

Chronic Pain in the Elderly with Cognitive Decline: A Narrative Review

Luca Cravello · Simona Di Santo · Giustino Varrassi · Dario Benincasa ·
Paolo Marchettini · Marina de Tommaso · Jacob Shofany ·
Francesca Assogna · Daniele Perotta · Katie Palmer · Antonella Paladini ·
Fulvia di Iulio · Carlo Caltagirone

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ABSTRACT

The presence of pain in elderly persons with cognitive decline is often neglected, under-reported, underestimated, misdiagnosed and not adequately treated, with consequences that have a strong impact on health, independence in activities of daily living and quality of life. There is no empirical evidence that people with dementia experience less pain; therefore, in

patients with severe cognitive impairment the progression of cognitive decline dramatically affects the ability to verbalize the presence of pain. Self-assessment scales are considered the “gold standard” for pain assessment, but the presence of cognitive impairment is likely to reduce the reliability of these measures. Treatment of pain in elderly with cognitive decline or dementia is based on non-pharmacological and pharmacological strategies. Pharmacological treatment should consider physiological changes, high comorbidity and drug interactions that occur frequently in the elderly. This narrative review aims to describe current knowledge, methods of detection and treatment approaches for chronic pain in elderly persons with cognitive deficits.

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L. Cravello (✉) · D. Perotta
Centro Regionale Alzheimer ASST Rhodense,
Passirana di Rho Hospital, Milan, Italy
e-mail: lcravello@asst-rhodense.it

S. Di Santo · J. Shofany · F. di Iulio · C. Caltagirone
IRCCS Fondazione Santa Lucia, Rome, Italy

S. Di Santo
Dipartimento di Medicina dei Sistemi, Università
Tor Vergata, Rome, Italy

G. Varrassi
Paolo Procacci Foundation, Rome, Italy

G. Varrassi
World Institute of Pain, Winston-Salem, USA

D. Benincasa
Istituto Regina Elena IFO-Neurologia, Rome, Italy

P. Marchettini
Istituto Scientifico Ospedale S. Raffaele, Milan, Italy

M. de Tommaso
Neurophysiology and Pain Unit, University of Bari
Aldo Moro, Bari, Italy

F. Assogna
Laboratory of Neuropsychiatry, Department of
Clinical and Behavioral Neurology, IRCCS Santa
Lucia Foundation, Rome, Italy

K. Palmer
Fondazione Ospedale San Camillo IRCCS, Venezia,
Italia

A. Paladini
Department of MESVA, University of L'Aquila,
L'Aquila, Italy

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INTRODUCTION

Chronic pain is defined as persistent and recurrent pain that is perceived over a pre-defined period of time, commonly 3 or 6 months after onset or, according to a broader definition involving no arbitrarily fixed duration, pain that extends beyond the expected healing period [1].

The worldwide prevalence of chronic pain is estimated to be between 25% and 50% in elderly people living in the community [2] and up to 83% in those living in nursing homes [3]. The prevalence of chronic pain increases with age, reaching a plateau at around 70–75 years [4].

The presence of pain in the elderly is often ignored, underestimated, underreported and thus improperly treated, with important consequences on health, the ability to perform the activities of daily living and quality of life. Sleep disorders, musculoskeletal problems, lower degree of mobility, falls, malnutrition, cognitive impairment, increased use of drugs, depressed mood depression and reduced social participation are usual manifestations of symptomatic pain in elderly patients [5].

Although chronic pain affects cognitive abilities, the inverse relationship is unclear. Neurodegenerative diseases, which lead to cognitive impairment, can influence the perception of pain. Given the progressive increase in the aging population and the high prevalence of dementia in the elderly, the topic of chronic pain, its detection and quantification in people with cognitive impairment and the identification of useful therapeutic approaches is of high interest and importance.

This narrative review aims to describe current knowledge, methods of detection and treatment approaches for chronic pain in elderly persons with cognitive deficits.

This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

PAIN IN ALZHEIMER'S DISEASE AND OTHER DEMENTIAS

Pain is a complex perceptual and subjective experience that has sensory, affective and cognitive dimensions. In vegetative and minimal states of consciousness there is a residual cortical response to nociceptive experimental stimuli [6], thus the perception of pain seems essential for survival and deserves evaluation in the absence of valid subjective reports, such as in people with severe cognitive impairment.

Neuropathological changes that occur in people with dementia are considered responsible for alterations in pain perception [7]. Although these alterations could be common in different types of dementia, the vast majority of clinical and experimental studies investigating pain assessment or treatment in dementia are focused on patients with Alzheimer's disease (AD).

The neuropathological changes that occur in AD selectively affect important areas involved in the medial pathway of pain, especially the medial nuclei of the thalamus, hypothalamus, cingulus and insula, whereas the brain areas involved in the lateral pathway of pain are relatively well preserved [8]. Thus, according to a widely accepted theory, typical degeneration of AD involves the affective-motivational component of pain (medial pathway) more than the sensory-discriminative dimension (lateral pathway) [9]. Furthermore, the typical cognitive impairment of AD, which is characterized by memory deficits and reasoning, could affect the individual assessment of a painful experience and the ability to describe it. According to this clinical theoretical construct, an unchanged pain threshold and a higher tolerance of painful stimuli should be observed in AD patients. Indeed, some authors found a higher tolerance for intense pain in AD patients than in controls [10] and some others suggested that in AD the perception of acute pain is preserved and that the experience of chronic pain may be altered [11]; a reduction in the autonomic response as a result of impending pain has also been reported [12].

Conversely, other studies have provided different results [13]. For example, after nociceptive stimuli administration a functional brain neuroimaging study did not show more reduced activity of specific brain areas involved in the medial pain pathway in AD patients than in healthy controls [14]. This indicates that the emotional aspects of the experience and emotional pain are not selectively reduced in these patients [14]. These data are still consistent with the results of previous works indicating that sensory-discriminative pain is preserved even in the advanced stages of AD [12], whereas pain tolerance is enhanced with increasing severity of the disease [10].

Another key point related to the neuropathological changes that occur in the prefrontal lobe of patients with AD is alteration of the response to analgesic drugs. An experimental study showed that the placebo mechanism, which is an important aspect of pain management, is reduced in patients with AD. This effect is particularly noticeable when the connections between the prefrontal lobes and the rest of the brain are extensively damaged [15]. It is, therefore, likely that patients with AD require a higher dosage of pain medication to obtain the analgesic effect that is normally reached in cognitively healthy persons. In addition, it is still unclear whether the changes in the blood–brain barrier that occur during the dementia process influence the effect of centrally acting pain medications, such as opioids [16].

Neuropathological changes differ, at least partially, between dementia syndromes. It has been, therefore, suggested that the prevalence of pain differs among different types of dementia. However, evidence from studies enrolling patients with dementia types other than AD is scarce.

Pain perception in vascular dementia (VaD) may increase because of white matter lesions of pathways ascending to the thalamus, such as the spinothalamic tract [17]. As far as we are aware, there are only a few studies on chronic pain in patients with VaD, observing that the level of pain reported by patients with VaD is significantly higher than that reported by persons without dementia [18–20]. Moreover, in a

recent study of Binnekade et al., patients with mild to moderate AD and mixed AD and VaD are less likely to report pain than patients with subjective cognitive impairment in an outpatient memory clinic setting [21].

There is overlap between AD and frontotemporal dementia (FTD) in affected pain-related areas. However, compared with AD, the degeneration of the cingulate cortex and the insula is higher in FTD, while atrophy of the amygdala and hippocampus appears milder [22]. It, therefore, might be argued that the evaluative and motivational-affective aspects, as well as the autonomic responses and memory for pain, should be particularly affected in FTD patients. Accordingly, in one study, the perception of pain and ability to withdraw from nociceptive stimuli in FTD was found to be significantly lower than in AD and VaD [23]. Nevertheless, no study was found to report the prevalence of pain specifically in patients with FTD.

Also, pain perception in dementia with Lewy bodies (LBD) may be altered due to brain atrophy and damage caused by Lewy bodies. However, studies reporting the prevalence of pain in people with LBD are scarce. Since LBD neuropathology may be a key feature of Parkinson's disease (PD), a specific reason for the lack of studies in LBD could be that these patients might be included within trials assessing pain in PD, in which prevalence of pain is estimated to be of 59.7% [24].

A recent review investigated pain prevalence in AD, VaD, FTD and LBD. The sample-weighted prevalence of pain could only be calculated for AD, VaD and mixed dementia: pain was estimated to affect 45.8% (95% CI 33.4–58.5%) AD patients, 56.2% (95% CI 47.7–64.4%) persons with VaD and 53.9% (95% CI 37.4–70.1%) with mixed dementia [7].

According to three studies found, the prevalence of pain in patients with LBD ranges between 50% and 70% [25–27]. In a recent review and meta-analysis on pain in atypical Parkinsonism, patients with LBD had a pooled pain prevalence of 38% with a multi-localized characterization [28].

ASSESSMENT OF PAIN IN ELDERLY WITH COGNITIVE DECLINE

Self-assessment scales are considered the 'gold standard' for assessing pain, but the presence of cognitive impairment decreases their reliability.

In 2002, the American Geriatrics Society established guidelines for the assessment of behavioral indicators of pain [29]. More recently, the American Society for Pain Management, with the Nursing Task Force on the assessment of pain in patients unable to verbally communicate, recommended a comprehensive hierarchical approach, incorporating measures of self-evaluation and the observation of behaviors related to pain [30]. On the basis of these recommendations, the assessment of pain in elderly patients affected by cognitive impairment should be carried out as follows:

1. An attempt should be made to obtain a self-rating by the patient; the severity of cognitive impairment is important for choosing the strategy and the evaluation tools. Self-assessment of pain is often possible in patients with mild to moderate cognitive impairment, but its accuracy decreases with the progression of dementia. The use of validated and standardized assessment scales is widely recommended to allow more accurate monitoring of patients, with the possibility of comparing the course of pain over time and more effective communication between the different operators. A high percentage (61%) of patients with severe dementia can understand at least a simple scale of pain self-assessment (e.g. Visual Analogical Scale, Verbal Rating Scale, Faces Scale). Observational scales for pain should not be administered routinely in patients with severe dementia if they are still able to provide pain self-assessment measures [31]. Communicative skill could, however, be compromised by the presence of delirium, an altered level of consciousness, medical devices such as endotracheal tubes, sedation or the effect of pharmacological treatments.
2. Researching possible causes of pain. Common etiological factors should always be investigated in elderly persons: pathological conditions (musculoskeletal or neurological problems), treatment procedures or other causes (infections, fecal retention, falls, entrapment, etc.) are common etiologies of chronic pain.
3. Observing and describing the patient's behavior, also using specific scales. When verbal expression is severely impaired (as in some forms of dementia or in severe stages of illness), behavior remains the primary source of communication. Modification of behavior can be an important sign of pain [32]. Behaviors that should be observed in patients with dementia include: facial expressions, verbalizations/vocalizations, body movements, changes in interpersonal interactions, changes in daily life, changes in cognitive status [29]. Although several studies have been conducted on this topic, the behaviors most often associated with pain in persons with dementia have not yet been unequivocally identified [33]. The observation should take place preferably while the patient is participating in an activity, since the pain may be minimal or absent at rest. Changes in vital parameters do not represent reliable pain indicators. Behavioral modifications can be described and quantified using validated scales appropriate to the patient's setting and clinical condition.
4. Obtaining information from a caregiver. Sufficiently reliable information can be obtained from formal and informal caregivers (family members, nurses, care personnel in nursing home/hospital) who have adequate knowledge of the patient's history and past and current behavior and may be adequately trained to assess pain. Pain assessment should be included in the training of all staff members involved in clinical care. There are discrepancies between patient self-assessment and that of family members and clinical staff, who tend to overestimate and underestimate the pain experienced by the individual [34].
5. Trying an analgesic treatment. It is important to try pain reduction by administering an analgesic; this should be done following

procedures and doses appropriate for the disease and after estimating intensity of pain and the patient's comorbidities [35].

Several tools have been developed to assess pain in elderly persons with cognitive impairment. Reviews in the literature [36, 37] concluded that the existing instruments need further implementation and psychometric validation before they can be commonly used in clinical practice. All scales designed to assess pain in elderly patients with dementia have significant limitations in terms of usability, construct validity, reliability and inter-rater and test-retest reliability [38]. In particular, observational scales should be validated versus the gold standard of self-rating assessment in people without cognitive impairment. Moreover, almost all research in the literature has focused exclusively on patients with moderate to severe dementia. To date only two studies have compared measures of self-evaluation and observational scales in people with and without cognitive impairment, i.e., a study on acute pain associated with physical therapy in patients with post-operative rehabilitation and research comparing patients with mild to moderate dementia with cognitively intact elderly persons [39]. There is, however, sufficient consensus that measures of self-assessment cannot represent the gold standard in patients who are unable to understand the scale instructions/requests and provide effective and uniquely interpretable verbal responses.

Direct assessment relies generally on simple analogue scales or on more complex instruments, which are, however, difficult to use in the presence of cognitive impairment. Indirect assessment is carried out with scales aimed at detecting and recording behaviors or attitudes indicative of pain, such as difficulty in breathing, restlessness, facial expressions, vocalizations and agitation.

TREATMENT OF CHRONIC PAIN IN THE ELDERLY WITH COGNITIVE DECLINE

Pain therapy in the elderly is different than in younger people. Clinical manifestations of

chronic pain are often complex and multifactorial. **Moreover, pain in elderly persons with cognitive disorders may be under-reported or underestimated.** The presence of comorbidity and polypharmacy must always be taken into consideration when choosing the painkiller treatment as it increases the risk of complications and adverse events. Current evidence from clinical trials on pain treatment cannot provide adequate indication in many situations commonly encountered in clinical practice: most of the evidence, in fact, is based on specific conditions and trials conducted in populations of young adults while few studies have been conducted on patients aged over 75 years and those on elderly people with cognitive decline are poor [40]. Age-related differences in efficacy, sensitivity, toxicity and in the pharmacokinetic and pharmacodynamic properties of drugs cannot be ignored in the formulation of an adequate therapeutic program.

The efficacy of pain-relieving treatments in patients with dementia could be influenced by the level of cognitive impairment, with a reduction of the awareness of the disease and of communication and relational skills. Moreover, behavioral symptoms such as agitation, aggression and delirium could be the only manifestation of pain [31]. Often, this type of patient receives a sedative treatment and the prescription of antipsychotic drugs, that have dubious efficacy on painful symptoms and expose the patient to potential even serious side effects, such as increased mortality, cardio- and cerebrovascular events and falls [41]. Referring then to the treatment of pain in elderly patients with cognitive impairment, the first consideration is to use appropriate pain assessment methods and to correctly set the diagnosis in order to choose the most appropriate drug therapy and avoid the use of inappropriate, potentially harmful drugs.

Given the lack of clinical evidence that can be extrapolated from clinical trials, the indications of interventions provided by the main guidelines for the treatment of pain are basically based on clinical experience.

The probability of obtaining adequate analgesic efficacy can be maximized by careful training of caregivers, analyzing the patient's

risk factors and comorbidities, and carefully monitoring the patient over time. Although realistic expectations about the possible benefits must be met and provided, especially in some persistent pain conditions, the goal in elderly patients, and even more so in those with cognitive impairment, is not to completely eliminate pain, but to reduce the intensity, duration and frequency of pain episodes, so as to maximize both independence in activities of daily living and quality of life, and to minimize the risk of side effects, often severe, that are associated with treatments [42].

Pain therapy can utilize non-pharmacological treatments, as well as pharmacological treatments. Among the non-pharmacological treatments, the following may be useful: physical therapy (physical exercises, TENS, vibratory therapy, massages, exposure to heat or cold sources) [43, 44], alternative therapies (acupuncture, acupressure, aromatherapy). There are also other types of non-pharmacological analgesic therapies used in elderly persons without cognitive impairment, such as educational programs, music therapy and psychological methods, which are difficult to apply in dementia patients, since cognitive impairment reduces treatment compliance.

Until now, the most recent guidelines for pharmacological treatment published by the British Geriatric Society [45] suggest that the choice of treatment should be dictated by the severity of the pain symptomatology and conducted gradually. The categories of pain medication to be used include non-opioid analgesics, opioids and adjuvant drugs. The first line drugs to be used are non-opioid analgesics and, if necessary, opioid analgesics can be added. In the case of severe pain, it is preferable to start with opioids by following the criterion of pain intensity.

Clinical practice requires a gradual increase in the dosage of drugs, in order to allow a better adaptation and tolerance to the therapy and avoid possible side effects of drugs. As the gradual titration of pain medication is requested at the beginning of the treatment, when the pain symptoms disappear, it is recommended to gradually reduce the dosages of drugs until the end of analgesic therapy.

Pain control through the use of psychoactive drugs (e.g. neuroleptics and benzodiazepines), often improperly used in elderly patients with dementia, should be avoided as these drugs can worsen the overall clinical condition. In addition, drugs that are indicated for the treatment of neuropathic pain in adults (e.g. gabapentinoids) should be used with caution in the elderly due to the increased risk of side effects. Other drugs, such as serotonin and norepinephrine reuptake inhibitors, may be a good alternative to non-steroidal anti-inflammatory drugs and opioids due to their ability to raise the pain threshold and the lower risk of side effects.

NON-PHARMACOLOGICAL PAIN MANAGEMENT IN THE ELDERLY WITH COGNITIVE DECLINE

Recent theories support the concept that psychological factors may influence the way in which people interpret, respond to and cope with pain. Although pharmacological therapy can be helpful in managing pain, it may not be completely effective and older people may be particularly susceptible to side effects and drug interactions [46]. In addition, non-pharmacological interventions may be helpful, not just when pharmacological therapy is ineffective, but as an adjunct to medication or as a first-line therapy [47]. Gagliese et al. proposed that pain in older people with dementia is the result of an intricate network of interactions between biopsychosocial phenomena; moreover, dementia and pain may have a reciprocal relationship [48]. Based on this model, pain in older people with dementia can be conceptualized as the final result of the interaction of three heterogeneous phenomena—pain, aging and dementia—which are created and influenced by the interactions of predisposing, lifelong, and current biopsychosocial factors [48]. Thus, interventions on biopsychological factors such as affective and social dimension can be effective on pain relief. For example, it has been found that treatment of depression in older people with osteoarthritis may have a significant impact on function and pain [47, 49];

moreover, there is some evidence that psychological interventions such as cognitive behavioural therapy may be effective in decreasing chronic pain in adults and improving disability and mood [47]. CIPHER et al. applied a multimodal cognitive behavioural therapy intervention consisting of comprehensive initial evaluation of several domains, including level of dementia, emotional distress and pain; the therapists worked collaboratively with nursing home residents, their families and others involved in their care and used structured and individualized treatment plans incorporating these to encourage behavioral change [50]. At the end of the program the 44 elderly participants showed a significant decrease in pain [50]. In another study, the authors examined the effects of mindfulness meditation on 27 older adults with chronic back pain and concluded that the patients experienced “numerous benefits” after intervention, including less pain, better sleep and improved quality of life [51].

Physical activity is important in the management of persistent pain in older people. Indeed, physical inactivity is common in elderly people and it can have impact on quality of life, with reduced level of functioning, leading to increased disability and pain. To date, studies exclusively focused on exercise and physical activity in people over 65 years with chronic pain are scarce and no randomized clinical trials are available on elderly persons with chronic pain and dementia. Data consistent with evidence from reviews of randomized clinical trials on populations with chronic pain that include, but are not exclusive to, people over 65 years [52, 53] support the use of programs that comprise strengthening, flexibility and endurance activities to increase physical activity and reduce chronic pain. Ellis et al. conducted a study on 95 participants at five residential aged care facilities in Australia [54]. The authors applied a pain management program using non-pharmacological approaches. The pain management program involved a physiotherapist implementing four sessions per week of treatments (massage therapy, TENS, exercises and stretching, or combinations of these). Resulting data showed a small but statistically significant decrease in the number of as

required medications, and a decrease in average pain ratings from “some to moderate pain” to “a little pain”. Notably, residents with dementia received lower pain ratings than those without. The authors concluded that non-pharmacological interventions may be effective in reducing pain and reliance on required medications in residential care settings, especially when two or more are used [54].

There is also evidence of the use of some types of complementary therapies (e.g. osteopathy, acupuncture, herbal medicine, homeopathy, aromatherapy, Ayurvedic medicine) for the management of painful conditions in older people [47]. However, no data from randomized clinical trials are available about the efficacy of complementary therapies on chronic pain in patients with dementia. Some studies highlighted that specific effects of aromatherapy on brain pathways, implicated in both emotional response and cognitive performance, might have a secondary effect on neuropsychiatric symptoms that can be an expression of pain in patients with dementia [55].

PHARMACOLOGICAL TREATMENT OF CHRONIC PAIN IN THE ELDERLY WITH COGNITIVE DECLINE

Below, we describe drugs that are indicated in the main guidelines for the treatment of chronic pain in elderly persons that can also be used for treatment of patients with dementia.

1. Non-opioid analgesics

They constitute a heterogeneous category of compounds (salicylic acid and its derivatives, Paracetamol, non-steroidal anti-inflammatory drugs—NSAIDs), which share some therapeutic actions and side effects. They represent the most commonly prescribed class of analgesics and are particularly useful especially for somatic pain, particularly if caused by inflammatory processes or tissue injury. Recent reviews of the literature [56], in agreement with current pain guidelines [29, 42, 45, 47] indicate paracetamol as the first-line approach for the management of pain also in patients

with dementia. The use of NSAIDs in patients with dementia differs significantly from elderly persons without dementia; a Scandinavian study reported the use of paracetamol in 46% of people with dementia compared to 25% of cognitively healthy elderly [57].

The greatest limitation of the use of NSAIDs is related to their “roof effect”, a phenomenon whereby increasing the dose above a certain level does not correspond to better analgesia, but only an increase in side effects, which may include potentially life-threatening gastrointestinal and cardiovascular disorders [45, 58–61]. NSAIDs should be carefully used, especially in the case of patients particularly at risk, such as the elderly, those with peptic ulcer disease, coagulation disorders, renal insufficiency and those under corticosteroid treatment. An NSAIDs treatment should be co-prescribed with a gastroprotection (i.e. proton pump inhibitor). It should also be taken into account that even paracetamol, although considered a drug without major side effects, can be hepatotoxic in excessive or long-term treatments [62].

2. Opioids

They include morphine and any other substance able to produce Morphine-like effects that can be blocked by specific antagonists, such as naloxone. Several neuropeptides and synthetic analogues are part of the opioid family. Evidence from randomized clinical trials (RCTs) indicates that different opioids are effective in the treatment of neuropathic pain and chronic pain related to musculoskeletal disorders. One RCT conducted on 25 subjects found that opioid treatment is effective in reducing the agitation of patients with advanced dementia [63]. However, evidence of efficacy for long-term treatment is poor and clinical trials in elderly patients are lacking.

The main side effects of opioids include tolerance, dependence, sedation, delirium, disorders of the gastrointestinal tract, interaction with the absorption of other drugs and respiratory depression which, although infrequent, constitutes the most dangerous

adverse event. The possibility of adverse events increases with increasing age, the number of comorbid diseases and existing pharmacological treatments. Interactions between opioids and psychotropic drugs are very frequent and some studies have shown that the combination opioids with psychotropic drugs increases the risk of falling and hip fractures four times [64, 65].

3. Adjuvants

The term “adjuvants” refers to drugs formulated for other therapeutic indications that have, however, shown an analgesic efficacy. Some adjuvants are particularly effective in neuropathic pain, such as tricyclic antidepressants and antiepileptics [47]. Tricyclic antidepressants are not recommended for the treatment of pain in the elderly as they are associated with anticholinergic effects and important side effects (urinary incontinence, hypotension, sedation, glaucoma, cardiac arrhythmia), which, besides increasing the risk of falls, are dangerous for this type of patient. Anti-depressant serotonin and norepinephrine reuptake inhibitors (SNRIs), such as duloxetine, are generally more effective and better tolerated. The evidence on other antidepressants, such as serotonin reuptake inhibitors (SSRIs), is insufficient and the guidelines advise against their use as painkillers [45]. Antiepileptic drugs, such as carbamazepine, sodium valproate and phenytoin, have been widely used in the treatment of neuropathic pain. However, their use in the elderly is not without problems due to central adverse effects, the need for regular monitoring of blood parameters and their potential interactions with other drugs. Other antiepileptic drugs, such as gabapentin and pregabalin, have become widely used in neuropathic pain and many studies have shown analgesic efficacy and fewer side effects than previous-generation antiepileptics [66]. However, there are currently no studies investigating the use of anti-epileptics for the treatment of pain in patients with dementia.

4. Other treatments

New approaches to pain control are aimed at multiple therapeutic interventions and they act at both neuronal and non-neuronal

levels. The most recent literature shows that this is possible by using active ingredients that can normally be found in foods in addition to drugs.

In recent years, increasing evidence has highlighted the functional significance of the interaction between immune and nervous systems in the mechanisms of pain [67]. More specifically, the role of mast cells has been recognized in peripheral sensitization mechanisms related to neurogenic inflammation and neurogenic pain and of microglia in the mechanisms of central sensitization, which is greatly involved in neuroinflammation and neuropathic pain [68]. The endogenous palmitoylethanolamide (PEA), a natural lipidic substance of the *N*-acyletanolamidic structure, which is contained in many foods widely used by humans and in particular in vegetable oils, is able to reduce neuroinflammation by means of inhibitory antagonist control on non-neuronal cells involved in the processes of peripheral sensitization and central pain; these include mast cells and microglia [69, 70]. When administered orally, PEA has been shown to be effective in treating painful peripheral neuropathies of various origins as well as pain symptomatology linked to carpal tunnel syndrome in diabetics and in persons without any other neuropathies [71]. Significant effects were also obtained in sensory and motor neuropathies induced by chemotherapy. When associated with certain polyphenols with antioxidant activity, PEA has also proven effective in treating chronic pelvic pain. From a clinical point of view, the administration of PEA to treat painful symptoms is of particular interest given the absence of severe side effects even after prolonged periods of use in frail elderly individuals. Therefore, the preclinical and clinical effectiveness of PEA against chronic pain has been widely documented [72, 73].

CONCLUSION

We performed a narrative review on the topic of chronic pain in the elderly with cognitive

Table 1 Chronic pain in elderly with cognitive decline: key points

1. Make a correct diagnosis of pain in patients with cognitive impairment
2. Use validated and standardized tools for pain assessment
3. Self-assessment pain scales are indicated for patients with mild to moderate cognitive impairment and observational scales for those unable to understand the scale instructions
4. Consider non-pharmacological interventions for the treatment of chronic pain in elderly with cognitive decline
5. Avoid using inappropriate and potentially dangerous drugs to treat pain in frail elderly people
6. In choosing analgesic drugs, take into account clinical variables and comorbidity of elderly patient with cognitive decline
7. According to severity of pain, start therapy with non-opioids and, if necessary, consider opioids later
8. Make a gradual titration of pharmacological treatment for pain (start low, go slow)
9. Avoid using neuroleptics and benzodiazepines as pain killers
10. Use antiepileptic drugs with care
11. Consider SNRI as adjuvants and/or an alternative to NSAIDs and opioids
12. Consider using natural compounds able to modulate the pain threshold

decline and the key points here discussed are summarized in Table 1.

Despite its high prevalence the diagnosis and treatment of chronic pain in cognitively impaired elderly people is still a challenge for clinicians. Neuropathological changes occurring in patients with AD and the loss of communication abilities could lead to under-assessment and under-treatment of pain in these patients. Self-report scales may represent

valid tools for the assessment of pain in people with mild to moderate cognitive decline. However, in severe stages of dementia nonverbal pain behaviors are useful in assessing pain symptoms. The complexity of patients with dementia makes it difficult not only to make a correct diagnosis of pain but also to start adequate treatment. Indeed, pharmacological treatment should take into account physiological changes, high comorbidity and drug interactions that occur frequently in the elderly.

Novel pharmacological approaches able to increase pain thresholds and with lower side effects may represent a valid alternative for the treatment of chronic pain in elderly persons with cognitive decline.

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Compliance with Ethics Guidelines. This article is based on previously conducted studies and does not contain any studies with human participants or animals performed by any of the authors.

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