111 Pain in the Older Adult

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Despite its increased prevalence in older adults, pain should not be considered a normal consequence of aging. Pain is always due to pathology, even if not easily identified or fully appreciated by the clinician. An understanding of the complex cellular, molecular, and genetic contributions to the experience of pain are beginning to emerge, along with their relationship to physical, psychological, and environmental factors. Persistent pain interferes with enjoyment of life and has deleterious effects on mood, social interaction, function, mobility, and independence. For many reasons, pain remains undertreated in this population. This chapter examines age-related changes in the prevalence and perception of pain and approaches to assessment and treatment. The focus is on pain and suffering, rather than the underlying causes of pain. The management of specific painful conditions is not discussed.

COMPONENTS OF PAIN

The pain experience is best understood by considering the influence of four determinants—nociception, pain perception, suffering, and pain behaviors.[1] Nociception is the detection of tissue damage by specialized transducers on primary afferent A delta and C nerve fibers in response to noxious stimuli. The subsequent perception of pain by the individual is affected by central processing of nociceptive input from the periphery or from lesions in the peripheral and central nervous systems. Pain consequent to nerve damage can occur with or without somatic nociceptive input. In the former case, the perception of pain is altered from what is usually reported following nociception. The intensity of pain under these circumstances bears little relationship to the extent and severity of observable pathology and tends to be less responsive to traditional analgesic medications. Adjuvant medications, or those formerly not used to treat pain, have demonstrated efficacy in treating pain that results from changes in the central and peripheral nervous systems.

Suffering is a negative emotional response induced by pain and also by fear, anxiety, loss, and other psychological states. Patients often use the language of pain to describe suffering, such as "heartache," although not all suffering is caused by pain. Pain behaviors, such as grimacing, lying down, limping, and avoidance of physical activity may result from pain perception and suffering. The clinician infers the existence of nociception, pain, and suffering from the patient's history, physical examination, and observation of pain behaviors.[1] Recognition of the multiple components of the pain experience will guide the clinician in assessing and planning age-appropriate pain management.

TYPES OF PAIN

A simple classification differentiates pain as acute or chronic. Acute pain can be of visceral or somatic origin. It usually has an identifiable temporal relationship with an injury or disease. Autonomic overactivity, such as diaphoresis and tachycardia, may be present. In this setting, pain may be seen to serve a useful role in drawing attention to injured tissues, altering behavior, and hence preventing further tissue damage. Acute pain often leads the individual to seek medical attention. Pain often resolves before healing is complete. As people age, there may be a blunting of protective warning signals. Age-related dysfunction along pain pathways may account for age-related differences in pain perception.[2-4] Pain associated with visceral causes are prevalent and may present atypically in older adults. Visceral pain associated with cardiac, pulmonary, and abdominal disease is associated with morbidity and mortality and can be difficult to diagnose in older adults. Clinicians need to be especially vigilant in their pain assessment technique in this population.

Chronic pain persists beyond the normal duration of injury or tissue damage or is associated with progressive disease. The time frame for the transition from acute to chronic pain is somewhat arbitrary, often determined by the underlying pathology, and not necessarily characterized by a change in quality or severity of symptoms. Thus, chronic pain is often defined as pain persisting for longer than 3 to 6 months or beyond the expected time of healing. There may be no identifiable pathology to account for the pain. Psychological and functional features are often associated with chronic pain, and autonomic overactivity is not usually present. Chronic pain may be persistent (always present) or intermittent, such as migraine headache. Pain intensity may vary during the day or be related to activity level. Musculoskeletal disease, arthritis, orofacial, and neuropathic pain conditions are common in older adults. Once reversible factors have been excluded, the pain rather than the pathology is considered the major problem. At this stage, the goal of treatment shifts from a disease focus to reduction of pain, suffering, and disability.

Prevalence Studies

Pain in older adults is common and has a tremendous impact on quality of life in this age group. Pain is an important health deficit, and its presence adds to the risk associated with health deficit accumulation, particularly in relation to this risk, it is greater in men than in women.[5] There is great variability in the reported prevalence, likely due to differences in the reporting period for pain, intensity of pain reported, and composition of the older population studies. Crook and colleagues[6] have reported age-specific rates of 29% for those between 71 and 80 years of age when asked "how often are you troubled by pain during the past 2 weeks…?" Brattberg and associates[7] have reported a 12-month prevalence of mild to severe pain in 75% of those older than 75 years. Persistent pain ranges from 26% to 30% in the population, with those between the ages of 60 to 69 years reporting the most pain.[8] Persistent pain has been reported in approximately half of community-dwelling older adults,[9,10] and older adults at the end of life report an even higher incidence of pain.[11] The fact that prevalence data has not changed significantly in the past 30 years illustrates the complexity of pain management in older adults.

Pain affecting the joints, feet, legs, and back is increased with age but pain in the head, abdomen, and chest is reduced. The high prevalence of degenerative joint disease overwhelms any contribution from other causes in all surveys. Osteoarthritis (OA) is reported in 12% of adults, with the incidence increasing with age. Painful OA is present in 26% of women and 13% of men older than 71 years, whereas OA of the knee is present in 17% of adults older than 45 years. These rates are significantly higher than those reported in younger adults.[12] Persistent intermittent

back pain ranges from 13% to 49% in persons 65 years of age and older.[13,14]

Other musculoskeletal noncancerous conditions contribute to pain in older adults. Bone demineralization leading to osteoporosis and vertebral compression fractures are common in postmenopausal women[15]and can contribute to traumatic long bone fractures.[16] Vitamin D deficiency can predict osteoporosis and OA and is associated with a significantly higher prevalence of chronic back pain in women.[17] Postherpetic neuralgia (PHN) and painful diabetic neuropathy (PDN) are common in older adults. In persons older than 60 years who develop acute herpes zoster, approximately 12.5% will develop PHN,[18,19] and PDN affects 15% of older patients with diabetes.[20] Persistent and inadequately treated pain can lead to decreased quality of life, including impaired sleep, mobility, and function and decreased socialization and independence, among other consequences. Efforts by clinicians to understand, assess, and treat pain in this population are imperative.

Age-Related Changes in Pain Perception

Pain may not be the cardinal symptom of disease in older adults. Silent myocardial infarction is more common with age.[21,22] Similarly, in a retrospective study of older patients with peritonitis, abdominal pain was absent in nearly 50% of cases.[4] The physiologic basis of these observations is uncertain. Clinicians should not underestimate the potential seriousness of underlying pathology in an older person because of the absence of severe pain.

There are widespread morphologic, electrophysiologic, neurochemical, and functional changes within the nociceptive pathways, and psychological factors may alter pain experience in older adults.[23] Most studies of experimental pain have supported the view that pain thresholds to short-duration noxious stimuli are increased in older adults.[24,25] There is controversy regarding the effect of age on pain thresholds; pain thresholds to thermal, ischemic, and mechanical stimuli have been shown to increase with age, but aging does not predict decreasing sensitivity to pain.[26] However, a decrease in the function of the descending inhibitory pain control pathway as a person ages[23] suggests greater sensitivity to noxious experimental pain. In other studies, reticence, self-doubt, and reluctance to label a stimulus as painful underlie the perception that stoicism to pain increases with age. However, when pain is perceived, the experience is the same or, under some circumstances, enhanced or prolonged.[27,28] Tolerance to severe pain may even be reduced in older adults.

Age-related loss of neurochemicals, such as serotonin,[29] glutamate, γ-aminobutyric acid GABA),[30] and opioid receptors,[31] implicated in pain modulation, may contribute to altered pain processing in older adults. Changes in the aging brain[32,33] have been associated with older adults processing and response to pain. Taken together, these studies suggest that pain is dependent on a complex neuroprocessing system that is affected by aging and has implications for the pain experience in older adults.

PATHOPHYSIOLOGIC PERSPECTIVE

Inferences about the underlying pathophysiology of a painful condition assist the clinician in the selection of therapy and determining prognosis. Clinicians must keep in mind that older adults often have more than one source of pain. Pain may be subdivided into three pathophysiologic subtypes—nociceptive, neuropathic, and psychogenic. Pain that arises from noxious stimulation of specific peripheral or visceral nociceptors is termed *nociceptive pain*. Examples include pain arising from OA, soft tissue injuries, and visceral pathology. Pain arising from pathology of the peripheral nerves or within the central nervous system leading to aberrant somatosensory processing is termed *neuropathic pain*. This term encompasses a diverse range of conditions, including painful peripheral neuropathies, phantom limb pain, postherpetic neuralgia, trigeminal neuralgia, and central poststroke pain. Pain of neuropathic origin is often associated with abnormal and unpleasant sensations (dysesthesia) and may have a burning or shooting quality. Mild, normally non-noxious stimuli in the affected region may cause pain (allodynia), normally noxious stimuli may result in a heightened sensitivity response (hyperalgesia), or repetitive stimulation can result in summation and pain persisting longer than the stimulus (hyperpathia). There may be a delay between the precipitating injury and onset of pain. The onset of central poststroke pain syndrome occurs commonly between 1 and 3 months following a stroke, but may occur more than 1 year later.[34] Pain often persists in the absence of ongoing tissue damage. Pain associated with psychological factors is termed *psychogenic pain*. It is probably more useful to consider the impact of psychological influences on the pain presentation, choice of treatment, and response to treatment than the potential influence that the label of psychogenic pain may convey.

The multidimensionality of chronic pain has long been recognized to include sensory-discriminative, affective-motivational, and cognitive-interpretative dimensions. These are influenced by biologic, psychological, and social factors. The ability of the individual to adapt to biopsychosocial changes in response to stress may be diminished with age. The term *pain homeostenosis* has been introduced to describe an organism's diminished ability to respond effectively to the stress of persistent pain.[5,33] Clinicians should be aware of factors that contribute to these phenomena, such as cognitive function, decreased density of opioid receptors, medical comorbidity, polypharmacy, and effect of aging on pharmacokinetics and pharmacodynamics, social isolation, depression, and altered activities of daily living. There are specific assessment techniques and tools to assist in assessing these factors.

Depression is common in people with chronic pain. Patients who are depressed may exhibit decreased energy, decreased engagement in treatment modalities, or avoidance of pleasant diversional activities. Anxiety has also been closely associated with pain[35,36] and often coexists with depression in this population. Anxiety may play a part in fear-related behavior that might inhibit participation in physical rehabilitation efforts. Social networks and economic resources are important assessment parameters. Involvement with family and friends can provide pleasurable experiences and diversion away from a constant focus on pain. In addition to the availability of social support, the type of relationship should be assessed. Negative social reinforcement may present in the form of overly solicitous family members who encourage sedentary behavior. Other negative effects are likely if long-term caregivers become resentful of their support role. Economic resources have a great impact on access to potential treatment options and must to be identified.[37] Finally, beliefs and attitudes about pain can affect the overall pain management plan. Pain can signify loss of independence, debilitating illness, or be regarded as a general consequence of the aging process and therefore underreported. If older patients have a good understanding of the underlying cause of pain, what it means in terms of function, and possible treatment options, it is likely that they will participate in the plan of care and obtain more satisfactory outcomes.

EVALUATION

Pain is inherently subjective; the individual's self-report is the gold standard for assessment. The history should focus on the onset and temporal pattern of the symptoms, site, and quality of the pain, severity, aggravating and relieving factors, and impact of the pain on the patient's lifestyle. The assessment of a patient with a complex pain problem may need to take place over several consultations. The reliability of the history can be affected by the chronicity of the pain, past interventions, and age-related

conditions that affect cognition. A collaborative history from a family member is often helpful. Special emphasis should be placed on musculoskeletal and neurologic examinations because of their importance in the genesis of pain in older adults. The assessment should include functional and psychological aspects and, where possible the individual should be assessed within his or her own environment. The open-ended question, "What would you do if you no longer had pain?" often reveals valuable information regarding mood state, attitudes, and disability. Part of the assessment needs to focus on the patient's comorbidities, how these affect function, their contribution to altered mood state their propensity to affect management with medications, and physical or psychological interventions.

Back pain is illustrative. An estimated two thirds of adults will experience back pain at some stage of their lives. Experimental studies have revealed that pain may originate from any one of many structures. However, after clinical evaluation, no precise pathoanatomic diagnosis can be established in 85% of cases.[38] Investigations are used to confirm a diagnosis and exclude more serious pathology. The diagnostic probabilities change with increasing age, with cancer, compression fractures, and spinal stenosis becoming more common. Plain radiology is not highly sensitive but findings on computed tomography (CT) and magnetic resonance imaging (MRI) are nonspecific and thus may be misleading. CT and MRI studies of asymptomatic individuals older than 60 years have shown that about 80% have abnormal findings, such as disc prolapse and spinal canal stenosis. Therefore, the identification of pathology on diagnostic investigation does not necessarily indicate causality. Deyo and Weinstein[38] have suggested that it is more helpful to address three questions during the assessment of a patient with low back pain:

1. Is a systemic disease causing the pain?
2. Is there social or psychological distress that may amplify or prolong pain?
3. Is there neurologic compromise that may require surgical evaluation?

Under most circumstances, these questions can be answered from a careful history and physical examination. without the need for further tests.

Although these scales only assess unidimensional pain intensity, older adults with mild to moderate cognitive impairment have demonstrated successful use of numeric rating scales[39,40] and verbal descriptor scales.[37,41] Several validated psychometric instruments can help quantify and communicate the patient's pain experience. The widely used McGill Pain Questionnaire[42,43] consists of 78 adjectives describing emotional, sensory, and evaluative dimensions of the pain experience. Words such as throbbing, sharp, cramping, burning, and aching describe a sensory dimension, whereas tiring, exhausting, cruel, punishing, fearful, and sickening describe an affective component. There is no shortage of geriatric assessment instruments available to clinicians. A recommendation from a comprehensive review of assessment of pain in older adults[44] has suggested the Brief Pain Inventory[45] combined with the Short Form-McGill Pain Questionnaire[43] as an appropriate 10-minute battery for cognitively intact older adults.

Modification to accommodate sensory, motor, perceptual, and cognitive changes in older adults may be necessary. Proper lighting, attention to tone, speed, and pacing of voice, reduction of extraneous noise, and using tools with large bold print is helpful. The Mini-Cog is a brief (3-minute) cognitive screen that includes a clock drawing and three-item recall,[46] which can establish the ability to obtain a self-report of pain.[47]

Psychological Assessment

A comprehensive psychological assessment is not usually required in the setting of acute pain. However, chronic pain may have profound effects on mood, interpersonal relationships, and activity level, and it may be difficult to ascertain which is cause and which is effect. A psychological evaluation is indicated when contributing factors are discovered on history taking or medical evaluation fails to explain the severity of pain behaviors adequately. Psychological evaluation can also be valuable when the pain results in excessive health service use or interference with normal activities or interpersonal relationships. Chronic pain patients are often resistant to psychological evaluation, considering this an inference that the pain is "in the head," rather than being a physical problem. Patients often require careful explanation regarding the complex interaction between mind and body, which often influences pain, suffering, and disability.[48] Acknowledging that the pain is real preserves the patient's sense of legitimacy and allows for a more complete evaluation of the psychological factors contributing to the maintenance of pain. Moreover, pain is commonly accompanied by depression, and this relationship persists, even for people who are frail, for whom it can affect disease expression.[49]

It is important to evaluate how the patient, family, and caregiver(s) conceptualize the pain and goals of treatment. They may believe that the pain has persisted because the medical assessment has been inadequate or specific interventions denied. Each time a new intervention is tried and fails, the psychological distress is reinforced. Psychological strategies are not likely to be effective in teaching the patient how to manage ongoing pain while the patient remains focused on seeking a cure. Pain behaviors such as limping, grimacing, inactivity, and verbalizing of pain complaints may be reinforced by social influences such as gaining attention, sympathy, or the ability to avoid unpleasant responsibilities. Fear of causing further pain or injury may lead to avoidance of activity. Attempts at management with medications and physical therapies, without addressing psychological factors, are often unsuccessful.

Assessment of Pain in the Presence of Cognitive Impairment

Cognitive impairment represents a major impediment to the evaluation and management of pain. A hierarchical approach is recommended as a guide to assess pain in persons not able to self-report pain.[50] Interpretation of a pain stimulus may be altered in persons with dementia.[51] Additional evidence has suggested that cognitive impairment does not necessarily change the pain intensity experienced.[52-54]

When assessing pain in severely cognitively impaired patients, the clinician must rely on behavioral indicators. These include nonverbal cues such as restlessness and guarding, verbal cues such as crying, moaning, and groaning, and facial expressions such as grimacing.[55-57] Changes in usual activity may also indicate pain. There is tremendous variability in pain behavior, and certified nursing assistants will often be the first to notice behavioral changes, including combativeness, resisting care, a decrease in social interactions, increased wandering, difficulty sleeping, and refusing to eat.[58] Behavioral indicators for pain in this population and pain assessment tools have been developed for cognitively impaired persons. The assessment instruments vary greatly on their reliability, validity, and applicability for easy clinical use.[59-61] Because pain behaviors may be absent during rest, observations should take place during movement such as bathing, dressing, or transferring.

Defining the Goals of Therapy

Before embarking on a treatment program, the patient and clinician should agree on the goals of therapy, particularly when pain eradication is not feasible. An essential outcome should include improvement in physical an psychosocial functioning.

Involvement of family members and caregivers often assists with enhanced compliance to treatment and successful outcomes. A frank discussion about the prognosis and therapeutic options is important, particularly for individuals who have had unsatisfactory experiences and expectations in the past. Even if the sensory component of pain cannot be eliminated, improved outcomes can be achieved by addressing factors such as disability and mood disturbance. Management of severe pain often requires establishing a balance between the severity of sensory symptoms, level of disability, and medication side effects. Disability may be more important to the patient than the pain. An improvement in the distance that an individual can walk before being stopped by pain may be considered a positive outcome, although the intensity of maximum pain remains unaltered. Medication side effects may be more troublesome than the condition for which they were prescribed. Pain management programs that combine cognitive and rehabilitative approaches to enhance coping strategies and minimize the impact of persistent pain on the individual can be helpful.

MANAGEMENT

Medications

The management of pain can be tricky. Pain medications can be less well tolerated in frail older adults, so attention to whatever other medications they are on is needed.[62] Selection of appropriate drug therapy for older patients requires an understanding of age-related pharmacokinetic and pharmacodynamic changes and needs to take into account any coexisting diseases and other medications, including those obtained without prescription. Selection of therapy needs to balance the potential efficacy with the potential for harm from the intervention. Physiologic changes associated with aging, such as intestinal motility, secretions, and blood flow, can alter drug absorption, bioavailability, and transit time, Hepatic and renal functions are diminished and alter the metabolism and excretion of water-soluble drugs. Guidelines are available to mitigate the potential risks of adverse effects and medication toxicity due to the age-related changes,[63] as summarized in Box 111-1.

The timing of drug administration is important. Analgesics may be prescribed on an "as required" basis for occasional pain or prophylactically for induced pain. However, for continuous pain, analgesics are best prescribed on a regular basis. Additional doses may be required before an activity known to exacerbate pain or for breakthrough pain. Medications with long half-lives may be used to reduce the frequency of dosing. In general, medications should be started at low doses, titrating upward and stopping at the lowest dose that achieves the desired outcome. Finding the appropriate medication and dose may take a long of time due to tolerability and efficacy and should be explained to the patient to reduce the potential for prematurely abandoning treatment.

Simple Analgesics

Acetaminophen (APAP, paracetamol) 500 mg qid is the preferred analgesic for older adults.[64-66] A trial of acetaminophen is warranted as initial therapy on the basis of cost, efficacy, and toxicity profile. Dosages should be limited to 4000 mg/day, with lower doses used for persons with diminished renal or hepatic function or for those requiring chronic use. It is absorbed rapidly and metabolized by the liver. Because of the risk of hepatoxicity, acetaminophen should be used with caution in patients with liver disease, chronic alcoholism, malnutrition, and dehydration.

As a class, nonsteroidal antiinflammatory drugs (NSAIDs) have been among the most frequently prescribed medications, particularly for pain associated with OA and inflammatory arthropathies. However, they should not be used as first-line analgesics for persistent pain. The side effect and drug interaction profile of NSAIDs is of particular concern. Dose-related and prolonged exposure to NSAIDs contribute to gastric mucosal adverse events, which are significantly increased in those older than 75 years.[67-69] Renal toxicity is another concern. Risk factors for renal failure in patients with intrinsic renal disease treated with NSAIDs include age older than 65 years, history of hypertension, congestive cardiac failure, and concomitant use of diuretics or angiotensin-converting enzyme (ACE) inhibitors. Most NSAIDs have a dose-response relationship, with a ceiling effect. Increasing the dose above the recommended level or adding a second NSAID does not impart any greater analgesia, but increases the likelihood of drug toxicity.

The rate of NSAID-related gastrointestinal (GI) complications has decreased in recent years, in part due to extensive medical education campaigns and a move away from NSAIDs as first-line management of OA.[70] Patients with inflammatory arthritides should preferentially be treated with disease-modifying drugs. The options for management of patients with NSAIDs who are at high risk of serious upper GI events are the use of a nonselective NSAID with gastroprotective therapy or the use of a cyclooxygenase-2 (COX-2) specific inhibitor. Coadministration of misoprostol has been demonstrated to reduce the upper GI complication rate of nonselective NSAIDs but is not well tolerated. Proton pump inhibitors are an acceptable alternative. Histamine H2 receptor antagonists have been shown to prevent duodenal ulceration only and cannot be recommended.[71] Celecoxib is the only COX-2 selective NSAID currently available in the United States.[4] The primary short-term advantage of this

BOX 111-1 Treatment Options

MEDICATIONS

Paracetamol

- First-line analgesic for older patients with chronic pain
- Often as effective as NSAIDs
- Best given regularly for persistent pain, rather than as required

NSAIDs

- Increased risk of GI and renal complications in older adults
- Avoid if possible

Selective COX-2 Inhibitors

- Preferable to nonselective NSAIDs
- Similar nongastrointestinal side effects to nonselective NSAIDs

Adjuvant Analgesics

These include antidepressants and anticonvulsants.

- Proven role in neuropathic pain states
- Total pain eradication is unlikely
- Selection of medication based on side effect profile rather than comparative efficacy
- Started at low dose, increased slowly

Opioid Analgesics

- Have a role in chronic noncancer pain
- Treat constipation preemptively
- Drug dependence uncommon in older adults

NONPHARMACOLOGIC APPROACHES

These include physical and psychological therapies.

- Will reduce reliance on medications
- Failure to use these strategies often accounts for treatment failure.

class of agents is its lack of effect on platelet function. Because these drugs are frequently prescribed for pain control in rheumatoid arthritis and OA, their usefulness for long-term therapy is limited. In addition, COX-2 inhibitors appear to affect renal function in a similar fashion as nonselective NSAIDs, and particular care is required in patients with renal impairment or those taking diuretics and ACE inhibitors. COX-2 inhibitors may diminish the antihypertensive effects of ACE inhibitors and diuretic effects of furosemide and thiazides. Celecoxib inhibits the cytochrome P450 (CYP450) enzyme (CYP2C9) and thus may cause elevation of plasma concentrations of drugs metabolized by this enzyme, such as some β-blockers, antidepressants, and antipsychotics.[72] Topical NSAIDs are an effective and safe alternative for some patients, especially for the management of pain associated with OA[73] and acute musculoskeletal and soft tissue inflammatory pain.[74,75] Diclofenac gel and patch formulations are currently available, with several other NSAID formulations under development. Although GI side effects are less common than with oral preparations, there is still a risk, especially in those who have previously experienced previous side effects from NSAIDs.[76]

Opioid Analgesics

Opioid analgesic medications are considered second- or third-line pharmacologic therapy for persistent moderate to severe pain.[65,77,78] Older patients tend to be more sensitive to equivalent doses and blood levels of opioids due to physiologic changes associated with aging and the effects of polypharmacy. For example, the analgesic effects of codeine (methylmorphine) are mediated by its conversion to morphine via the CYP450 D6 (CYP2D6) system. About 8% of whites and 2% of Asians are genetically deficient in CYP2D6 and obtain little pain relief with codeine. A number of medications frequently prescribed for older patients are capable of inhibiting CYP2D6, including cimetidine, quinidine, amitriptyline, and the selective serotonin reuptake inhibitors (SSRIs; e.g., fluoxetine, paroxetine, fluvoxamine). Starting doses should be 25% to 50% lower than standard adult doses, and titration should be done cautiously and slowly.[66] For patients requiring round the clock dosing, a steady state is generally reached through five half-lives of repeated dose administration.[78,79] Effectiveness of the drug therapy can then be evaluated. Clinicians, therefore, need to be familiar with specific opioid pharmacology, starting doses, titration schedules, and monitoring of effectiveness, side effects, and potential for abuse and diversion.

All opioid analgesic medications carry the side effect profile of potential nausea, constipation, sedation, respiratory depression, and cognitive alterations. Older adults should be placed on a prophylactic bowel regimen. They may be at greater risk for accident-related injuries when starting therapy.[80] Methadone should only be prescribed by those familiar with the drug. An initial electrocardiogram (ECG) with periodic reassessments are necessary due to the potential for prolonged QTc intervals, especially with doses above 100 mg/day.[65,81,82] Older adults without a prior history of substance abuse disorder are at low risk for developing an addiction to opioid analgesics, but opioid misuse is a public health concern. Strategies to assess for misuse and diversion need to be in place for all older adults receiving opioid therapy. These include periodic pill counts, urine drug screening, use of a prescription drug monitoring program, and securing medications in a locked container.[78,83] Newer abuse-deterrent formulations have the potential to mitigate abuse and diversion of opioid analgesic medications.

Weak opioids include tramadol, tapentadol, and buprenorphine and may be better tolerated by older adults. Tramadol is a centrally acting synthetic analgesic with opioid-like effects. Its mode of action is through binding to the μ-opioid receptor and inhibition of noradrenaline and serotonin reuptake. The efficacy of tramadol is comparable to that of ibuprofen in patients with hip and knee OA. Dose reduction may be required in older patients, Tapentadol is a centrally acting analgesic and acts as a μ-opioid receptor agonist and noradrenaline reuptake inhibitor.[84] Buprenorphine is a semisynthetic opioid analgesic that acts primarily as a partial agonist at the μ-opioid receptor. The transdermal formulation provides continuous delivery of buprenorphine, resulting in a relatively consistent plasma drug concentration throughout a 7-day dosing interval.[85] The more traditional weak opioids may be effective but have a ceiling effect for analgesia due to the combination and limits of acetaminophen. If adequate pain relief is not obtained at optimal doses, change to a strong opioid should be considered.

Morphine is the prototypic opioid. Its analgesic properties are not limited by a ceiling effect, but side effects are common. Tolerance to side effects develops more rapidly than tolerance to analgesic effects, although constipation tends to persist. Once the daily opioid requirements have been established through the administration of a short-acting opioid on a regular basis, the use of delayed-release opioid agents should be considered. Delayed-release morphine and oxycodone preparations may be used in older patients but care must be taken to prevent drug accumulation. Other strong opioids include methadone, hydromorphone, and fentanyl. Methadone must be used with caution because it has a long half-life of up to 2 or 3 days, resulting in accumulation in older patients.

When carefully monitored, opioid analgesics can be very effective in treating pain in older adults. However, achieving efficacy and tolerability is sometimes compromised by two related clinical manifestations of this treatment approach, opioid tolerance and opioid-induced hyperalgesia (OIH). Tolerance may develop with repeated administration of all opioids whereby higher doses are required to maintain equivalent analgesic effects. The rate of development of tolerance varies greatly, but is not as common as once believed. OIH is described as a paradoxic response in which prolonged opioid administration results in an atypical increase rather than a decrease in pain that appears unrelated to the original nociceptive stimuli.[86,87] Clinical differences between the two conditions have been described. Opioid tolerance is characterized by a decrease in the efficacy of the drug, which can be overcome by increasing the drug dosage. Conversely, OIH is not overcome by increasing the drug dosage and will worsen the pain. In this scenario, pain is improved by reducing or eliminating the drug.[88] Clinical recognition and management is a challenge for clinicians.

Before tolerance is suspected in a patient with a previously established opioid dose, evidence of advancing disease, new-onset disease or injury, or psychosocial cause should be investigated. If these are negative, the dose or frequency of dosing may be increased. Cross-tolerance with other opioids is not complete because they often act through different combinations of receptors. The problem may be overcome by changing to another oral opioid, commencing at 50% of the equianalgesic dose. When a patient is unable to tolerate oral opioids or has refractory pain, parenteral analgesia by the transdermal, subcutaneous, venous, epidural, or intrathecal route should be considered. A transdermal fentanyl patch offers the advantage of one application every 72 hours. It has a similar side effect profile to other opioids, although some patients report less constipation than with other preparations. Fentanyl accumulates in skeletal muscle and fat and then is slowly released into the blood. Minimum effective concentrations are reached approximately 6 hours after application. Serum fentanyl concentrations decrease by 50% approximately 17 hours after removing the patch. The clearance of fentanyl is delayed in older, cachectic, and debilitated patients. The 25-μg/hr transdermal fentanyl patch is equivalent to about 90 mg of morphine/day. It is not recommended for opioid-naive patients.

Clinical criteria for diagnosing OIH have been proposed, including the following: (1) increased pain intensity during ongoing opioid treatment; (2) no evidence of underlying disease progression; (3) no evidence of opioid withdrawal; (4) no evidence of opioid tolerance (tested by decreased pain in response to added dose); (5) decrease in pain intensity in response to dose reduction; and (6) no evidence of addictive behavior.[87] Several mechanisms for neural changes in response to exposure to μ-opioid agonists that lead to OIH have been proposed. Although not fully understood, management approaches are related to the sensitization of glutamenergic systems, *N*-methyl-D-aspartate (NMDA) receptor activation, and enhanced descending descending facilitation to the dorsal horn of the spinal cord.[86,87] Opioid-sparing strategies with adjuvant drug therapies, such as anticonvulsants and antidepressants, and heat, cold, and exercise programs have been used to treat OIH. Opioid rotation has demonstrated effectiveness in treating opioid tolerance and increased opioid sensitivity.[89-91] NMDA receptor blockade studies have had mixed results. Ketamine, methadone, dextromethorphan, and COX-2 inhibitors all have a theoretical rational in OIH treatment[87] but should be used cautiously in older adults.

Clinical strategies to manage these potential opioid administration–related conditions as well as other potential opioid side effects begins with vigilant monitoring and early problem identification. Treatment can be time-consuming and may require multiple office visits. Rational polypharmacy, including nonopioid medications and nonpharmacologic approaches in conjunction with opioid analgesics, can be very effective in older adults.

Adjuvant Analgesics

Adjuvant analgesics are drugs that have a primary indication other than pain, are analgesic in many pain syndromes, but have been most studied in neuropathic pain syndromes. They include medications from heterogeneous therapeutic classes, including selected antidepressants, anticonvulsants, topical lidocaine, and herbal remedies. Antidepressants act by modulating pain through direct pathophysiologic mechanisms or by treating underlying depression that might augment pain perception. Tertiary amines (e.g., amitriptyline, imipramine, doxepin) should be avoided in older adults because of anticholinergic side effects, including sedation, constipation, urinary retention, delirium, and dizziness. Amitriptyline entails the risk of cardiac arrhythmia. Secondary amines (e.g., nortriptyline, desipramine) tend to have a more favorable adverse event profile in older adults.[92] Serotonin norepinephrine reuptake inhibitors (SNRIs), such as duloxetine and venlafaxine, have been approved for the treatment of diabetic peripheral neuropathic pain, but SSRIs do not appear to be effective for pain management. Among the anticonvulsant drug class, the calcium channel alpha-2/delta-1 ligands (gabapentin and pregabalin) are associated with a more favorable adverse event profile and with fewer drug-drug interactions.[92]

Neuropathic pain (NeP) has been defined as pain arising as a direct consequence of a lesion or disease affecting the somatosensory nervous system.[93] Toth and Au[94] have reported a prevalence rate for NeP of 45% for patients presenting with polyneuropathy from a variety of causes. Treatment based on clinician and patient preference, usually gabapentin, pregabalin, topiramate, and amitriptyline, suggests an average number needed to treat (NNT) of 2 to 3 for more than 30% relief. The average NNT was 5 to 7 for more than 50% relief. Average NeP pain relief was 31% to 42% on a visual analogue scale (VAS) after 6 months, and amitriptyline had a slightly greater intolerable side effect profile.[94]

The selection of an adjuvant analgesic agent for the management of neuropathic pain should be based on the side effect profile and the potential for drug interaction rather than on the relative efficacy of different agents. There is considerable individual variation in the response to these agents. Failure to respond to one agent is not predictive of the response to another agent in the same therapeutic class.

Topical lidocaine patches have been licensed for use in PHN in the United States[95] and are an effective treatment for diabetic neuropathy.[96] In addition, herbal products and dietary supplements are used by many Americans. Marinac and coworkers have found that 21% of persons older than 60 years were using at least one herbal or dietary supplement, with 19% at risk for a potential adverse drug reaction.[97]

Nonpharmacologic Therapies

Nonpharmacologic approaches, alone or in combination with pharmacologic treatment, should be an integral part of the care plan for older adults with chronic pain. These approaches encompass a broad range of physical, psychological, and other treatment modalities. They are widely used by patients, often without the knowledge of their health care provider. Nonpharmacologic interventions can also refer to invasive approaches such as epidural steroid injections and spinal cord stimulators. This section will focus on noninvasive approaches.

Psychological Approaches

Psychological factors may contribute to the maintenance of pain or be causally related to the pain. Regardless of the pathophysiologic basis of chronic pain, psychological strategies have a role in management. The essence of management is to establish appropriate pain-coping strategies and discourage behaviors that may perpetuate the pain syndrome. Generally, a combination of behavioral and cognitive strategies is used. Cognitive strategies are aimed at modifying belief structures, attitudes, and thoughts to modify the experience of pain and suffering. This approach also includes distraction therapy, relaxation, biofeedback, and hypnosis. The patient is encouraged to take an active role and accept responsibility for pain management, rather than being a passive victim. These strategies have been demonstrated to be effective for managing pain in older adults.[98] Although difficulties in accessing treatment have been cited, models to mitigate the access barrier have been emerging.[99-101]

Other self-management strategies such as yoga, tai chi, and music therapy, have shown promise for reducing pain and increasing function in older adults.[100,102-104] The use of telephone- and Internet-delivered interventions may increase access to these therapies for older adults.

Physical Therapies

Simple adjustments in posture and daily routines, such as preparing meals in a seated position, breaking up the housework, or providing a walking aid can reduce the impact of pain on daily life. The use of a walking frame, which causes a mild degree of lumbar flexion, will often ease the pain of lumbar canal stenosis.

Exercise is a major component of most pain management programs, alone or in conjunction with pharmacologic and other nonpharmacologic approaches. Even frail and institutionalized older adults may benefit. Exercise can lead to decrease in pain, improvements in function, and elevation of mood.[105,106] Low-impact exercises, such as walking and water aerobics, may be helpful in reducing pain and improving function.[107,108] Hydrotherapy should be considered when weight-bearing exercises aggravate pain.[105,109] The buoyancy effect of water reduces the weight of the body, allowing joints to be moved with minimal friction through a full range of movements. The warmth of the water decreases pain and muscle spasm. Transcutaneous electrical

nerve stimulation (TENS) is a popular method of symptom relief for a wide range of painful conditions in older adults, such as low back pain, OA, and PHN.[105,110] Other physical therapies used for a wide range of painful conditions include massage, cold and heat treatments, acupuncture, and electrotherapies such as ultrasound, low-level laser therapy, and biofeedback. Combined with drug therapies, nonpharmacologic interventions may have an additive or synergistic effect on the management of pain and improved function in older adults.

Pain and Cancer

Half of all cancers occur in those older than 60 years.[111] In the advanced stages of cancer, 64% experience pain, and the pooled prevalence of pain in all types of cancer at all stages is more than 50%. Many patients (>33%) report moderate to severe and persistent pain.[112] Despite clear guidelines, pain associated with cancer persists in older adults.[113]

The World Health Organization (WHO) method for relief of cancer pain is based on a three-step approach to the use of analgesia. The first step of the WHO analgesic ladder is nonopioid analgesics, including acetaminophen and NSAIDs. The second step is weak opioids, and the third step is the strong opioid group. Nonopioid analgesics are usually combined with an opioid in steps 2 and 3 to give additive analgesia.[114] The relevance of this approach has come into question due to newer pharmacologic delivery systems (e.g., rapid-onset opioid analgesics) and the need to bypass earlier steps in many cases.[115-118] The use of strong opioids as first-line therapy compared to the WHO analgesic ladder has demonstrated better pain control, with fewer changes in therapy.[119] A more recent guideline has supported the role of opioid analgesics as first-line therapy for patients with pain associated with cancer.[120]

CONCLUDING REMARKS

Advancing age is associated with an increased incidence of painful pathology. Anyone who has persistent pain, despite what appears to be conventional treatment, should be carefully reassessed to determine why there has been a failure of response to therapy. One should never conclude that it is the patient who has failed to respond to treatment; it is the treatment that has failed to achieve the desired result. Severe unrelieved pain has a profound impact on an individual. Various factors may preclude the older patient from the benefit of definitive therapy to eradicate pain and, under these circumstances, symptom management is indicated. This must take into consideration the effect of comorbidities on the expression, assessment, diagnosis, and treatment of the painful condition. Overemphasis on pharmacologic approaches ignores the potential benefits of physical and cognitive-behavioral strategies. The persistence of pain despite apparently appropriate therapy raises the possibility of unrecognized mood disturbance, pain of neurogenic origin, or advancing pathology. Under these circumstances, a multidisciplinary pain management approach involving medical, physical, and psychological therapeutic modalities is often more effective than a single disciplinary approach.[121] Multidisciplinary pain management clinics have emerged over the past 30 years, but are limited geographically and by expertise in geriatric medicine. Age should not, however, be regarded as a barrier to successful outcomes from the multidisciplinary management of pain problems. Even if pain cannot be eradicated, worthwhile improvements can often be achieved by addressing pain as a problem in a broader sense, not simply as a sensory symptom.

KEY POINTS

ASSESSMENTS

- Contribution of nociceptive and neuropathic factors
- Impact of pain on function and mood state
- Comorbidities affect assessment, function, and treatment selection.

INVESTIGATIONS

- Presence of radiologic abnormalities does not prove causality.
- Unexplained change in symptoms warrants reassessment to exclude serious pathology.

For a complete list of references, please visit www.expertconsult.com.

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