



Geriatric pain management, pharmacological and nonpharmacological considerations

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Abstract

Persistent pain is prevalent in the elderly population, although it is not an inevitable part of aging. It is important to understand how to manage pain effectively in old age, particularly because an increasing number of individuals are becoming older, or living longer. Several problems, less common in younger adults, may complicate the treatment of pain. An accurate pain assessment is required for the most efficient strategy of pain treatment. Challenges to an effective pain assessment include: pain underreporting by patients, atypical manifestations of pain in elderly, age-associated pharmacodynamic and pharmacokinetic changes to specific drugs, other general age-related changes, and misconceptions about tolerance or addiction to opioids. However, physicians are able to provide geriatric patients with appropriate analgesia by using comprehensive assessment involving a multidisciplinary approach, and the appropriate use of various treatment modalities. **Keywords:** geriatric pain management, pain assessment, pain threshold, geriatric pharmacokinetics

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Introduction

Elderly men and women represent the fastest growing demographic in the world's population. By 2040 the number of people aged 65 and older worldwide will increase to 1.3 billion from the current 506 million. In the United States alone, the elderly population will increase from 40 million to 80 million by 2040. Although pain is not part of normal aging, a significant proportion of the elderly experience physical discomfort. Studies

suggest 25% to 50% of community-dwelling elders report pain, and that for elderly residents in nursing homes the prevalence of pain is as high as 80% (Kaye, Baluch, & Scott, 2010; Charette & Ferrell, 2007; Berdine & Mihalyo, 2004).

Chronic geriatric pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage for persons who are either aged (65 to 79 years old) or aged (80 and over) and who have had pain for greater than 3 months." (Kaye et al., 2010) With inadequate treatment, this pain produces functional impairment and decreased quality of life for elderly patients. Other consequences may include sleep disturbances, depression, anxiety, decreased socialization, cognitive dysfunction, polypharmacy, malnutrition, and increased costs associated with health care (Kaye et al., 2010; Manchikanti, Singh, Datta, Cohen, & Hirsch, 2009; Bruckenthal, 2008). Pain-related lessened activity may also lead to gait impairments, which may result in injuries from falls and accidents.

The prevalence of chronic pain increases with age (Crook, Rideout, & Browne, 1984) along with neuralgias and joint pain (Badley & Tennant, 1992). A significant proportion of elderly individuals experience daily pain but fail to receive adequate treatment. In one study of

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elderly cancer patients with pain, 21% between 65 and 74 years of age received no pain medication; in those 75 to 84 years old, 26% received no pain medication, and for those above the age of 84, 30% received no pain medication (Kaye et al., 2010; Cleeland, 1998). Undertreatment is exacerbated further by a lack of efficient methods for detection and management of geriatric pain (Woo, Ho, Lau, & Leung, 1994). A study of elderly nursing home residents found 66% with pain; however, physician assessment detected only 34% (Kaye et al., 2010; Sengstaken & King, 1993; Ferrell, 1991).

Barriers to effective pain assessment in elderly patients

Geriatric pain assessment is a complex clinical process influenced by several factors. Complicating factors include cognitive or language impairments that diminish communicative abilities, coexisting illnesses, concomitant medications, and the cost of drugs. Assessment can be impacted specifically by negative mood states such as depression, heightened anxiety, psychosocial concerns, poor memory, and failing health. Elderly patients may underreport discomfort, thinking that pain is an inevitable part of aging or because they believe their physician is too busy to hear such concerns. Additionally, the elderly may fear the meaning of the pain and worry about the possible side effects of medications. Patients and healthcare providers alike may also avoid the use of opioids because of misconceptions about addiction and tolerance.

There are needs for more reliable and valid methods of identifying, diagnosing, and understanding pain in older individuals. These problems have been the focus of an increasing number of papers related to pain measurement in patients with dementia, in addition to pain assessment research more generally (Kaye et al., 2010; Ferrell, Ferrell, & Rivera, 1995; Kovach, Weissman, Griffie, Matson, & Muchka, 1999; Warden, Hurley, & Volicer, 2003).

Pain assessment and the physical examination

Geriatric pain assessment requires a comprehensive and multidisciplinary approach to the description, diagnosis, and management of chronic pain. Physicians, psychologists, psychiatrists, and physical therapists work together to develop pain management strategies based on their individual evaluations of the patients. Meetings with patient caretakers, as well as laboratory or imaging studies, may be necessary if the initial workup does not provide sufficient information for a diagnosis.

Evaluations of patient functional abilities and performances are included in the assessment. Impairments in functional status may impact degree of independence, quality of life, and need for caretakers. Assessment of patient daily activities and habits such as using Activities of Daily Living (ADL) and

Instrumental Activities of Daily Living (IADL) ferrets out possible functional limitations. This information can then be incorporated into treatment plans toward the goals of maximizing patient function and decreasing pain perception (Kaye et al., 2010).

Pain assessment scales

Verbal Descriptor Scales (VDS), Numerical Rating Scales (NRS), and Visual Analogue Scales (VAS) are commonly used to assess pain intensity. Current data support the validity of all three methods. The VDS has been recommended specifically for use with elderly patients, and patients often prefer it to the other measures because it is the easiest to complete (Herr, Spratt, Mobily, & Richardson, 2004). Because studies have shown an association between the VAS and unscorable or incorrect responses in the elderly, the measure is used best with caution (Gagliese, 2002; Gagliese, & Melzack, 1997). However, in clinical and research settings the VAS has proven reliable and provides the advantages of simplicity, easy administration, and minimal obtrusiveness (Kaye et al., 2010). Difficulty has been reported in elderly patients with answering the NRS, particularly when administered verbally (Kaye et al., 2010; Herr & Mobily, 1993; Benesh, Szigeti, Ferraro, Gullicks, 1997; Gagliese & Melzack, 1997).

The McGill Pain Questionnaire (MPQ) assesses the sensory, affective, evaluative, and miscellaneous components of pain (Melzack, 1975). The validity, reliability, and discriminative capabilities of the scale are supported and are not age-related. Pain may be described in terms of intensity, affect, location, or several other domains (Ferrell, 2000). However, the MPQ tends to be time-consuming and difficult to use in clinical settings.

Pain history and examination

In addition to the evaluation of pain intensity and its characteristics, a thorough examination is needed. A detailed history is taken, and a physical examination is performed including a review of systems and relevant laboratory data, imaging studies, and diagnostic tests. An in-depth review of the location, intensity, and other factors associated with reported pain is conducted. Baseline functionality is determined by evaluation of ADLs, balance, and gait. Additionally, evaluation of patient psychological functioning and present social and living situations is conducted. The temporal relationship among significant life events, medical interventions, and various pain and emotional complaints are noted.

Any self-reported pain is thoroughly explored. Pain that is persistent, recurrent, and impacts patient quality of life or functional capacity is considered significant. Many elderly do not complain specifically of "pain", but instead they use a variety of terms such as "hurting", "burning", or "aching" to refer to their problems. As a result, terms other than "pain" may be targeted to screen

for symptoms. Behavioral cues such as vocalizations and changes in behavioral or physical functioning can indicate the presence and severity of pain. These are primarily important in the assessment of individuals with cognitive impairments. Reports from caregivers and close relatives are essential, especially in patients with cognitive or language impairment.

History

If pain symptoms have increased from the previous visit or treatment session, the physician should increase the frequency of assessment using clinical judgment. Since the older population commonly has multiple medical problems, it is not uncommon to find multiple sources of pain. The intensity, character, frequency, location, and duration of pain are included in the history. The physician should determine whether symptoms are due to one underlying pathology or multiple overlapping pathologies. Factors that exacerbate or ameliorate pain can help to elucidate the diagnosis. Therefore, questions related to effects of past treatments as well as a thorough analgesic history should be asked. After determining these factors, inquiry should be made concerning the patient's response to current treatments and subsequent effects on the patient's physical, mental, social, and functional status. In addition, a quantitative assessment of patient pain is obtained with the most appropriate measurement scale. To the extent possible, physicians review the previous medical, surgical, and psychiatric condition daily, as well as records of injuries and accidents. Coexisting diseases along with current and previous treatments can impact treatment decisions.

It is not uncommon for an older patient with pain to have anxiety or depression or both, and oftentimes it is unclear if chronic pain is causing depression or anxiety or if depression and anxiety are causing chronic pain. A depression assessment using the Geriatric Depression Scale (GDS) may be used in these situations to help determine which occurred first. The medication history consists of listing all current and past medications, dosages, and adverse effects, and prescribed, over-the-counter, and herbal supplements are included.

Physical examination

The physical exam assesses the neuromuscular systems with attention to impairments, weakness, numbness, tingling, hyper/hypoalgesia, hyperpathia, or allodynia. Certain pathologies may be suggested by the presence of local inflammation, bony deformities, or trigger points at specific sites. Gait and balance are also assessed to determine functional mobility.

Functional assessment

Physical function is determined by assessing patient ability to perform ADLs. Mobility impairments may contribute to deficits in physical functioning and are evaluated by gait, balance, and range of motion testing.

Psychosocial assessment

Patient psychosocial functioning can be determined by exploring factors including mood, social support systems, family or caregiver relationships, and financial resources. Heightened anxieties and mild to severe depression symptoms are common in individuals with chronic pain and behaviors associated with anxiety or depressive disorders are noted. The availability and type of relationship in social support systems are explored. Patients with greater interpersonal involvement and more supportive social contacts spend less time focusing on their painful condition and consequently can exhibit greater reductions in pain. Conversely, interpersonal isolation and negative social relationships may impede treatment outcome.

Follow-up interval

Once the initial assessment has been completed, a follow-up interval is determined in relation to the severity of the pain and dysfunction. Follow-up visits aid in reassessing improvement or worsening of the condition, patient compliance, and complications with medications. Evaluators observe and record the positive and negative effects of the therapeutic modalities and analgesics and modify the treatment plan accordingly (American Geriatrics Panel on chronic pain in older persons, 1998).

Pain assessment in the cognitively impaired

Pain assessment is more challenging in individuals with cognitive impairments. These patients may lack the capacity to report pain accurately and reliably, although cognitively impaired individuals who have retained adequate communication skills are more likely to provide physicians with a valid pain report. Research suggests that self-reports from patients characterized by mild to moderate cognitive impairments are as valid and reliable as reports from those with normal cognitive functions (Parmelee, Smith, & Katz, 1993; Weiner, Peterson, Logue, & Keefe, 1998). As a result, these mildly to moderately impaired individuals can be assessed similarly to patients with normal cognitive function, beginning with a self-report and thorough examination. The VDS is generally recommended for measuring pain intensity in patients with mild to moderate cognitive impairment (Herr & Mobily, 1993; Herr & Garand, 2001).

The assessment of pain in individuals who exhibit cognitive impairments and/or frank deficits in receptive and expressive language poses major challenges. There is currently no clearly best method or guidelines for evaluating pain in these patients. Behavioral cues may be used to evaluate pain in non-communicative patients, including observing vocalizations, facial expressions, withdrawn/agitated behavior, and changes in gait or posture. Nevertheless, studies show many of these assessments underestimate pain intensity (Pautex et al., 2005; Pautex et al., 2006). It may be helpful for patient caregivers or close relative to provide reports containing information regarding patient pain and observed changes

in behavior and emotional responsiveness, although there are limits to these assessments (Ferrell, 1991; Lin, Lum, Mehr, & Kane, 2006).

Pathophysiological changes in the elderly

During normal aging there is a steady reduction of organ system function and homeostatic functions. The central nervous system, hepatic, renal, and respiratory systems are the most important organ systems affected with aging.

Central Nervous System

Elderly patients present a higher prevalence of neurological diseases and dysfunctions resulting from or associated with age-induced changes in the central nervous system (CNS). Mental processing deficiencies are present in 15% of the total geriatric population, whereas 50% of elderly subjects who live in nursing homes have either a psychological illness or dementia (Ferrell, 1996). Other conditions include strokes, transient ischemic attacks, and movement disorders, which may affect pain assessment and treatment efficacy (Kaye et al., 2010; Broe, 1989).

In many patients seeking pain relief, the number of neurotransmitter cell receptors decreases with age-associated cortical and subcortical atrophy of brain tissue. Synaptic efficiency decreases as neurons fail to regenerate and are replaced by proliferating glial cells (Long, 1985). The greatest loss of neurons is observed in the locus coeruleus and substantia nigra and has an effect on pain transmission (Ghafoor, 2003). Reduction in dendritic synapses and intracellular enzymes additionally contribute to the decreased synaptic ability (Kaye et al., 2010; Coleman & Flood, 1987).

Age-induced changes in the CNS are responsible for deficits in cognitive and motor functions and may occur as early as 50 years of age. The development and onset of CNS conditions are influenced by important factors such as heredity and genetics, concomitant disease, level of intellectual complexity or ability, and stresses from daily activities or trauma (Samorajski, 1976).

Neuroendocrine function decreases with age and contributes to common neurological diseases present in elderly adults. Parkinson's disease and Alzheimer's disease show reduced dopaminergic and cholinergic/hypothalamic/noradrenergic function, respectively (Rehman & Masson, 2001).

Minor alterations in memory resulting in neurological changes are thought to be a normal feature of aging. However, dementia is present in 5% to 20% of adults age 65 and older. Alzheimer's disease is the most common cause of dementia, constituting 60% of all cases. There are other possible causes or corollaries of dementia that require exploration including Parkinson's disease, vascular disorders, normal-pressure hydrocephalus, neoplastic diseases, alcoholism and other long-term additions, genetically transmitted neurodegenerative diseases, CNS infections, metabolic

disorders, and pseudodementias (Kaye et al., 2010; Simon, Aminoff, & Greenberg, 1989).

Hepatic

An elderly liver may prolong the clearance of drugs from the body secondary to prehepatic, intrahepatic, or posthepatic causes. Prehepatic dysfunction includes decreased first-pass metabolism and blood extraction, which may be secondary to reduced arterial and portal blood flow and lower gastrointestinal absorption. Intrahepatic dysfunction may be caused due to hepatocellular pathology, for example, cirrhosis. Additionally, posthepatic dysfunction is caused by either biliary tree or enterohepatic circulation pathology (Kaye et al., 2010).

Renal system

Starting at the age of 40, renal function declines ~1% per year or a 1 mL/min/yr decline in creatinine clearance (Kaye et al., 2010; Stiff, 1993). In healthy elderly individuals, however, the overall function of the kidneys appears to be maintained (Kohli et al., 2006). In a recent report, more than 5% of elderly patients were determined to exhibit renal failure, primarily as a result of diabetic nephropathy.

Pain threshold

Several studies have focused on the relationship between aging and pain threshold. Gibson (2003) conducted a meta-analysis of 50 previous studies that examined age differences in sensitivity to induced pain. Of these 50 studies, 21 reported data that supported an increase in pain threshold with increasing age, three reported a decrease, and 17 reported no difference. The effect size was 0.074 ($p < 0.0005$), indicating evidence of an increase in pain threshold with advancing age (Kaye et al., 2010; Gibson, 2003).

Further studies have shown that the effect of age on pain threshold depends on the method of pain induction. Lautenbacher, Kunz, Strate, Nielsen, and Arendt-Nielsen (2005) compared pain perception from different stimuli in two groups. Each consisted of 20 men classified according to age, with the mean age of the older group 71.6 and the younger at 27.1. Results revealed that for older individuals somatosensory thresholds for non-noxious stimuli were increased, whereas pressure thresholds decreased. No age-associated changes were observed for heat pain threshold (Lautenbacher et al. 2005). These results confirm previous studies (Kaye et al., 2010; Gibson, 2003; Lin, Hsieh, Chao, Chang, & Hsieh, 2005; Verrillo, Bolanowski, & Gescheider, 2002; Woodrow, Friedman, Siegel, Collen, 1972; Pickering, Jourdan, Eschaliere, & Dubray, 2002).

The difference in pain perception may be related to age-associated changes in CNS. Research has focused primarily on the differential changes in A δ - and C-fibers that transmit epicritic/phasic pain and protophasic/tonic pain, respectively. Results from these studies support the presence of a deficit in the ability of older people to

perceive A δ -mediated pain, but there was no evidence of age-related differences in the perception of C-fiber mediated pain (Chakour, Gibson, Bradbeer, & Helme, 1996).

Common comorbidities in the elderly

The prevalence of certain pain-associated conditions increases with age. Comorbidity represents an important consideration in the assessment and treatment of pain. The most effective treatments are based on a solid base of knowledge concerning common geriatric pain conditions, thus allowing delivery of the most efficient treatments. A list of common geriatric pain syndromes is shown in Box 1.

Rheumatic disease (i.e., osteoarthritis, rheumatoid arthritis)
Cancer pain
Angina
Herpes zoster
Postherpetic neuralgia/shingles
Temporal arteritis
Pain associated with atherosclerosis and diabetic peripheral neuropathy
Trigeminal neuralgia
Alcohol abuse
Malnutrition

Box 1. Description of chronic geriatric pain syndromes

Modified from Kaye A. D., Baluch A., & Scott J. T. (2010). Pain management in the elderly population: A Review. *The Ochsner Journal*, 10, 183.

Pharmacokinetic changes

Increased body fat, decreased total body water, and decreased muscle mass are age-related changes in body composition that effect drug distribution (Kaye et al., 2010; Turnheim, 2003; Vuyk, 2003).

Diuretics may further decrease body water, and these drugs are commonly in the elderly. Hydrophilic drugs such as ethanol, lithium, and cimetidine are less used, distributed effectively, and result in more rapid onset of action and increased peak concentrations. Consequently, there is a greater risk of side effects for hydrophilic medications in the elderly. Lipophilic drugs such as diazepam and lidocaine have an increased distribution and slow onset of action. With repeated dosing, accumulation of lipophilic drugs will occur. Frailty and malnourishment are common in elderly patients and additionally influence drug distribution (Kaye et al., 2010; ElDesoky, 2007).

Decreases in serum albumin concentrations increase the proportion of free drug in the plasma. Therefore, highly protein bound drugs such as NSAIDs, benzodiazepines, and anti-epileptics will cause higher levels of adverse effects in elderly patients. Poor nutritional status may also affect free drug concentrations (Kaye et al., 2010).

Age-associated decreases in liver size and hepatic blood flow reduce the clearance of drugs that undergo first-pass metabolism in the liver such as lidocaine and narcotics (Bresler & Bahl, 2003). The amount of free drug in the plasma is increased and, as a consequence, elderly patients are at risk for a greater chance of side

effects and adverse reactions. The presence of frailty, comorbidities, or polypharmacy can additionally increase these chances (Kitani, 1986; Kinirons & Crome, 1997). To avoid complications in the elderly, drugs that undergo significant first-pass metabolism should be initiated slowly at low doses (Crooks & Stevenson, 1981). The renal elimination of drugs and their metabolites is reduced with age as a result of decreased glomerular filtration and tubular reabsorption and decline in renal mass and blood flow (Shi, Mörrike, & Klokz, 2008). Drugs that are eliminated primarily renal, including several antibiotics and lithium, will have increased drug levels for a prolonged duration (Wright & Warpula, 2004). Patients experiencing age-associated renal insufficiency and dehydration should be cautiously administered renally cleared drugs, and the dosage should be decreased while the frequency of administration increased. Overall reduction in kidney and liver function increases the half-life of many benzodiazepines and tricyclic antidepressants.

Hepatic phase I oxidation metabolism including oxidation, reduction, and hydrolysis is more susceptible to age than hepatic phase II conjugation reactions such as acetylation, glucuronidation, sulfation, and glycine conjugation (Wright & Warpula, 2004). Drugs that undergo phase I metabolism have reduced elimination in the elderly. Acetaminophen and diazepam are metabolized at the same rate for all ages. However, drugs metabolized by the same enzyme system including carbamazepine, lidocaine, and fentanyl undergo reduced metabolism in the elderly. Glucuronidation of morphine and glutathione conjugation of acetaminophen are phase II reduction reactions and are not affected by age. To decrease side effects that are a result of reduced metabolism and elimination, physicians should be cautious when administering drugs that undergo hepatic phase I metabolism (Kaye et al., 2010).

Pharmacodynamic changes

In the elderly, the decline in drug sensitivity is associated strongly with age-related decline in CNS function (Kaye et al., 2010). Geriatric patients exhibit increased sensitivity to drugs that act centrally or have centrally mediated effects including benzodiazepines, opioids, and psychotropic drugs. As a result, these drugs produce exaggerated effects in older individuals. In contrast, the adrenergic and cholinergic autonomic nervous system has reduced sensitivity to receptor-specific drugs with age. Reduced response to β -adrenergic stimulation results the decreased effect of β -blockers (Muravchick, 1998).

Observance to physician in the elderly population

Poor medical compliance prevents physicians from providing effective pain management and can be attributed to multiple factors. Factors include poor physician-patient communication, cost of care, ethnic

and cultural beliefs, drug and dosage form, and insurance coverage (Kaye et al., 2010; Steinman & Hanlon, 2010). Approaches to involved efforts to increase compliance include communicating the purpose and side effect profile of medications, prescribing simple dosing regimens, decreasing the total number of drugs needed, scheduling regular follow-ups, preparing individualized medication cards, establishing medication review by pharmacists, and using of multi-compartment dose administration aids (George, Elliott, & Steward, 2008). Many studies have been conducted to determine the best way to address non-compliance; however, inconsistent study methodologies and findings have prevented the drawing of firm conclusions in favor of any specific method over another.

Pain management options in the elderly

A multidisciplinary approach to pain management is recommended to provide the most effective and comprehensive addressing of all the components of pain. Pain treatment modalities for the elderly may be classified into the following four groups (Kaye et al., 2010):

1. Pharmacotherapy
2. Physical rehabilitation
3. Psychological support
4. Interventional procedures

Pharmacotherapy

Pharmacotherapy is the most common method used to control geriatric pain and, in addition, is relatively easy to implement. Drug treatment consists of NSAIDs, muscle relaxants, opioids, and adjuvant therapy. Analgesic drugs are effective and safe when properly used; however, the elderly have an increased risk of adverse reactions. The cognitive, functional, and physiological status of the patient may be affected. The American Geriatric Society (AGS) and the World Health Organization (WHO) have formed counsels to conceptualize and develop better approaches to managing geriatric pain (Kaye et al., 2010; American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons, 2009).

A. Nonopioids

I. Acetaminophen is considered as initial and ongoing pharmacotherapy in the treatment of persistent pain, particularly musculoskeletal pain, owing to its demonstrated effectiveness and good safety profile (high quality of evidence; strong recommendation).

a. Absolute contraindications: liver failure (high quality of evidence, strong recommendation).

b. Relative contraindications and cautions: hepatic insufficiency, chronic alcohol abuse or dependence (moderate quality of evidence, strong recommendation).

c. Maximum daily recommended dosages of 4 g per 24 h are not to be exceeded and must include “hidden

sources” such as from combination pills (moderate quality of evidence, strong recommendation).

II. Nonselective NSAIDs and COX-2 selective inhibitors may be rarely considered and with extreme caution in highly selected individuals (high quality of evidence, strong recommendation).

a. Patient selection: other (safer) therapies have failed; evidence of continuing therapeutic goals not met; ongoing assessment of risks and complications outweighed by therapeutic benefits (low quality of evidence, strong recommendation).

b. Absolute contraindications: current active peptic ulcer disease (low quality of evidence, strong recommendation), chronic kidney disease (moderate level of evidence, strong recommendation), heart failure (moderate level of evidence, weak recommendation).

c. Relative contraindications and cautions: hypertension, *Helicobacter pylori*, history of peptic ulcer disease, concomitant use of corticosteroids or SSRIs (moderate quality of evidence, strong recommendation).

III. Older persons taking nonselective NSAIDs should use a proton pump inhibitor or misoprostol for gastrointestinal protection (high quality of evidence, strong recommendation).

IV. Patients taking COX-2 selective inhibitors with aspirin should use a proton pump inhibitor or misoprostol for gastrointestinal protection (high quality of evidence, strong recommendation).

V. Patients should not take more than one nonselective NSAID or COX-2 selective inhibitor for pain control (low quality of evidence, strong recommendation).

VI. Patients taking aspirin for cardioprophylaxis should not use ibuprofen (moderate quality of evidence, weak recommendation).

VII. Patients taking nonselective NSAIDs and COX-2 selective inhibitors should be assessed routinely for gastrointestinal and renal toxicity, hypertension, heart failure, and other drug-drug and drug-disease interactions (weak quality of evidence, strong recommendation).

B. Opioids

VIII. Patients with moderate to severe pain, pain-related functional impairment, or diminished quality of life because of pain may be considered for opioid therapy (low quality of evidence, strong recommendation).

IX. Patients with frequent or continuous pain on a daily basis may be treated with around-the-clock time-contingent dosing aimed at achieving steady-state opioid therapy (low quality of evidence, weak recommendation).

X. Clinicians should anticipate, assess for, and identify potential opioid-associated adverse effects (moderate quality of evidence, strong recommendation).

XI. Maximal safe doses of acetaminophen or NSAIDs should not be exceeded when using fixed-dose opioid combination agents as part of an analgesic

regimen (moderate quality of evidence, strong recommendation).

XII. When long-acting opioid preparations are prescribed, breakthrough pain should be anticipated, assessed, and prevented or treated using short-acting immediate-release opioid medications (moderate quality of evidence, strong recommendation).

XIII. Clinicians well versed in the use and risks of methadone should initiate it and titrate it cautiously (moderate quality of evidence, strong recommendation).

XIV. Patients taking opioid analgesics should be reassessed for ongoing attainment of therapeutic goals, adverse effects, and safe and responsible medication use (moderate quality of evidence, strong recommendation).

C. Adjuvant analgesic drugs

XV. All patients with neuropathic pain are candidates for adjuvant analgesics (strong quality of evidence, strong recommendation).

XVI. Patients with fibromyalgia are candidates for a trial of approved adjuvant analgesics (moderate quality of evidence, strong recommendation).

XVII. Patients with other types of refractory persistent pain may be candidates for certain adjuvant analgesics (i.e., back pain, headache, diffuse bone pain, temporomandibular disorder) (low quality of evidence, weak recommendation).

XVIII. Tertiarytricyclicantidepressants (amitriptyline, imipramine, doxepin) should be avoided because of higher risk for adverse effects (i.e., anticholinergic effects, cognitive impairment) (moderate quality of evidence, strong recommendation).

XIX. Adjuvant agents may be used alone, but often the effects are enhanced when used in combination with other pain analgesics and nondrug strategies (moderate quality of evidence, strong recommendation).

XX. Therapy should begin with the lowest possible dose and increase slowly based on response and side effects, with the caveat that some agents have a delayed onset of action and therapeutic benefits are slow to develop. For example, gabapentin may require 2 to 3 weeks for onset of efficacy (moderate quality of evidence, strong recommendation).

XXI. An adequate therapeutic trial should be conducted before discontinuation of a seemingly ineffective treatment (weak quality of evidence, strong recommendation).

D. Other drugs

XXII. Long-term systemic corticosteroids are reserved for patients with pain-associated inflammatory disorders or metastatic bone pain. Osteoarthritis should not be considered an inflammatory disorder (moderate quality of evidence, strong recommendation).

XXIII. Patients with localized neuropathic pain are candidates for topical lidocaine (moderate quality of evidence, strong recommendation).

XXIV. Patients with localized nonneuropathic pain may be candidates for topical lidocaine (low quality of evidence, weak recommendation).

XXV. Patients with other localized nonneuropathic persistent pain may be candidates for topical NSAIDs (moderate quality of evidence, weak recommendation).

XXVI. Other topical agents including capsaicin or menthol may be considered for regional pain syndromes (moderate quality of evidence, weak recommendation).

XXVII. Many other agents for specific pain syndromes may require caution in older persons and merit further research (i.e., glucosamine, chondroitin, cannabinoids, botulinum toxin, alpha-2 adrenergic agonists, calcitonin, vitamin D, bisphosphonates, ketamine) (low quality of evidence, weak recommendation).

The WHO developed an approach to cancer pain management that may be applied to management of geriatric pain because of their significant overlap. To manage pain effectively, the WHO recommends oral administration of analgesics “around the clock” (determined regular intervals), individualized for the patient, and following the “analgesic ladder.” This treatment is inexpensive and estimated to be 80% to 90% effective (Kaye et al., 2010; Tapsell et al., 2006). According to this approach:

1. For mild pain conditions, acetaminophen is the most appropriate first choice because it has the least known side effects.
2. For mild to moderate pain conditions or pain uncontrolled with acetaminophen, NSAIDs are the most appropriate.
3. For pain initially rated moderate or pain refractory to NSAID treatment, a weaker opioid (i.e., codeine) is the most appropriate first choice. Other weak opioids include hydrocodone, propoxyphene, and oxycodone in combination with acetaminophen.
4. For pain initially rated as severe or pain refractory to the previously mentioned weaker opioids, an opioid agonist (i.e. morphine) is chosen. Other opioid agonist drugs include hydromorphone, fentanyl, methadone, and levorphanol.
5. Adjuvant medication may be used for pain and anxiety relief and for synergism with medications mentioned above.

Adjuvants

Adjuvant drugs are non-analgesics that may enhance the efficacy of other analgesics, independently provide analgesia for specific types of pain, or treat certain symptoms of pain. Adjuvant drug therapy is necessary to increase the analgesic effects of other medications. Regimens of multiple drugs may be implemented before the optimal treatment combination for each individual is obtained. Common adjuvant drugs used in pain treatments include but are not limited to the medications listed in Box 2.

Antidepressants (i.e., amitriptyline)
Anticonvulsants (i.e., gabapentin)
Muscle relaxants (i.e., carisoprodol)
Psychostimulants (i.e., dextroamphetamine)
α -2-adrenergic agonists (i.e., clonidine)
Antihistamines (i.e., hydroxyzine)
Neuroleptics (i.e., methotrimeprazine)
Local anesthetics (i.e., lidocaine)
Corticosteroids (i.e., prednisone)
Antiarrhythmics (i.e., β -blockers)
Topical cream/gels (i.e., diclofenac 1% gel)
Calcitonin

Box 2. Common drugs in the geriatric population

Modified from Kaye A. D., Baluch A., Scott J. T. (2010). Pain management in the elderly population: A Review. *The Ochsner Journal*, 10, 185.

Studies are currently being conducted to evaluate the efficacy of herbs and supplements in the treatment of pain. For example, Level II evidence supports that ginger in studied dose ranges from 510 mg to 1 g per day reduces osteoarthritis and rheumatoid arthritis, including arthritic knee pain, ranking slightly below ibuprofen. Further, anti-inflammatory effects are known for omega fatty acids. To determine how these modalities compare with current drug therapies, more studies and comparison trials are required (Tapsell et al., 2006).

Physical therapy and alternative modalities

rehabilitation allows geriatric pain patients to live a more functional and independent life as a result of their adapting to the loss of psychological, physical, or social skills. Individual-specific treatment plans are created to minimize pain and enhance function. ADL assessments are used to evaluate the level of patient disability and guide treatment. The objectives of the rehabilitation process include stabilizing the primary order, preventing secondary disabilities, decreasing pain perception using a multidisciplinary approach, treating deficits in function, and promoting overall adaption to the disability and life demands (Brummel-Smith, 1997). The beneficial effects of spinal manipulative therapy and acupuncture on the attenuation of pain sensation have been established by recent studies; however, their effects in elderly populations remain to be elucidated (Bialosky, Bishop, Robinson, Zepieri, & George, 2009; Lang, Stoer, Schober, Audette, & Irnich, 2010).

Therapeutic Exercises

Therapeutic exercises are used to improve or to maintain strength. They also help to maintain flexibility, prevent contractures, improve joint range of motion (ROM), and improve both proprioception and balance. Some classifications of these modalities include passive, active, active-assisted, resistive exercises, flexibility (stretching) exercises, and aerobic conditioning (Javier & Montagnini, 2011). Devices used during therapy may include rowing machines, ergometers, and treadmills. An example of a therapeutic regimen may be any resistive exercise whereby the patient performs a set of 8–12 repetitions at 60–70% of one maximal rep over a

12-week program in the affected portion of the body. Studies have shown that such a regimen may improve quality of life, decrease fatigue, and increase strength (Segal et al., 2003).

Physical modalities

Physical modalities for pain control may contribute to improved physical function and may include cold, heat, massage, ultrasound, and transcutaneous electrical nerve stimulation (TENS), among others. Cryotherapy may be applied to the affected areas to reduce blood flow, metabolism, swelling, and muscle spasms that consequentially decrease nerve activity and pain. Application of cryotherapy should be limited to less than 30 min at a temperature ~59°F (15°C) and should be used with caution or not at all in patients with nerve damage or perfusion problems. Heat may also be employed via a hot pack, hot water bottle, or heating pad with temperatures ranging from 109–113°F (43–45°C) for 3–30 min at a time. The resultant vasodilation increases the supply of oxygen and nutrients to the site while simultaneously eliminating carbon dioxide and metabolic waste. It is especially useful for muscle spasms, myalgia, contractures, bursitis, and fibromyalgia.

Massage therapy, one of the most common forms of manual therapy, may be used to mobilize a joint, stretch adhesions, reduce swelling, and mobilize fluids by manipulating the surface of the body mechanically. Generally, a physical therapist or massage therapist will apply this technique by stroking, compressing, tapping, or using sustained pressure on the affected soft tissue. The most commonly used form of electrical delivery is transcutaneous electrical nerve stimulation (TENS). Small pads with conducting gel may be applied to the painful area, which eventually lead to changes in perfusion, improved healing, and restoration of proper nerve signaling.

Acupuncture

One of the oldest healing techniques, acupuncture, is part of traditional Chinese medicine and has become more prevalent in the Western hemisphere. Practitioners will stimulate specific points on the body that often have no anatomic correlation or relationship to the nervous system. Stimulation is via insertion of thin needles through the skin in an attempt to regulate the flow of “qi,” vital energy, along pathways referred to as meridians. Acupuncture has been used to help treat common ailments in the geriatric population including back pain, joint pain, neck pain, severe headaches, and recurring pain. Acupuncture stimulation has a resultant increase in tissue vasodilation for several hours, mediating or modulated by a number of chemicals being released or activated. These include, among others, acetylcholine, endorphins, norepinephrine, dopamine and 5-hydroxytryptamine.

Currently, results for acupuncture versus other treatments (NSAIDS, lidocaine injections, manual

manipulation) have been mixed (Furlan et al., 2008). Further randomized clinical studies with larger study populations must be undertaken to determine effectiveness of this modality compared to others currently available.

Psychological modalities

Current psychological modalities utilized to manage chronic pain attempt to achieve increased self-management, behavioral change, and cognitive change instead of focusing directly on the actual locus of pain. Psychological interventions target emotional, behavioral, and cognitive aspects of chronic pain with some of the more frequently employed modalities including psychophysiological techniques, behavioral modification, cognitive behavioral therapy, and acceptance-based interventions.

Psychophysiological techniques such as biofeedback allow for patients to learn to interpret feedback in the form of physiological data based on certain physiological functions. For example, equipment may be used to recognize areas of body tension so the patient can subsequently learn to relax those areas. Feedback may come in the form of blood pressure, muscle tone, heart rate, skin temperature, or brain electrical activity. These modalities have been shown to be efficacious and have shown significant improvements in certain conditions (Nestoriuc & Martin, 2007).

Behavioral approaches may include relaxation techniques such as breathing exercises, visualization/guided imagery, and graded activation. Collectively these techniques have shown to be efficacious for acute and chronic pain quality of life (Baird & Sands, 2006; Carroll & Seers, 1998; Morone & Greco, 2007). However, these techniques are not necessarily applicable to individuals with significant cognitive impairment or severe depression (Kaye et al., 2010; Norelli & Harju, 2008).

The presence of depression and/or anxiety in patients can affect abilities to improve the quality of life and manage pain; therefore, co-morbid mental disorders can be addressed using psychotherapy, medication, or meditation. Socio-environmental factors may be adjusted to help patients cope with pain. A solid support system consisting of involved relatives and caregivers should be established as results in pain reduction.

Interventional modalities

Interventional modalities are invasive treatments used for a number of reasons and are important in pain management. First, these interventions assist to determine the precise cause of pain, which consequently helps physicians to make a more accurate diagnosis. Second, they remain a mainstay of chronic pain treatment, even though many of the procedures suffer from lack of research-based validity related to the difficulty of obtaining prospective randomized controlled studies. In this regard, placebo-controlled trials are difficult to obtain secondary to ethical considerations and patient enrollment challenges. Interventions generally target

the actual neural structure involved in pain generation. Mechanisms of action vary but include infiltration with local anesthetics, steroids, opioid agents, and/or adjuvant agents, spinal cord stimulation, or ablation with either radiofrequency or neurolytic agents.

Intraspinal opioid therapy may be used to enhance efficacy and to minimize systemic side effects when compared to oral medication. Delivery may be via programmable, implanted pumps, accessible reservoir systems, or tunneled, exteriorized catheters. Studies performed have demonstrated improved analgesic efficacy and reduced toxic side effects when compared to patients who are on high dose oral opioid treatment (Smith et al., 2003; Rauck et al., 2003).

Neurolytic blockade is commonly used for end-stage cancer pain related to potential neurodestruction from either phenol or alcohol. An example would be a celiac plexus neurolytic block for terminal intra-abdominal cancer. The ganglia are situated in the retroperitoneal space and the approach, in general, has been reserved for severe pain in terminal end of life patients. This neurolytic block has been shown to significantly reduce pain, reduce opioid-related side effects, and increase quality of life (de Oliveira, dos Reis, & Prado, 2004).

“Gate theory” proposed that the balance of small and large neural fiber firing influences the sensation of pain. Retrograde stimulation of large fibers would cause “closing” of the gate and thereby provoke nonpainful stimulation. Currently, pain stemming from the periphery and ischemic pain sites are the most common reasons for use of nerve stimulation for pain management. Complex regional pain syndrome and chronic radicular pain are examples of indications for nerve stimulation techniques. Statistically significant reductions in pain severity have been found with this treatment as well as marked reduction in analgesic requirements (Harke, Gretenkort, Ladleif, & Rahman, 2005; Kemler, de Vet, Barendse, van den Wildenberg, & van Kleef, 2006; Calvillo, Racz, Didie, & Smith, 1998; Ebel, Balogh, & Klug, 2004; Oakley & Weiner, 1999).

Spinal pain is the most rampant noncancer pain syndrome and physicians have used radiofrequency to mitigate symptoms. Radiofrequency ablation has been used to attack pain stemming from the facet joint, which are paired synovial joints formed by the inferior articular process of one vertebra and the superior articular process of the vertebrae below. Two studies have demonstrated long-lasting efficacy with this procedure where percutaneous radiofrequency neurotomy was performed (Lord, Barnsley, Wallis, McDonald, & Bogduk, 1996; Van Kleef et al., 1999).

Other studies dealing with facet-type pain have shown little benefit diagnostically or therapeutically with intra-articular facet joint injection with local anesthetic and steroid (Carette et al., 1991; Jackson, Jacobs, & Montesano, 1988).

It should be noted that literature support for transforaminal nerve root injection, epidural steroid

Table 1. Numerous liver changes observed in the elderly population

Size	Liver mass decreases by 1% per year after age 50
Blood flow and velocity	33% decrease in flow and 21% decrease in portal blood velocity over age 65
Liver function	No significant changes in liver function tests
Conjugation	Not significantly changed
Microsomal hydroxylation/oxidation	Not significantly changed
Nonmicrosomal oxidation	Not significantly changed
Demethylation	Decreased with aging, caution with benzodiazepine use
Protein synthesis	Slightly decreased serum albumin levels, reduced quality of albumin, increased free fraction of protein bound drugs
Serum and biliary cholesterol	Increased change of cholelithiasis and atherosclerosis
Liver regeneration and capacity	Decline in regeneration rate, regeneration capacity remains unchanged

Modified from Lynch, D. (2000). Geriatric pain. In: P. Raj (Ed.), *Practical Management of Pain*. [3rd ed.] St. Louis, MO: Mosby, 278.

Table 2. Numerous kidney changes observed in the elderly population

Size	Kidney decreased in size by 20%–30% by age 70
Renal tubules	Decreased length, number, and thickness
Interstitial tissue, tubular diverticula of renal tubules	Increased
Renal blood flow	Decreased by 10% per decade after age 20
Glomerular filtration rate	Decreased 10 cc/min/decade
Free water absorption	Decreased by 5% per decade after age 50

Modified from Kielstein, J. T., Bode-Boger, S. M., Haller, H., & Lynch, D. F. (2003). Functional changes in the ageing kidney: is there a role for asymmetric dimethylarginine? *Nephrology Dialysis Transplant*, 18, 1245–1248, and Lynch, D. (2000). Geriatric pain. In: P. Raj (Ed.), *Practical Management of Pain*. [3rd ed.] St. Louis, MO: Mosby, 278.

injection, and sacroiliac joint injection has been established and is generally accepted (Manchikanti, Cash, McManus, Pampati, & Benyamin, 2010a; Manchikanti et al., 2010b, Buenaventura, Datta, Abdi, & Smith, 2009; Manchikanti, Singh, Falco, Cash, & Pampati, 2010c, Rubinstein & van Tulder, 2008). Radiofrequency of the sacroiliac joint has not been firmly established. It is clear, however, that information gained from nerve blocks may help with several aspects of pain control including the diagnosis of the precise pain generator and the overall prognosis of the pain state.

Pain injections play a role in the elderly with regard to preemptive analgesia, which involves blocking pain pathways before surgical incision or damage to tissue. Finally, interventional pain interventions can play a definitive therapeutic role in numerous common and atypical pain states. Further studies must be conducted in order to determine which patients may benefit from each type of interventional technique. However, the preponderance of evidence suggests a critical and important role for interventional pain procedures in all populations for many pain states, in particular in the geriatric population.

Summary

Persistent pain is prevalent in the elderly population, although it is not an inevitable part of aging (Kaye et al., 2010). It is important to understand how to manage pain effectively in old age, particularly because an increasing number of individuals are becoming older or living longer. Several problems, less common in younger adults, may complicate the treatment of pain. An accurate pain assessment is required for the most efficient strategy of pain treatment. Challenges to an effective pain assessment include pain

underreporting by patients, atypical manifestations of pain in elderly, age-associated pharmacodynamic and pharmacokinetic changes to specific drugs, other general age-related changes, and misconceptions about tolerance or addiction to opioids. Pain specialists can be invaluable to the diagnosis and treatment of many pain states common in the elderly population (Kaye et al., 2010). In summary, physicians are able to provide geriatric patients with appropriate analgesia by using comprehensive assessment involving a multidisciplinary approach and the appropriate use of various treatment modalities.

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