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Management of chronic pain in older adults

Silvia Carino,[1] Mariagiovanna Cozza[2]

[1]Geriatrics Complex Operative Unit, Renato Dulbecco University Hospital, Catanzaro; [2]Intermediate-Long Term Care Complex Operative Unit, Integration Department, Local Health Unit Authority of Bologna, Italy

Abstract

Chronic pain is highly prevalent among older adults. In this population, comorbidities and polypharmacy often complicate pharmacological management due to an increased risk of adverse effects and drug-drug interactions. At the same time, many patients experience undertreated pain, significantly affecting quality of life. This review highlights current challenges and therapeutic strategies, emphasizing a stepwise, individualized approach that integrates pharmacological and non-pharmacological interventions.

Key words: opioids, pharmacological treatment, non-pharmacological treatment, chronic pain.

Correspondence to: Mariagiovanna Cozza, Intermediate-Long Term Care Complex Operative Unit, Integration Department, Local Health Unit Authority of Bologna, Italy. E-mail: mariagvzster@gmail.com

Introduction

The new definition of pain, coined by the International Association for the Study of Pain (IASP), is: "an unpleasant sensory and emotional experience caused, or similar to that caused, by ongoing or potential tissue damage". Pain perception in older adults is influenced by age-related changes in both peripheral and central nervous system function, leading to altered pain thresholds and modulation mechanisms.[1] Although some studies suggest increased pain thresholds with aging, the clinical experience of pain is highly variable and often influenced by cognitive, emotional, and social factors.[1-3] The presence of pain in older adults is associated with several negative outcomes, such as reduced functional autonomy, falls, decreased appetite, sleep disturbances, depression and anxiety, up to delirium and cognitive impairment, with a consequent worsening of quality of life.[2] Chronic pain occurs in 25-76% of community-dwelling older adults and in 83-93% within residential care settings.[3] The predominant origin of pain is musculoskeletal (joint pain from polydystrectal arthritis, especially gono- and coxo-arthritis) and polyneuropathic (diabetes, shingles, peripheral vasculopathy). However, even older adults constitutes a category of patients at high risk of under-assessment and analgesic under-treatment,[4] due to the presence of comorbidity, disability-with risk of traumatic falls, adverse drug reactions from polypharmacotherapy,[5] in those with cognitive impairment, where communication difficulties may obscure its recognition and assessment, the lack of randomized controlled trials conducted specifically on this population,[6] but also several commonplaces including: pain as a natural part of the aging process; pain worsens over time; biases toward opioids. In older adults, treatment selection should be guided not only by pain intensity but also by clinical context, including frailty, comorbidities, cognitive status, and risk of adverse drug reactions.

Methods

This narrative review was conducted to summarize current evidence on the assessment and management of chronic pain in older adults. A literature search was performed using major electronic databases (*e.g.*, PubMed, Scopus, and Cochrane Library). Key words included combinations of "chronic pain", "older adults" and "pain assessment". Articles were selected based on relevance, prioritizing systematic reviews and clinical guidelines published in English. Given the narrative nature of the review, no formal meta-analysis was conducted. However, to enhance transparency, levels of evidence were assigned to key findings based on study design and methodological rigor, following a simplified hierarchical classification, from levels of evidence categorized in Table 1.

Classification

Chronic pain is recognized as pain that persists or recurs for more than 3 months. It can be the sole or a leading complaint: chronic primary pain, according to the IASP classification proposal. Chronic primary pain should be considered a disease. It occurs in conditions such as fibromyalgia or nonspecific low-back pain. On the other hand, when chronic pain is secondary to an underlying disease, the IASP classification proposed the umbrella term of chronic secondary pain, where pain may at least initially be considered as a symptom (chronic cancer-related pain, chronic neuropathic pain, chronic secondary visceral pain, chronic posttraumatic and postsurgical pain, chronic secondary headache, orofacial pain, and chronic secondary musculoskeletal pain).[7] Background pain is defined as persistent pain controlled by chronic therapy, while breakthrough pain, defined as transient exacerbations of high intensity compared with baseline pain, requires additional treatment. In

addition, two different types of pain were historically and traditionally distinguished based on the involved receptors or based on some hypothesized mechanisms: i) nociceptive pain, when pain results from nociceptors damage and/or activation. In turn, it can be classified as either somatic (localized pain from muscles, bones, or skin) or visceral (defined pain from internal organs); ii) neuropathic pain, caused by a lesion or disease of the somatosensory nervous system, as happens in trigeminal neuralgia, painful polyneuropathy, postherpetic neuralgia, and central poststroke pain.

More recently, nociplastic pain has been described as different from nociceptive and neuropathic pains. Currently, nociplastic pain is defined as "pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage that causes peripheral nociceptor activation or evidence of disease or lesion of the somatosensory system causing the pain". It appears in chronic pain conditions such as headaches, fibromyalgia, and low back pain, commonly being an expression of chronic primary pain. However, cancer-related pain (which is a type of secondary chronic pain) can sometimes be a nociplastic pain. As for today, a diagnostic gold standard has not been developed yet. Consequently, identification of nociplastic pain is complex, and its prevalence could be underestimated.[7,8]

Pain assessment

Assessment of pain is crucial for its impact on the patient's overall health condition and to achieve proper therapeutic management. Self-assessment scales, chosen according to the patient's level of consciousness and ability to verbalize, are generally used to measure pain intensity. Numerical or verbal scales are the most frequently used, due to their simplicity and reliability.[9] The main scales used to measure pain fall into two categories: unidimensional and multidimensional. The unidimensional scales are the Visual Analog Scale (VAS), the Verbal Rating Scale (VRS) and the Numeric Rating Scale (NRS).

The VAS proposes a 10-cm rod with two ends corresponding to "no pain" and to "maximum possible pain".

The VRS re-proposes the 10-cm rod, in which the choice is facilitated by the presence of adjectives that quantify pain.

Lastly, NRS proposes the 10-cm rod in which, however, the choice is made explicit by a number, from zero to ten (0=no pain, 10=maximum pain imaginable).

In most older adults, given the objective difficulty in assessing pain due to comorbidities (some conditions may, in fact, mask symptoms), impaired hearing and vision, and cognitive deficits,[10] pain is manifested atypically, with vocal, postural, motor, and mimicry symptoms (agitation, restlessness, moaning, crying, shouting, busyness, insomnia). Therefore, it is necessary to research it using appropriate scales based on the analysis of behaviors and body language, such as PAINAD (Assessment of Pain in Advanced Dementia).[11] PAINAD scale evaluates five specific behaviors: breathing, negative vocalization, facial expression, body language, and ability to console. Each behavior score is on a 0 (not present) –2 (completely present) scale based on a direct observation. The total score can range from 0 to 10, where higher scores indicate greater pain severity. A score ≥2–3 may suggest the presence of pain and the need for inter-

Table 1. Levels of evidence.

Level of evidence	Study	Study design	Population	Main findings
I	Abdulla *et al*. (2013)[3]	Systematic review/Guidelines	Older adults (≥65 years)	Comprehensive recommendations for pharmacological and non-pharmacological management; emphasizes individualized care
I	Reid *et al*. (2015)[6]	Systematic review	Community-dwelling older adults	High prevalence of chronic pain; strong association with disability, depression, and reduced quality of life
I	Cohen *et al*. (2021)[8]	Review (multidisciplinary)	Adults including older adults	Highlights complexity of chronic pain and need for multimodal, biopsychosocial management
I	Raja *et al*. (2020)[1]	Consensus/Review (IASP)	General population	Updated definition of pain; emphasizes subjective and multidimensional nature of pain
I	International Association for the Study of Pain (IASP Terminology)[7]	Expert consensus	General population	Standardized terminology and definition of pain used globally in research and clinical practice
II	American Geriatrics Society[28]	Clinical guidelines	Older adults	Recommends cautious pharmacologic use and prioritization of non-pharmacological strategies
II	Schofield *et al*. (2020)[23]	Review/Guideline-oriented	Older adults	Focus on assessment and management strategies tailored to frailty and comorbidities
III	Cherubini *et al*. (2021)[22]	Observational/Review	Older adults	Highlights undertreatment and need for better pain recognition in geriatric populations

IASP, International Association for the Study of Pain.

vention (clinical judgment required). PAINAD is useful for non-verbal patients with dementia, helps guide pain management decisions, should be used alongside clinical assessment and caregiver input, but it does not replace a full clinical evaluation. Besides, behavioral changes may also reflect factors other than pain (*e.g.*, anxiety, discomfort, delirium). It is important to note that multiple validated scales are available for this population, rather than a single instrument. The Doloplus 2 is a tool based on the Douleur Enfant Gustave Roussy scale for young children, adapted for use in older adults, evaluating three distinct pain equivalents (facial expression, psychomotor behaviors, and psychosocial behaviors), with a score of 5 out of 30 for pain suggestion.[12] Algoplus is a 5-item scale consisting of different facial, body, and movement-related behavioral indicators, with a cut-off score of 2 out of 5 indicating pain.[13] The Non-Communicative Patient's Pain Assessment Instrument is a nursing assistant-administered instrument consisting of four main sections (activity chart checklist, pain behavior presence, pain behavior intensity, and pain intensity).[14] The Checklist of Nonverbal Pain Indicators includes a 6-item scale including non-verbal vocalizations, facial grimacing or wincing, bracing, rubbing, restlessness, and vocal complaints, without a clear cut-off established.[15] The Abbey Pain Scale includes six behavioral indicators (vocalization, facial expressions, change in body language, behavioral changes, and physiological and physical change), with a score of ≥3 that indicates pain.[16] The Pain Assessment for the Dementing Elderly of 24 items includes three dimensions: facial expressions, activities of daily living, and the overall healthcare provider's judgment of pain symptoms; however, no cut-off is clearly established.[17] The Discomfort Scale in Dementia of the Alzheimer's Type (DS-DAT/DS-DAT modified) is used to measure discomfort in older adults with advanced dementia of the Alzheimer's type, with nine items and a total score from 0 to 27.[18] Systematic reviews comparing different suggest variability in psychometric properties, feasibility, and clinical utility, with no single tool emerging as universally superior. However, despite their usefulness, behavioral scales have inherent limitations. They may be influenced by factors unrelated to pain (*e.g.*, neuropsychiatric symptoms, environmental distress), and their interpretation requires clinical judgment. Therefore, whenever possible, even limited forms of self-report (*e.g.*, simplified scales, yes/no responses) should be attempted before relying exclusively on observational tools. The assessment of pain in non-communicative older adults remains a significant clinical challenge.[19-21]

Pain management: general principles

The management of chronic pain in older adults is very complex and requires an individualized and multidimensional approach that considers comorbidities, polypharmacy, functional status, and psychosocial factors. The main goals of treatment are to reduce pain intensity, preserve functional autonomy, and improve quality of life.[6,8] A comprehensive assessment of pain characteristics, underlying mechanisms, and patient-related factors should guide therapeutic decisions. In older adults, pharmacological treatment should follow the principles of geriatric pharmacotherapy, including starting at low doses, slow titration, preference for the oral route when feasible, and regular monitoring for both efficacy and adverse effects.[22] Given the increased susceptibility to drug-related complications, non-pharmacological interventions should always be integrated into the treatment plan. The goals of therapy must be mutually agreed upon in the physician-patient or physician-care giver relationship, also considering psychological aspects such as depression, anxiety, fear of movement, and social factors such as isolation, family context, and economic conditions, which influence adherence to treatment, with the aim of managing pain at a level that allows the person to carry out his or her daily activities and achieve an acceptable quality of life.[8]

The choice of effective analgesic therapy should consider three guiding criteria:[6]

i) the use of the World Health Organization analgesic scale. Based on pain intensity measured with a scale from 1 to 10 (*e.g.*, NRS), pain is distinguished into mild (1 to 4), moderate (5 to 6), and severe (7 to 10). Although the method has been validated for the management of oncological pain, much data in the literature affirms the possibility of using the analgesic scale for the management of chronic non-oncological pain as well;[9]
ii) scientific studies, which show the efficacy of certain drugs in precise pain conditions;
iii) the evaluation of the pathophysiological mechanisms underlying the origin of pain.

In older adults, a "stepped" approach is usually recommended (Figure 1). Initially, the least potential risk interventions should be

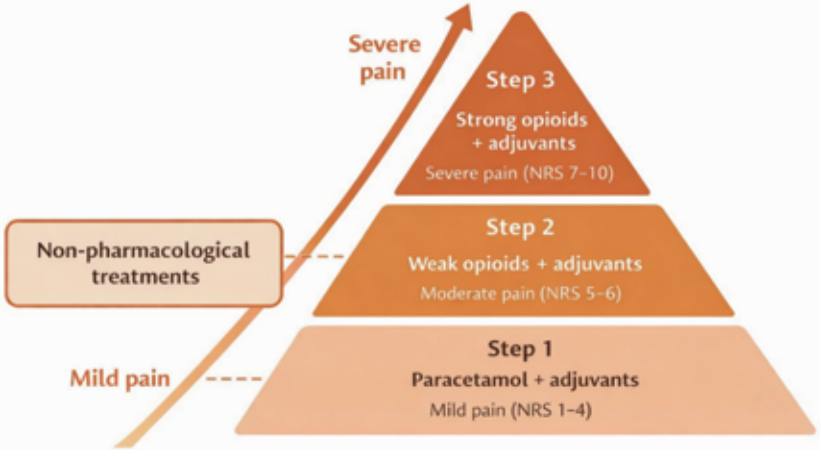

Figure 1. Pain management through a stepwise approach. NRS, Numeric Rating Scale.

used, if necessary, by therapies associated with higher risks (Table 2). It is preferable to start at low dosages, with slow titration, and to prefer the oral route. Provision should be made for the administration of an additional dose or a ready-acting drug to control incident pain (breakthrough pain). Systemic drugs are generally introduced at a later stage than in young adults because of the increased potential for side effects, fluctuations related to their absorption, toxicity, and interactions with drugs used for chronic diseases in older adults. However, the subcutaneous, transdermal, rectal, and transmucosal routes are considered appropriate in reduced level of consciousness, dysphagia, nausea, and malabsorption.[23] Once a drug has been introduced, its efficacy and tolerability must also be evaluated over a sufficiently long and consistent time interval to improve efficacy and limit adverse events. For some classes of analgesic drugs, older adults have shown increased sensitivity, a condition that exposes them to a higher risk of adverse reactions and side effects. In addition, the age-adjusted/adjusted dose is often not available for most analgesics. Timing in drug administration is critical; for chronic pain, analgesics should be taken at regular intervals and not "as needed". For those patients in whom no single drug can produce pain relief without dose-limiting adverse effects, a combination of multiple active ingredients at reduced doses may be beneficial, as the combination of two or more drugs with complementary mechanisms of action may work synergistically to provide greater relief with less toxicity than higher doses of one. Unfortunately, there is also the flip side of the coin, in that taking multiple drugs at the same time increases the risk of side effects related to the complex but extremely important phenomenon of interactions, both between the same drugs prescribed for pain control and between the other drugs that the comorbid patient takes for the rest of their other chronic conditions.[24]

Pain management: pharmacological management

Current drug therapy for chronic pain has drugs that act by different mechanisms: at the peripheral level on nociceptors (anti-inflammatories and steroids), at the nerve fiber level (sodium channel inhibitors), at the synaptic level as modulators (paracetamol, opioids) or as reducers of established spinal sensitization [α-2 delta ligands (such as gabapentin and pregabalin), some antidepressants, baclofen, *etc*.].[25]

Step 1

Mild-to-moderate pain

There is unanimous agreement that the drug of first choice in the treatment of mild and mild/moderate pain in older adults is acetaminophen, particularly in pain of musculoskeletal origin. Paracetamol exerts its analgesic effect mainly through central inhibition of prostaglandin synthesis and modulation of serotonergic pathways, with minimal anti-inflammatory activity. The recommended starting dose is 325-500 mg every 4 hours, or 500-1000 mg every 6-8 hours, up to a maximum of 3 g per day, which should be reduced to a maximum of 2 g per day for the frail old patients, aged ≥80 years, at risk of hepatotoxicity (*e.g.*, regular alcohol consumption or malnutrition.[26,27] Paracetamol interacts with warfarin by prolonging the International Normalized Ratio. Nonselective and selective COX-2 inhibitor nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase (COX-1 and/or COX-2) enzymes, thereby reducing prostaglandin synthesis involved in inflammation and pain.[15] NSAIDs are used in older adults as a second choice, in the presence of nociceptive pain sustained by a certain inflammatory process, for a limited period, strictly necessary to restore the threshold of the nociceptor "sensitized", and then continue with modulatory drugs. NSAIDs, although more effective than acetaminophen for inflammatory pain, are burdened with more side effects, such as gastrointestinal and renal toxicity, cardiovascular damage, and may cause interactions with other drugs (*e.g.*, concomitant use of corticosteroids or selective serotonin reuptake inhibitors). For these reasons, older adults taking NSAIDs should be routinely reassessed and monitored.[28]

Step 2

Weak opioids for mild-to-moderate pain can be combined with non-opioids and/or adjuvants.

Opioids are opioid receptor agonist drugs (μ, κ, δ), stimulation of which results in a variety of responses, including analgesia. Opioids are effective in the treatment of persistent pain associated with musculoskeletal conditions and in the management of various neuropathic pain conditions.[25,27] Older adults taking opioids chronically should be treated with opioids at fixed doses and at set times with the aim of achieving a steady state of analgesic therapy. It is advisable to use low doses initially, titrating the dose gradually to reduce the risk of accumulation and overdose. Evidence shows that the use of opioids in older (especially frail) adults with chronic pain is preferable to that of NSAIDs because of the serious consequences already mentioned on the gastrointestinal, cardiovascular systems,

Table 2. Indication of main class of analgesics in older adults.

Class of analgesics	Main side effects in older adults	Preferred *vs.* Avoid
Opioids	Sedation, respiratory depression, neurotoxicity (especially meperidine), delirium, constipation, falls, neuropsychiatric effects	Use with caution; avoid meperidine & pentazocine; prefer safer opioids (*e.g.*, low-dose morphine)
NSAIDs (including ketorolac)	Gastrointestinal toxicity (ulcers, bleeding), renal impairment, fluid retention, hypertension, major CV risk	Use with caution (short-term only)
Paracetamol (acetaminophen)	Generally safe; risk of hepatotoxicity at high doses or in frail patients	Preferred first-line
Muscle relaxants	Sedation, anticholinergic effects, confusion, falls	Avoid
Adjuvant analgesics (TCAs, gabapentinoids, antiepileptics)	Sedation, dizziness, ataxia, cognitive impairment, falls; TCAs: anticholinergic effects	Use with caution; prefer gabapentinoids over TCAs; avoid amitriptyline if possible

NSAIDs, nonsteroidal anti-inflammatory drugs; TCAs, tricyclic antidepressants; CV, cardiovascular.

and renal function. It is appropriate to select patients who may benefit from low-dose opioid therapy in combination with other therapies (*e.g.*, somatic, peripheral, or neuropathic pain). The initial dose should be lower in older adults, with a reduction of about 25% after age 60 and 50% after age 80.[23,24,26] Situations in which opioids may be useful include pain related to advanced tumors, severe persistent pain, or continuous daily pain related to serious underlying conditions, intense neuropathic pain due to a partially or not fully correctable pathology (*e.g.*, spinal nerve root compression). It is appropriate to avoid opioids in chronic central or visceral pain syndromes such as fibromyalgia, headaches, or abdominal pain. "Weak" opioids (*e.g.*, codeine, tramadol) are indicated for patients who fail to obtain adequate relief after being treated with a nonopioid analgesic or who present with moderate pain, possibly in combination with a nonopioid or an adjuvant to obtain an additional analgesic effect. However, their use in older adults requires careful consideration. Codeine should be used with caution due to its variable metabolism *via CYP2D6*, which may result in unpredictable analgesic effects and an increased risk of toxicity or lack of efficacy. A typical starting dose in older adults is 15 mg every 6-8 hours, with careful titration; doses rarely exceed 120 mg/day in this population. Tramadol, due to its dual mechanism of action, may be effective but carries a risk of central nervous system adverse effects, including dizziness, confusion, and increased risk of falls. Additionally, tramadol may lower the seizure threshold and increase the risk of serotonin syndrome, particularly in patients receiving antidepressants. A recommended starting dose is 25 mg once or twice daily, with gradual titration up to 100-200 mg/day, depending on tolerability. Doses above 300 mg/day should generally be avoided in older adults. Extended-release formulations should be used cautiously. Their use should be avoided or carefully reconsidered in patients with significant cognitive impairment, history of falls, or concomitant use of central nervous system depressants.[3-6,22,28]

Step 3

Patients who fail to obtain adequate relief despite adequate prescription of Step 2 drugs, or who present with severe pain, should be treated with a strong opioid (morphine, hydromorphone, oxycodone, fentanyl, and buprenorphine) with possible addition of adjuvants. Among opioids, the drug of choice in clinical practice of moderate/severe oncologic and nononcologic pain has always been considered morphine. Lower initial doses are recommended in older adults (approximately 25% reduction after age 60 and up to 50% after age 80), followed by careful titration. Long-acting formulations may be considered after stabilization. Older adults are particularly susceptible to opioid-related adverse effects, including sedation, respiratory depression, delirium, constipation, and orthostatic hypotension.[3-6,22] Constipation should be proactively managed with laxatives. Continuous monitoring is essential to reduce risks and optimize treatment. Opioid-induced constipation is a common and persistent adverse effect in older adults receiving opioid therapy, resulting from peripheral μ-opioid receptor activation in the gastrointestinal tract. Prophylactic use of laxatives is recommended at treatment initiation; in patients with inadequate response, peripherally acting μ-opioid receptor antagonists, such as naldemedine, may be considered, as they improve bowel function without compromising central analgesia.[29-31] Morphine is hepatically metabolized, so it is well tolerated in patients with mild to moderate hepatic impairment, while in those with severe hepatic impairment, it can be used with a reduced dose. Morphine is mainly eliminated in the urine, so if creatinine clearance is reduced, there is an increased risk of accumulation of active metabolites and subsequent adverse effects.[32-34] Oxycodone is a pure opioid agonist with affinity for κ, μ, and δ receptors in the central nervous system and spinal cord; it has a lower first-pass metabolism than morphine and, as a result, its bioavailability (of 60-87%) is higher than that of morphine (this availability increases by 15% in older adults and, approximately, by 50% in renal failure). Oxycodone and its (inactive) metabolites are excreted by the urinary route [32-34]. Hydromorphone is a semisynthetic opioid, a pure μ-receptor agonist. Adequate hydromorphone therapy requires preserved bowel function and no surgical outcomes, no pathology of the last intestinal tract, and no short bowel syndrome. This is because the drug is constantly released into the intestines for 24 hours by the tablet, which acts like a reservoir with a semi-permeable membrane; the tablet wrapper is not digested and is eliminated with feces. Fentanyl is a synthetic opioid analgesic, about 75 times more potent than morphine. The antalgic effect of these formulations is rapid onset (5-15 min) and short duration (1-2 hours), features that make the molecule suitable for use even at close intervals. In chronic pain, the most used formulation is transdermal. It is used for maintenance therapy after titration with rapid-release morphine or for an opioid rotation. The fentanyl patch should be replaced every 72 hours; however, in some patients, a change may be necessary after 60-48 hours for inadequate antalgic coverage by day 3. Impaired elimination or insufficient fat stores and muscle hypotrophy (patients with hepatopathy, cachectic, or debilitated) may result in abnormal pharmacokinetics with prolonged half-life. Any change in dosage can be implemented after 3 days, at which time the patch will have to be changed and will need at least another 24 h to become constant.[32-34] Buprenorphine is a potent opioid analgesic that, when administered at antalgic doses, behaves as a pure μ agonist with very high affinity for the μ receptor and a slow rate of dissociation. Buprenorphine is one of the few opioid analgesics that does not significantly interfere with immune system function.[35] The transdermal formulation of buprenorphine is the one that ensures a steady release of active ingredient, prevents the occurrence of absorption spikes, has good tolerability, and side effects are generally modest and transient.[35] Tapentadol represents the progenitor of a new generation of drugs, indicated for severe pain, with a combined mechanism, due to its action on opioid receptors and noradrenergic pathway: it is a μ opioid receptor agonist and noradrenaline reuptake inhibitor; both mechanisms of action contribute in a complementary and synergistic way to its analgesic efficacy, in chronic conditions such as neuropathic or mixed pain. It is recommended that patients begin treatment with a single dose of a 50 mg tapentadol extended-release tablet administered twice a day. After instituting therapy, the dose should be titrated on an individual basis to a level that will produce adequate analgesia and minimize side effects. Studies in patients with arthritis or chronic low back pain have demonstrated analgesic efficacy like that of a strong opioid in comparison. The efficacy of tapentadol is also evident in neuropathic pain. Tapentadol has a good safety profile for older adults, in relation to its low risk of drug interactions, reduced binding to plasma proteins, minimal CYP450 relevance on its metabolism, and absence of pharmacologically active metabolites.[36] Table 3 summarizes interactions between renal function, risk of delirium, and opioids.

If necessary, naloxone can also be used in older adults.[23] Naloxone can be safely used in older adults when clinically indicated, particularly in cases of suspected or confirmed opioid overdose. However, special considerations are required in this population due to age-related physiological changes, comorbidities, and polypharmacy. Lower initial doses are often recommended to avoid precipitating acute withdrawal symptoms, severe pain, or sympathetic overactivation, which may lead to complications such as hypertension, arrhythmia, or pulmonary edema. Careful titration is essential,

starting with small doses and repeating as needed to achieve adequate respiratory function rather than full reversal of analgesia. Additionally, older adults should be closely monitored after naloxone administration, as the duration of action of some opioids may exceed that of naloxone, increasing the risk of recurrent respiratory depression. Continuous observation and supportive care, including airway management and oxygen therapy if needed, are therefore crucial. Concomitant drugs such as benzodiazepines and central nervous system depressants increase the risk and severity of such adverse effects. Ongoing overdose education should be encouraged, and take-home naloxone training for older patients and their families/friends/caregivers should be increasingly proposed.

Adjuvant drugs

Adjuvants are drugs that have been originally developed and used for indications other than pain control, but which have beneficial analgesic properties, especially when a neuropathic component is preponderant. Adjuvant drugs may have an independent analgesic effect (consequently, they may be used alone), additive, or synergistic analgesic effects when used with conventional analgesics. When added to conventional analgesics, they enable a reduction in their doses and side effects while increasing analgesic efficacy. Typically, the analgesic effects derived from some adjuvants, such as antidepressants and anticonvulsants, occur at dosages lower than those used for their primary indication; this usually involves less frequent and severe adverse effects. Adverse effects vary by class but may include sedation, dizziness, cognitive impairment, and anticholinergic effects. These risks are especially relevant in older adults with multimorbidity and cognitive decline. In clinical practice, gabapentinoids (gabapentin and pregabalin) and serotonin-norepinephrine reuptake inhibitors are commonly considered first-line options for neuropathic pain, while tricyclic antidepressants should generally be avoided in older adults due to their anticholinergic effects and increased risk of cognitive impairment and falls. Their use may enhance analgesic efficacy and allow dose reduction of primary analgesics, thereby improving overall tolerability.[37,38]

There is no defined pattern to be used. However, considering their mechanism of action, it can be said that prescriptive appropriateness is based on the following considerations:

i) drugs that act in the presence of peripheral nerve fiber damage, as in the case of polyneuropathy and mono-neuropathy: anticonvulsants (carbamazepine, lamotrigine, gabapentin, pregabalin), tricyclic antidepressants, and local anesthetics (lidocaine);
ii) drugs that act in the presence of sensitization of spinal neurons by nociceptive afferents, reduction of inhibitory systems, and others (spinal neuroplasticity). Clinically, this eventuality results in increased pain, with onset of referred pain and reduced response to analgesic drugs, opioid and non-opioid: gabapentinoids (gabapentin, pregabalin), clonazepam, and antidepressants (tricyclic and non-cyclic);[37]
iii) drugs that act in the presence of nerve pathway inflammation, where the role of peripheral receptors of small nociceptive endings in the perinervum plays an important role: corticosteroids.[39]

According to the guidelines compiled by the American Geriatrics Society,[28] all older adults with neuropathic pain and those with fibromyalgia should be candidates for adjuvant therapy; tricyclic antidepressants should be avoided because of the high risk of side effects (*e.g.*, anticholinergic effects, cognitive impairment...); although these drugs are also effective in monotherapy, their effect is enhanced when they are used in combination with other analgesics or complementary nonpharmacological measures; adjuvant therapy should be started at low doses and increased slowly according to clinical response, with the awareness that some drugs in this class manifest their response in a long time; steroid therapy should be reserved for patients with rheumatologic disease and with bone metastases; older adults with localized neuropathic and nonneuropathic pain should be candidates to receive topical lidocaine; many pharmacologic remedies used in the treatment of pain in older adults should be used with caution and would need further experimental confirmation (*e.g.*, cannabinoids, ketamine, glucosamine, chondroitin, cholecalciferol, bisphosphonates, calcitonin, botulinum toxin, α-2 adrenergic). Table 4 summarizes the main molecules used as adjuvants.

Table 3. Opioids and renal adjustments with delirium risk.

Opioid	Renal impact (metabolites)	Dose adjustment in CKD	Delirium risk	Key mechanism for delirium
Morphine	↑↑ Active metabolites (M3G, M6G)	Avoid or ↓↓↓ dose	High	Neurotoxic metabolites confusion, sedation, hallucinations
Hydromorphone	Metabolite accumulation	↓ dose	Moderate-High	Agitation, delirium for neuro-excitation
Oxycodone	Metabolites accumulation	↓ dose	Moderate	CNS accumulation sedation/confusion
Fentanyl	Minimal active metabolites	Caution in frail	Low	Less accumulation, lower neurotoxicity
Buprenorphine	No significant accumulation	Usually	Lowest	Minimal renal clearance, ceiling effect on CNS depression

CKD, chronic kidney disease; CNS, central nervous system.

Table 4. Maximum dose of adjuvants in the management of pain in older adults.

Drug	Maximum dose (old population, analgesic use)	Key considerations in older adults
Amitriptyline	25-50 mg/day	Strong anticholinergic effects, high risk of confusion, falls, urinary retention: often avoided
Nortriptyline	50-75 mg/day	Better tolerated than amitriptyline but still monitor for sedation and orthostatic hypotension
Carbamazepine	600-800 mg/day	Risk of hyponatremia, drug interactions, dizziness: monitor sodium
Pregabalin	300 mg/day (lower if renal impairment)	Adjust for kidney function; risk of sedation, falls
Gabapentin	1800 mg/day (often less)	Renal adjustment essential; sedation and gait instability common
Clonazepam	≤2 mg/day (generally avoid)	High risk of falls, cognitive impairment: usually discouraged

Pain management: nonpharmacological interventions

Current approaches recommend that interventions for chronic pain in older adults should always be part of a comprehensive, multidisciplinary treatment [physical activity and complementary therapies such as oxygenzonotherapy, physiotherapy, acupuncture, transcutaneous electrical nerve stimulation (TENS), active and passive motor activation, psychoeducational interventions such as cognitive-behavioral therapy (CBT), meditation, and patient education]. Non-pharmacological interventions represent a cornerstone of chronic pain management in older adults and should be systematically integrated into treatment plans, either alone or in combination with pharmacological therapies, in line with current guideline recommendations (Table 5). Non-pharmacological interventions include physical therapy and structured exercise programs (aimed at improving strength, flexibility, and endurance), which have been shown to reduce pain and improve functional outcomes in older adults. Physical therapy and structured exercise programs have consistently demonstrated positive effects on pain intensity, mobility, and functional independence. Exercise interventions, particularly those focusing on strength, flexibility, balance, and endurance, can reduce disability and mitigate the risk of falls, which is a critical concern in older adults. Furthermore, regular physical activity has been associated with anti-inflammatory effects and improved neuromuscular coordination, contributing to long-term pain modulation.[40,41] CBT is also effective in addressing maladaptive thoughts and behaviors associated with chronic pain and has demonstrated benefits in improving coping strategies and psychological well-being. CBT has been shown to improve coping strategies, reduce perceived pain intensity, and alleviate comorbid symptoms such as anxiety and depression. Importantly, these psychological benefits may enhance adherence to both pharmacological and non-pharmacological treatments. Patient education and self-management strategies play a key role in enhancing adherence to treatment and promoting active participation in care, leading to better long-term outcomes. These interventions improve treatment adherence, promote realistic expectations, and encourage behavioral changes that support long-term pain control. Self-management programs have been associated with sustained improvements in symptom control and healthcare utilization.[42,43] In addition, complementary therapies, such as acupuncture and TENS, may provide adjunctive pain relief in selected patients, although evidence in older adults remains variable. These approaches are generally well tolerated and may be particularly valuable in patients with contraindications to pharmacological therapies.[44] In selected patients, especially those with localized or refractory pain, interventional procedures may be considered as part of a multimodal approach. These include nerve blocks, intra-articular injections, and minimally invasive techniques such as radiofrequency ablation (RFA). RFA, which involves the thermal disruption of nociceptive nerve fibers, has shown efficacy in conditions such as facet joint pain and certain neuropathic pain syndromes. In older adults, these procedures may offer a valuable alternative when pharmacological treatments are contraindicated or poorly tolerated. However, careful patient selection and evaluation of procedural risks are essential.[45] Furthermore, psychosocial interventions and a multidisciplinary care approach are essential in the

Table 5. Non-pharmacological approaches for chronic pain in older adults.

Intervention	Main indications	Clinical benefits	Level of evidence
Physical therapy and exercise	Chronic musculoskeletal pain (*e.g.*, osteoarthritis, low back pain), frailty	Improves pain, mobility, balance, and quality of life; reduces fall risk	High (Cochrane reviews, guidelines)
Manual therapy	Mechanical and musculoskeletal pain syndromes	Short-term pain relief, improved joint mobility	Moderate
Cognitive-behavioral therapy	Chronic pain with psychological comorbidities (depression, anxiety, pain catastrophizing)	Improves coping strategies, reduces pain perception and disability	Moderate-High
Transcutaneous electrical nerve stimulation	Localized musculoskeletal or neuropathic pain	Non-invasive pain relief; variable response among patients	Low-Moderate
Acupuncture	Chronic low back pain, osteoarthritis functional improvement	Modest pain reduction and	Moderate
Heat and cold therapy	Acute or chronic musculoskeletal pain inflammation	Symptomatic relief: improves muscle relaxation or reduces	Low
Multidisciplinary rehabilitation	Complex chronic pain, multimorbidity, functional impairment	Improves overall function and quality of life	High
Intra-articular injections (*e.g.*, corticosteroids, hyaluronic acid)	Osteoarthritis (especially knee, shoulder)	Short-term pain relief and improved joint function	Moderate
Nerve blocks	Localized neuropathic or nociceptive pain	Diagnostic and therapeutic role; temporary pain relief	Moderate
Radiofrequency ablation	Facet joint pain, selected neuropathic pain conditions	Longer-lasting pain relief compared to nerve blocks	Moderate
Neuromodulation techniques	Refractory neuropathic pain	Pain reduction in selected patients	Moderate (selected populations)

management of chronic pain in older adults, as they address emotional, behavioral, and social factors that influence pain perception and overall quality of life. Chronic pain in older adults is frequently associated with social isolation, depression, and reduced participation in daily activities. Multidisciplinary approaches, integrating medical, psychological, and rehabilitative expertise, have been shown to improve functional outcomes, reduce pain-related disability, and enhance quality of life. These models also facilitate individualized care, which is crucial in a population characterized by heterogeneity in clinical conditions and functional status.[8,23]

Conclusions

In older adults, the recommended treatment of chronic pain is multimodal, non-pharmacological, and pharmacological, because it allows for obtaining the best results while reducing the risks of side effects. It is necessary, therefore, to implement a customization of the treatment plan, which goes to consider the right dosage of the drug, the most suitable modalities of use for the patient, as well as the type of nonpharmacological intervention to be implemented, to manage pain at a level that preserves as much as possible functional autonomy and that allows for achieving an acceptable quality of life.

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