

INSIDE THIS ISSUE

Use of Opioids in the Older Patient
Penny Tenzer, MD **3**

CASE STUDY:
How Would You Treat This Patient?
Srinivasa N. Raja, MD **6**

TARGET AUDIENCE Neurologists, family physicians, general practitioners, internal medicine specialists, rheumatologists, physical medicine and rehabilitation specialists, pharmacists, and other physicians and healthcare professionals who treat patients with pain

LEARNING OBJECTIVES After reading this newsletter, participants should be able to:

- Recognize the biopsychosocial issues and clinical challenges in treating pain in the aging patient population
- Identify the benefits and risks of using opioid analgesics in the older patient
- Determine a treatment regimen for managing neuropathic pain associated with postherpetic neuralgia

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Pain in the Elderly



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Dr Ferrell has indicated that he has no relevant financial relationships to disclose.

The approach to pain assessment and management is different in elderly versus younger persons. Older persons may underreport pain for a variety of reasons, despite functional impairment, psychological distress, and the needless suffering related to pain.¹ They often present with concurrent illnesses and multiple problems, making pain evaluation and treatment more difficult.² Older persons have a higher incidence of side effects to medications and a higher potential for complications and adverse events related to many treatment procedures.^{1,2} Despite these challenges, pain can be effectively managed in most older patients. Moreover, clinicians have an ethical and moral obligation to prevent needless suffering and provide effective pain relief, especially for those near the end of life.

Age-Related Changes in Pain Perception

Elderly persons have presented with painless myocardial infarction and painless intra-abdominal catastrophes. The extent to which these incidents are attributable to age-related changes in pain perception remains uncertain. Studies of pain sensitivity across the lifespan have shown mixed results.³ Inducing pain in normal volunteers has shown both increased and decreased pain threshold as well as no change in pain threshold across the lifespan. Decreased pain sensitivity (ie, increased threshold) with aging can be supported by evidence of decreased numbers of receptors and changes in nerve conduction. Increased pain sensitivity (ie, decreased threshold) with aging can also be supported by evidence of alterations in spinal cord and central nervous system processing (poorer endogenous analgesia).³ If these observations are correct, overall pain perception may not change much with aging.¹ Clearly, additional studies are needed to define age-related changes specific to nervous system function and pain perception.

Pain is associated with a number of negative outcomes in elderly people, including depression, decreased socialization, sleep disturbance, impaired ambulation, and increased healthcare utilization and costs.¹ Older patients rely heavily on family and other caregivers near the end of life. For these patients and their caregivers, pain can be especially distressing. Caregiver strain and caregiver attitudes can have a substantial impact on pain.

Assessment of Pain in the Elderly

Accurate pain assessment includes an estimate of pain intensity, usually with a valid and reliable pain scale. Pain scales can be grouped into multidimensional and unidimensional scales. In general, multidimensional scales with multiple items, such as the McGill Pain Questionnaire and the Brief Pain Inventory, often

CONTINUED ON PAGE 4



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EDITOR'S PERSPECTIVE

On the Disadvantages of No Longer Being Young

Eric Chevlen, MD

Dr Chevlen has indicated that he has no relevant financial relationships to disclose.

My esteemed father, who will soon be 86 years old, recently sighed deeply and said, "Oh, to be 70 again!" He was not unaware of the humor of the statement—nor was he unaware that its humor derives from its truth.

Old age isn't for sissies. All of the realms of life—biologic, intrapersonal, and interpersonal—seem to take a hard hit as the years lumber along. Pain is no exception. Old people are more likely than young ones to experience chronic pain, more likely to have comorbidities that complicate its treatment, more likely to tolerate therapies poorly, more likely to be inadequately assessed, and more likely to be inadequately treated. Otherwise, they do just fine.

This issue of *Pain Management Today* is devoted to the problem of pain in the elderly. In the lead article Bruce Ferrell, MD, introduces the vast topic with an overview that ranges from age-related changes in pain perception to the challenges of assessing and managing pain in the elderly. An accompanying article by Penny Tenzer, MD, discusses the benefits and risks of using opioid analgesia to treat pain in elderly patients. Finally, Srinvasa Raja, MD, presents a case profile of one of the most common conditions seen in the elderly, postherpetic neuralgia.

If it is true—and it is—that effective pain management requires the integration of a broad range of clinical skills, then treating pain in the elderly doesn't merely require it. It *demand*s it. But equal to the challenge of managing chronic pain in the elderly is the enormous reward of doing so successfully. Although our armamentarium is still incomplete, we are blessed to have available a wide variety of agents that can reduce the suffering of our elders. What a joy it is to be able to diminish their pain and assuage their suffering.

Most of us will grow old. Most of us will experience pain in our advanced years. Yes, sometimes this field of pain medicine gets personal.

Oh, to be 50 again! 

NIPC EDUCATION STATEMENT

This educational activity is a component of the National Initiative on Pain Control® (NIPC®) and is designed to heighten the knowledge of physicians and other healthcare providers about the serious impact of unresolved pain on patient care. Some of the agents included in this newsletter are discussed in the context of uses for which they have not been approved by the FDA, and will be identified by an asterisk (*).

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ABOUT THE NIPC

The National Initiative on Pain Control® (NIPC®) is an integrated CME education initiative that was established in 2001 to help physicians improve outcomes for their patients who have pain. Living with pain has deleterious effects on many aspects of the patient's life including deterioration of physical functioning, the development of psychological distress and psychiatric disorders, and impairment of interpersonal functioning. Of special

concern, less than optimal training of physicians in pain disorders has led to the underassessment and undertreatment of patients who are living with pain. The program heightens physician awareness of the impact of pain on patient's daily living in terms of quality of life, lost workdays, and societal/familial consequences.

NIPC addresses the barriers to achieving pain control by providing physicians with potential pathways for action and expected amelioration of their patients' pain. Communicating with physicians about the latest advances and strategies in pain management helps them be better able to translate clinical data into clinical practice.

All NIPC programs are developed and continuously evaluated by the NIPC Education Council, an expert, multidisciplinary team of specialists, researchers, and practicing physicians in pain management. The NIPC faculty includes nationally respected experts in the pain management field.

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Use of Opioids in the Older Patient



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Dr Tenzer has indicated that she has no relevant financial relationships to disclose.

As the population ages, the number of individuals with persistent pain is anticipated to grow proportionately. Persistent pain affects more than 50 million Americans, with between 20% to 50% of community-dwelling older persons and up to 80% of institutionalized geriatric patients experiencing pain.¹ Although older patients suffer disproportionately from pain, it continues to be underreported and underdiagnosed in this population.

A variety of physiologic changes occurs with aging and influence pain management. Total body fat increases, while the body's water content and muscle mass decrease. As a result, water-soluble drugs may have a higher initial concentration, while fat-soluble drugs may exhibit a longer half-life due to slow release from fatty tissue. The glomerular filtration rate also decreases approximately 10% per decade of life, affecting drugs that are cleared renally. In addition, there

is decreased synthesis of mixed-function oxidases (CYP 450) with aging, which impact medications metabolized by this pathway.

Further challenging clinicians is the issue of polypharmacy. More than 90% of elderly patients presenting to the emergency department (ED) take one or more medications (average, 4-8 medications).² While physicians should be concerned about adverse reactions and drug-drug interactions, it is also imperative to treat pain promptly and effectively to prevent future complications, suffering, and pain syndromes. Ideally, pain treatment is multimodal and interdisciplinary, and utilizes pharmacologic and nonpharmacologic therapies. This article focuses on one component of the comprehensive pain management plan, the use of opioids for managing pain in older patients.

Short-Acting vs Long-Acting Opioids

Opioids are available in short- and long-acting formulations and are a mainstay of pain treatment, with proven efficacy in acute, chronic, inflammatory (sometimes called nociceptive), and neuropathic pain. Yet, many physicians and patients exhibit "opiophobia" (patients fear taking opioids, and physicians fear prescribing them).¹

Short-acting agents include transmucosal fentanyl and immediate-release forms of codeine, tramadol, hydrocodone, morphine, hydromorphone, oxycodone, and oxymorphone. Codeine, tramadol, hydrocodone, and oxycodone are available in combination with acetaminophen or a nonsteroidal anti-inflammatory drug (NSAID).

Long-acting opioids include the transdermal fentanyl patch and 12- to 24-hour-release formulations of tramadol, morphine, oxycodone, and oxymorphone. Anticipated in upcoming months is the release of several controlled-release agents, including combinations and long-acting opioids in tamper-resistant formulations. New combinations such as morphine/naloxone and oxycodone/naltrexone are being evaluated for release, claiming to have abuse-deterrent effects.

Opioid therapy in the older patient is initiated at a low dose and gradually increased. The amount of opioid used during 24 hours is then converted to a sustained-release form of the same drug, with an immediate-release medication available as needed for breakthrough pain. The optimum dose must be determined with the patient, who is the best indicator of the balance between pain relief and side effects.

Short-acting opioids display a rapid rise and fall in serum opioid levels, whereas long-acting opioids increase gradually to therapeutic levels that are sustained for an extended time and then decline slowly. Short-acting opioids may be utilized for moderate to severe

Table 1. Mu-agonist Dose Chart^a

Opioid	Approximate Equianalgesic Dose (mg)		
	Oral	Parenteral	Dosing Interval
Morphine	30	10	q4h
Hydromorphone	7.5	1.5	q3-4h
Fentanyl	-	0.1	q3d
Oxycodone	20	-	q4h
Methadone ^b	2.5-5	2.5-5	q8-12h ^c
Levorphanol	4 (acute) 1 (chronic)	2 (acute) 1 (chronic)	q6-8h
Oxymorphone	10	1	q3-4h
Hydrocodone	30	-	q4-6h

^a Ratio for short-term opioid therapy; not for conversion to methadone.

^b Should only be initiated by a prescriber familiar with the use of methadone in chronic pain.

^c Dosing interval varies by patient due to metabolite accumulation.

Ashburn MA et al. *Principles of Analgesic Use in the Treatment of Acute Pain and Cancer Pain*. American Pain Society, 2003. Opana [package insert].

Pain in the Elderly

CONTINUED FROM THE COVER

provide a more stable measurement and evaluation of pain in several domains. These scales are often long, time consuming, and may be too difficult to use with some elderly patients.⁴

Unidimensional scales consist of a single item that usually relates to pain intensity alone. Examples include the verbally administered 0-10 scale, a single item visual analog scale, or one of the several word descriptor scales available. These scales are easy to administer, require little time or training to produce reasonably valid and reliable results, and can be used in many clinical settings to monitor treatment effects and for quality assurance indicators.⁴

Unidimensional pain scales often require framing the pain question appropriately for maximum reliability. Subjects should be asked about pain in the present tense (here and now). Questions that require accurate memory and integration of pain experiences over time may be more difficult for older patients, especially those with cognitive

pain-relieving medications (opioids, for example). However, the elderly are a heterogeneous population. Thus, optimum dosage and known side effects are difficult to predict. Recommendations for age-adjusted dosing are not available for most analgesics, and dosing for most patients requires beginning with low doses with careful upward titration, including frequent reassessment for dosage adjustments and optimum pain relief.¹

Acetaminophen is the drug of choice for older persons with mild to moderate pain, especially pain due to osteoarthritis and other musculoskeletal problems.² Although acetaminophen may have deleterious effects on renal function (dose related over many years) and may occasionally interfere with the concomitant administration of warfarin,⁵ if given in a dose of 650 mg to 1,000 mg four times a day (not to exceed 4,000 mg/day),¹ it remains the safest analgesic medication compared with traditional NSAIDs and other analgesic drugs for most patients (see Table).

NSAIDs are appropriate for short-term use in inflammatory arthritic conditions

periods of time should be avoided in elderly patients. For those with multiple medical problems, NSAIDs are associated with increased risk of drug-drug and drug-disease interactions that may exacerbate a condition.

Opioid analgesics have no ceiling to their analgesic effects and have proved effective for all types of pain. Advanced age is associated with a prolonged half-life of opioid drugs, so that older people may achieve pain relief from smaller doses of opioids than younger people. The corollary is that the full effect of any dose will not become apparent until it has been given steadily for 5 half-lives, which will, of course, be longer in older patients.² [For specific details about using opioids in the older patient, see article on page 3. Ed.]

Non-Analgesic Medications

A variety of other medications not formally classified as analgesics are helpful for certain specific pain problems, such as neuropathic pain conditions, including diabetic neuropathies, postherpetic neuralgia, and trigeminal neuralgia. The term “adjuvant analgesic drugs,” although frequently used, is a misnomer in that some of these non-opioid drugs may be the primary pain-relieving pharmacologic intervention in certain cases.

Tricyclic antidepressants (TCAs), anticonvulsants, and local anesthetics, such as the lidocaine patch 5%, are the most frequently used non-opioid analgesics for neuropathic conditions. In general, these drugs have had limited success in pain syndromes that are not associated with neuropathic mechanisms. These drugs are rarely totally successful as single agents, and usually work better in combination with other traditional drug and non-drug strategies in an effort to improve pain and keep other drug doses to a minimum.⁶

As is the case with opioids, treatment with these agents should usually start with lower doses than those recommended for younger patients, and doses should be escalated slowly based on the known pharmacodynamics of individual

Advanced age is associated with a prolonged half-life of opioid drugs, so that older people may achieve pain relief from smaller doses.

impairment. Although pain is an individual experience, family and caregivers may be an excellent source of qualitative information about general behavior, medication usage, and actions that seem to reduce or aggravate pain.⁴

Management of Pain

Analgesic Medications

Although analgesic medications are safe and effective in elderly people, they carry a balance of benefits and burdens. Elderly patients have increased analgesic sensitivity for some classes of

(eg, gout, calcium pyrophosphate arthropathy, acute rheumatoid arthritis) and other mild to moderate pain syndromes. Individual drugs in this class vary widely regarding anti-inflammatory activity, potency, analgesic properties, metabolism, excretion, and side-effect profiles. Failure of response to one NSAID may not predict the response to another. A disadvantage is that NSAIDs demonstrate a ceiling effect, which is the level at which an increased dose results in no further increase in analgesia.² High-dose NSAIDs for long

drugs.⁷ Most of the non-opioid medications for pain management have high side-effect profiles in elderly people and must be monitored carefully. Because of the high level of anticholinergic side-effects, most TCAs are no longer considered first-line therapy for neuropathic pain.⁸

Anticonvulsants, in general, are limited by their high side-effect profiles in elderly people. Since most patients respond only partially, the overall risk/benefit ratio is rather large in this population. These drugs are not simple analgesics and should not be used for the relief of trivial aches and pains. Gabapentin, FDA approved for treating diabetic neuropathy and postherpetic neuralgia, has a significant analgesic effect on neuropathic pain with a much lower side-effect profile compared with other anticonvulsant drugs and most antidepressants as well.⁹⁻¹¹ The elimination of gabapentin is nearly entirely renal. Since kidney function declines in the elderly, gabapentin must also be dosed carefully in the elderly. Other new anticonvulsant drugs, especially pregabalin, are proving useful in managing pain.

Several local anesthetics, primarily the lidocaine patch 5% and capsaicin,¹² are also used to relieve neuropathic pain. Mexiletine, similar to lidocaine but active orally, has also shown some

Nonpharmacologic strategies...used alone or in combination with the appropriate analgesic medications should be an integral part of the care plan for most elderly patients with significant pain problems.


activity against the neuropathic pain of diabetic neuropathy.¹³ Although this drug also has a high risk/benefit ratio, some studies have reported response rates at lower doses than are often recommended for cardiac arrhythmias.

Nonpharmacologic Therapy

Nonpharmacologic strategies, such as physical exercise, cognitive and behavioral therapies, and alternative medicine approaches, used alone or in combination with the appropriate analgesic medications, should be an integral part of the care plan for most elderly patients with significant pain problems. These interventions often enhance therapeutic effects while allowing medication doses to be kept low to prevent adverse drug effects.¹

Conclusion

Pain is a common problem among the elderly and, as the population ages, the problem will only continue to escalate. Although there are numerous challenges facing the physician when

treating pain in the elderly, identifying appropriate treatment strategies will lead to improved functionality and quality of life for the older patient. 

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Table. Organ System Changes in the Older Patient Affect Pharmacodynamics

	GI	Renal	Cardiac	CNS
Tramadol	-	-	-	+
Opioids	+	-	-	+
Local Anesthetics (systemic)	-	-	+	+
Local Anesthetics (topical)	-	-	-	-
Antidepressants	+	-	+	+
Anticonvulsants	+	-	+	+
COX-2s	+/-	+	+	+
NSAIDs	+	+	+	+

Some drugs generally considered inappropriate in older patients: propoxyphene, meperidine, naproxen, indomethacin, diazepam, alprazolam
 - = does not affect drug pharmacodynamics.
 + = does affect drug pharmacodynamics.

GI = gastrointestinal; CNS = central nervous system; COX-2 = cyclooxygenase-2; NSAID = nonsteroidal anti-inflammatory drug.

How Would You Treat This Patient?



Srinivasa N. Raja, MD, Professor, Department of Anesthesiology and Critical Care Medicine, Director, Division of Pain Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland

Dr Raja has indicated that he receives grant/research support from Allergan, Alkermes, and Celgene Corporation; and is a retained consultant for Allergan.

A 72-year-old widow visits her primary care physician with complaints of burning pain and itching in her right forehead and frontal scalp region. The symptoms have persisted for 2 days and began shortly after she tried a new hairspray. There is an area of redness in the region. The physician suspects that she has an allergic dermatitis and prescribes a topical steroid ointment. Two days later, the patient returns to the physician's office with worsening symptoms, a swollen right eye, and photophobia.

Her medical history is significant for hypertension controlled with extended-release metoprolol 100 mg/day, and glaucoma treated with brimonidine eye drops. She gives a history of depression following the death of her husband after a prolonged illness a year ago.

On examination, vesicular lesions are observed in the right forehead and scalp.

The lesions do not extend to the left of the midline. The eyelids are edematous and she complains of difficulty opening her eye and a feeling of a foreign body in her eye. She complains of severe pain during the past 2 days that has prevented her from sleeping. She lives alone and states that her independence is important to her.



Optimal therapy consists of early initiation of antiviral therapy after the onset of the disease and aggressive pain control. Placebo-controlled trials of acyclovir have demonstrated that therapy started within 72 hours of onset of rash shortens the period of new vesicle formation, speeds healing of rash, decreases pain severity during the acute phase, and reduces ocular complications of ophthalmic HZ. The limited oral bioavailability of acyclovir necessitates frequent dosing (800 mg 5 times daily for 10 days for patients with normal renal function).

In contrast, the newer antivirals famciclovir and valacyclovir have better oral bioavailability and can be dosed less frequently (500 mg q8h, and 1g q8h, respectively, for 7 days for patients with normal renal function). Studies suggest that these agents may reduce the incidence of HZ-associated pain. HZ in the trigeminal distribution may be associated with lesions in the cornea and an ophthalmologic consultation is appropriate. Visceral, ocular, and central nervous system complications and HZ in immunocompromised patients should be treated with intravenous acyclovir (10 mg/kg q8h for 7 to 14 days for patients with normal renal function).

The clinical evidence suggests that neuraxial and sympathetic nerve blocks provide short-term pain relief and may decrease the severity and duration of the eruption.^{1,2} The effectiveness of sympathetic ganglionic blockade in relieving the acute pain of HZ is well accepted, but there is controversy as to whether these nerve blocks reduce the incidence of postherpetic neuralgia (PHN).

While tricyclic antidepressants have shown to be effective in treating PHN and may possibly help during the acute zoster phase, amitriptyline would be relatively contraindicated in this patient because of her age.³ Amitriptyline should be used with caution in patients with cardiovascular disease, glaucoma, urinary retention, hyperthyroidism, and psychosis. (Correct answers: a, b, d, e)

1. Based on the information presented, which of the following treatment strategies should be considered in managing this patient? (Select all that apply)

- a. Initiate therapy with valacyclovir 1 g tid**
- b. Treat her pain with acetaminophen and opioids**
- c. Treat her depression and sleep disturbance with amitriptyline 25 to 50 mg at bedtime**
- d. Refer her to an ophthalmologist**
- e. Inform her that if the pain persists, you may refer her to a pain clinic for possible nerve blocks**

This patient's clinical history is typical of acute herpes zoster (HZ). HZ, or shingles, is common in the elderly, with an annual incidence of about 10 per 1,000 among octogenarians. HZ is a clinical diagnosis, and since the prodromal symptoms may be present for 2 to 4 days prior to the development of vesicular lesions, the diagnosis may be missed initially. The course of the disease is often self-limiting, with healing of the vesicles after crusting in 3 to 4 weeks. Secondary infections resulting in conjunctivitis, keratitis, and iridocyclitis may occur. Systemic signs and symptoms during HZ may include fever, signs of meningismus, headache, nausea, gastrointestinal disturbance, and adenopathy. The pain associated with zoster can be severe and adversely affect the patient's quality of life.

Four months later, the patient continues to have sharp, shooting pains in the region of her shingles and the surrounding area, including her scalp, and rates her average pain intensity as 7 out of a highest pain score of 10. She states that the skin over her forehead and scalp feels partly numb, but even mild stroking of the area or combing her hair causes severe pain. She has lost weight and complains of a loss of appetite and poor sleep. On examination, the skin affected by shingles is well healed. She has decreased sensation to pinprick and a cotton swab in that region. However, light brushing of the right side of the forehead elicits excruciating pain.

2. Complaints of increased sensitivity to pain despite clinical observation of decreased sensation in the affected region raise the suspicion of a psychological problem being the cause of her pain.

- a. True
- b. False

Allodynia (pain induced by stimuli that are normally not noxious) is a common clinical presentation in PHN. The herpes virus can cause destruction of neurons in the dorsal root ganglia, which can result in sensory loss. A number of different mechanisms, including sensitization of the spinal cord and/or loss of spinal inhibitory mechanisms, can lead to allodynia when the skin is stroked, even in the presence of sensory deficits. Depression is common among patients with chronic PHN, and referral for psychiatric consultation is sometimes helpful for PHN patients who have signs and symptoms of mood disturbance. Even those who are free of overt depression and anxiety can

benefit from cognitive behavioral strategies to help manage their pain and sleep disturbance. Detectable mood disorders may need to be treated concurrently as efforts to reduce pain continue. (Correct answer: b)

3. Which of the following is an appropriate next step in managing this patient? (Select all that apply)

- a. Initiate therapy with a topical local anesthetic, such as the lidocaine patch 5%
- b. Treat her pain as a neuropathic pain and use anticonvulsant drugs, such as gabapentin and pregabalin
- c. Treat her depression and consider referral to a psychiatrist if her depressive symptoms worsen
- d. Avoid using opioid analgesics because they are not likely to be beneficial and will cause cognitive dysfunction
- e. Inform the patient that her pain is likely to resolve spontaneously in the next couple of months and she needs to be patient and conservative with her use of medications

Several classes of drugs are effective in attenuating the pain and hyperalgesia (increased sensitivity to pain or enhanced intensity of pain sensation) caused by PHN, but usually no single drug leads to the complete relief of symptoms. Treatment for established PHN should begin with medications with good evidence for favorable efficacy and safety profiles; however, a proportion of patients will experience pain that is refractory to both initial and subsequent therapies.

Lidocaine patches are FDA approved for PHN and appear to be safe and effective for many patients.⁴ The patch can be applied

over the area of allodynia and left intact for 18-24 hours. Some patients may not apply the topical patch because of cosmetic reasons. An alternative is ointments or creams of local anesthetics applied 3 to 4 times a day. Topical capsaicin (0.025% to 0.075%) can desensitize nociceptors, but the burning pain associated with its application can limit its utility.

Gabapentinoids, such as gabapentin (1,800 to 3,600 mg/day for patients with normal renal function) and pregabalin (150 to 600 mg/day for patients with normal renal function), should be considered first-line treatment, as these drugs have been shown to be effective in randomized trials and are FDA approved for this indication.⁵⁻⁷

The number needed to treat (pooled from multiple studies) to achieve 50% pain reduction for gabapentin and pregabalin are 4.4 and 4.9, respectively.⁴ Recent studies suggest that combination therapy with an opioid and gabapentin may provide better reduction in pain than either drug alone and may decrease the dose requirements of both drugs.⁶ Although short-acting opioids may be used during the titration period, controlled-release opioids such as morphine, oxycodone, and oxymorphone, or transdermal fentanyl are preferred for longer-term therapy.⁸ In patients being maintained on stable doses of opioids, no significant cognitive dysfunction is observed.⁹ In the subset of patients resistant to pharmacotherapy or intolerant to the side effects associated with the drugs, neuromodulation therapies, such as spinal cord stimulation, are being used. Their efficacy needs to be investigated further in prospective studies.⁴

(Correct answers: a, b, and c)

To view an algorithm on the prevention and treatment of PHN, please visit www.painknowledge.org/physiciantools. See details on page 12.

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Use of Opioids in the Older Patient

CONTINUED FROM PAGE 3

acute pain, breakthrough pain, and during initial dose-finding and titration to long-acting opioids. The repetitive dosing schedule of short-acting opioids is inconvenient and may be a constant reminder of the pain. These opioids may also be associated with less compliance and increased dosing errors. Short-acting opioids are not ideal for chronic pain and may increase the end-of-dose breakthrough (ie, troughs) and potential for euphoria or side effects (ie, peaks).³

Since long-acting opioids display a more stable blood level, these drugs are commonly used to manage persistent acute pain or chronic pain. Long-acting opioids may reduce the frequency of end-of-dose breakthrough pain, lower the potential for peaks, decrease side effects, and improve quality of life. They also provide dosing convenience, a more uniform effect, and may improve compliance.

Different Types of Opioids

Tramadol is an atypical analgesic. It has some activity at the mu-opioid receptor, but it also affects processing of serotonin, norepinephrine, acetylcholine, substance P, and G-coupled protein receptors.⁴ It is clearly analgesic, but the exact mechanism of action is far from clear. Tramadol has been well studied in the older patient population and overall is well tolerated and effective.

Codeine is classified as a “weak” opioid. Codeine itself has little analgesic effect; it must be converted to morphine to provide analgesia. Many people, including up to 10% to 20% of the white population, lack the enzyme for this conversion. Also, several drugs can inhibit the conversion of codeine into morphine. In these populations, a different opioid is required for pain relief.

Morphine acts as a pure opioid agonist, effecting analgesia, sedation, and mood alterations. For mostly historical reasons, most other opioids are compared with

morphine in equianalgesic tables. Morphine has 6 times the potency of codeine and is metabolized in the liver; the kidneys excrete the active metabolites. These metabolites can accumulate if the patient has reduced glomerular filtration rate. Therefore, clinicians should consider using decreased doses or another opioid in elderly patients or in patients with impaired kidney function. Morphine is available in a variety of formulations, including sustained release. Equianalgesic tables are used to convert and adjust treatment between different opioids (see Table 1).

Most studies of the effects of aging on opioid analgesia involve the use of morphine for postoperative pain and therefore may not necessarily be generalizable to management of chronic pain. These studies reveal similar pain intensity in young and older populations. Although the initial morphine loading dose was similar between these groups, there was a clear trend toward a lower maintenance dose in elderly patients,

with men tending to use more morphine than women.⁵

Hydromorphone is more expensive than equianalgesic doses of morphine and is about 5 times as potent. Its metabolites undergo renal clearance and there are fewer metabolite-related side effects. Hydrocodone is commercially available only in combination with acetaminophen or NSAIDs. These co-ingredients limit the dose of hydrocodone and present special concerns of toxicity for the elderly. The older patient may be more sensitive to the renal and gastrointestinal effects of NSAIDs. Although hydrocodone is metabolized to an active metabolite, hydromorphone, hydrocodone is a potent analgesic itself.

Oxymorphone, a semisynthetic opioid and metabolite of morphine, is available in both immediate-release and extended-release formulations. Oxymorphone is not significantly metabolized by CYP 450 isoenzymes, which may be an advantage in treating the older patient, who usually is taking

Table 2. Opioid Side-Effect Management

SYMPTOM	TREATMENT
Constipation	Bowel stimulants such as fiber or senna, stool softeners, suppositories, and enemas such as the milk-molasses enema (8-oz warm water, 3-oz powdered milk, 4.5-oz molasses)
Nausea	Antiemetics such as metoclopramide or other dopamine antagonists, antihistamines such as diphenhydramine, some of the 5-HT ₃ agonists such as ondansetron
Fatigue/sedation	Dose reduction: add nonsedating co-analgesic or stimulants such as caffeine
Dizziness/confusion	Antivertiginous agents
Central nervous system functions/myoclonus	Dose reduction or benzodiazepines
Itching	Antipruritic therapy such as antihistamines
Urinary retention (rare)	Rotate to different opioid; discuss catheterization
Respiratory depression (rare) ^a	Care with the opioid-naïve patient: avoid medication with long half-life during rapid titration; care with other medications such as benzodiazepines

^a Cheyne-Stokes respiration can be normal in sleeping elderly patients.

multiple medications. However, the bioavailability of orally administered oxymorphone may be increased in patients with moderate to severe liver disease. In a clinical trial comparing oxymorphone extended release with oxycodone controlled release and placebo in patients with chronic low back pain, oxymorphone was shown to be equianalgesic to oxycodone at half the milligram daily dose, with a comparable safety profile.⁶

Although oxycodone and many of its metabolites are renally excreted, the metabolites are inactive. This makes oxycodone, with appropriate dose reduction, a suitable choice for opioid therapy of patients with renal insufficiency. It is available in immediate-release or sustained-release formulas and in combination therapies.

Meperidine is a synthetic opioid, producing normeperidine as a metabolite, which is not naloxone reversible. Normeperidine's half-life is 15 to 30 hours, and it is renal-function dependent. Side effects of normeperidine include respiratory distress and neurotoxicity (hyperreflexia, myoclonus, seizures, and agitation, described as occurring after 24 hours). Meperidine has anticholinergic effects, including urinary retention. Serotonin syndrome has occurred when combined with fluoxetine. Given this information and the physiologic changes that occur with aging, meperidine is not recommended for the elderly.

Methadone has a highly variable half-life—averaging about 23 hours—and complex pharmacokinetics. Increasing the dose too quickly can increase risk of overdose. Recent increased use and overdoses of methadone, as well as drug-drug interactions with agents (such as fluconazole or paroxetine) that inhibit its hepatic clearance, have resulted in an FDA black-box warning. Methadone has also been associated with QRS prolongation, which can lead to sudden cardiac death. Physicians must be cautious when converting patients from other opioids to methadone. Patients who respond

well initially may need a lower dose of methadone as it accumulates, and dosage changes should be made no more frequently than every 5 days to avoid overdosing.

Propoxyphene is a synthetic opioid analgesic metabolized in the liver to norpropoxyphene. This metabolite is not naloxone reversible, is poorly dialyzed, and has been associated with seizures, arrhythmias, and pulmonary edema. Previous studies have questioned

and commitment to work with patients to improve function. It also entails addressing the emotional, cognitive, behavioral, and physiologic alterations that cause pain in the elderly patient population. Age should not be an excuse for inadequate analgesia.

Prescription of opioids should be based on thorough evaluation, ongoing review of risks and benefits, and individualized treatment plans with pain diaries. Regular review, adjustment,

...opioids are safe and effective in managing pain in the older patient when they are prescribed and monitored appropriately, especially for adverse reactions.


its efficacy as an analgesic. The United States General Accounting Office has listed propoxyphene among the drugs “inappropriate in the elderly.”

Fentanyl is extremely potent and fast-acting in a buccal formulation. When used as a patch, it may have a better side-effect profile in the elderly and in patients with renal impairment. However, because of its potency, patients should be taking at least the equivalent of 50 mg of morphine per day before even the 25 mcg/h patch is tried. A 12.5 mcg/h patch was recently released. Because the onset of action of the patch is slow, dosage changes should be made no more frequently than every 3 to 6 days.

Conclusion

Overall, opioids are safe and effective in managing pain in the older patient when they are prescribed and monitored appropriately, especially for adverse reactions (see Table 2). Due to significant variability in bodily function the complete effects of aging on opioid pharmacology and analgesia are unclear.⁴

Effective pain management in the elderly involves proper assessment

and monitoring are essential. Current issues such as “opioid rotation” and medication coadministration are worthy of further research and evaluation. Patients should take an active role in pain management. Approaching pain as a team with the patient as a full participant improves outcomes, function, and patient satisfaction. 

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IN THIS ISSUE, WE INTRODUCE A NEW SECTION CALLED



This will be a place for the practice tips, clever ideas, and novel approaches clinicians have found useful in treating patients with pain. Many of these ideas may involve off-label or investigational uses of medications and/or treatment approaches not supported by randomized, clinical trials, and these ideas will be identified accordingly.

Think of these *pearls* as tips that may be informally shared in the doctor's lounge of a hospital.

If you'd like to share a *pearl* that has improved your clinical practice with colleagues, please email it to info@painknowledge.org. We'll review the entries and feature the best *clinical pearl* in each issue.

Staggered Rotation of Transdermal Fentanyl Patches

From time to time, I treat patients who will experience a sudden drop in analgesia as their transdermal fentanyl patch "runs out of juice" after 2 or 3 days. For patients who require more than one patch, I encourage them to change the schedule of patch rotation. For example, a patient prescribed 150 mcg/hour of transdermal fentanyl will be instructed to wear three 50-mcg/hour patches constantly, and to change one of them daily. Each patch is dated with a magic marker when it is applied, so the patient can easily identify the oldest patch. Since each patch is still worn for 3 days, this staggered rotation schedule costs the patient no more than would the use of three 50-mcg/hour patches all changed every 3 days. Since it seems that fentanyl absorption is greatest on the first day of use, changing one patch a day smoothes out the drug's analgesic effect.

~Eric Chevlen, MD, Rootstown, Ohio

Self-Assessment Test

FERRELL ARTICLE

1. Which of the following is true of unidimensional pain scales?

- They cannot be used to monitor treatment effects and quality assurance indicators
- They are often time consuming and may be too difficult to use with elderly patients
- They require pain questions be framed appropriately for maximum reliability
- They often provide more stable measurement and evaluation of pain than multidimensional scales

2. Recommendations for age-adjusted dosing are available for most analgesics; often this includes initiating treatment with low doses and careful upward titration for most patients.

- True
- False

3. Which of the following is true of opioid analgesics?

- No "ceiling effect" for their analgesic properties
- Pain relief can be achieved with smaller doses of opioids in older patients
- They carry low risks for adverse effects
- a and b
- None of the above

TENZER ARTICLE

4. Physiologic changes that occur with aging *do not* include:

- Increased total body fat
- Increased water content in the body
- Decreased glomerular filtration rate
- Decreased synthesis of mixed-function oxidases

5. Short-acting opioids

- Can be used for persistent acute or chronic pain
- Provide a uniform analgesic effect
- Are associated with decreased dosing errors
- May increase the end-of-dose breakthrough

RAJA ARTICLE

6. Systemic signs and symptoms of herpes zoster (HZ) can include:

- Meningismus
- Nausea
- Adenopathy
- Gastrointestinal (GI) upset
- b and c
- All of the above

7. Which of the following agents are FDA approved for postherpetic neuralgia (PHN)?

- Pregabalin
- Lidocaine patch 5%
- Morphine
- Gabapentin
- Oxycodone
- a, b, and d
- a and d only

ANSWERS 1. c. Unidimensional pain scales consist of a single item that usually relates to pain intensity alone. These scales are easy to administer, require little time or training to produce reasonably valid and reliable results, and can be used in many clinical settings to monitor treatment effects and for quality assurance indicators. Unidimensional pain scales often require framing the pain question appropriately for maximum reliability; subjects should be asked about pain in the present tense. In contrast, multidimensional scales are often long, time consuming, and may be too difficult to use with elderly patients. 2. b. Elderly patients are a heterogeneous population, thus optimum dosage and known side effects are difficult to predict. Recommendations for age-adjusted dosing are not available for most analgesics. Dosing for most patients requires beginning with low doses with careful upward titration, including frequent reassessment for dosage adjustments and optimum pain relief. 3. d. Opioid analgesics have no "ceiling" to their analgesic effects and have proven effective for all types of pain. Advanced age is associated with prolonged half-life and prolonged pharmacokinetics of opioid drugs so that older people may achieve pain relief from smaller doses of opioids than younger people. 4. b. A variety of physiologic changes occur with aging that may influence pain management. Total body fat increases, while the body's water content and muscle mass decrease. The glomerular filtration rate also decreases approximately 10% per decade of life. In addition, there is the decreased synthesis of mixed-function oxidases (CYP 450) with aging, which impact medications metabolized by this pathway. 5. d. Short-acting opioids may be utilized for moderate to severe acute pain, breakthrough pain, and during initial dose-finding and titration to long-acting opioids. These opioids may also be associated with less compliance and increased dosing errors. Short-acting opioids are not ideal for chronic pain and may increase the end-of-dose breakthrough (ie, troughs) and potential for euphoria or side effects (ie, peaks). 6. f. Systemic signs and symptoms during HZ may include fever, signs of meningismus, headache, nausea, gastrointestinal disturbance, and adenopathy. The pain associated with HZ can be severe and adversely affect the patient's quality of life. 7. f. Lidocaine patches are FDA approved for PHN and appear to be safe and effective for many patients. Gabapentinoids, such as gabapentin and pregabalin, should be considered first-line treatment, as these drugs have been shown to be effective in randomized trials and are FDA approved for this indication.

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Bruce D. Nicholson, MD	Tue., Oct. 16	B176-01	12:00 PM	11:00 AM	10:00 AM	9:00 AM
Charles E. Argoff, MD	Tue., Oct. 16	B176-02	7:00 PM	6:00 PM	5:00 PM	4:00 PM
Grace Forde, MD	Wed., Oct. 17	B176-03	8:00 PM	7:00 PM	6:00 PM	5:00 PM
Charles E. Argoff, MD	Thurs., Oct. 18	B176-04	9:00 PM	8:00 PM	7:00 PM	6:00 PM
Bruce D. Nicholson, MD	Tue., Oct. 23	B176-05	12:00 PM	11:00 AM	10:00 AM	9:00 AM
Grace Forde, MD	Wed., Oct. 24	B176-06	9:00 PM	8:00 PM	7:00 PM	6:00 PM
Charles E. Argoff, MD	Thurs., Nov. 1	B176-07	8:00 PM	7:00 PM	6:00 PM	5:00 PM
Charles E. Argoff, MD	Wed., Nov. 7	B176-08	12:00 PM	11:00 AM	10:00 AM	9:00 AM
Grace Forde, MD	Thurs., Nov. 8	B176-09	7:00 PM	6:00 PM	5:00 PM	4:00 PM
Bruce D. Nicholson, MD	Thurs., Nov. 15	B176-10	7:00 PM	6:00 PM	5:00 PM	4:00 PM

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Professional Postgraduate Services® (PPS), known for its award-winning healthcare Websites, has launched a new educational resource on pain management. Originating from the successful National Initiative on Pain Control® (NIPC®), known for its expert faculty and innovative certified activities, PainKnowledge.org will be the home of all certified enduring materials, educational resources, physician tools, and patient materials created by PPS on the treatment and management of pain.

SPOTLIGHT ON PHYSICIAN TOOLS

TABLE OF OPIOID ANALGESIC AGENTS

This downloadable physician tool lists the dosage forms and side effects of opioid analgesics currently available for use in the treatment of pain.

PHN FLOWCHART

This algorithm provides an outline of how to effectively prevent postherpetic neuralgia (PHN) with the Zostavax vaccine and how to treat PHN using several pharmacologic therapies. Download your own personal copy of this tool.

For a treatment regimen for managing neuropathic pain associated with PHN see case study on page 6.

OPIOID ANALGESIA TOOLKIT

This toolkit is a comprehensive compilation of practical tools and references for the management of patients prescribed opioid therapy. Features include an interactive algorithm to help clinicians maximize the benefits and minimize the risks of opioid therapy.

The screenshot displays the PainKnowledge.org website interface. At the top, it features the 'PAINKNOWLEDGE' logo and a 'Finalist MIM AWARDS 2007' badge. The navigation bar includes links for Home, Site Map, About PainKnowledge.org, Contact Us, FAQs, Register, and My Briefcase. A search bar is located on the left side. The main content area is titled 'Physician Tools for Treating Patients with Pain' and includes a disclaimer about pop-up windows. Three red arrows point from the text on the left to specific sections on the website: the 'Table of Opioid Analgesic Agents' table, the 'PHN Flowchart' diagram, and the 'Opioid Analgesia Toolkit' link. The 'PPS Educational Links' section lists various partner websites like PPS-CME.org, NDEI.org, and CCMDweb.org.

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