication that has as its main pharmacologic property and intended action a reduction in pain.

- ♦ *Adjuvant* – a medication or therapy with little or no direct impact on a symptom or condition which is expected to add to the benefit of a standard or known effective treatment for the symptom or condition.

Pathophysiology of Pain

The pathophysiology of pain is complex, our understanding continually evolving and beyond the scope of this article. A brief review of the basics of pain generation is useful.

- ❖ *Nociception*, the most upstream signal in pain physiology, occurs when damage results in the stimulation of peripheral neuro-receptors in tissues; these transmit a signal to a peripheral nerve.

- ❖ *Transmission* is the traversing of a pain signal from the nociceptor to the peripheral nerve to the spinal cord to the brainstem to the midbrain to the sensory cortex to the association cortex.

- ❖ Next is *modulation*, when, at least at the levels from the spinal cord and above, descending and local signals serve to either dampen or accentuate the ascending pain signals from the periphery.

- ❖ After modulation comes *cognition*, the final summed subjective sensation of pain and modifying influences as experienced by the patient.

- ❖ *Expression* is the communication of this cognition to others, verbally or non-verbally. Although simplistic, this schema allows us to get from a painful site in the body to the person telling the physician about their pain in the context of their life and illness. It also shows us the levels at which any intervention might have an impact upon the pain.

Assessment of Pain

Adequate assessment of pain is vital to treat the pain optimally and the disease appropriately. This is true for end-of-life as well as curable conditions. Important factors in assessment of pain include: location – subjective and anatomic description of where the pain occurs; chronicity – duration of the pain complaint; temporal pattern – how the pain

changes over time; severity – intensity of the pain complaint, often measured¹⁰ from 0-10 or on a visual analog scale¹¹; character – pain description (sharp, dull, stabbing, burning, etc.); and associated findings – at the end-of-life, many other findings may be present-dyspnea, cachexia, fever, depression, etc.

This complete assessment of pain plus a work-up of possible etiologies or unique pathophysiology will usually lead to successful relief of suffering.

The Pain Work-Up

The pain work-up includes: a physical examination with special attention to the neurologic and musculoskeletal findings; laboratory examination – to confirm or refute suspected conditions related to the pain complaint (infection, liver or bone metastasis); radiographic evaluation – including plain films, computed tomography, ultrasound, magnetic resonance imaging, positron emission tomography scanning, and other tests.

Biopsies may be required to confirm a diagnosis of primary cancer or recurrence. Pulmonary function tests or echocardiograms establish the severity of chronic obstructive pulmonary disease or congestive heart failure. This evaluation narrows the numerous possible causes of pain, and allows for targeted therapeutics.

Multidisciplinary Patient-Centered Approach

Pain relief therapy should begin simultaneously with the diagnostic process, not upon completion of the work up. Either outpatient or inpatient settings may be appropriate for evaluation and management, depending upon the severity of the pain, symptoms and the ease of control.

The primary physician, nurse, psychosocial



professional, and consultants should be involved from the beginning and communicate daily, preferably face-to-face. The target of their efforts should be the relief of the patient's pain, suffering, and symptoms.

Modalities of Pain Therapy

Physicians and nurses tend to focus predominantly on pharmacologic management of pain. There are multiple other important therapeutic modalities for relieving pain. These include surgery, other interventional techniques, palliative or radical radiotherapy, physiatry, massage, and electromagnetic therapy (ultrasound, magnet, electrical stimulation). Successful treatment of patients in pain often requires an individualized, thoughtfully selected mix of therapies.

Pharmacological Therapy for Pain Relief

The principles of pharmacologic therapy for pain are well established and have not changed dramatically in over three decades. Unfortunately, these principles are not applied uniformly or effectively even in the United States. The World Health Organization (WHO) analgesic ladder was formulated in 1986 to serve as a worldwide guide to physicians for rational, effective use of non-opioid and opioid analgesics.¹²



Opioids are the main pharmacologic therapy for pain at the end-of-life. They are

safe, effective, easy to use, and relatively inexpensive. There is no maximum dose of any pure opioid agonist. These medications have several drawbacks, including regulatory constraints, limited supplies (in some countries), and the real but uncommon problems of abuse, diversion, and addiction.

Opioids come in weak, moderate, and strong analgesics, single and combination products, and long and short acting formulations. Delivery routes include oral tablets, capsules, and liquids; sublingual or oral transmucosal liquids or lozenge preparations; transdermal patches, suppositories, and intravenous, subcutaneous, and intramuscular delivery.

Most patients with chronic or end-of-life pain will do best with both a long-acting agent to prevent most pain and a short acting agent to treat episodic or breakthrough pain.⁹ It is relatively simple to choose an

Table 1
Equianalgesic Dosing Conversion Table

Oral or Rectal Dose (mg)	Agent	IV/IM/SQ Dose (mg)
100	Codeine	--
15	Hydrocodone	--
10	Oxycodone	--
15	Morphine	15
4	Hydromorphone	1.5
--	Fentanyl	25mcg/hr patch ~50mg morphine PO/24 hours

Adapted from Ref. 14

appropriate agent(s), dose, route, and schedule. With careful follow-up and adjustments this plan should relieve pain. If not, switching to another type of opiate is often effective. This is called opioid rotation, and it is successful about 50 percent of the time.¹³ In order to change from one opiate to another, or from one administration route to another, or to a different agent, an equianalgesic-dosing table¹⁴ is quite helpful. An example is shown in Table 1.

In addition to opioids, other agents can have a direct or indirect effect on pain sensation or transmission. These other

medications are called co-analgesics if they have analgesic properties of their own and adjuvants if they don't. Research has shown these medications have some chemical and therapeutic similarities. Depending upon the type of pain-nociceptive, neuropathic, inflammatory, central, etc. - these agents may greatly potentiate opioids.

On the WHO analgesic ladder, the first step is the use of acetaminophen, aspirin or other non-steroidal anti-inflammatory agents (NSAID) alone without an opioid.¹² These weak analgesics often can control mild pain, even at the end-of-life. Other categories of adjuvants or co-analgesic medications include anti-inflammatory agents (corticosteroids and NSAIDs), true adjuvants/neuromodulators (tricyclic antidepressants, anticonvulsants), psychiatric agents (antidepressants, anxiolytics, neuroleptics), and topical agents (lidocaine lotion or patches, capsaicin cream). Other medications are

commonly utilized to minimize side effects from opioids and other medications. These include stool softeners, laxatives, anti-emetics, anti-acid medications, psycho-stimulants, and sedatives.

Goals and Reassessment

Adequate control of pain at the end-of-life often requires aggressive application of multi-modality therapy. The treatment plan should be as aggressive and multifaceted as is needed to achieve the goals of reasonable comfort and minimal suffering in the dying process. Rapid, frequent reassessment is vital. Reassessment includes serial pain scale measurements over time; regular repeat physician visits with physical examinations, appropriate laboratory tests and radiographs, ongoing nursing assessments, and analysis of home health and hospice evaluations.

Each assessment should be followed by appropriate alterations of the treatment plan and discussion of the plan with the patient and family. Changes in old symptoms or appearance of new symptoms warrant thorough investigations to look for treatable etiologies. The patient should be carefully observed for medication or treatment side effects. These may

require changing drug dosage, changing medications or adding drugs directed at the side effects.

Conclusion

The problem of under-treated or non-treated pain at the end-of-life is a major challenge. In the United State, all of the resources to solve this problem are at hand. For the vast majority of patients, the full and appropriate use of these resources will result in satisfactory to excellent relief of pain and pain producing symptoms. The most important factor at this point is for physicians to make pain control a matter of paramount importance in the care of dying patients.

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