Effective Treatments for Pain in the Older Patient

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Abstract By 2050, the number of older persons across the globe will exceed the number of younger people for the first time in history. Chronic conditions, especially pain, will rise in prevalence as the population ages. Controlling pain in this unique subset of the population demands careful attention to pharmacokinetic and pharmacodynamic factors and their specific impact on pharmacotherapies, relevant complementary and alternative medicine therapies, and interventional strategies.

Keywords Older adults · Elderly · Aging · Seniors · Pain control · Pharmacotherapy · Analgesia · Opioids · Biopsychosocial · Complementary and alternative medicine · Nerve blocks · Injections · Interventional techniques · Neuromodulation · Vertebroplasty · Kyphoplasty · Geriatric pain

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Introduction

As a growing portion of the population enters the latter portion of their lives, the treatment of pain becomes an integral part of practice for nearly all physicians and surgeons. By 2050, the number of older persons across the globe will exceed the number of younger people for the first time in history [1]. Chronic conditions, especially pain, will rise in prevalence as the population ages. Effective pain control in this demographic requires special consideration of the pharmacodynamic and pharmacokinetic impact on analgesic pharmacotherapies, appropriate nonpharmacologic therapies such as complementary and alternative modalities, and knowledge of the more prevalent pain conditions in older persons and the applicability of procedural interventions.

Pharmacotherapy

General Principles

When pain is insufficiently controlled by nonpharmacologic means alone, pharmacotherapy becomes an important component of pain management. Safe and effective use of pain-reducing drugs in older individuals requires a thorough understanding of patient-specific factors, including the presence of comorbidities, drug–disease interactions, adherence to therapy, and cost. Clinicians must assume that there may be age-associated differences in the effectiveness and toxicity of the therapy, and that pharmacokinetic and pharmacodynamic drug properties will be altered in the older populations [2].

The optimal treatment regimen is one that has a good probability of reducing pain and associated disability and

improving function and quality of life. At the outset, the practitioner needs to establish realistic goals with the patient and primary caregivers to reach a level of comfort that can improve quality of life.

Because older adults use an average of two to five prescription medications on a regular basis, drug–disease and drug–drug interactions must be considered when selecting an analgesic regimen [3]. In addition, age-related alterations in drug absorption, distribution, metabolism, and excretion can result in greater variability in duration of action and plasma concentration for many analgesics (Table 1). Therefore, lower initial dosing and slower titration are recommended to optimize safety [4••, 5].

Most analgesics have not undergone clinical trials in geriatric cohorts, and therefore, do not have empirically derived recommendations for age-adjusted dosing. Also, because older adults comprise a very heterogeneous group, it is difficult to predict common side effects or derive an optimum dose. The dosing adage of "start low and go slow" is largely based on pharmacokinetic considerations and the desire to avoid adverse reactions, and not data from clinical trials. But in the absence of dosage guidelines that can be generalized to a wide population, the initiation of therapy at a low dosage followed by careful upward titration, with frequent monitoring and follow-up, is advisable for older adults [3, 4••].

The least invasive method of drug administration also should be used. For most patients, the oral route is the most convenient and provides relatively steady blood concentrations of the drug [6]. Individuals with swallowing difficulties may benefit from transdermal, rectal, and oral transmucosal routes of administration.

Matching temporal characteristics of pain with onset and duration of analgesic formulations is highly important to optimize treatment outcomes. For example, rapid-onset and short-acting analgesics are required for severe episodic pain, while long-acting or modified release formulations for continuous pain provide around-the-clock relief. Scheduled administration is recommended for cognitively impaired patients who may be unable to request pain relief [4••].

The integration of one or more pharmacologic agents that have a synergistic effect may be more effective than monotherapy in managing painful conditions [7, 8]. While monotherapy eliminates potential competing mechanisms of metabolism and drug–drug interactions, a single therapeutic agent may require dose escalation for adequate pain control. This increases the risk of adverse events. A multidrug approach should be considered when dose-limiting side effects occur before therapeutic goals are met.

Specific Recommendations for Classes of Pharmacologic Agents

The recommendations in Table 2 summarize the conclusions reached by the American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Patients [4••]. Quality of evidence and strength of recommendation are provided.

Table 1 Physiology and effect on drug therapy in older individuals

Physiologic change	Age-related physiologic change	Effect on pharmacology
Volume of distribution	Body fat increases by 20% to 40% and body water decreases by 10% to 15% in old age	Leads to an increased concentration of water-soluble drugs and a prolonged elimination half-life for lipid-soluble drugs
Hepatic Function	Arterial hepatic blood flow may decline with aging, but splenic and venous blood flow does not change with normal aging. The effect of a decline in arterial blood flow has not been well characterized. Decreased cardiac index can result in stiffening vasculature, increasing systolic blood pressure, and reduced myocardial reserve and reduce both hepatic and renal function; decreased liver mass and hepatic blood flow.	Decreased hepatic function only applies to those drugs that are largely metabolized by oxidation mechanisms. Oxidative enzyme function may change with aging and some liver diseases in some individuals. Most opioid medications are metabolized by conjugation, which usually is not affected by aging or many liver disease processes. May cause a 30% to 40% reduction in elimination of drugs metabolized by the liver. Bioavailability of drugs with high first-pass elimination will be increased; decreased activity of certain drug-metabolizing enzymes.
Renal function	Glomerular filtration rate and renal blood flow decreases with advancing age in many patients	Can increase the half-life of drugs eliminated via the kidneys; accumulation of drug or active drug metabolites increases the risk of toxicity and the severity of adverse events
Gastrointestinal absorption or function	Gastrointestinal transit time may slow down	Can lengthen effects of continuous release enteral agents; bowel dysmotility related to opioids might be enhanced

(*Adapted from* Ferrell et al. [101])

Table 2 Medication recommendations for pain in older adults

#	Medication	Recommendation			Quality of evidence & strength of recommendation
		Role	Condition	Comments	
Non Opioid Analgesics					
I	Acetaminophen	As initial and ongoing therapy	Persistent pain, especially musculoskeletal.	A. Absolute contraindications: liver failure	High quality of evidence, strong recommendation
				B. Relative contraindications and cautions: hepatic insufficiency, chronic alcohol abuse/dependence	A. High quality of evidence, strong recommendation
				C. Maximum daily recommended dosages should not be exceeded and must include "hidden sources" such as from combination pills.	B. Moderate quality of evidence, strong recommendation C. Moderate quality of evidence, strong recommendation
II	Nonselective NSAIDs and COX-2 selective inhibitors	Use rarely, in highly selected individuals, with extreme caution		A. Patient selection: other (safer) therapies have failed; evidence of continuing therapeutic goals met; ongoing assessment of risks/complications outweighed by therapeutic benefits. B. Absolute contraindications: 1) current active peptic ulcer disease; 2) chronic kidney disease; 3) heart failure C. Relative contraindications and cautions: hypertension, *H. pylori*, history of peptic ulcer disease, concomitant use of steroids or SSRIs	High quality of evidence, strong recommendation A. Low quality of evidence, strong recommendation B. Low quality of evidence, strong recommendation; 2) moderate level of evidence, strong recommendation; 3) moderate level of evidence, weak recommendation C. Moderate quality of evidence, strong recommendation
III	Proton pump inhibitor or misoprostol	Use If taking NSAIDs	Gastrointestinal protection		High quality of evidence, strong recommendation
IV	Proton pump inhibitor or misoprostol	Use If taking COX-2 selective inhibitor with aspirin			High quality of evidence, strong recommendation
V	On one nonselective NSAID/ COX-2 selective inhibitor			Avoid other nonselective NSAID/ COX-2 selective inhibitor	Low quality of evidence, strong recommendation
VI	If using ASA	For cardioprophylaxis		Avoid ibuprofen	Moderate quality of evidence, weak recommendation

VII	Patients on nonselective NSAIDs and COX-2 selective inhibitors			Routinely assessed for gastrointestinal and renal toxicity, hypertension, heart failure, and other drug–drug and drug–disease interactions	Low quality of evidence, strong recommendation

Opioid analgesics

VIII	Opioid therapy	Moderate to severe pain, pain-related functional impairment, or diminished quality of life due to pain			Low quality of evidence, strong recommendation
IX	Opioid therapy	Frequent or continuous pain on a daily basis		Provide time-contingent, around-the-clock therapy aimed at achieving steady state	Low quality of evidence, weak recommendation
X	Opioid therapy			Anticipate, assess for, and identify potential opioid-associated adverse effects	Moderate quality of evidence, strong recommendation
XI	Fixed-dose opioid and NSAID or acetaminophen combinations			Do not exceed maximal safe doses of NSAIDs or acetaminophen	Moderate quality of evidence, strong recommendation
XII	Short-acting opioids	Used for breakthrough pain	Use while on long-acting opioids	Anticipate, assess, prevent, and treat breakthrough pain	Moderate quality of evidence, strong recommendation
XIII	Methadone			Should be initiated and titrated cautiously only by clinicians well versed in its use and risks	Moderate quality of evidence, strong recommendation
XIV	Opioid therapy			Reassess for ongoing attainment of therapeutic goals, adverse effects, and safe and responsible medication use	Moderate quality of evidence, strong recommendation

Adjuvant analgesics

XV	Adjuvant analgesics		Use in neuropathic pain		Strong quality of evidence, strong recommendation
XVI	Adjuvant analgesics		In fibromyalgia	Begin trial of "approved" agents	Moderate quality of evidence, strong recommendation
XVII	Adjuvant analgesics		Use in refractory persistent pain (eg, back pain, headache, diffuse bone pain, temporomandibular disorder)		Low quality of evidence, weak recommendation
XVIII	Tertiary tricyclic antidepressants (amitriptyline, imipramine, doxepin)			Avoid because of higher risk for adverse effects	Moderate quality of evidence, strong recommendation
XIX	Adjuvant analgesics			Agents may be used alone but effects are often enhanced when used with other analgesics and/or non-drug strategies	Moderate quality of evidence, strong recommendation
XX	Adjuvant analgesics			Begin with lowest possible dose and increase slowly based on response and side effects, with the understanding that some agents have a delayed onset of action and therapeutic benefits develop slowly (eg gabapentin)	Moderate quality of evidence, strong recommendation

Table 2 (continued)

#	Medication	Recommendation			Quality of evidence & strength of recommendation
		Role	Condition	Comments	
XXI	Adjuvant analgesics			An adequate therapeutic trial should be conducted before discontinuation	Low quality of evidence, strong recommendation
Other drugs					
XXII	Long-term systemic corticosteroids		Use only 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	Topical lidocaine	Potential role	In all patients with localized neuropathic pain		Moderate quality of evidence, strong recommendation
XXIV	Topical lidocaine	Potential role	In patients with localized non-neuropathic pain		Low quality of evidence, weak recommendation
XXV	Topical NSAIDs	Potential role	In all patients with localized non-neuropathic persistent pain		Moderate quality of evidence, weak recommendation
XXVI	Other topical agents, including capsaicin and menthol	Potential role	In patients with regional pain syndromes		Moderate quality of evidence, weak recommendation
XXVII	Other agents (eg. glucosamine, chondroitin, cannabinoids, botulinum toxin, alpha-2 adrenergic agonists, calcitonin, vitamin D, bisphosphonates, ketamine)		In patients with specific pain syndromes	May require caution in older persons, and merit further research	Low quality of evidence, weak recommendation

ASA aspirin; *COX-2* cyclooxygenase 2; *NSAIDs* nonsteroidal anti-inflammatory agents; *SSRIs* selective serotonin reuptake inhibitors.

(*From* Ferrell et al. [4••], with permission.)

Biopsychosocial, Complementary and Alternative Medicine Approaches

Psychological Approaches

The multidimensional, biopsychosocial model of pain acknowledges the important role that psychological factors play in mediating persistent pain. Two psychological models frequently used in the treatment of persistent pain include behavioral operant therapy, which reinforces healthy behaviors and ignores or extinguishes maladaptive pain behaviors (eg, inactivity, excessive medication use), and cognitive therapy, which alters the belief structures, attitudes, and thoughts of the person. The combination of the two in a cognitive-behavioral approach is the mainstay of psychological therapy for the management of chronic pain, including pain in older adults.

Maladaptive behaviors are considered as either operant or respondent in nature. Respondent behavior refers to the responses to painful inputs, while operant behavior is what becomes reinforced by social and environmental influences. The aim of cognitive treatment is to identify maladaptive thoughts and reconceptualize such thoughts with alternative cognitions and more effective coping strategies. The person is encouraged to accept responsibility for the pain and its impact rather than act as a passive victim of the condition. Relaxation therapy, biofeedback, guided imagery exercises, stress reduction techniques, attention to family dynamics, sleep problems, and communication skills also are added to standard cognitive programs.

Apart from coping methods, effective therapy must be given in a structured and systematic fashion [9–11]. Initial sessions focus on the historical, physical, and psychological aspects of the pain and the success of prior therapies. Cognitive-behavioral methods and expected treatment gains are explained to the patient. Later sessions focus on new skill acquisition, maintenance of gains, preventions of flare ups and relapse, and review and consolidation of training [9–11].

Studies have shown post-treatment reductions in pain severity, self-rated disability, depression, anxiety, and mood disturbance as well as improved coping skills, engagement in social activity, and quality of life [12–14]. A few randomized controlled trials show efficacy of cognitive-behavioral therapy in older adults living in the community [15–17] or nursing home [18]. Despite supportive evidence of cognitive-behavioral therapy, this treatment modality is grossly underutilized at present. Several specific complimentary/alternative medicine strategies for pain control in older adults are here examined.

Physical Therapies

Exercise

Therapeutic exercise often is prescribed for older adults with chronic pain with the aim of slowing physical deterioration and maintaining or improving functional capacity and range of motion.

Pain can lead to disuse muscular atrophy and reduced range of motion in a joint. Studies have shown that strengthening exercises reduce the intensity of musculoskeletal pain in older people by nearly 30% [19, 20] and increase functional capacity and range of motion in the frail elderly population [21–23]. Further evidence demonstrates an elevation in mood of older people with depression [24, 25] including those with high levels of comorbidities [26]. While both isotonic and isometric strengthening exercises are beneficial, the evidence indicates that isometric exercises may have less impact on pain reports [27].

Physical Modalities

Physical modalities, such as superficial heat, vibration, therapeutic massage, and transcutaneous electrical nerve stimulation (TENS) are designed to reduce pain intensity. Most physical modalities for pain relief have relatively brief periods of efficacy and are not practical for managing more persistent pain, although repeated applications may be warranted for a limited time during acute pain episodes or exacerbation of persistent pain states.

Thermotherapy

Superficial heat provides short-term pain relief [28•] and is generally well-tolerated by older persons, although it may cause superficial burns. Intact thermal sensory afferents and adequate communicative and cognitive abilities must be present in older adults to help prevent cutaneous burns. Heat packs are useful for activities likely to provoke incident-related pain or an exercise-induced exacerbation of musculoskeletal pain. Superficial heat should not be applied within 48 h of acute injury because it may increase swelling, and promote hyperalgesia [29].

Superficial cooling also provides temporary pain relief, but is more effective in acute pain conditions particularly if the area is inflamed [30]. Older adults are less tolerant of cold-based, rather than heat-based, treatments, and the reduction in continuous pain may be less in persons of advanced age [31]. The frequent application of superficial cooling requires active and ongoing

management with little expectation of improvement based on the chronic pain experiences of older people [32, 33].

Vibration

The gate-control theory of pain (ie, activation of large nerve fibers [touch] inhibit small nerve fibers [pain]) is presumed to explain the therapeutic effect of vibration. Though vibration has shown to produce slight improvements in pain, the analgesic effects were reversed within seconds once the treatment had ceased [34]. Hence, strong evidence supporting its use is lacking.

Massage

The combination of therapeutic touch and the enhanced blood flow after palpation of soft tissues is argued to produce a dual palliative effect on mind and body [35]. Several different types of massage are available including shiatsu, Thai, Swedish, and relaxation massage, but the exact mechanisms of action for massage therapy are not fully known. Massage therapy should be avoided over areas of superficial cancer, infection, or local trauma [36].

Electrotherapy

Electromagnetic energy, ultrasound, and TENS have been trialed in a variety of clinical conditions common in older adults, including osteoarthritis and postherpetic neuralgia, although recent evidence questions the efficacy of such treatments and have noted significant methodological shortcomings in many studies [37–39]. Perhaps the most widely used and accepted electrotherapeutic modality is TENS, which involves the application of a low-frequency electrical current to the skin (typically 2 Hz to 100 Hz), with limited adverse reactions. It is recommended that TENS be used to produce a strong but comfortable tingling sensation that exceeds the perception threshold, but optimal TENS parameters for pain relief are yet to be determined. TENS electrodes should not be positioned where they may interfere with cardiac pacemakers or over the carotid sinuses. TENS can be applied for many hours consecutively if pain persists throughout the day and night, and may relieve pain for several hours even after a single 1-hour daily application [40]. TENS can be used for long periods, requires minimal supervision, and permits the user to control stimulation parameters; therefore, this technique remains a viable option for managing pain in seniors.

Interventional Analgesic Strategies

Epidural Steroid Injections

Currently, low back pain is the most common source of pain and disability in the United States, incurring billions of dollars in health care costs each year [41]. Mechanical compression of spinal nerve roots by a herniated disc or spinal stenosis accounts for the major pathologic findings; the resulting back or radicular pain are amenable to treatment with epidural steroid injections (ESIs) with varying degrees of success [42]. Recently, use of ESIs has increased dramatically in seniors. For instance, there was a 271% increase in lumbar ESIs in the Medicare population between 1994 and 2009 alone [43]. As the cost and utilization of ESIs have escalated, there has not been a concurrent rise in evidence to support long-term efficacy of this treatment. Further, there is debate over which approach may be more effective: caudal, interlaminar, or transforaminal. However, a systematic review of the management of chronic spinal pain reported that interlaminar ESI in the cervical region was supported by moderate evidence for both short- and long-term pain relief [44]. For instance, the evidence was strong for short-term pain relief and limited for long-term pain relief in the lumbar region, and evidence was indeterminate for the management of axial neck, axial low back, and lumbar stenosis pain. For transforaminal ESIs in the cervical region, the evidence was moderate for both short- and long-term pain relief. In the lumbar region, the evidence for transforaminal ESI was strong for short-term relief, moderate for long-term relief, and indeterminate for the management of axial neck, axial low back, and lumbar disc extrusion pain. For caudal ESIs, the evidence was strong for short-term and moderate for long-term relief of chronic lumbrosacral radiculopathy and postlumbar laminectomy syndrome. Complications of ESI can be categorized as either needle or drug induced. They include dural puncture, spinal cord trauma, infection, epidural hematoma, epidural abscess, subdural injection, intravascular, spinal cord infarction, pneumocephalus, pneumothorax, headache, nerve root injury, drain damage, and death [45]. While more randomized controlled trials are underway, the careful application of ESI within a multidisciplinary treatment program can provide beneficial pain relief, especially to patients with radicular pain.

Facet Joint Injections and Radiofrequency Denervation

The zygapophysial joint is a true synovial joint located at the junction of the inferior articular process of the cephalad vertebra and the superior articular process of the caudal

vertebra. The facet joints may be a frequent source of pain in older patients, though the prevalence varies widely, from 5% to 90%, in the general population principally due to the variability of diagnostic methods associated with the investigator [46].

Like other pain treatment interventions, there is controversy about the efficacy of these procedures. Yet, well-designed studies with stringent patient selection and attention to technique have demonstrated excellent results for both facet joint blocks (eg, medial branch blocks) and denervation procedures. For example, facet joint blocks undertaken after confirmation of intra-articular inflammation with single-photon emission computed tomography scanning have been reported to significantly relieve pain in 87% of patients, though other studies with less-established selection criteria and technique report pain relief as low as 42% (compared with 33% relief with placebo) [47]. For radiofrequency (RF) denervation of the medial branch nerves, there also have been a number of prospective studies, reporting various degrees of success. For instance, Dreyfuss et al. [48] reported that 60% of patients achieved 90% pain relief at 12 months after RF ablation. A more recent study has shown that performance of RF denervation without diagnostic blocks is more cost effective than those performed after the blocks, even after considering the percentage of patients who may undergo the more expensive RF procedure without gaining significant pain relief thereafter [49]. Serious complications as a result of facet joint injections or RF denervations are rare. Those occurring are either related to the injectate (ie, steroid) or improper needle position [50, 51].

Sacroiliac Joint Interventions

The sacroiliac (SI) joint is a diarthrodial joint designed primarily for stability, yet it can rotate in all three axes and is the largest axial joint in the body, with an average surface area of 17.5 cm^2 [52, 53]. Degenerative changes within the SI joint may begin as early as puberty and become symptomatic when ankylosis occurs around the capsule in the sixth decade of life, and by the eighth decade of life there is marked erosion and plaque formation [54]. Of all chronic axial back pain 15% to 20% can be attributed to dysfunction of the SI joint [55]. Current literature suggests that the anterior portion of the SI joint is innervated by L2-S2, while the posterior aspect is innervated by the lateral branches of L4-S3 [55, 56]. Pain can be referred to buttock (94%), lower lumbar region (72%), lower extremity (50%), groin (14%), upper lumbar region (6%), and abdomen (2%) [56]. Smal-volume diagnostic blocks with local anesthetic have become the "gold standard" of diagnosing SI joint pain because other diagnostic modalities such as physical examination and radiographic imaging offer less sensitivity and specificity [55].

Interventions for SI joint pain include intra-articular injections of steroids with local anesthetics (LA), RF denervation, proliferative therapy (prolotherapy) [57], and, in extreme cases, surgical instrumentation. Intra-articular injection of LA and steroid has been shown in various studies to be both diagnostic and therapeutic for a duration of 6 months to 1 year [55]. A recent systematic review demonstrates level II-2 evidence for diagnostic SI joint injections, level III-3 for RF neurotomy, and no evidence supporting or refuting therapeutic intra-articular SI joint injections [58•]. Advancements in cooled-tip RF technology have shown effective pain treatment of the SI joint with cooled-tip RF denervation of L4/L5 dorsal rami and S1-S3 lateral branches [59]. Based on the best available evidence, the literature supports the use of diagnostic SI joint injections followed by therapeutic RF neurotomy.

Vertebroplasty and Kyphoplasty

Each year there are estimated 1.4 million vertebral compression fractures that present for medical consultation worldwide due to pain and/or disability [60]. Osteoporosis is the most common cause of new vertebral compression fractures (VCF), accounting for 700,000 new cases per year [61]. In fact, the incidence of VCFs in women over 50 years of age is about 26% and increases to 40% at the age of 80 years or greater [62]. VCFs are associated with pain symptoms in up to 84% of cases, and are further linked to pulmonary dysfunction, immobility, spinal deformity, chronic pain, and depression [63]. The annual cost of treating VCFs was estimated at $13.8 billion in 2001 [64]. While conservative medical management remains the gold standard and surgical intervention is typically reserved for patients with neurologic deficit, vertebroplasty (VF) and kyphoplasty (KP) offer minimally invasive solutions to alleviating pain and restoring function.

Vertebroplasty consists of percutaneously injecting an acrylic cement called polymethyl methacrylate (PMMA) into the affected vertebral body to stabilize the bone and promote pain relief. It was developed to treat vertebral angiomas [65], though its use has now expanded. Balloon kyphoplasty uses catheters with inflatable bone tamps that are inserted inside the affected vertebral body to re-expand the compressed bone before the injection of PMMA [66•]. Indications for vertebroplasty include painful osteoporotic VCFs that are refractory to medical management, metastatic vertebral fractures, multiple myeloma, avascular necrosis (Kummell's disease), and vertebral hemangiomas [67]. Kyphoplasty carries similar indications for osteoporotic and osteolytic vertebral compression fractures, but offers the potential benefit of partly restoring vertebral body height and angular deformity [68].

To date, a small number of retrospective and prospective trials have shown short-term efficacy of vertebroplasty or kyphoplasty. For instance, one study reported a cohort of 245 patients who underwent vertebroplasty between 1996 and 1999. Within a median time of 7 months, patients reported reduction of pain from 8.9 to 3.4 on a 10-point scale and a 50% improvement in their ability to ambulate [69]. A separate prospective analysis of 100 consecutive patients undergoing vertebroplasty with a mean age of 73.7 years reported a 93% reduction in pain on the visual analogue scale (VAS) over a period of 21.5 months [70]. Other cohort studies have confirmed the efficacy and safety of vertebroplasty and kyphoplasty [66, 71]. Most recently, the VERTOS II (Percutaneous Vertebroplasty Versus Conservative Therapy) study compared vertebroplasty to conservative management for acute osteoporotic VCFs in an open-label randomized trial in which 202 patients over the age of 50 years (mean age of 75 years) with acute VCFs were randomized to either vertebroplasty or conservative treatment. At the 1-month and 1-year follow-up periods, patients who underwent vertebroplasty reported statistically significant reduction in VAS scores compared to the conservative treatment group. This was the first prospective randomized study supporting the efficacy and safety of vertebroplasty in patients with acute compression fractures [72•].

Interestingly, two recent randomized trials comparing vertebroplasty for osteoporotic vertebral fractures to sham procedure sparked much controversy and debate over the efficacy of this minimally invasive procedure [73, 74]. Both studies showed no improvements in pain and disability compared to sham procedure. However, neither study compared intervention to conservative management.

Potential complications occur in about 5% of patients who undergo vertebroplasty. They include hematoma, infection, rib fracture, neuritis, pedicle fracture, and extravasations of bone cement [75]. Serious complications include cement extravasation into the spinal canal causing neuropathy and/or paraplegia [76]. Systemic extravasation of PMMA also may lead to pulmonary cement embolism in 3.5% to 23% of cases [77]. Of note, the incidence of cement leakage is seen less often after kyphoplasty than vertebroplasty [68].

Compared to optimal medical management, there is good evidence from a level I study that supports the use of vertebroplasty [71] for osteoporotic VCFs and fair evidence from level II and III studies that supports the use of kyphoplasty [78••].

Spinal Cord Stimulation

During the past 30 years, spinal cord stimulation (SCS) has been used for managing chronic pain and carries a US Food and Drug Administration (FDA) approval for the treatment of chronic intractable pain of the trunk or limbs associated with failed back surgery syndrome (FBSS), intractable low back pain, and leg pain [79]. SCS therapy also has been successfully applied to treat refractory neuropathic pain conditions, ischemic limb pain, refractory angina, and complex regional pain syndrome (CRPS) types I and II [80]. Although the exact mechanism of action is unclear, neuromodulation may be partly explained by the gate-control theory of pain advanced by Wall and Melzack [81]. That is, by electrically stimulating the large myelinated $\alpha\delta$ fibers (touch and vibration) located in the dorsal horn of the spinal cord, one can "close" the gate to the transmission of pain signals carried by smaller, unmyelinated C fibers [80]. Moreover, dorsal column stimulation has been shown to produce inhibition of second-order afferent nerves and interneurons, creating a down regulation of pain transmission [82].

To date, there are a few randomized-controlled trials validating the efficacy of SCS in chronic pain management. For the treatment of persistent radicular pain after lumbosacral surgery (ie, FBSS), North et al. [83] conducted a randomized controlled trial of 50 patients who either underwent SCS or reoperation. At the 3-year follow-up, SCS was found to be more effective than reoperation. There were significantly fewer patient crossovers from the SCS group to the surgical group, and the SCS group required fewer opiate analgesics.

In a multicenter international trial, Kumar and colleagues [84] compared SCS to SCS plus medical therapy in 100 patients with FBSS. They showed that SCS in addition to medical management was significantly better than medical management alone. Specifically, 48% of patients undergoing SCS compared to 9% of patients with medical management reached the primary outcome of 50% or greater pain relief at the 1-year follow-up. Incidentally, this study also showed a surprisingly high 32% complication rate attributed to the SCS device, of which 24% required corrective surgery. Notable complications included electrode migration (10%), wound infection (8%), and loss of paresthesia (7%).

For the treatment of CRPS, Kemler et al. [85] compared SCS with physical therapy to physical therapy alone. In the group of 24 patients with SCS, there was a mean reduction of 2.4 on the VAS compared to a 0.2 reduction with physical therapy alone. This was augmented by an overall increase in the global perceived effect of "much improved" among the SCS group (39%) versus the control group (6%). Although the sample size was relatively small, the length of follow-up was impressive. For instance, at the 6-month and 2-year follow-up, the SCS group continued to show a greater than 50% reduction in burning pain compared to the control group [86]. Unfortunately, at the 5-year follow-up, SCS with physical therapy demonstrated no difference

compared to the physical therapy alone group [87]. Long-term follow-up revealed that the effects of SCS faded over time; yet, a subset analysis revealed that 95% of the study patients would repeat the procedure despite the diminished benefit.

There are several refractory pain conditions for which SCS therapy may be applied, including FBSS, CRPS, phantom limb pain, ischemic pain, peripheral neuropathy, diabetic neuropathy, chronic abdominal pain, and postsurgical pain. A dual approach that involves a psychological professional as well as the pain specialist is crucial in selecting the best candidates for neuromodulation therapy. Overall, SCS offers a broad range of treatment applications for persistent and refractory pain syndromes to which older adults are susceptible, and serious complications are infrequent.

Intrathecal Analgesia

When treatment of persistent and refractory pain with conventional therapies such as oral medications, neural blockade, and complimentary/alternative medicine strategies becomes less effective or limited by side effects, certain analgesics may be delivered directly to the central nervous system to regions of the dorsal horn of the spinal cord such as the substantia gelatinosa (lamina II) [88]. Intrathecal (IT) delivery of opioids can be quite effective in reducing cancer pain [89], from which older adults suffer more than the general population [90–92]. Data from clinical outcomes and cost analyses recommend using IT analgesic therapy for patients with terminal, painful malignancies, and tunneled epidural catheters for patients with terminal cancer with life expectancies less than 3 months [93]. The treatment of nonmalignant persistent pain with IT agents, and specifically opioids, is controversial due to concerns of opioid-induced hyperalgesia, tolerance, and the potential for abuse [94, 95]. Three agents are FDA approved for IT delivery: morphine, baclofen, and ziconotide. However, several additional medications and drug combinations are commonly used to achieve adequate analgesia and these options can be found in the Poly-analgesic Consensus Conference 2007 statement [96].

In the older population, maintenance of an implantable drug delivery system (IDDS) can pose challenges due to transportation limitations to the clinic for IT pump medication refills. Alternatively, these refills now can be performed at home by specific home infusion providers. The unique pharmacokinetic and pharmacodynamic effects of opioids and analgesic medications in seniors require careful titration and monitoring. Before IDDS implantation for nonmalignant pain, patients must undergo a thorough psychological screening process to uncover psychosocial predictors of success as well as untreated conditions like depression or anxiety [97]. Successfully screened patients then undergo a trial of IT therapy to demonstrate pain relief and/or adverse effects. Finally, the patient and physician decide to implant the IDDS based on the trial outcome, weighing the intensity of pain relief with any adverse effects.

Complications of IT therapy include cerebrospinal fluid leak, catheter malfunction, wound infection, seromas, and granuloma formation at the catheter tip [98•]. Potential drug related side effects with long-term use of IT analgesics include constipation, nausea, urinary retention, confusion, hypogonadism, pruritus, and psychological disturbances [99]. A systematic review of IT therapy for chronic noncancer pain, reported 15 observational studies that provide level II-3 or level III (based on the US Preventative Services Task Force criteria) evidence supporting the use of intrathecal drug delivery systems for the treatment of chronic noncancer pain [100•]. With insufficient data in older adults to guide specific treatment, IT therapy should be considered in controlling cancer pain foremost, and then regarded as an option in carefully selected seniors with persistent nonmalignant pain.

Conclusions

The approach to managing pain in the older patient requires close attention to age-specific factors as well as the likelihood of diseases. Pharmacotherapy should be considered for all patients with pain that negatively impacts quality of life. Understanding the pharmacology of all potentially useful agents and patient-specific factors, coupled with ongoing monitoring of therapeutic goals and adverse effects, helps to optimize outcomes. Prescription of highly effective therapies such as cognitive-behavioral therapy, along with judicious use of physical modalities such as superficial heat, cold, vibration, and TENS in selected individuals, also may increase the yield of positive patient results. Interventional treatments represent an important opportunity for both the reduction of pain and polypharmacy.

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