ECHO Idaho: Behavioral Health in Primary Care

Management of Chronic Non-Cancer Pain in Older Adults without Opioids and Tramadol: the ATMAN approach

September 4, 2019
Abhilash K. Desai MD
Psychiatrist
Dr.abhilashdesai@icloud.com
Financial Disclosures


• I have no other financial relationships with commercial interests to disclose.
Learning Objectives

• Describe risks of opioids and tramadol in older adults.

• Discuss potential risks and benefits of various psychopharmacological agents commonly used to manage chronic non-cancer pain in older adults.

• Discuss non-pharmacological interventions for management of chronic non-cancer pain in older adults.
Pre-Test

• Question 1: All of the following statements about chronic pain in older adults are true except:
  – (a) After diabetes, chronic pain is the most common medical condition
  – (b) It is a significant cause of depression and disability.
  – (c) It is commonly under-treated or mistreated.
  – (d) Research to date does not support use of opioids and tramadol for treatment of chronic pain
Pre-Test

• Question 2: Which two pain assessment tools and strategies are reliable in older adults with mild dementia?
  – (a) PAINAD and Doloplus 2
  – (b) Verbal descriptors and PAINAD
  – (c) PAINAD and Numerical rating scale
  – (d) Numerical rating scale and verbal descriptors
Pre-Test

• Question 3: Allodynia is:
  – (a) experiencing more severe pain from stimuli that would normally be only mildly painful
  – (b) experiencing pain from stimulus that would normally be nonpainful
  – (c) abnormal nonpainful sensation that is either spontaneous or evoked
  – (d) pain that reflects tissue injury
Pre-Test

• Question 4: Opioid use is associated with all of the following risks except?
  – (a) hypogonadism
  – (b) intoxication delirium
  – (c) withdrawal delirium
  – (d) hyperalgesia
Pre-Test

• Question 5: Which analgesic is associated with significant drug-drug interaction risk with many psychopharmacological agents through the 2D6 and 3A4 liver enzyme system?
  – (a) hydrocodone
  – (b) tramadol
  – (c) duloxetine
  – (d) acetaminophen
Pre-Test

• Question 6: Which of the following non-pharmacological interventions has best research support for chronic non-cancer pain management?
  – (a) hot and cold remedies
  – (b) massage
  – (c) cognitive behavioral therapy
  – (d) music therapy
  – (e) mindfulness and meditation
Pre-Test

• Question 7: Which of the following topical analgesics is associated with burning?
  – (a) diclofenac
  – (b) menthol
  – (c) lidocaine
  – (d) capsaicin
  – (e) cannabidiol
Pre-Test

• Question 8: Which of the following agents used to manage neuropathic pain is approved for treatment of generalized anxiety disorder in Europe but not in US?
  – (a) duloxetine
  – (b) venlafaxine
  – (c) gabapentin
  – (d) pregabalin
  – (e) desvenlafaxine
NIDA director Nora Volkow M.D.

• During a brief hospital stay following a car accident, Dr. Volkow received Demerol (meperidine) for her pain. She stopped taking it when she came home and went into withdrawal (severe restlessness etc.). She knew that body becomes biologically dependent on opioids quickly but "I ignored all my knowledge about opioids and became ill."
Chronic Pain

• Complex experience with physical, emotional, cognitive and spiritual/existential dimensions.
• Up to one in five adults (up to 50% older adults; up to 75% with advanced cancer) may have chronic pain.

Chronic Non-Cancer Pain in Older Adults

• More common than diabetes, heart disease and cancer combined.

• Common cause of depression, agitation, insomnia and decline in ability to do activities of daily living.

• Generally under-treated and or inappropriately treated with opioids and tramadol.

Pain Assessment

- Comprehensive assessment (ideally part of Comprehensive Geriatric Assessment [CGA]): Goal is to identify all specific pain sources.
- Pain scales (e.g., numeral rating scale and verbal descriptors [also okay in mild-moderate cognitively impaired individuals], Pain In Advanced Dementia [PAINAD] and Doloplus-2 recommended for severe cognitive impairment).

Key Terms

• Nociceptive pain (occurs with tissue injury)
  – Somatic, visceral
• Neuropathic pain (caused by abnormal functioning of nervous system)
  – Peripheral, central
• Allodynia: experiencing pain from stimulus that would normally be nonpainful
• Hyperalgesia: experiencing more severe pain from stimuli that would normally be only mildly painful
• Paresthesia: abnormal nonpainful sensation that is either spontaneous or evoked.

Why should we avoid opioids?

- Lack of high-quality studies supporting effectiveness of opioids for chronic non-cancer pain in older adults
- High risks: respiratory suppression, overdose related death, intoxication delirium, dependence, tolerance, withdrawal effects (does not cause withdrawal delirium), addiction, abuse, diversion, falls and serious injuries (e.g., fractures, TBI), hypogonadism, hyperalgesia, allodynia, cognitive impairment, adverse drug interactions, and other adverse effects (e.g., constipation, pruritis, day-time somnolence, agitation in individuals with dementia, depression, dysphoria/irritability, hallucinations in individuals with dementia).

---

Why should we avoid opioids?


- Use of opioids for management of chronic (more than three months) non-cancer pain should be restricted to intractable pain that is not adequately managed with conservative and interventional methods (American Society of Pain Medicine http://www.painmed.org/files/use-of-opioids-for-the-treatment-of-chronic-pain.pdf).
Why should we avoid opioids?

- Current guidelines discourage use of opioids for chronic pain.
- No RCTs (except Krebs 2018 JAMA study) on effect of opioids on long-term pain, function or quality of life.

- VA Guidelines on Opioids for Chronic Pain
  https://www.healthquality.va.gov/guidelines/Pain/cot/VADoDOTCPG022717.pdf
Why should we avoid opioids?

- Opioids did no better (in terms of function) than non-opioid analgesics for chronic moderate to severe osteoarthritis pain (knee, hip) and back pain. Adverse effects were significantly more common in opioid group compared to nonopioid group. Pain intensity less in acetaminophen-NSAIDs group. Mean age: 58 years.

Why should we avoid opioids?

• Nonopioid group: Step 1: acetaminophen and NSAID. Step 2: adjuvant oral (nortriptyline, amitriptyline, gabapentin) and topical (capsaicin, lidocaine). Step 3: pregabalin, duloxetine, tramadol.

Why should we avoid opioids?

- The 2019 Beers criteria recommends to avoid use of opioids in older adults with history of falls or fractures except for pain management in setting of severe acute pain (e.g., recent fractures or joint replacement). Level of Evidence: Moderate. Strength of Recommendation: Strong.

Why should we avoid opioids?

- The 2019 Beers criteria recommends to avoid simultaneous use of opioids and gabapentinoids (gabapentin, pregabalin) in older adults because of severe sedation-related adverse effects including risk of respiratory suppression or death. Level of Evidence: Moderate. Strength of Recommendation: Strong.

- Exceptions: When transitioning from gabapentinoids to opioids or when using gabapentinoids to reduce opioid dose although caution is advised in all circumstances.

Opioid Use Disorder in Older Adults

• First-time treatment admissions for heroin and prescription opioid use disorder has increased in the last decade.

• Medication-Assisted Treatment (MAT) use (naltrexone, buprenorphine, methadone) is low (7-9%) in older adults with OUD.

Why should we avoid tramadol?

- Lack of high-quality studies supporting effectiveness of opioids and tramadol for chronic non-cancer pain in older adults
- High risks (although lower than opioids): risks similar to opioids as it is a partial mu receptor opioid agonist but risks lower than opioids; drug-drug interaction risks (especially with antidepressants); dizziness in more than 10% of cases. Higher risks in patients with chronic kidney disease.
- Check out the podcast by pharmacist and internist Dr. David Juurlink: https://www.geripal.org/2018/06/Tramadont-dangers-of-tramadol.html

Why should we avoid tramadol?

• Tramadol use is associated with significant risk of adverse drug-drug interactions with many psychopharmacological medications through 2D6 and 3A4 liver enzyme system posing serious risks (e.g., serotonin syndrome, seizures) (https://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020281s032s033lbl.pdf).

• There is little evidence for use of tramadol for management of pain for more than three months (http://www.who.int/medicines/areas/quality_safety/6_1_Update.pdf).
Why should we avoid tramadol?

- Seizures reported within the recommended dose range.
- Seizure risk higher in individuals with history of seizure, with conditions that increase risk of seizure (e.g., stroke, TBI), and with medications that also increase risk of seizure (e.g., bupropion).
- Interaction with 2D6 inhibitors: diphenhydramine, haloperidol, cimetidine, sertraline, paroxetine, fluoxetine.

Why should we avoid tramadol?

• 2D6 rapid metabolizers: 1-10% Caucasians, 3% African Americans, 1% Hispanics and Asians.
• Orthostatic hypotension may occur in older adults.
• Tramadol use is associated with SIADH / hyponatremia.

ATMAN approach

- A: Acetaminophen, Anti-depressants
- T: Topical analgesics
- M: Muscle relaxants
- A: Anti-convulsants, Anti-inflammatory agents
- N: Non-drug interventions
Acetaminophen

• Despite lack of RCT support, it is generally considered first line agent for mild to moderate chronic musculoskeletal pain.
• A 2014 Lancet study: no better than placebo for acute low-back pain
• A trial of acetaminophen may be considered in patients with dementia and agitation/insomnia

Anti-depressants - TCAs

- Tri-cyclic antidepressants: imipramine, amitriptyline, nortriptyline, desipramine (neuropathic pain, chronic headaches). Nortriptyline and desipramine preferred over amitriptyline and imipramine in older adults.
- Significant anti-cholinergic and cardiac toxicity. Hence, minimize its use in older adults. Safer alternatives available.

Anti-depressants - SNRIs

• Selective Serotonin Norepinephrine Reuptake Inhibitors for chronic pain management: duloxetine, milnacipran, levomilnacipran
• Milnacipran and Levomilnacipran: Approved by the FDA for treatment of fibromyalgia.
• Levomilnacipran (an enantiomer of milnacipran) is also approved by the FDA for treatment of depression.
• Note: Venlafaxine and desvenlafaxine are also SNRIs (venlafaxine at doses up to 150mg per day is only an SSRI and becomes an SSRI at higher doses) but do not have high-quality research to support their use for management of chronic pain in older adults.

Anti-depressants - Duloxetine

- Duloxetine: medication of choice for chronic non-cancer pain
- Approved by the FDA for diabetic neuropathic pain, fibromyalgia, chronic low back pain, osteoarthritis pain
- First line treatment for neuropathic pain.
- Not recommended if creatine clearance less than 30.
- Rapid onset of action (separation from placebo beginning at week 1)
- Well studied in older adults with depression.

---

Anti-convulsants

• Gabapentin: neuropathic pain
• Pregabalin: neuropathic pain, fibromyalgia; schedule V; at doses of 150mg it was generally ineffective
• Valproate: migraine
• Carbamazepine: trigeminal neuralgia
• Lamotrigine: HIV-related neuropathy, central poststroke pain

Gabapentinoids

- Gabapentin: postherpetic neuralgia
- Pregabalin: diabetic neuropathy and spinal cord injury, postherpetic neuralgia, fibromyalgia
- “Clinicians who prescribe gabapentinoids off label for pain should be aware of the limited evidence and should acknowledge to patients that potential benefits are uncertain for most off-label use” (Goodman and Brett 2019)

---

Anti-inflammatory agents - NSAIDS

- NSAIDs: ibuprofen, naproxen, meloxicam.
- Due to cardiovascular (heart attacks, strokes) and renal toxicity risks besides gastrointestinal bleeding, their use for chronic non-cancer pain is limited and hence, their chronic use should in older adults should be minimized.
- Meloxicam may be considered in some patients as it has lower gastrointestinal bleeding risk compared to other NSAIDs.
- May need to use misoprostol or high-dose H2 antagonists or PPIs to reduce risk of GI bleed.

Anti-inflammatory agents - Celecoxib

- Cox-2 inhibitor Celecoxib also has risks similar to NSAIDs but lower likelihood of adverse events compared to NSAIDs.
- It may be considered in some older patients for short term use.

Anti-inflammatory agents

- Avoid in patients taking aspirin for cardiovascular protection due to increased risk of GI bleed and interference with aspirin’s anti-platelet effect.
- Avoid in patients receiving anticoagulant therapy.
- Avoid in patients with chronic kidney disease (creatinine clearance less than 30) and compromised liver function.
- Require close clinical and laboratory monitoring (e.g., CBC, renal function, liver function)

Topical analgesics

- Lidocaine patch (5% [only prescription], 4% [available OTC]): post-herpetic neuralgia, other neuropathic pain, occasionally helpful for musculoskeletal pain; on for 12 hours, off for 12 hours. Up to 3 patches.
- Capsaicin: Alkaloid derived from chili peppers (0.025%; 0.075%). Try higher strength for 6 weeks before declaring treatment failure. Causes initial burning sensation; so best used in combination with menthol. Avoid touching eyes.
- Menthol
- Cannabidiol (CBD)

Topical NSAIDs

• OTC methyl salicylate,
• Diclofenac gel [2g tid/qid, may increase to 4g qid). Max for single joint: 8g. Avoid use in combination with aspirin or other NSAIDs. Periodic transaminase monitoring recommended for chronic use.
• Diclofenac: also available as topical patch, solution, spray.

Muscle relaxants

- Baclofen (pills, baclofen pump): spasticity (e.g., in patients with Multiple sclerosis)
- Tizanidine
- Cyclobenzaprine (some evidence supporting its use in fibromyalgia; best studied muscle relaxant in musculoskeletal disorders; 5mg tid as effective as 10mg tid)
- Carisoprodol, dantrolene, methocarbamol, chlorzoxazone, orphenadrine
- In older adults, all muscle relaxants carry significant risk of falls, cognitive impairment, mood changes, and delirium. In individuals with dementia, they may cause agitation.
- Baclofen, tizanidine, cyclobenzaprine are preferred over other agents.
- Start low, go slow.

Neuropathic pain

- First-line agents: gabapentin, pregabalin, duloxetine, lidocaine patch.
- Second-line agents: desipramine, nortriptyline (in younger adults, these could be first-line agents), capsaicin high concentration
- Third-line agents: carbamazepine

Cannabidiol (CBD)

• Preliminary evidence has found beneficial effects of CBD for pain management.
• There are potentially serious safety risks with all supplements including CBD due to possible contaminants because U.S. Food and Drug Administration does not regulate over-the-counter supplements with the same rigor as prescription medications.
• Furthermore, some CBD products that claim to be from industrial hemp (defined as Cannabis sativa with a THC content of less than 0.3% per dry weight) may contain much higher amounts of THC. Some CBD products may have much less CBD than what they claim.

Cannabidiol (CBD)

- Three consecutive days of oral CBD solution (400mg and 800mg) significantly reduced cravings and anxiety induced by drug cues in individuals with heroin addiction compared to placebo.
- No significant adverse effects.

Cannabidiol (CBD)

- CBD inhibits THC-induced paranoid symptoms and hippocampal-dependent memory impairment.
- Cannabis users report that strains with a high amount of CBD (especially if quantity of THC is low) will be less intoxicating than a strain with low concentration of CBD and high concentrations of THC.

THC

- Dronabinol, nabilone, and medical marijuana have been found some effectiveness for neuropathic pain and pain associated with multiple sclerosis.
- A retrospective chart review of 81 patients (Mechter 2018, NY) found medical cannabis safe and effective for pain management in older adults with 32% reducing their opioid use.
- A study of more than 3000 subjects found medical cannabis useful in patients with cancer pain (Abuhashira 2018)

  - Laszlo Mechter MD. American Academy of Neurology May 2018 meeting.
THC

• THC is a high risk medication in older adults, as it may cause delirium, psychotic symptoms, severe agitation and aggression, and panic attacks. Until more research becomes available, its use in older adults should be minimized and when used, the patient should be closely monitored for adverse events.

• Short-term risks also include impaired judgment and cognitive impairment (so increased risk of driving accidents)

• Long-term risks include permanent cognitive impairment besides other risks.

‘Dysfunctional Pain’

• Term for pain syndromes that are common, cause considerable distress and disability, have absence of evidence of tissue injury, their etiology/pathophysiology is not well understood, prevalence of childhood trauma, and treatments not very effective.

• Three key syndrome: Fibromyalgia, Irritable Bowel Syndrome, Interstitial cystitis.

• Central Sensitivity Syndrome includes fibromyalgia, chronic tension headaches and myofascial pain and shares similar characteristics.

• Functional somatic syndromes: Fibromyalgia, IBS, Temporomandibular joint disorder, interstitial cystitis

Pain systems

- Evolutionary perspective: pain is a strong motivational signal (indicates threat) with negative affective connotations, while pain relief can be conceptualized as a form of relief and reward, and therefore represent potent factors directing behavior.

Pain systems

• Higher attention and perceiving/framing it as “high-grade threat”: greater catastrophic reactions, pain sensitivity, and avoidance behaviors.
• Avoidance behaviors, once acquired, are notoriously persistent and maintain pain-related fears.
• Distraction and reframing it as “low-grade threat”: reduced intensity of pain experienced.

Nonpharmacological Treatments for Chronic Pain

• Multimodal rehabilitation may be needed in many cases.
• Pain self-management.
• Cognitive Behavior Therapy – Pain (CBT-P) has the best evidence amongst all nonpharmacological interventions for treatment of chronic pain.
• Exercise has the next best evidence.
• Support groups, posture training, music therapy, hot-cold remedies, massage, acupuncture, and mindfulness / mind-body-based approaches (e.g., meditation, gentle movements, Tai Chi, yoga), weight-loss strategies, balneotherapy (spas; hydrotherapy) may provide additional benefits.

CBT-P

- CBT-P is different module than CBT for depression, anxiety, and insomnia (CBT-Depression; CBT-Anxiety; CBT-Insomnia CBT-I)
- Cognitive Therapy (to address unhelpful / counterproductive ABCs [attitudes, beliefs, coping styles] and automatic negative thoughts [ANTs 😞], catastrophizing [“I will never get better,” “This pain will never go away,” Excessive fear that movement or activity will worsen pain]).
- Relaxation training (e.g., deep breathing exercises, progressive muscle relaxation, relaxation response, guided imagery).
- Reinforcing positive health behaviors and positive activities.

Interventional pain management

• Nerve blocks
• Trigger point injections
• Ultrasound or fluoroscopy guided interventions.

Assessment

- Pain prevalence increases with age up to 85 years and then decreases.
- Multidisciplinary approach to assessment and treatment is essential.
- Self-report measures recommended: numeral rating scale (0-10 scale) and verbal descriptors (no, mild, moderate, severe, as bad as it can be) okay in mild-moderate cognitively impaired individuals, Pain In Advanced Dementia [PAINAD] and Doloplus-2 recommended for severe cognitive impairment.
- Presence of depression, social isolation and loneliness need to be assessed.

Treatment

• Interdisciplinary approach
• Primary care providers, nurses, social workers, psychiatrists, psychologists, physiatrists, pharmacists, neurologists, anesthetists.
• Individualized Pain-relieving Activities Schedule (IPAS) that takes into account patient preferences, attitudes, views and beliefs.
• Address comorbidity (e.g., Major depression).

Patient attitude and beliefs

- Belief that pain is a normal part of aging
- Stoicism and pride
- Vocalizing pain is an expression of weakness
- Do not want to seem as a difficult patient, bother busy staff, or be perceived as a medication seeker

Geriatric Pharmacology Principles

• Usual starting dose approximately half of the usual dose
• Raise dose in small increments
• Some may need the full dose (but most don’t)
• Almost all oral analgesics increase risk of falls and injuries (e.g., fractures, head injury)
• Choose drugs with least risk of anticholinergic effects, sedation, postural hypotension, parkinsonism, and drug-drug interactions.
• Response to treatment is less predictable
• Drug-drug and drug-disease interactions prevalent

Role of Consultant Pharmacist

• Referral to consultant pharmacist for medication review to discontinue medications that are inappropriate in older adults (using Beers criteria, STOPP-START criteria) and other medications that may cause or contribute to pain and adverse drug interactions should be done routinely (especially for frail older adults and older adults with dementia).

• Reducing anticholinergic load should also be a routine part of comprehensive chronic pain management plan. Check anticholinergic burden score: www.acbcalc.com. Consider checking information on www.trchealthcare.com (Therapeutic Research Center).

Resources

- The American Chronic Pain Association [https://www.theacpa.org](https://www.theacpa.org).
- September is Pain Awareness Month
- Cleveland Clinic Wellness app (Free): mindful moments by ccw for Guided meditation
- CBTi Coach app (Free): Cognitive Behavioral Therapy for insomnia by Veterans Administration. Free. It has excellent relaxation exercises.
Post-Test Answers Key

• 1: (a)
• 2: (d)
• 3: (b)
• 4: (c)
• 5: (b)
• 6: (c)
• 7: (d)
• 8: (d)
In summary

• Use of opioids and tramadol for chronic non-cancer pain should be avoided (except during end-of-life care where opioids are preferred over tramadol).

• All other oral pharmacologic interventions for chronic non-cancer pain have limited data in older adults and also carry substantial risks that are generally underappreciated. Chose wisely 😊

(http://www.choosingwisely.org/wp-content/uploads/2018/03/Avoid-Opioids-For-Long-Term-Pain_8.5x11-Eng.pdf )

• Robust use of non-pharmacological interventions and topical agents for management of chronic non-cancer pain in older adults (starting with CBT-P) should be first line therapy for all patients.