Pain Management in the Elderly

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KEYWORDS

• Pain • Older adult • Pain assessment • Pain management

KEY POINTS

- The critical first step in effective pain management is adequate pain assessment. In the elderly population, this includes an assessment of cognition and sensory impairment.
- An appropriate selection of analgesic entails attention to pain etiology along with physiology of aging and comorbidities.
- Opioids are generally safe and effective analgesics for moderate to severe pain when initiated at low doses and preemptive strategies are incorporated to minimize adverse effects.
- Acetaminophen and topical nonsteroidal anti-inflammatory drugs remain first-line therapies for mild to moderate pain, particularly in osteoarthritis; duloxetine's role in pain management continues to evolve.

INTRODUCTION

Persistent pain is common in older adults and results in substantial morbidity. A recent, nationally representative sample of community-dwelling older adults found that 67% reported pain of moderate or greater intensity over the past 4 weeks.[1,2] The prevalence of pain did not vary significantly between age groups of persons age 60 to 74, 75 to 84, and 85 and older.[1] However, pain prevalence may increase as older adults approach the end of life.[3] Also, older patients often have pain in multiple sites, compounding pain-related suffering and disability.

Pain presence is associated with worse health and those in pain may experience greater functional impairment, falls, depression, decreased appetite, impaired sleep, and social isolation compared with persons not in pain.[4–6] Moreover, the multidimensional impact of pain may leave older adults more vulnerable and less able to effectively respond to physiologic stressors, ultimately contributing to the development of frailty.[7,8] Although pain can be adequately managed in most elderly patients, it remains undertreated, especially in the oldest old, African Americans and other ethnic

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minorities, and those with cognitive impairment.[9–11] See **Box 1** for patient and provider factors that contribute to the undertreatment of pain in the elderly.

As with any clinical decision, shared decision making is essential to balance the benefits and burdens of pain management interventions, including nonpharmacologic and pharmacologic approaches. Pain management goals should be delineated before the initiation of any therapy with ongoing monitoring of treatment targets and adverse effects over time. Patients and families should be educated that pain can be reduced with currently available treatments; however, the complete elimination of pain is generally not an achievable goal. Also, treatment should generally be targeted at improvements in pain-related disability rather than pain intensity, because improvements in disability are more tangible outcomes among persons with persistent pain. In this review, we provide an overview of pain assessment and management for older adults with management focusing on the initiation and monitoring of commonly used analgesics.

PAIN ASSESSMENT

Adequate pain assessment is the lynchpin of optimal pain management. Given that older adults often suffer with persistent pain for years, clinicians should integrate a comprehensive history and physical examination along with relevant diagnostic tests before developing a treatment plan.[4,12] Family and/or professional caregivers should also be interviewed when possible to corroborate key aspects of the pain history. **Table 1** provides essential components of a standardized pain assessment. Note that an evaluation for sensory and cognitive impairment is an integral part of pain assessment in the elderly patient. For example, hearing loss may make it more difficult for an older adult to interpret and self-report pain on a standard scale.

Pain assessment in persons with cognitive impairment or the nonverbal patient can be particularly challenging and should include an attempt at patient self-report, review of painful conditions, evaluation of pain behaviors, caregiver report of patient's

Box 1
Factors leading to undertreatment of pain in elderly patients

Patient factors that may contribute to under treatment of pain

- Pain represents a new or worsening disease process
- Fear of being prescribed an opioid
- Fear of addiction
- Fear of analgesics losing effect and not being effective once pain is severe
- Previous dismissal of pain report by healthcare providers
- Labeled as a weak or difficult patient or a complainer
- Cultural and/or religious beliefs

Provider factors that may contribute to under treatment of pain

- Lack of training in pain assessment and/or management
- Fear of state and federal initiatives scrutinizing physicians who prescribe opioids
- Fear of diversion when an opioid is prescribed
- Fear of opioid-related side effects including increased risk of falls and confusion
- Fear of litigation surrounding any use of opioids

Table 1
Overview of a comprehensive pain assessment

Domain	Components
Pain presence	At rest, with activity
Pain intensity	Now, on an average day, worst pain, lowest level of pain
Pain characteristics	Location, frequency, exacerbating and relieving factors, character, and natural history
Pain physiology	Nociceptive, neuropathic, or mixed
Pain interference with activity and pain-related morbidity	Physical, psychological, spiritual, and social functioning, falls, sleep, appetite, etc
Painful conditions	Osteoarthritis, osteoporosis, previous bone fractures, diabetic neuropathy, post-herpetic neuralgia, myofascial pain syndromes, etc
Pain behavior	Facial expressions, vocalizations, body movements, changes in interpersonal interactions and routines, and mental status changes
Pain treatment	Nonpharmacologic and pharmacologic including injections, surgical interventions, and alternative therapies
Coping style	Distraction, ignoring pain sensations, reinterpreting pain sensations, catastrophizing, praying, and hoping
Sensory	Hearing, vision, and cognition
Proxy report	Professional and family caregiver

experience, and if necessary an empiric analgesic trial.[13] An empiric analgesic trial is an invaluable tool to help distinguish between actual pain and pain perseveration. Persons with cognitive impairment may exhibit pain perseveration (ie, repetitive pain reporting) while not displaying any nonverbal pain behaviors or impaired activity related to pain. A common scenario would be (1) a patient who reports pain and discusses it very frequently during the visit and at home with family, (2) a family caregiver reports the patient consistently talks about pain even though most of the time the patient seems to be comfortable, and (3) few pain behaviors at rest and with activity. When the multifaceted assessment remains inconclusive, an empiric analgesic trial can help to determine whether or not the patient is experiencing significant pain or pain that interferes with function.

GUIDELINES FOR TREATING PAIN

General principles of pain management are well-established and supported by several consensus guidelines, including those from the American Pain Society and the American Geriatrics Society.[4,14] As part of a comprehensive treatment plan, analgesics are often considered to decrease pain intensity and to help improve a patient's well-being.[15] The World Health Organization's 3-step pain ladder, initially developed as an approach for managing cancer-related pain, has been widely accepted and adopted as a guide for selecting analgesics.[4] The underlying premise of the ladder is that pain intensity guides analgesic selection. Step 1 corresponds with mild-intensity pain and includes the use of acetaminophen, nonsteroidal anti-inflammatory drugs (NSAIDs), or both. Step 2 is associated with moderate pain and promotes the use of "mild opioids," generally considered to be combination products, such as acetaminophen or an NSAID added to an opioid or tramadol. Step 3 represents severe pain and suggests the use of "strong opioids," such as morphine,

oxycodone, and hydromorphone. Co-analgesics (medications with pain-relieving properties that were not primarily identified as an analgesic but in clinical practice demonstrate either independent or additive analgesic properties) should be considered with each step, with analgesic selection based on the underlying etiology of the pain. For instance, an older adult with moderate to severe pain secondary to post-herpetic neuralgia may be treated first with gabapentin, with the subsequent addition of a combination opioid, such as oxycodone plus acetaminophen.[16]

The adoption of guidelines including opioids for the management of moderate to severe noncancer pain in older adults has led to a dramatic increase in their use over the past decade.[14] This approach is supported by research that indicates opioid use in older adults is associated with decreased pain intensity and improved function.[15] These benefits must be tempered with safety concerns including increased risk of falls, fractures, and hospitalizations.[17,18] A decision to use opioids requires an individualized approach and consideration of drug–drug and drug–disease interactions, as well as benefits and burdens of treatment, including an assessment of risk of diversion and addiction.

PHARMACOLOGIC MANAGEMENT

Acetaminophen

Acetaminophen is the most commonly used analgesic in the United States and is indicated for the management of mild to moderate pain. It does not exhibit significant anti-inflammatory or antiplatelet effects because it does not inhibit thromboxane.[19]

Acetaminophen taken at recommended doses is considered safe. However, inadvertent overdose is possible when patients unknowingly consume multiple acetaminophen-containing products simultaneously; more than 600 over-the-counter products contain acetaminophen for the management of pain, fever, insomnia, and cold and flu symptoms. In fact, nearly one-half of cases of liver failure in the United States are owing to unintentional acetaminophen overdose.[20] The risk of hepatotoxicity led the US Food and Drug Administration (FDA) to lower the recommended maximum daily dose from 4 to 3 g, as well as limit the amount of acetaminophen contained in combination products to 325 mg.[21] Lower doses ($\leq$2 g/d) or avoidance altogether is recommended for patients with underlying liver disease or those who consume 3 or more alcoholic beverages daily. Also, a black box warning was placed on acetaminophen-containing products to highlight the risk of acute liver failure and subsequent need for a liver transplant or death.

Nonsteroidal Anti-inflammatory Drugs

Although studies suggest NSAIDs may be more effective for the management of mild inflammatory pain compared with acetaminophen, the most recent American Geriatric Society guidelines for pain management now state that NSAIDs should be considered "very rarely and with extreme caution."[22] Recommendations against its use, particularly long-term use, stems from its high risk of adverse effects, including on the gastrointestinal (GI), cardiovascular, and renal systems.[23] The risk of GI bleeding with NSAIDs increases with age, dose, and duration of therapy and the presence of GI symptoms, such as dyspepsia and abdominal pain, do not predict who will or will not develop bleeding complications.[24] GI prophylaxis with a proton pump inhibitor with NSAID use may mitigate some of the risk of GI toxicity.[25,26] NSAID cardiovascular effects represent another significant risk to older adults, and include fluid retention, worsening hypertension, congestive heart failure, myocardial infarction, and cerebrovascular accidents. NSAIDs significantly impact the renal system as well contributing to water and sodium retention, decreased renal blood flow, electrolyte imbalances,

and acute and chronic renal failure. If an NSAID is being considered for osteoarthritis pain, topical NSAIDs are generally preferred, but a short course of oral NSAIDs may be indicated in the appropriate patient (eg, adequate renal function, no risk factors for GI bleed, and no cardiovascular disease). Common clinical scenarios in which NSAID use may be considered with caution include acute pain, such as a musculoskeletal injury, an episode of acute-on-chronic pain, or someone with arthritis pain unable to tolerate an opioid and not deriving adequate analgesia from scheduled acetaminophen.

Opioids

Opioid medications are recommended and effective for the management of moderate to severe pain and cancer pain in particular. Studies of opioid rotation suggest inter-individual variability in both analgesic response and tolerability.[27] As a result, older adults should be questioned about prior opioid exposure, such as with dental work or after a surgical procedure, along with beneficial or adverse responses to help guide initial opioid selection. Finally, any discussion of opioid therapy in older or younger adults necessitates dialogue and documentation around addiction and diversion, with patients who may be at high risk for addiction being considered for referral to a pain specialist.

Opioid selection in older adults

As in younger adults, important considerations when selecting an initial opioid include response to specific opioids in the past, hepatic and renal function, drug interactions, and available formulations of the agent. Important characteristics of commonly prescribed opioids in older persons are outlined in **Table 2**. Side effects of most are similar and are also outlined in the table. Morphine or oxycodone at a dose of 2.5 mg every 6 hours with a plan to follow up within 48 to 72 hours to assess for efficacy and adverse effects represents a reasonable starting regimen for patients with moderate to severe pain; details of opioid choice and dosing are discussed elsewhere in this article.

Tramadol, a weak mu-opioid agonist with additional serotonin and norepinephrine reuptake inhibition, is not routinely recommended for older adults with moderate to severe pain, but is commonly used. Importantly, its mu-opioid receptor activity results in a similar side effect profile as other opioids and necessitates similar cautions described herein. In addition, tramadol increases seizure risk, particularly at doses higher than 300 mg/d, the maximum daily dose recommended in an older adult. Also, tramadol may increase suicide risk and should not be prescribed in patients with suicidal ideation. Last, the development of serotonin syndrome may occur with the use of tramadol, particularly with concomitant use of serotonergic drugs. Tramadol should be initiated at 25 mg/d or twice daily and increased in 25-mg increments every 2 to 3 days to an initial goal of 100 mg/d.

Dosing opioids in older adults

Another key component to safe opioid prescribing once appropriate treatment goals have been elucidated and agreed upon and an initial short-acting agent has been selected is the initial dose.[28] The “start low and go slow” approach is essential when dosing opioids. Patients who report severe pain or those who have experienced uncontrolled pain for prolonged periods of time will likely require ongoing titration of opioid therapy to balance pain relief with adverse effects. Frequent reevaluation for analgesia and adverse effects is critical in older persons, should be tailored to the patient’s condition, comorbidity, and support system, and may include phone calls, offices visits, or visiting nurse services.

Table 2
Characteristics of commonly prescribed opioids in older adults

Opioid	Potency	WHO Step	Metabolism/Excretion	Common Side Effects	Additional Considerations
Tramadol	Weak	2	Hepatic/renal	Constipation, nausea, appetite loss, drowsiness, dizziness, sweating	Lowers seizure threshold; may precipitate serotonin syndrome in SSRI/SSNRI users
Codeine	Weak	2	Hepatic (CYP2D6)/renal	Constipation, nausea, appetite loss, drowsiness, dizziness, sweating, falls	Variability in metabolism both slow and rapid can cause variability in response
Hydrocodone	Weak	2	Hepatic (CYP2D6)/renal	Anxiety, constipation, dry mouth, headache, nausea	Formulated with acetaminophen, which can increase liver toxicity
Morphine	Strong	3	Hepatic/renal	Constipation, nausea, vomiting, appetite loss	Metabolites accumulate in renal insufficiency
Hydromorphone	Strong	3	Hepatic/renal	Constipation, dizziness, drowsiness, dry mouth	Considered safer in renal insufficiency
Oxycodone	Strong	3	Hepatic (CYP 3A4)/renal	Constipation, dizziness, drowsiness, heartburn, nausea, vomiting	No parenteral preparation available in the United States
Fentanyl[a]	Strong	3	Hepatic/renal	Anxiety, confusion, constipation, headache, indigestion, nausea	Prolonged elimination may occur; structurally different than morphine, thus can be used in morphine allergy
Methadone[b]	Strong	3	Hepatic ($\geq$6 CYP450 enzymes)/fecal	Constipation, dizziness, dry mouth, headache, sweating, nausea	Multiple potential drug interactions; variable PK; associated with QT prolongation; mainly excreted in feces, thus safer in renal failure
Buprenorphine	Strong	3	Hepatic/fecal	Less constipation, nausea, and respiratory depression than other opioids	Can be used safely in the context of renal failure

Abbreviations: CYP, cytochrome pigment; PK, pharmacokinetics; SSNRI, selective serotonin–norepinephrine reuptake inhibitors; SSRI, selective serotonin reuptake inhibitors.

[a] Fentanyl should never be initiated in an opioid-naive patient.

[b] Methadone should be initiated only by experienced practitioners.

Data from Refs.[52–54]

Opioids should be started at 25% to 50% of the recommended dose for adults.[28] For example, a typical oral starting dose of morphine or oxycodone in a younger person is 5 to 10 mg, whereas 2.5 to 5 mg represents an appropriate dose for older persons. As with pain management in other age groups, the dose of the opioid is increased gradually until prespecified treatment targets are reached or unmanageable side effects develop. When a dose increase is considered, it should not be escalated until a steady state has been reached. In general, only 1 analgesic agent should be initiated and titrated at a time to optimally ascertain efficacy and adverse effects.

The time to maximal effect of opioids does not change with aging. The onset of action for oral preparations is approximately 30 minutes (6–10 minutes intravenously and 15 minutes subcutaneously), reaching peak plasma levels (peak effect) in approximately 1 hour and lasting approximately 3 to 4 hours. However, many experts in older adult pain management recommend a longer time interval (usually 6 hours) between doses of short-acting preparations at the initiation of opioid therapy, given the heterogeneity in response found in older persons. A steady state is generally reached at around 4 to 5 half-lives of the drug.

After successful initiation of a short-acting opioid, a sustained-release preparation can be considered to decrease medication complexity. Although sustained-release preparations may improve adherence and patient satisfaction, these products have not been demonstrated to improve analgesic outcomes.[29] In addition to sustained-release preparations, immediate-release medications should be continued to control breakthrough or incident pain at a dose typically 10% of the total 24-hour sustained-release dosage.

Opioid pharmacokinetics and pharmacodynamics

Numerous factors can affect the pharmacokinetics and pharmacodynamics of opioids, including factors associated with normal aging, such as a natural decline in organ function, and comorbidities, which are more common in elderly persons. A review of these issues follows.

Impact of normal aging Numerous well-documented pharmacokinetic alterations have been described as a result of the natural decline in the functioning of all organs caused by the normal aging process.[30] Reduced intravascular volume, organ volume, and muscle mass may alter drug distribution, resulting in increased plasma levels relative to that of a younger person.

The volume of distribution of fat-soluble opioids, namely fentanyl, may increase because of the increased fat-to-lean body mass ratio that accompanies aging, increasing the drug's effective half-life. The decreased volume of distribution that occurs owing to decreased total body water with aging may also result in increased plasma levels of more hydrophilic opioids (eg, morphine) compared with levels observed in younger persons.[30] In general, oral bioavailability does not seem to be affected by age, and although first-pass metabolism may be affected, dosage adjustments are not routinely necessary beyond the 25% to 50% dose reduction recommended at opioid initiation.[31]

Renal clearance (glomerular filtration, tubular reabsorption, and secretion) decreases with age by about 6% to 10% per decade beginning at age 30 years, so that by age 70 a person may have a 40% to 50% reduction in renal function without underlying kidney disease.[31,32] Opioid clearance may be significantly delayed because most opioids are highly reliant on renal elimination, with methadone and buprenorphine being noteworthy exceptions. Hepatic clearance is also reduced, affected mainly by the reduction of hepatic blood flow while hepatic enzyme activity

is minimally impacted with age. Although the effects of aging itself may not dramatically impact the pharmacokinetics of opioids, increased sensitivity to opioid analgesics (or pharmacodynamic alterations) are observed in older adults, suggesting an altered intrinsic potency. Taken together, opioid use requires lower dosages and less frequent administration in the elderly.

Impact of comorbidities In addition to the altered intrinsic potency of opioids that are dependent on age, underlying comorbidities must also be considered before initiation of these agents.

Liver dysfunction Hepatitis, cirrhosis, or hepatic malignancies that significantly affect hepatic function can substantially increase opioid bioavailability, so close monitoring of dose effectiveness and duration of action is essential in these patients. In general, older adults with significant liver dysfunction should have initial opioid doses decreased by 50%, and the dosing interval should be doubled.[33]

Cardiovascular disease and renal function In addition to the normal decrease in renal clearance that occurs with age, comorbidities that increase in frequency with age, such as hypertension, diabetes, and vascular disease, can adversely affect renal function. Decrements in renal function may decrease the excretion of some neurotoxic opioid-related metabolites. This caution is particularly true for codeine, morphine, hydromorphone, and oxycodone, and dose adjustments with even low doses of these agents should be made accordingly, along with close monitoring for toxicity (eg, myoclonus).[34–36] In general, hydromorphone and oxycodone are preferred over codeine and morphine for use in patients with renal insufficiency.[36]

Codeine should be not be used in patients with a creatinine clearance of less than 30 mL/min/1.73 m^2 because there have been reports of substantial toxicity, even with relatively low doses. Oxycodone has several active metabolites that may accumulate in renal dysfunction, but is considered to be safer than morphine. Limited case reports and pharmacokinetic data suggest that fentanyl can be used at usual doses in mild to moderate renal insufficiency and in patients undergoing dialysis if the drug's use is accompanied by proper monitoring of respiratory and cardiovascular status, blood pressure, and heart rate.[36]

Methadone is primarily excreted in the feces; thus, it is considered safe for use in persons with renal insufficiency. However, equianalgesic ratios between morphine and methadone are dose dependent, the half-life is highly variable, and numerous drug interactions must be considered; therefore, methadone should be used only by practitioners experienced with this agent.[37] Buprenorphine is also excreted primarily in the feces and is considered safe in persons with renal impairment.[38]

Assessment and management of opioid-related risks and side effects One common reason cited for noncompliance with opioid therapy is the fear of side effects. The side effects of most concern include constipation, nausea and vomiting, sedation, confusion, and respiratory depression. Tolerance develops to most of these side effects, with the exception of constipation. Falls represent a more recent concern based on the findings of recent studies.[17] Given the heterogeneity of opioid-related side effects, older adults should be instructed not to drive until a steady state has been achieved and no impact on driving capabilities has developed. Reassurance to the patient coupled with proactive management of common side effects are key strategies for reducing complications and increasing adherence to opioid therapy.

Nausea develops in about one-third of patients initiated on opioids and occurs because these agents slow down the motility of the GI tract, stimulate the

chemoreceptor trigger zone, and sensitize the vestibular apparatus. If severe nausea occurs, low-dose haloperidol (0.5 mg) or ondansetron (4 mg) scheduled or "as needed" typically manage nausea until it resolves over the first week of therapy. Opioid-related constipation should also be considered and treated if present when a patient on opioids presents with nausea.

Constipation is common in older persons with serious illnesses and nearly universal in patients taking an opioid, which is often cited by older adults as a reason to refuse opioid therapy. Constipation results from μ-receptor binding in the GI tract, resulting in slower transit time and subsequent increased water reabsorption. Prevention is the cornerstone of constipation management with a bowel stimulant of senna or bisacodyl scheduled daily at initiation and increased to twice daily if needed.[39] Osmotic agents, such as polyethylene glycol or milk of magnesia, as monotherapy generally lack sufficient action to counteract opioid GI effects, but can be helpful in conjunction with stimulant laxatives when needed. Bulk-forming agents such as psyllium are ineffective and can worsen symptoms if patients do not ingest an adequate amount of fluid.

The relationship between pain, falls, and opioids is complex and not completely understood. Cohort studies support that pain interference is associated with an increased risk of falls among community-dwelling older adults. At the same time, the use of opioids, particularly short acting, at time of initiation, may increase the likelihood of falls compared with those with arthritis pain treated with an NSAID.[40] However, published studies examining the relationship between analgesic use and falls have noteworthy limitations, including opioid patients reporting greater comorbidity versus comparison groups, as well as a lack of adjustment for starting opioid dose. The relationship among pain, cognition, and opioids also remains inconclusive. Undertreated pain may predispose to an increased likelihood of confusion, particularly in the hospital. For example, a study of hospitalized hip fracture patients found that persons taking higher opioid doses had a lower delirium risk compared with patients taking low-dose or no opioid.[41]

Black box warning

All opioids contain a black box warning for the risk of abuse, diversion, and fatal overdose owing to respiratory depression. Respiratory depression is rare in opioid-naive patients whose treatment is initiated at low doses. Risk has been shown to increase with age, opioid dose, and with underlying pulmonary conditions, such as chronic obstructive pulmonary disease and sleep apnea. The concomitant administration of opioids with other central nervous system depressants (eg, benzodiazepines, alcohol, barbiturates) can also significantly increase the risk of respiratory depression for which patients should be educated.

Any patient being considered for opioid therapy must be treated with "universal precautions" against addiction and misuse. Prescribers need to understand state laws and regulations when prescribing opioid therapy, because active legislation is ongoing in many states. Addiction and misuse is another cited reason why older adults may decline a trial of opioid therapy for the management of moderate to severe pain. Each patient requires risk stratification for addiction and misuse with adherence monitoring commensurate with risk. Patients at moderate or greater risk for addiction or misuse should be considered for referral to a pain specialist. Patients must be educated about safe drug storage and sharing, which is a federal crime.

To date, research on opioid addiction and the older adult is lacking, including prevalence data and risk factors. Available research suggests addiction risk is much lower in older adults compared with younger adults, but data specific to newer aging cohorts, such as the baby boomers, is lacking. Experts recommend asking about

and documenting risk factors of addiction in younger persons, which include (1) personal or family history of alcohol and/or drug abuse, (2) a history of preadolescent sexual abuse, and (3) psychiatric disease. Opioid risk stratification tools may also be employed and are often recommended by guidelines to help identify and mitigate risk of addiction and misuse; however, research documenting their benefits and harms in primary care and older populations is lacking. Commonly used risk tools include the Screening Tool for Addiction Risk (STAR) and Screener and Opioid Assessment for Patients with Pain (SOAPP).

Adherence monitoring should be integrated into the pain management plan with patient risk of addiction and misuse determining which steps to incorporate into the care plan. For lower risk patients, adherence protocols may include monthly physician visits with pill counts, required use of only 1 pharmacy, home health to better supervise patients in the home setting, and documentation of pain-related outcomes. For higher risk patients, strategies may include urine toxicology screens; use of long-acting medications without breakthrough; prescribing small quantities at a time, although this strategy can be problematic with some insurance carriers (particularly Medicaid); prescribing opioids less prone to abuse such as methadone and buprenorphine; and use of a patient–prescriber agreement. Patient–prescriber agreements should not be thought of as punitive, but as an opportunity to openly discuss the benefits and risks of opioid therapy and how the provider and patient are going to work together to mitigate the risks.[42]

Nonopioid Analgesics

Duloxetine

Duloxetine is a serotonin and norepinephrine reuptake inhibitor with analgesic efficacy purportedly related to its central effect with influence on descending inhibition. Randomized, controlled studies have established the analgesic efficacy of duloxetine in 4 chronic pain conditions: diabetic peripheral neuropathy, fibromyalgia, chronic low back pain, and osteoarthritis knee pain.[43–45] Each of these studies predominately enrolled younger patients, with the exception of the knee pain studies, where the average patient age was in the mid 60s. FDA indications for use of duloxetine include each of these conditions, with the exception of chronic low back pain. Duloxetine is usually started at 30 mg/d and may be increased to 60 mg/d after 2 weeks if appropriate.

The most commonly experienced adverse events associated with duloxetine are dry mouth, nausea, constipation, diarrhea, fatigue, dizziness, somnolence, and insomnia. Nausea is typically mild to moderate in severity and generally resolves within 1 week. A small, statistically significant but clinically insignificant increase in hemoglobin A1C levels has been reported in the diabetic peripheral neuropathy studies with duloxetine use compared with placebo. Duloxetine should not be prescribed to patients with hepatic impairment or heavy alcohol use because cases of elevated liver enzymes, hepatitis, jaundice, and hepatic failure have been reported.

Given the available evidence, duloxetine may be considered for the management of moderate to severe, persistent pain from osteoarthritis of the knees or back where acetaminophen or opioids have been unsuccessful (duloxetine monotherapy) or not provided enough relief (combination therapy with addition of duloxetine).

Gabapentin and pregabalin

Gabapentin and pregabalin are antiepileptic drugs that, through alterations in ascending nociceptive pathways, have been shown to be effective in the management of several painful neuropathic conditions that occur commonly in older adults.

Gabapentin carries FDA indications for post-herpetic neuralgia, whereas pregabalin has FDA indications for post-herpetic neuralgia, diabetic peripheral neuropathy, fibromyalgia, and neuropathic pain associated with spinal cord injury. Both of these medications have few drug interactions.[46] They are excreted renally as unchanged drug and dose reduction with renal insufficiency is necessary. Gabapentin dosing requires slow titration starting at doses as low as 100 mg/d. The dose can be increased every 3 to 7 days based on analgesic response and tolerance up to maximum dosage of 3600 mg/d in divided doses. This process can take several months. Pregabalin can be titrated more easily. The starting dose is 100 mg/d and increased incrementally to 300 mg/d over several weeks if necessary. The medication is given in 2 or 3 divided doses. Dizziness, sedation, and peripheral edema are the most common side effects and are more common in older adults.

Gabapentin and pregabalin therapy should be considered first line agents or for use as co-analgesics among older adults with post-herpetic neuralgia and/or diabetic peripheral neuropathy. Clinicians should start at a low dose and increase slowly the dose every few days until desired analgesia is achieved, limiting side effects emerge, or the maximum recommended dose is reached. As with opioids, older adults should abstain from driving until a steady state has been achieved and no impact on driving capabilities has developed.

Topical Therapies

Topical nonsteroidal anti-inflammatory drugs

Even though oral NSAIDs are effective for the management of mild pain, significant adverse GI, cardiovascular, and renal effects, particularly in the older population limit their widespread use. Topical NSAIDs represent an alternative to oral NSAIDs, so that patients may benefit from local analgesia with lower risk of systemic adverse effects.[47] In the United States, 2 topical diclofenac formulations, namely, diclofenac sodium 1% topical gel and diclofenac sodium 1.5% topical solution, have been approved for the treatment of osteoarthritis pain. Diclofenac epolamine 1.3% topical patch has also been approved for the treatment of pain owing to minor strains and sprains. A recent Cochrane review reported topical NSAIDs were as effective as oral NSAIDs for the relief of chronic musculoskeletal pain with fewer systemic adverse effects, particularly in hand and knee osteoarthritis.[48]

Capsaicin

Capsaicin, primarily studied for the management of neuropathic pain, is derived from the chili pepper and stimulates the ion of the transient receptor potential vanilloid-1 (TRPV1). It is available as a topical agent in a low dose (0.075%) applied several times a day for several weeks and a high-dose (8%), 1-time preparation that may be repeated. Upon application to the skin, a brief initial sensitization is followed by prolonged desensitization with depletion of substance P. Although low-dose capsaicin has not resulted in good efficacy, the larger dose 8% topical capsaicin has had some benefit in select patients for the treatment of post-herpetic neuralgia and HIV neuropathic pain.[49,50]

Topical lidocaine

Lidocaine 5% topical patch has been shown to be safe, effective, and well-tolerated for the treatment for post-herpetic neuralgia. Although it may be reasonable to use a topical lidocaine patch for similarly focal neuropathic pains, such as post-thoracotomy pain, we strongly recommend against its use for other painful conditions, including osteoarthritis and back pain, given a lack of evidence demonstrating efficacy.[51] Placement is advised for only 12 hours daily; however, pharmacokinetic studies of use up to

24 hours demonstrate minimal systemic absorption. The most common side effects are mild skin reactions and no drug–drug interactions have been reported in clinical trials.[51]

SUMMARY

Persistent pain in older adults is a common problem linked to significant morbidity. Effective pain management begins with thorough and multidimensional assessment and goal setting. Normal physiologic changes and the impact of comorbidity have to be considered in both the selection of analgesic agents and their initial and subsequent dosing. Successful medication management is possible with attention to detail, careful titration, and monitoring of analgesic effect and adverse effects.

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