

Treatment of Chronic Pain in the Elderly in the Era of the Opioid Crisis: Implications for our Vulnerable Elders

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Objectives

- Describe the scope of and problems associated with detection and management of chronic pain in the elderly, especially nursing facility nursing residents
- Identify appropriate and inappropriate choices in the pharmacologic approach to management of pain in the elderly, including the appropriate use of opioids in the era of the "opioid crisis"
- Formulate an appropriate plan for management of pain in the elderly that encompasses both pharmacologic and non-pharmacologic interventions
- Discuss potential adverse consequences to elderly nursing facility residents of the CDC guidelines and societal initiative to reduce opioid prescribing

Epidemiology of Pain

- Pain is the most common reason for office visit
- 64-78% of independent elderly with current pain complaint
- Musculoskeletal largest category of pain
- Physicians have generally done poor job of adequately treating chronic pain
- Enormous consequences of unrelieved pain

Persistent Pain is Prevalent in the Elderly

- As many as 50% of community-dwelling elderly with chronic pain disorder (pain on most days for > 3 months)
- >80% of older adults with OA take daily OTC or Rx pain meds
- 59% of community dwelling older adults with chronic pain of diverse causes report routine use of analgesic
- Substantial literature documents chronic pain under detected and undertreated with advancing age

Pain in the Nursing Facility

- 49-84% prevalence of persistent pain in various populations
- 66% with intermittent pain, 34% with constant pain
- 55% with intermittent pain have daily pain
- Pain is inconsistently and often inadequately managed, typically just with prn acetaminophen
- Only 15% have had medication in last 24 hours
- Some evidence of improvement in recent years

Pain in the Nursing Facility

- Largest category of pain: musculoskeletal
- Low back (40%), arthritis (24%), previous fracture site (14%), foot (8%), neck (6%)
- Other sources: neuropathies (11%), leg cramps (9%), claudication (8%), headache (6%)
- Cancer only 3% but source of some of most severe pain encountered in NF

Consequences of Unrelieved Pain in Older Adults

- Impaired ability to enjoy activities
- Impaired ambulation
- Sleep disturbances
- Depression
- Decreased socialization
- Deconditioning, falls, slow rehabilitation
- Malnutrition
- Increased health care utilization and costs

Difficulties in Detection and Treatment of Pain in Elderly and NF

Heterogeneous population in many NFs

- Short stayers: differing needs
 - Hospice/end of life care—often needing aggressive palliative care and pain management
 - Rehab to home—often have to deal with post-op pain, possibly mixed with preexisting chronic pain
- Long stayers
 - Many with dementia and susceptible to adverse CNS effects of analgesics
 - Others with advanced age, multiple co-morbidities and physical frailty

Difficulties in Detection and Treatment of Pain in Elderly and NF

Geriatric factors

- Age related changes in drug pharmacokinetics and pharmacodynamics
- Multiple concurrent illnesses and accumulated deficits of disease
- Multiple possible sources of pain
- Multiple medications
- Increased sensitivity to anticholinergic effects of commonly prescribed analgesics
- Increased risk of ADRs

Difficulties in Detection and Treatment of Pain in Elderly and NF

Attitudes and fears of older adults/residents

- Ageist expectation that pain inevitably associated with aging
- May fear meaning of pain
- May think pain cannot be relieved
- Afraid of being labeled a “complainer”
- May fear pain complaint will lead to more testing
- May see others around them as worse off
- May fear if opioid used now it won’t be effective when really needed later
- May quickly reject therapy if adverse effects encountered

Difficulties in Detection and Treatment of Pain in Elderly and NF

Staff and physician factors

- Inappropriate concerns about addiction
- Extra work involved with schedule II drugs
- Concern over regulatory scrutiny
- Poor understanding of differences between tolerance, dependence and addiction
- Inadequate knowledge of pain management principles
- Ageist attitudes
- Misconceptions about elderly pain experience and elderly opioid tolerance
- Failure to inquire directly about pain

Difficulties in Detection and Treatment of Pain in NF Residents

Nursing facility system factors

- Limited access to diagnostic facilities
- Limited staff with different levels of education and responsibility
- Limited on-site pharmacy services and controlled substance storage
- Limited routes of administration for pain medications
- DEA policies unique to NF (nurse as agent issue)

Difficulties in Detection and Treatment of Pain in NF Residents

Research and educational factors

- Limited research in epidemiology of pain in LTC
- Limited research on pharmacokinetics and pharmacodynamics of pain medications in elderly
- Limited research on safety of various pain medications in elderly
- Validity and reliability of pain assessment instruments not well-established in LTC and elderly population in general

Depression and Pain in the Elderly

- Significant association of pain with depression
- Major depression associated with more intense pain and greater number of localized pain complaints
- Association strong even after functional disability and health status controlled for

Pain in Demented NF Residents

- High prevalence of dementia in NF
- Physicians do poor job of identifying persistent pain in demented NF residents
 - 43% of communicative residents
 - 17% of non-communicative residents
- Analgesic drugs used sparingly
- Pain can be assessed using scales tailored to individual disabilities and questions framed in present
- No evidence demented “mask” cognitive deficits with pain complaints; self-report is as valid as in cognitively intact

Misconceptions About Pain and Opioid therapy in Elderly

- Elderly don't experience pain like younger pts
- Elderly can't tolerate side effects of opioids
- Patients will become addicted
- "Weaker" opioids will be tolerated better
- Escalating dosages in advancing pain (cancer) will ultimately lead to respiratory depression and hasten death

Opioid Tolerance

- A state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of a drug's effects over time
- Pharmacologic effect characteristic of all opioids
- Occurs rapidly to sedation, more slowly to nausea and vomiting, very slowly if at all to analgesic effect in stable adequately treated pain
- No tolerance to constipation
- Need for increasing dose in previously stable chronic pain usually indicates disease progression, worsening pain—particularly common in cancer pain

Opioid Dependence

- A state of adaptation that 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
- Neuro-pharmacologic property of all opioids
- Occurs with regular opioid dosing > 1 week
- Not a sign of addiction, but can coincide with addiction
- Withdrawal a sign of mismanagement of opioid therapy, either by physician or patient
- When pain gone, most patients have no lingering desire for drug

Opioid Addiction

- A primary, chronic, neurobiologic 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.
- Rare in chronic pain patients without prior history of substance abuse disorder
- Always associated with decreased functionality

Opioid Pseudoaddiction

“In the setting of undertreated pain, some patients develop aberrant behaviors that may be quite similar to those associated with addiction. When the pain is relieved, the behaviors cease and opioids and other drugs are used responsibly.”

Weisman and Haddox (1989)

Categories of Pain

- Nociceptive
- Neuropathic
- Bone
- Psychogenic?

Nociceptive Pain

- **Somatic**
 - Localized
 - Observable tissue injury often evident
- **Visceral**
 - Deep, aching, cramping
 - Often associated with stretching of organ capsule

Bone Pain

- Subset of nociceptive pain
- Prostaglandin mediated
- Often seen in metastatic cancer pain
- NSAIDs and steroids often effective

Neuropathic Pain

- Often described as burning, tingling, shooting, stabbing, electrical
- Often radicular
- Radiculopathies
- Diabetic and other peripheral neuropathies
- Post-herpetic neuralgia
- Pain may exceed observable injury
- Less responsive to typical analgesics

Post Herpetic Neuralgia

- Dermatomal pain persisting >120 days after onset of HZ rash
- Stimulus-dependent burning, throbbing, electric shock-like sensation, hyperalgesia
- >90% have tactile allodynia
- Key is prevention by early treatment with antiviral agents—start w/in 72 hours of rash onset
- Acyclovir may have benefit for prevention of PHN even if given after 72 hours of rash onset

Acute Pain

- An adaptive, beneficial response necessary for the preservation of tissue integrity
- Usually nociceptive
- Severity usually correlates well with demonstrable tissue pathology
- Sympathetic signs often present
- Easier to detect and assess

Persistent (Chronic) Pain

- Pain that has outlived its usefulness
- Any type; often becomes regionalized
- Severity correlates poorly with demonstrable tissue pathology
- Sympathetic signs usually absent
- Assumes emotional dimension
- Frequently disrupts sleep, interpersonal and family relations, work
- More difficult to detect and assess

Evaluation of Pain

- Obtain full description of pain: “PQRST”
 - P alliative or provocative factors
 - Q uality of pain
 - R adiation of pain
 - S everity of pain
 - T emporal factors

Evaluation of Persistent Pain

- Functional evaluation
- Sleep history
- Psychosocial effects
- Assess for depression
- Assess for associated health concerns (substance abuse/addiction history, smoking)
- Physical exam: focus on ms and nervous systems
- Limited, but appropriate diagnostic evaluation
- Treat pain while proceeding with workup

Pain Scales in Older Adults

- Numeric rating scale and verbal descriptor scale preferred in older adult population
- Numeric rating scale: patient rates pain on 0-10 scale; 0 = no pain; 10 = most severe pain imaginable
- Verbal descriptor scale (“pain thermometer”): vertical scale from “no pain” to “excruciating”
- Use same scale each pain assessment

Goals of Pain Management

A delicate balancing act in the elderly:

- Relief of pain
- Preservation or restoration of function
- Avoidance of adverse effects of treatment

Pharmacotherapy: Nonopioids

Acetaminophen

- Good safety profile
- Few adverse effects
- Effective in chronic osteoarthritis
- Low ceiling effect
- Narrow therapeutic window: hepatotoxicity with doses > 4 gm/day
- In elderly, avoid doses > 2.6 gm/day chronically
- Cumulative dose-dependent risk for ESRD
- Initial and ongoing choice in elder persistent pain

Pharmacotherapy: Nonopioids

NSAIDs

- Prostaglandin inhibition + central effects
- Effective for bone pain, inflammation
- Low ceiling effect
- High incidence of adverse effects, more common in elderly

NSAID Adverse Effects

- Renal effects: reversible renal dysfunction; Na and fluid retention
- CV risks (dose dependent): exacerbation of CHF; worsening of hypertension; increased risk of atrial fibrillation/flutter; increased risk of stroke, MI, post MI reinfarction and death
- Implicated in 25% of ADRs resulting in hospitalization > age 65
- Cox-2 inhibitors may have somewhat better GI safety profile, other adverse effects same as other NSAIDs
- Increased risks present even with short term use of NSAIDs

NSAID GI Complications

- 16,500 deaths/year*
- 103,000 serious GI events/year**
- 60-80% of hospitalized patients had no prior GI events
- 13 fold increase in risk for hemorrhagic PUD when used concomitantly with warfarin

*Singh, G., Am J Ther 2000;7:115-121
**Singh, G., J Rheumatol. 1998;25 (suppl 51):8-16

Pharmacotherapy: Opioids

- Relieve all types of pain
- No ceiling effect
- Elderly more sensitive, longer half life
- High potential for adverse effects in frail elderly
- Regular dosing best in persistent pain
- Mu agonists drugs of choice in persistent pain

Opioid Adverse Effects

- No major organ toxicity
- Respiratory depression antagonized by pain
- Rapid tolerance to cognitive effects (drowsiness, dysphoria) with regular dosing
- Anticholinergic effects: cognitive impairment may not show tolerance effect
- Slower tolerance to nausea/vomiting
- No tolerance to constipation—use stimulant laxative from outset
- Switching opioids may be effective
- Claims study indicates opioids may be associated with increased risk of falls w/fractures, safety events w/hospitalization, all cause mortality c/w NSAIDs

Management of Opioid-Induced Nausea and Vomiting

- Prevent or treat with dopamine-blocking antiemetics
 - Prochlorperazine 10 mg. q 6h
 - Haloperidol 1 mg. q 6h
 - Metoclopramide 10 mg. q 6h
 - Olanzapine 2.5 mg. daily
- Other antiemetics often effective
- Alternative opioid if refractory

Management of Opioid-Induced Constipation

- Occurs with all opioids, no convincing evidence of superiority of any opioid
- Etiology: opioid effects on CNS, spinal cord, myenteric plexus of gut
- Must use stimulant laxative +/- softener
- Easier to prevent than treat

Management of Opioid-Induced Urticaria and Pruritis

- Etiology: mast cell destabilization
- Can occur with any opioid
- Not an allergic reaction (not IgE mediated)
- Try treating with routine long-acting non-sedating antihistamine—variable response
 - Fexofenadine 180 mg po daily
 - Cetrizine 10-20 mg po daily
 - Loratadine 10-20 mg po daily
- Often switch to another opioid effective

Opioid-Induced Androgen Deficiency

- Common, often overlooked, consequence of long-term opioid therapy
- Mechanism: central suppression of hypothalamic-pituitary-gonadal axis
- Much more clinically significant in men
- Symptoms same as primary male hypogonadism
- All opioids in all forms probably pose same risk
- Diagnose in elderly men with bioavailable testosterone (free + weakly bound)
- Treatment same as for primary male hypogonadism

Opioid Selection: Considerations

- Cost
- Rapidity of pain relief
- Oral route preferred
- Minimize side effects
- Convenience
- Presence of active or neurotoxic metabolite, esp. with elderly or renal insufficiency
- SR/long acting forms vs. short acting

Opioid Selection

- **Short-acting**
 - Incident or breakthrough pain
 - To permit activity, e.g. PT
 - Exacerbations of pain
 - Initial choice for opioid therapy
- **Long Acting**
 - Persistent moderate to severe pain
 - Baseline analgesia
 - Avoidance of acetaminophen toxicity from high dosages of combination opioids

Short-acting Opioids

- **Combination opioids**
 - Hydrocodone, codeine, oxycodone combined with acetaminophen, occasionally ibuprofen
 - Dosing limited by non-opioid ingredient
- **Single entity opioids**
 - Oxycodone
 - Morphine
 - Hydromorphone
 - Oxymorphone
 - Fentanyl buccal

Long-acting Opioids

- All are single entity opioids
- Sustained-release morphine
- Sustained-release oxycodone
- Methadone
- Transdermal fentanyl
- Transdermal buprenorphine

Benefits of Long-acting Opioids

- More reliable round-the-clock pain control
- Better overall pain control
- Improved convenience and compliance
- More rapid tolerance to cognitive side effects and nausea
- No maximum dose of single entity opioids

Opioid Metabolism/Elimination Considerations in the Elderly

- Most elderly have diminished renal function
- For chronic pain avoid opioids with active metabolites, esp neurotoxic metabolites—will accumulate with regular dosing in face of renal insufficiency
- Morphine has active, non-neurotoxic metabolite; will accumulate in renal insufficiency; use with caution
- Fentanyl and methadone have no active metabolites and can be used in mild to moderate renal insufficiency, but have other limitations

Opioid Metabolism/Elimination Considerations in the Elderly

- Oxycodone has no clinically significant active metabolites; with long and short acting forms and generic availability is considered by many drug of choice in elderly, esp with mild-mod renal insufficiency
 - Reduce dose and increase dose interval with severe renal insufficiency due to reduced elimination of parent drug
- Transdermal buprenorphine
 - Metabolized in liver and excreted in feces—can be used even in severe renal insufficiency
 - Reduced risk respiratory depression c/w other opioids due to ceiling effect on respiratory depression, but not analgesia
 - Only long acting opioid in DEA Schedule III

Opioids Not Recommended for the Elderly

- Codeine
 - High incidence of adverse effects relative to analgesia
 - Efficacy dependent on presence of CYP2D6 enzyme
- Meperidine
 - Active, neurotoxic metabolite accumulates rapidly; common cause of delirium, can cause seizures
 - Oral form much less effective; short duration of action

Opioids Not Recommended for the Elderly

- Tramadol
 - Weak opioid, partial antagonist, yet significant withdrawal syndrome
 - Responsible for 27,000 ER visits/year
 - Lowers seizure threshold
 - Risk of serotonin syndrome, esp with SSRIs and SNRIs
 - Risk of hypoglycemia
 - Risks greatest in elderly

Opioids Cautiously Recommended for the Elderly

- Methadone
 - Complex metabolism with biphasic elimination, slower in elders
 - High risk of accumulation; difficult to use unless very familiar and experienced with this drug
 - Good and inexpensive choice for younger patients
 - Can be used in elderly with appropriate caution
- Agonist-antagonist drugs
 - Most have ceiling effect on analgesia
 - High incidence of CNS effects

Opioid Dosing for Chronic Pain in Elders

- Determine whether patient is opioid naïve
- Usually start with low dose short acting single entity or combination opioids if opioid naïve
- Dose on schedule, slowly increase dosage to best clinical effect with tolerable side effects
- “Start low and go slow” does not mean “start low and stay low;” often leads to undertreatment
- Use equianalgesic conversion tables to convert between opioids; reduce dose 25-50% initially (methadone up to 90%)

Opioid Dosing in Chronic Pain

- When converting from maximum doses of fixed opioid combinations, usually start with
 - Oxycodone CR 20 mg q 12 hr
 - Morphine SR 30 mg q 12 hr or 50-60 mg q 24 hr
- If pain was not controlled on previous regimen, increase above by 25-50%

Opioid Dosing in Chronic Pain

- Provide rescue dose of immediate release form of opioid equal to 10-15% of 24 hour base dose q 3-4 hr.
- Assess pain at frequent intervals, daily if cancer pain
- Increase dose 25-50% if pain not controlled
- Titrate to best control of pain with acceptable side effects
- Assess for and manage opioid adverse effects regularly
- No maximum dose of single entity opioid

Adjuvant Drugs for Neuropathic Pain

- Antidepressants
 - Tricyclics
 - SNRIs (duloxetine in diabetic neuropathy)
- Anticonvulsants
 - Gabapentin and pregabalin FDA approved for PHN
- Antiarrhythmics
- Capsaicin
- Opioid therapy often needed, usually at least partly effective

Tricyclic Antidepressants in Neuropathic Pain

- Inhibit pain neurons by prolonging synaptic activity of norepinephrine and serotonin
- More selective NE inhibitors more effective (amitriptyline, imipramine)
- Dose 10-50 mg @ hs; response 4-7 days
- Significant adverse effects, esp. in elderly
- Strongly anticholinergic
- Desipramine as effective as amitriptyline in diabetic neuropathy, better tolerated

Duloxetine in Diabetic Neuropathy

- FDA approved (also for fibromyalgia)
- Better tolerated than tricyclics
- Mechanism of action probably same as tricyclics
- Use antidepressant doses: 60 mg best

Anticonvulsant Drugs in Neuropathic Pain

- Alter perception of pain centrally
- Especially effective in trigeminal neuralgia
- Carbamazepine and gabapentin mainstay; generic
 - Adverse effects: ataxia, dysphoria, sedation, esp. in elderly
- Gabapentin: no protein binding, excreted unchanged in urine, minimal if any interactions
- Pregabalin indicated for diabetic neuropathy, post-herpetic neuralgia, fibromyalgia
 - Similar pharmacokinetics to gabapentin
 - Generally well-tolerated, but expensive

Adjuvant Drugs for Bone Pain

- NSAIDs: major agent
 - Long term use associated with significant adverse effects, esp. in elderly
- Corticosteroids
 - Bone and spinal cord compression pain
 - High rate of adverse effects
- Calcitonin nasal spray
 - Analgesic activity in osteoporotic compression fxs
- Opioid therapy often needed in addition

General Principles of Pharmacotherapy for Persistent Pain

- Establish a reasonable plan of treatment
- Use long acting analgesics for daily pain
- Prevent pain by routine analgesia, avoid prn dosing in persistent pain
- Use short acting analgesics for breakthrough pain or prior to painful activities
- Be alert for adverse effects

What About the CDC Guideline?

- CDC issued Guideline for Prescribing Opioids for Chronic Pain in 2016
- Reaction to opioid crisis in the country with significant rise in opioid misuse and overdose deaths
- Provides recommendations for PCPs prescribing opioids for chronic pain *outside of active cancer treatment, palliative care, and end of life care*
- Recommend non medication and non-opioid medication therapy over opioid therapy.

Is the CDC Guideline Appropriate for Elderly, NF?

- Opioid misuse rates rising among elderly, but still fraction of rate in younger adults (2% vs 8%)
- Elders with opioid use disorders (OUD) are more likely to die from their chronic illnesses than drug-related causes, c/w younger adults with OUD
- CDC study recently showed 67% of drug-related hospitalizations in elders caused by anticoagulants, insulin, antiplatelet drugs and oral hypoglycemics; far exceeded rate for opioids.
- OUD much less problem in NF where dosing monitored and controlled

Implications of CDC Guideline for Elders with Chronic Pain

- Many elders, esp NF residents, with chronically painful conditions being well managed with well tolerated judicious (palliative) opioid therapy
- With pressure from CMS, insurers, regulatory agencies, pharmacies, foreseeable response by many providers will be to limit or deny such elders opioids that have been controlling their pain, resulting in worsened pain, or possibly substitute more dangerous analgesics and alternatives, such as high dose acetaminophen, tramadol, NSAIDs, TCAs, anticonvulsants

Nonpharmacologic Pain Management Strategies

- Physical modalities: heat, cold, massage, PT
- TENS
- Psychologic maneuvers and CBT: effective, but generally not suitable for cognitively impaired
- Activities programs: may decrease perception of pain, avoid depression and worsening of pain caused by inactivity and immobility
- Combining pharmacologic and nonpharmacologic pain management strategies found to enhance pain relief for many elders
- Limited RCT trials of nonpharmacologic measures in elderly persistent pain

Invasive Therapies

- Acupuncture
- Trigger point injections
- Epidural steroid injections and nerve blocks
- Opioid infusions and PCA pumps
- Epidural morphine pump
- Spinal cord stimulators
- Nerve ablation

Role of Coordination of Care

- Medical home model
 - PCP/NF attending takes responsibility for coordination of pain management
 - Takes into account complex needs of elderly with persistent pain
 - Multidisciplinary approach to formulate appropriate and effective for the individual
 - Coordination of pharmacologic and nonpharmacologic therapies, specialist referrals

What About the Regulatory Agencies?

1990s: Pendulum Began to Swing

- APS and AAPM consensus statement “The Use of Opioids for the Treatment of Chronic Pain” (1996)
- Federation of State Medical Boards’ “Model Guidelines for the Use of Controlled Substances for the Treatment of Pain” (1998)
- State initiatives: Intractable Treatment Acts (1990s)
- State Medical Boards began issuing guidelines for opioid prescribing in chronic nonmalignant pain based on Federation Model Guidelines

Missouri Initiatives

Missouri’s Intractable Pain Treatment Act (1995)

- Defines “intractable pain” and “therapeutic purpose”
- Physician may not be disciplined solely for prescribing controlled substances for therapeutic purpose to person with intractable pain
- Drug dependency not a reason to withhold opioid prescribing
- Does not protect nontherapeutic or careless prescribing

Missouri Initiatives

- MO State Board of Registration for the Healing Arts issued "Guidelines for the Use of Controlled Substances for Pain" (2004)
 - Based on Federation's Model Guidelines
 - Board encourages physicians to view pain management as part of quality medical practice for all patients with pain, acute or chronic
 - Appropriate pain management is the treating physician's responsibility
 - Inappropriate treatment of pain includes nontreatment, undertreatment, overtreatment, and continued use of ineffective treatments
 - Board will consider the inappropriate treatment of pain to be a departure from standards of practice and will investigate such allegations

Conclusions

- Persistent pain is prevalent in elderly and NF residents
- Many barriers exist to recognition and effective treatment of pain in elderly and NF residents
- Despite these barriers most pain in elderly and NF residents can be managed effectively
- Opioids are mainstay of pharmacologic pain management for more severe persistent pain
- Caution and appropriate selection must be utilized with opioid therapy in elders
- Effective pain management requires coordinated approach utilizing pharmacologic and nonpharmacologic interventions
