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Overcoming Opiophobia & Doing Opioids Right

CURRENT COMMENTS

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A More Practical Perspective on Opioids

Only opioids go to the heart of the matter, which is the endogenous opioid receptor system. Any direct attack on pain must target this system.

Most arguments against the use of opioids for a significant short-term or long-term pain problem are usually based on irrational fears, or so-called "opiophobia." However, this ignores a more practical perspective.

The only *direct* biologic pain-relief system in the human body is the endogenous opioid receptor system, consisting of endorphins and their tissue-based action sites, or receptors. Any potent attack on pain must trigger or enhance this system. All other systems in the human body that may relieve pain must do it indirectly. Hence, pain treatment agents that exert their biologic effects by suppressing inflammation, blocking synapses or anion channels, or activating hormones for growth or healing must all act indirectly.

Only opioids (see ***Table***) go to the heart of the matter, which is the endogenous opioid receptor system. When pain is severe, whether acute or chronic, indirect treatment agents such as antiinflammatory or neuro-synaptic blocking agents may not only fail to adequately control pain, they may produce significant complications.

Opioids Commercially Available for Ambulatory Use in the U.S.

Buprenorphine	Methadone
Butorphanol	Morphine
Codeine	Nalbuphine
Dihydrocodeine	Opium
Fentanyl	Oxycodone
Hydrocodone	Oxymorphone
Hydromorphone	Pentazocine
Levorphanol	Propoxyphene
Meperidine	Tramadol

Astonishingly, there is still widespread belief that pain is merely a psychological phenomenon with no inherent physical complications of its own, and aggressive medical treatment is, therefore, unwarranted. For example, some drug detoxification centers promote the self-serving concept that withdrawal from opioids can cure pain.

While some rare forms of pain may be purely psychic manifestations, the notion that opioids should be withheld from a patient with severe pain in favor of various psychological, behavioral, or physical therapies is folly and dangerous. The scientific literature and extensive clinical experience abundantly demonstrate that the failure to adequately treat severe acute or chronic pain may produce a plethora of serious complications, including death from pain-related cardiovascular collapse [Brookhoff 2000; Tennant 2004].

Opioid Treatment of Post-Surgical, Accident, and Other Acute Conditions

Acute pain, be it from an injury, infection, or post-surgical procedure, is clearly known to over-activate the pituitary-adrenal axis and interfere with healing [Greisen et al. 1998, 1999]. Opioids have clearly been shown to shorten recovery and promote healing in acute conditions, to say nothing about the humanitarian relief of suffering [Brookhoff 2000; Yakota et al. 2000]. There remains a belief by some, however, that a patient recovering from surgery, accident, or myocardial infarction is better served by writhing in a hospital bed rather than having their pain relieved.

There are excellent controlled studies demonstrating the positive effects of pain control following surgery, including dental and obstetrical procedures. Opioids stabilize cortisol, catecholamines, and blood pressure among other restorative homeostatic mechanisms [Greisen et al. 1998, 1999; Yakota et al. 2000]. Post-operative patients who have excellent pain control are routinely observed to begin eating, ambulating, and socializing within hours after surgery. See ***Table***.

Benefits and Risks of Post-Surgical Opioid Treatment

Benefits

- Shorter recovery time
- Homeostasis of endocrine, cardiovascular, and immune systems

Risks

- Respiratory depression

Since most patients who present to the healthcare system due to accident or in need of surgical intervention are not opioid tolerant, the only significant risk of opioid administration is respiratory suppression. This complication can be easily avoided if the initial opioid dosage is low and raised as necessary. Severe pain appears to have the affect of "absorbing opioids" and preventing respiratory depression. In the event, however, that respiratory depression does occur, naloxone, an opioid antagonist, will immediately reverse this complication.

Opioid Treatment of Headache and Other Pain-Flare Conditions

Chronic medical conditions that periodically flare and require emergency pain treatment with opioids plague emergency rooms and primary care physicians. While headaches are the predominant condition, there are other diseases that produce periodic, debilitating pain flares including sickle cell disease, pancreatitis, porphyria, and some gastrointestinal diseases, including ulcerative colitis and regional enteritis.

Opiophobia relating to the treatment of pain-flare conditions is prevalent.

Simple, short-term opioid therapy consistently, rapidly, and effectively relieves pain flares from these conditions, particularly when given by injection, suppository, sublingual, or buccal administration. See ***Table***. Although many opioids for pain flare conditions are routinely stocked and used in hospitals and emergency rooms, there is great reluctance to prescribe opioids for at-home, pain flare treatment by the patient and family.

Benefits and Risks of Opioid Treatment of Pain-Flare Conditions

Benefits

- Rapid pain relief
- Avoid bed/house-bound state
- Eliminate emergency room and hospital visits
- Facilitate safer driving
- Eliminate toxic effects of excessive triptans and antiinflammatory agents

Risks

- Overdose with respiratory depression or accidents

Broader prescribing and patient-teaching of safe, at-home techniques for opioid administration are the most effective ways to treat pain flares and avoid a bed/house-bound state, and to prevent emergency room and physician visits. The irrational fear of opioids for at-home use is simply unfounded. It is this restriction that leads many patients to overuse triptans and antiinflammatory agents to toxic levels and serious complications.

Another misplaced fear is that patients who self-administer opioids for flare conditions will drive poorly. In reality, an untreated patient with a pain flare from headache, pancreatitis, or sickle cell disease is clearly a driving hazard since uncontrolled pain may adversely affect attention span, muscle coordination, and vision.

Still, opiophobia relating to pain-flare treatment is prevalent. For example, some hospitals and other medical institutions have removed meperidine (Demerol®) from their formularies due to fear that a seizure may occur in some patients if meperidine metabolites accumulate to toxic levels. This fear is valid only with chronic administration and not the occasional use normally required for pain-flare conditions. Injectable meperidine remains the superior "stop-the-pain now" opioid for many patients. Another concern is that pain-flare treatment with opioids will be overdone and cause a fall or auto accident. This can happen, but these risks can essentially be eliminated if the patient is accompanied by an advocate who can observe the patient after opioid administration.

Opioid Treatment in Chronic Pain Conditions

Untreated, severe chronic pain has multiple, major complications (see ***Table***), which debilitate patients and shorten their life spans [Tennant 2000]. For example, if chronic pain is severe, it will produce a negative biologic state characterized by high pulse rate, hypertension, abnormal adrenal hormone levels, insomnia, anorexia, immobility, and other effects. Regardless of clinical risks, this condition must usually be treated with high doses of opioids.

Clinical risks after initiation of opioid treatment include the nuisance problems of constipation, edema, nausea, dizziness, and itching. (See lower ***Table***.) Other than constipation these side effects usually disappear after a few days of opioid treatment. Weight gain commonly occurs with chronic opioid administration. Once opioid tolerance and an effective pain-control dosage is achieved following upward titration from a starting dose, the major risk is suppression of testosterone and possibly dehydroepiandrosterone (DHEA) [Daniell 2001]. This complication may occur in males and females, and no other hormone suppression has been documented. There is no conclusive evidence that chronic opioid administration in a tolerant patient causes mental, neurologic, or immune deterioration. However, since chronic opioid administration does have documented testosterone suppression, constipation, and weight gain, it is recommended only after nonopioid therapies have failed to adequately control the chronic pain condition.

Major Complications of Severe Chronic Pain

Underuse of Musculoskeletal System

a. "Overuse" of ancillary musculoskeletal tissue with degeneration
b. Decreased mobility
c. Obesity
d. Muscle atrophy, contractures
e. Neuropathies

Hormonal

a. Excess catecholamine production with hypertension and tachycardia
b. Glucocorticoid excess or deficiency
c. Insulin and lipid abnormalities
d. Immune suppression

Neuropsychiatric

a. Nerve and spinal cord degeneration
b. Cerebral atrophy/dementia
c. Depression/suicide
d. Insomnia
e. Attention deficit
f. Memory loss
g. Cognitive decline

Chronic opioid administration benefits are profound (see ***Table***). In the patient whose pain is severe, constant, and alters blood pressure, pulse rate, and pituitary-adrenal hormones due to its stressor properties, opioid administration is the only treatment that can consistently and predictably control pain. Chronic opioid therapy is documented to normalize blood pressure, pulse rate, and pituitary-adrenal secretions [Tennant and Hermann 2002]. Even milder forms of chronic pain may benefit from low-dose opioid treatment as demonstrated by a number of clinical studies.

Opioid treatment leads to enhanced biologic functions, including eating, sleeping, socializing, and sexual relations. Physical functions, including the ability to walk, drive, and work usually improve. Patients and clinicians commonly refer to the benefits of chronic opioid administration as improving "quality of life." Much of the improved quality is in the stability brought to a chronic pain patient who, without opioids, is in-and-out of the hospital or sickbed and unable to participate in normal family, vocational, and other desired pursuits.

Benefits and Risks of Chronic Opioid Treatment

Benefits

- Improved quality of life
- Able to perform activities of daily living
- Normalization of cardiovascular, immune, and adrenal abnormalities
- Neurogenesis

Risks

- Testosterone suppression
- Weight gain
- Itching
- Constipation
- Edema

An emerging revelation involving chronic opioid administration is *neurogenesis*. There exists the outdated belief that nerves cannot regrow or regenerate and that pain that results from damaged nerve tissue is fixed and permanent. Numerous animal and laboratory studies reveal that nerve tissue can at least partially regenerate. Clinically, chronic pain patients who have taken opioids for extended periods are now being observed to permanently reduce their pain levels presumably due to neurogenesis. Opioids appear to function as a type of "splint," allowing homeostasis and healing to take place. Conversely, uncontrolled pain suppresses immune function and does not permit such rehabilitative nerve growth.

There is no ceiling or maximal level of opioid dose in chronic pan. The appropriate dosage is determined by starting low and titrating upward until a dose is reached that reduces pain 70% to 90%, but does not impair or sedate the patient. Multiple opioids may be required for this purpose. Overdoses, deaths, and accidents that occur in chronic-pain patients whose dose is initially determined in this fashion are due to patients failing to take their opioids as prescribed. Patients may also take other drugs or substances unknown to the prescribing physician and produce a drug interaction, with potential cardiac arrest and death. Simply stated, opioids as formulated, marketed, and properly prescribed in the United States are quite safe and have minimal clinical risk – *when they are taken as prescribed*.

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The Harmful Consequences of Misinformation

Prescribing physicians and the general public are constantly barraged with negative and misleading information about opioids. The worst misinformation is that patients who take opioids chronically become "addicted." It is remarkable, and instructional, to observe that patients who daily take insulin, antihypertensives, antidepressants, or sedatives are never referred to as "addicts."

Just as with chronic pain patients, these patients need daily medication. Chronic pain patients who take opioids become physiologically dependent and experience withdrawal symptoms when their daily opioids are abruptly stopped. This is also true for patients who daily take most antihypertensives, antidepressants, and sedatives, among other drug classes. When a chronic pain patient is able to totally eliminate pain as a result of effective treatment, they can easily withdraw and remain off opioids.

Another bit of misinformation thrust upon us is that a patient taking chronic opioids cannot drive, work, or volunteer. In a tolerant patient, this is simply false. The American Society of Addiction Medicine and every other professional physician group basically defines an "addict" as someone who compulsively takes a drug, such as an opioid, for a nonmedical purpose, like euphoria or pleasure. However, is not pain a most legitimate *medical* purpose?

Yet another harmful media effect has been perhaps unintended, but the onslaught of attention given to celebrities and other persons who sell, abuse, overdose, or die from opioids gives the public a false impression that no opioid drug should ever be prescribed by physicians. In reality a mere glance at the high-profile media cases reveals these people did not take opioids legitimately or as prescribed. The number of celebrities and street users combined who misuse and die from opioid overdose is miniscule, compared with the many millions of ordinary persons with painful conditions who daily take their opioids as prescribed and greatly benefit from them.

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So why the constant onslaught of negative misinformation? There appear to be two basic reasons. The first is economic – parties with an economic reason to reduce or deny clinical opioid treatment constantly feed and goad the media. They include health insurance plans, because opioid treatment may be expensive and prolong survival. Opioids also reduce the need for costly care from some healthcare institutions and practitioners, such as hospitals, surgeons, and mental health specialists. Lastly, there is the ugly reality that heroin dealers want pain patients to buy illegal opioids from them, rather than receive legitimately prescribed opioid medications from the local pharmacy.

A second reason for the constant negative onslaught on opioids is religious and emotional bias. Apparently, there are some persons in society, including some physicians, who have a

belief that pain and suffering are "good." There are others who believe that persons who take opioids are weak-willed and should not be allowed these drugs in order to live or function.

For example, the author recalls a recent severe pain patient with only a few months to live who remorsefully related that her son refused to see her because he would rather have her die in pain than have her take opioids to function and prolong her life. These beliefs are irrational because every human nervous system and blood system are already filled with the opioid, endorphin. The simple fact is that persons who propagandize against opioids might be shocked to know they constantly have opioids floating in their blood and cannot live without them.

Prescribing Opioids the "Right" Way

The argument that opioids should not be used for long-term pain management is nonsensical, if they are prescribed under these two circumstances:

1. There is a legitimately diagnosed pain condition;
2. Nonopioid pharmaceuticals have failed to control the pain.

The correct response to confirmed drug-seekers is detoxification and psychiatric or addiction referral – no physician should prescribe opioids for these people.

Unfortunately, physicians today are being deluged by a suspicious population of patients who do not exhibit *obvious* causes of pain. They claim to hurt "all over" or have a diffuse back, head, or limb pain that does not appear to have any causative event or physical evidence of neuropathy. These patients also present with no medical records or 3rd-party person to validate evidence of legitimate pain. Sadly, these persons have become such a plague on some physicians and medical institutions that they have given both opioids and patients who *legitimately* need opioids a poor reputation. The correct response to confirmed drug-seekers is recommending detoxification and psychiatric or addiction referral – no physician should prescribe opioids for these people.

Conversely, there are millions of Americans who have authentic structural tissue damage and legitimate pain. Medical practitioners should not prejudge patients who complain of pain, but do a careful history-taking and physical exam, review x-rays and medical records, and do validation interviews with family members to separate the bona fide, opioid-deserving patients from those who need psychiatric or addiction referral.

Once a legitimate, structural cause of pain has been identified, a prescribing practitioner should attempt the various nonopioid agents that are available. Recent research has produced several new analgesic drugs to go with some older agents, and these should be attempted before opioids are prescribed. See ***Table***.

Agents to Rx Before Opioids Are Used

- NSAIDS
- Duloxetine (Cymbalta®)
- Pregabalin (Lyrica®)
- Tramadol (Ultram®)

If the agents listed in this table are not effective in controlling pain, it is appropriate to add or substitute a Schedule III or IV opioid. These include opioids that may contain acetaminophen, such as propoxyphene, hydrocodone, codeine, and dihydrocodeine. The addition of acetaminophen potentiates the opioid's pain-relieving capability and reduces its abuse potential, since it is difficult to inject, ignite, or nasally inhale acetaminophen. Mixed agonist-antagonist preparations – including nalbuphine, butorphanol, buprenorphine, and pentazocine – are sometimes excellent pain relievers and have relatively low abuse potential.

There are some patients with severe chronic pain who will require the use of long-term Schedule II opioids, such as methadone, morphine, oxycodone, oxymorphone, or hydromorphone. These agents should only be prescribed by practitioners who have a well-structured pain-treatment program as part of their regular practice or as their sole practice. Why? The initial evaluation of these patients may require 1 to 3 hours and extensive record-keeping. Patients needing ongoing Schedule II opioids also require regular clinic visits for monitoring of complications and compliance.

A Commonsense Conclusion

The clinical benefits of opioid treatment dwarf the clinical risks.

Only opioids can effectively treat significant pain resulting from surgery, injury, and certain disease processes. The idea that there are meaningful alternatives in many clinical situations is nonsensical, since opioids are the only class of drugs that can directly enhance the body's natural endorphin system. Opioids have many detractors, reflecting a variety of economic and emotional biases. Common sense, however, dictates that all physicians, along with their clinical allies and the general public, need to reject the opioid naysayers and their campaign to under-treat pain. Currently, misuse of opioids by persons failing to take the medications as prescribed is resulting in some high profile media cases that are giving opioids an unwarranted negative image. The clinical benefits of opioid treatment, however, dwarf the clinical risks.

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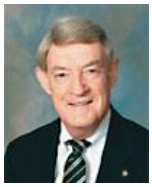

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