

Approach to Pain in the Elderly

Raim Iliaz^{1*}, Gulistan Bahat Ozturk¹, Timur Selcuk Akpinar², Asli Tufan¹, Irem Sarihan², Nilgun Erten¹ and Mehmet Akif Karan¹

¹Department of Internal Medicine, Division of Geriatrics, Istanbul Medical Faculty, Istanbul University, Turkey

²Department of Internal Medicine, Istanbul Medical Faculty, Istanbul University, Turkey

Abstract

Pain is the most common complained symptom in the elderly. Acute pain prevalence does not change with aging. However, chronic pain is much more prevalent in the elderly compared to young individuals. Despite these facts, pain in the elderly is commonly assessed and treated inadequately. The treatment goal of pain in the elderly is not always complete eradication of pain but decrease in pain allowing the improvement in activities of daily living and quality of life. Nonpharmacological-pharmacological approaches and anesthetic/invasive interventions can be used for pain treatment. During pharmacological treatment, the changes related to aging should be considered enabling increased side effects and drug-drug interactions. Generally, the stepwise guideline suggested by World Health Organisation for cancer pain is valid also for the treatment of chronic pain. Acetaminophen is the safest and mostly preferred analgesic in treating mild-moderate pain in the elderly. Metamizole is also free of gastrointestinal and thrombocyte related side effects. It is widely used in available countries for the pain in elderly with more intense and spasmolytic analgesic effect compared to other non-opioids. Nonsteroidal anti-inflammatory drugs can be used in moderate-severe pain. However, they should not be used in high doses and/or for a long time due to their severe side effect profile. Opioids are effective in all pain types and used in severe pain. The elderly is more prone to both analgesic effect and side effects of opioids. The most important side effects of opioids are respiratory depression, sedation, cognitive problems, emesis and constipation. Recently, they are being more suggested for the treatment of chronic non cancer pain in the elderly. If the pain is not controlled with these measures, the next step is the use of anesthetic/invasive modalities. In these cases, the elderly should be referred to centers specialized on pain. The aim of our study is to summarize the general approach to acute and chronic pain in elderly.

Keywords: Elderly; Pain; Approach; Assessment; Treatment

Approach to Pain in the Elderly

With average life expectancy rising, a significant shift in the age distribution takes place in favor of the elderly population all over the world. In developed countries, the percentage of individuals over the age of 65, which was 17.5% in 2002, are expected to rise to 36.3% in 2050, and individuals over the age of 80 are expected to triple [1]. However, health-related issues in the elderly are still more neglected. The elderly, due to physiological changes in the body, multiple drug use and increased co-morbidities with aging, are tend to get sick more often than non-elderly population, also prone to drug-drug interactions, atypical presentation instead of the usual symptoms, and more sensitive to the side effects of treatment. For these reasons; diagnosis, treatment and follow-up in older individuals requires a special approach. Pain is the most frequently reported symptom in the elderly and is one of the most serious problem affecting the quality of life. In elderly population, it is more common than young people. However, it usually stays unnoticed by physicians and caregivers or treated inadequately [2]. For example, more than ¼ of patients (%26) with cancer over the age of 65 who are in chronic pain do not take any analgesic agent [2]. On the other hand, evaluation and treatment of this problem is more difficult than in the young population. Untreated pain can result in many additional problems such as depression, anxiety, cognitive impairment, social isolation, sleep or appetite disorders, weight loss, movement disorders, restriction of functionality that can negatively affect the quality of life and may lead to significant increases in health care costs [3,4]. For instance, in patients with hip fracture, severe pain following surgery or inadequate analgesia may increase the confusion, slow down the recovery and worsen the ambulation and function [5,6]. Elderly with 'chronic pain' describe their health status as worse and use health services more than pain free group [7,8]. Effective treatment of pain in these patients also contributes to the treatment of disorders above that is secondary to pain and a reduction in costs. For all these reasons the AGS (American Geriatrics Society) published guidelines

in 1998 and 2001 about the treatment of pain in the elderly [9,10], IASP (International Association of Study for Pain) dedicated 2006-2007 global campaign to 'pain in the elderly' [11]. In this paper, pain issue will be examined as its frequency in elderly individuals holds an important place in neglect of health and determining quality of life, the prevalence of pain in the elderly, types of pain, pain sites, pain assessment and treatments will be summarized, considerations specific to this age group will be highlighted.

Pain in the Elderly: Prevalence, Types and Regions

Pain is the most frequently reported symptom in the elderly [12]. Acute pain is probably at similar rates in all age groups. Chronic pain, however, increases with years until the age of 65-70 and reaches plateau (70-75 years) [13-16]. It is reduced in middle-aged group (75-84 years) and elderly (85+) [17,18]. Lessened reporting in pain in the elderly is only valid for mild to moderate pain. Severe pain is expressed as it is in young adults [19].

As a result, in total, older individuals suffer from chronic pain more than young people. Chronic pain affects more than 50% of the elderly living in the community, and more than 80% of those living in nursing homes [20,21]. In one study, 45.8% of the elderly admitted to the hospital had reported pain [22]. In the elderly, the pain is usually

*Corresponding author: Raim Iliaz, M.D., Department of Internal Medicine, Division of Geriatrics, Istanbul University, Istanbul Medical Faculty 34093, Fatih-Istanbul, Turkey, Tel: +90212-4142000/31464; Fax: +902126319743; E-mail: raimiliaz@gmail.com

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moderate to severe intensity, will continue for many years, and tend to be multifocal and multifactorial [15].

The elderly often have chronic pain in the joints, legs and feet [23]. The prevalence of joint pain is twice as high in individuals over the age of 65 than in young adults. Frequency of foot and leg pain increase significantly parallel with aging. Central post-stroke pain and post-herpetic neuralgia also increases with the aging. However, some of the other regional pain is seen less than young people. The prevalence of headache decreases with aging after a peak at 45-50 years-old [16,24-27]. Facial/dental pain, abdominal/stomach pain frequency also decreases with the aging [26]. The prevalence of ischemic chest pain probably culminates with the last period of middle ages. And then it decreases with aging, despite the continued high mortality rate of ischemic cardio-vascular diseases [16,24,28]. Both silent ischemia and myocardial infarction without pain is seen more common with increasing age [29]. According to retrospective studies more than 1/3 of heart attacks in patients over the age of 65 are silent [30]. Despite the increase in atherosclerosis, pain due to ischemia of the internal organs does not increase parallel to this. In fact, in general, the severity of all acute visceral pain (such as pneumothorax, intestinal obstruction, peptic ulcer and peritonitis) is decreased in the elderly [31]. 45% of the elderly with appendicitis do not present any pain in the right lower quadrant as a symptom, while this rate is only 5% in young population [32]. It is been reported that visceral pain associated with various malignancies is again low in intensity in the elderly group than young's [33]. For this reasons, clinicians interested in the elderly should have a lower threshold of suspicion in terms of such pathologies. In the case of back pain, there is no consensus on the increase and decrease [23].

Pathologies that cause chronic pain in the elderly often are: osteoarthritis, spinal canal stenosis, myofascial pain, fibromyalgia, post-herpetic neuralgia, post-stroke pain syndrome, diabetic peripheral neuropathy, and cancer. There is usually more than one clinical diagnosis that causes chronic pain [34].

Cause of Age-Related Changes in the Prevalence of Pain

The prevalence of most diseases increase with aging. Though each disease is not painful, increased prevalence of diseases is the main factor that contributes to the increased prevalence of pain with aging. There are different opinions on the causes of the lack of increase in the prevalence of pain after 65 years, and even decrease after 75 years.

Disorders in nociceptive function of the nervous system occur with aging. This situation may result in decreased sensitivity of pain in the elderly. Thus, formation of the balance between increased pain causes and decreased pain perception, following the reduction of pain perception takes precedence over the increase of the pathology that causes pain, may be responsible for age-related changes in the prevalence of pain. Many studies have shown a progressive decrease in pain sensitivity with increasing age. Especially pain due to some visceral diseases (e.g., angina pectoris, acute intra-abdominal infections, etc.) is shown to decrease with aging. Showing that pain related to exercise associated myocardial ischemia weakens with aging supports the thesis that a decrease in the perception of ischemic pain occurs with aging [35]. The "anatomical" and "neurochemical" changes with aging may change "pain perception". "Sensory changes" are caused by the decrease in the number of Pacini corpuscles, Meissner and Merkel discs. However, aging does not decrease the number of free nerve endings. There is limited evidence of the age-related changes in nociceptive pathways of peripheral and central nervous system (CNS). Decrease in the density of myelinated and unmyelinated nerve fibres in elderly individuals,

slowed down rate of transmission of myelinated fibres, prolonged peripheral sensory nerve latency period have been reported [36-38]. In the central nervous system, number of neurons is reduced in the cortex, midbrain, and the brain stem. Decreased cortical activation in response to painful input, slowed down cognitive processing of pain is thought to be age-related. A decrease in the density of nociceptors, A-delta fiber function impairment, changes in the metabolism of serotonin, an increase in the spinal non-opioid analgesic pathways and a decrease in neuronal response to nitric oxide are likely to include effective mechanisms [31,39]. Again, high prevalence of medical conditions such as diabetes and hypertension that can go with a decrease in pain perception in the elderly, can lead to a decrease in visceral pain sensitivity with age [40,41].

Excruciating pain states such as cancer and fractures are often not reported in cross-sectional pain prevalence studies as they are short-term. This, in turn, may lead to the detection of understate the prevalence of pain in the elderly [23].

Pain occurs due to a sensorial warning or a neurological damage, but the degree of the feeling of the pain varies in one's memory, expectations and emotional structure. For these reasons, older individuals may not be caring enough the symptom of "pain", or distinguish to declare it due to loss of spouse or close friends, loss of functional independence and the high morbidity and disability caused by concomitant diseases, or depression and dementia which are more common in the elderly. There is also a general agreement that elderly individual more "patient" [42]. In addition, the elderly and elderly caregivers may accept the symptom of pain as a natural part of aging, like in many other pathological conditions that can accompany aging (amnesia, incontinence, decreased vision, social isolation, etc.) and not express any complaint [43]. Factors such as misconceptions about pain management, difficulty in the utilization of standard pain scales in elderly people and the mistake of expressions ("pain" instead of "ache", etc.) may also lead to the detection of low prevalence of pain in the elderly.

Despite all these factors as outlined above that can reduce the expression or feeling of the pain in the elderly, pain is the most common symptom complained in older population and chronic pain is seen significantly more than in younger ones.

Assessment of Pain in the Elderly

All seniors admitted to health facilities should be assessed for the presence of 'chronic pain' during first application [4]. Every chronic pain hat have an impact on physical, psychological function, and other aspects of quality of life should be considered as a significant problem and approached in that way [4]. For an effective treatment of pain, pain assessment should be comprehensive and repeated at required intervals.

While acute pain is usually a symptom of illness or injury, chronic and recurrent pain in itself is regarded as a specific health problems and disease. Chronic pain is never a natural part of aging. As a cause of chronic pain in the elderly, physical pathology and/or psychopathology are a must [27]. However, even though the factors that cause chronic pain cannot be spotted or eradicated all the time, the pain itself is a condition that can be treated and should be evaluated and treated as a separate entity (e.g. osteoarthritis pain) [44].

The proper evaluation of the pain is necessary for determination of "pain" the source and planning the most appropriate treatment. As in young's, identifying the type of pain may help the clinician choose

the appropriate treatment and predict the prognosis. There are two types of pain: a) nociceptive pain, b) neuropathic pain. Nociceptive pain is caused by the stimulation of pain receptors. May be visceral or somatic nature and is a result of tissue damage or inflammation. Usually responds to widely used classic analgesics. Neuropathic pain is caused by the peripheral or central nervous system pathology, and usually does not respond to classic pain relievers but responds to non-classical ones, such as antidepressants and anticonvulsants. However, compared with the younger age groups, "pain assessment" in the elderly is often a more difficult task. Pain is a subjective symptom and there are no measurement methods or a biological indicator that allows us to determine the amount of pain or its character (type). For this reason, in the elderly, like in all age groups, the factor we are depending on the assessment of the pain factor is the "the patient's own words" (medical history) [45]. However, older individuals often tend to report pain less than it is. And on the other hand, there may be other medical problems and symptoms in the elderly that make the assessment even more difficult. For example, cognitive impairment not only may interfere the patient's expression of pain in the first place but also may block the physician to be cooperative to questions asked during the history and physical examination and make the pain assessment quite difficult. In such cases, caregivers can help the physician, but the validity of this approach is unclear [46]. Other limiting factors may also block review (for example, visual and auditory problems can affect the dialogue with the patient and prevent the use of scales).

As in all symptoms, the first phase of understanding the pain begins with a good history. During the assessment of pain, some points should be learned such as "when it began", "where is it", "how the patient define his pain," "whether it spreads or not", "what are the factors that increase and decrease it", "intensity, quality, time, and its changes according to circumstances", "the effects of living", "ways of coping with pain" and "how analgesic treatment effected if previously received" [38]. On the other hand, patients' all medication should be known even if they are not used for the pain because they may be the reason of the current pain (for example, aspirin, which is used due to ischemic heart disease, or NSAIDs for osteoarthritis, can cause dyspepsia and epigastric pain). "Pain scales" can help to determine the amount of pain and categorize it. Although there is a large number of rating scales there is limited data on their use in geriatric population. Both "one-dimensional" (only reviewing pain) and "multi-dimensional" (pain and its effects to daily living activities (ADL) and mood) "pain scales" can be useful in geriatric population. "Geriatric Pain Measure", have been developed to assess the validity and reliability of multi-dimensional pain scales in the elderly. In addition to pain, it reliably assesses pain's effect to ADL [47]. However, in patients with significant physical or cognitive limitations, one-dimensional pain scales are more helpful because of possible other problems effecting mood and ADL other than pain [38]. The important point here is if a scale will be used for the assessment of pain, it should be appropriate for the patient and the same scale should be used during follow-up visits. Pain scales are easy to use and are based on the patient's expressions. Visual analog scales, different faces, figures, or colors used representing different levels of pain. Pain assessment tools based on the patient's own words (e.g., verbal descriptor scales, numerical scales, and facial scales) have proven the validity and reliability for their use in the elderly [48,49]. Pain diaries may also be useful in the elderly for assessment. However, to avoid focusing and increasing the perception of pain, after determining painful periods for once, the elderly may be asked to note the pain when felt, not at regular intervals on a regular basis [10].

Religious and moral beliefs, attitudes about the pain and other

medical diseases must be considered, cognitive function should be considered. If so, "functional limitations" and "psychological effects of pain" (and its effects on mood) that are caused by the pain should be considered and noted in the assessment of pain in the elderly. Controlling the depression in the early period may affect positively the treatment of the pain. If depression is not treated enough, approaches for the treatment of pain are hard to be successful [10]. In addition, anxiety accompanying the pain, if the elderly has secondary gains from the pain (for example, more and more people visits, etc.), whether or not the elderly focuses on pain should be considered in the assessment [10]. These conditions may affect the success of treatment.

In some specific elderly populations, for example who has cognitive impairment or sensorial (visual or auditory) loss, pain assessment is particularly difficult. Because of this, these elder ones are at risk of inadequate treatment of pain. It has been showed that they take smaller amount of analgesics than elderly who has similar pathology [50,51]. An assessment based on the patient's statement may not be reliable enough in elderly who has cognitive problems. However, in elderly who has cognitive impairment but preserved verbal communication, and who has audio-visual disorders, assessment of pain can be achieved with the help of one-dimensional and multidimensional pain scales with appropriate approaches (for example, a patient with visual impairment can be asked for numerical scoring on the severity of pain, and auditory scales in patients with visual problems). The majority of elderly people with mild to moderate cognitive impairment may report pain reliably [7,8]. Most patients with dementia can use such scales appropriately [52], but it may have to be asked to the patient if there is any pain. Individuals who cannot verbally express pain, especially in the elderly with dementia, pain can be expressed not verbal like "this hurts" but rather, behavioural symptoms: agitation, moaning, delirium, functional limitation: reduced mobility, and pain-suffering-sad facial expressions. In these cases, pain should be judged on the basis of these non-verbal markers.

Detailed medical story should be followed by a detailed and comprehensive examination. Physical examination should include referred pain area, as well as the musculo-skeletal system and the nervous system, and if needed, psychiatric and cognitive examination should be deepened. There is often more than one pathology that contributes to the chronic pain in the elderly. For this reason, a comprehensive physical examination should be performed routinely [46,48]. On the other hand, it should be known that it is common for elderly to have coincidental pathologies (for example, radiological OA without any symptoms). Therefore, additional diagnostic tests should be requested according to the findings of the collected history and physical examination.

In this age group, there is an increase in the presentation of atypical pain due to diminished physiological reserve and co-morbidities accompanied by (e.g., delirium due to the pain associated with a heart attack in a patient with dementia) [21]. Again there is a decrease in sensitivity of painful stimuli in the elderly. However, a decrease in sensitivity to pain does not mean that they feel less pain when reported suffering. On the contrary, when the pain reported, the pathology that causes pain may indicate a more serious level as compared with younger individuals reporting [53,54]. These factors should be considered when making an assessment of pain.

Treatment of Pain in the Elderly

Treatment of pain in the elderly especially is a difficult issue, and requires specialized knowledge and training about pain for an effective

treatment. As summarized above, the main factors that make it difficult for the treatment of pain in the elderly are: pain to be accepted as a natural part of aging by the elderly and their caregivers, problems in expression of pain (usage of other definitions than pain, unable to express pain in patients with cognitive problems, not complaining because of religious and moral beliefs (fatalism), wanting to be patient and the “good patient”, problems related to cognitive, visual or sensory difficulties in usage of pain scales), older people, their relatives and health professionals’ potential fear and avoidance of pain medications and non-pharmacological methods, fear of addiction with treatment, health care professionals not caring, not questioning and accepting the pain in the elderly as a natural part of aging, health care professionals to be unequipped on the principles of pain management in the elderly, drug action, side effects and a number of co-morbidity and the presence of the pharmacokinetic, pharmacodynamic changes that effect the bioavailability, so that increased sensitivity to the adverse drug effects, legal regulations that restrict the use of opioids, the difficulty in reaching health facilities and cost-refund problems (economic problems) (Table 1) [55].

Although persistent pain it is more common in the elderly population, pain treatment studies were mostly done in young adult population. Age-related changes in affection of the treatment were rarely taken into consideration. For this reason, there is a significant lack of scientific evidence that approaches which are widely used and accepted are valid in the elderly [56]. However, with an appropriate approach, pain can be controlled more than 90% of the elderly and can be treated effectively [38,57].

Every type of pain that has an impact on functional status or quality of life should be treated [9]. However, the goal in the treatment of pain in the elderly is not cut off pain completely all the time, but to reduce the level of pain to improve activities of daily living and quality of life. In the elderly, the treatment of persistent pain, should be planned individually for each patient. We must not forget that all elderly individuals are not the same. Among individuals with the same chronological age, there is significant heterogeneity in terms of physiological, psychological, and functional capacity [58].

In older people with dementia, treatment of pain is often known insufficient [59]. In this group, as interventions for the treatment of pain have an higher risk/benefit ratio, it should be known that aggressive treatments are required to be adapted proactively but with more cautious approach [4].

The underlying cause of the pain should be investigated at the first evaluation phase and treatment should be given if possible [60]. When

treatment of the underlying problem is not possible, pharmacological and non-pharmacological methods of treatment therapy, minimally invasive procedures, surgical procedures and psychiatric treatment alternatives should be considered and should be combined if necessary. Non-drug strategies alone or in combination with a suitable analgesic drug can be applied. The most successful treatment approach is achieved through a combination of pharmacological and non-pharmacological therapies [3]. Because most of the elderly patients are less tolerated to opioids, tricyclic antidepressants, and anti-inflammatory drugs than young patients. These treatments in the elderly often results in sedation and confusion. Therefore, it is particularly important in the elderly to take advantage of non-pharmacological treatment strategies. It should be known that in the treatment of chronic pain, drug therapy is more effective when combined with non-drug approaches in all cases and rehabilitation should be seen as a way to improve compliance [4].

Non-Pharmacological Approaches to the Treatment of Pain in the Elderly

Non-pharmacological approaches to the treatment of pain are physical therapy, educational programs, social interventions (such as music therapy), psychological methods (relaxation, distraction, hypnosis, meditation, cognitive-behavioural therapy) and alternative therapies (acupuncture, acupressure, and aromatherapy). Most of their side effects are very low. However, this approach is not used sufficiently nowadays. The reason for that are adequate pain treatment in elderly individuals is not made, such treatments are not offered to them, and that they are addressed to fewer treatment options [38,55]. Exercise programs, assistive devices, TENS (electrical nerve stimulation transcutaneous), vibration, massage, manipulation, hot or cold applications can be made in physical therapy [61,62]. In TENS, electrodes are placed in the painful area and nerve stimulation is made by continuous or intermittent bursts. It depresses nociceptive pain and usually effective in musculoskeletal pain and neuropathic pain due to nerve compressions in particular. Hot application effects by stimulating the release of endorphins while cold application effects by preventing the release of substances from the damaged tissue that stimulates nociceptive pathways. With training programs, patients can be educated about types of pain, pain assessment, measurement, implementation of non-drug methods at home and appropriate analgesic drugs. Studies have shown that education alone improves pain control [63,64]. Psychological therapies reduce the perception of pain by taking away attention from it. Alternative therapies may increase the release of endorphins. Behavioural treatment or social arrangements may be applied against elderly who are thought to have secondary gain and or increase in pain by focusing on the perception of it.

1	To take pain as a natural part of aging by the elderly and their caregivers
2	Problems to express their pain in older individuals
3	To use other definitions other than pain
4	Being unable to express pain like in patients with cognitive problems
5	Not complaining about pain because of religious and moral beliefs (fatalism), desire to be patient and to be a 'good patient'
6	Problems in use of pain scales due to cognitive, visual or sensory difficulties
7	Older people, their relatives and health professionals' possible fear and shyness, fear of addiction to pain medication and non-drug methods
8	Not caring and not questioning the pain in the elderly by healthcare professionals and to accept it as a natural part of aging
9	Unequipped health workers on the principles of pain management
10	The number of co-morbidity, the presence of pharmacokinetic and pharmacodynamic changes in the elderly that can effect the drug action, side effects and bioavailability, increased sensitivity towards adverse effects
11	The legal regulations that restrict the use of opioids
12	The difficulty for to reach the health facility
13	Economic problems (cost-refund problems)

Table 1: The main factors that make the treatment of pain in the elderly difficult.

Pharmacological Treatment of Pain in the Elderly

When forming a treatment plan for pain in the elderly, it is needed to be aware of the medication that the elderly is already taking and potential but important effects of co-morbid, medical and psychosocial problems. Therefore, analgesic choices are limited. Pharmacokinetics and pharmacodynamic with aging, possible side effects, relative and absolute contraindications, significant drug-drug interactions should be known about the analgesics and adjuvant drugs that are frequently used by the elderly and if necessary, dose adjustment should be made [3,4,65]. All analgesics have a number of side effects and they are only effective and safe when used properly.

The basic principles of pharmacological therapy in the elderly are to start low doses of analgesics and to titrate slowly. Type of pain, kidney and liver function, non-opioid, opioid and adjuvant drugs affects the choice. In addition, existing polypharmacy, pain type and severity, drug availability, associated symptoms, cost and drug accessibility are the other factors affecting the selection of analgesics.

In pharmacological treatment, World Health Organization (WHO)'s suggested model for the treatment of cancer pain is generally recognized and recommended for also chronic non-cancer pain [3,60]. World Health Organization recommends that pain treatment should be chosen by the severity of pain, and increased step by step. If the pain is severe, non-opioid agents should not be tried and opioid therapy should be started directly. Apart from that start of treatment should be made with non-opioid analgesics, followed by an addition of an opioid analgesic if needed, and in the presence of each phase, an indication of adjuvant (co-) drug recommended to be added.

Pharmacological treatment should always be started with the least invasive medication. Topical and/or oral way should be used firstly if there is no contraindication for the patient. The oral way is the most convenient and

Parenteral way is used when rapid analgesia is required, or high doses are needed in oral or rectal use. Intravenous (iv), intramuscular (im) and subcutaneous (sc) ways can be used. The fastest analgesia is obtained with bolus injections. However, in these cases, the toxicity of the drug effect is seen faster and breakthrough sudden pain attacks are more common as the drug effect will disappear quicker. Therefore, bolus injections are not recommended for long-term pain control. On the other hand, repeated im injections are painful. Subcutaneous infusions are less painful and the pain from repeated injections can be reduced by leaving sc catheter in place.

Continuous infusion is more preferred, and may provide the continuity of pain control. Both i.v. and s.c. ways can be used for continuous infusion. And this way the disadvantages of bolus injections are eliminated. On the other hand, during the continuous infusion, bolus injections could be added to the treatment of patients with "breakthrough" pain. Subcutaneous infusion can be made with 25-27 gauge butterfly needle. These needles can be left in place up to one week. There are devices available for continuous infusion in ambulatory (outpatient). With subcutaneous infusion, similar blood levels with intravenous can be achieved [66,67]. However, the effect starts slower in sc infusion and the peak effect is lower [38]. 10 mL per hour is the maximum infusion in subcutaneous way. With faster infusion than this, it can be both painful and absorption does not occur properly.

Transdermal, sublingual, and transmucosal drug application ways can also be used. Fentanyl and buprenorphine are opioids

with transdermal forms. Although dose adjustments are difficult with transdermal preparations, longer duration of effect, easy to use pain free application and less likely to have side-effects are the advantages of them. Sublingual absorption may be with all opioids, but the bioavailability will be less if the drug is not lipophilic enough. Sublingual preparations are limited.

Dose Intervals

The time of drug administration is important for the proper effect. In non-chronic (acute pain) and episodic pain short-acting medications should be used when the patient has the pain. For continuous pain, a stable level of analgesia should be provided. To do this, medications should be given at regular intervals. While release-controlled drugs can provide a constant basal pain control, short and fast-acting pain relievers should be planned for "breakthrough" pain intervals.

Medications

The drugs used in the treatment of pain are a) Non-opioid analgesics, b) Opioid analgesics and c) Adjuvant (auxiliary) drugs.

Non-opioid Analgesics

Non-opioid analgesics include: acetaminophen, aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), metamizol and tramadol.

Acetaminophen

Acetaminophen should be preferred in the elderly for mild-to-moderate pain. Side effects are few and tolerance is good. It has no anti-inflammatory activity but is effective in musculoskeletal system and osteoarthritis (OA) pain [68]. Safer than NSAIDs and can easily be combined with other drugs in chronic painful conditions. It can be used up to 4 times per day to 1000 mg; this dose should not be exceeded [69]. Excessive doses can cause irreversible hepatotoxicity. Overdose should be considered as toxicity may occur at lower doses and more severe in alcohol users and patients using combination preparations rather than pure acetaminophen.

NSAIDs

NSAIDs are potent inhibitors of prostaglandin synthesis. The reasons for their effects of pain relief are reducing inflammation, reducing pain perception directly and their central effects on pain [70]. Classical NSAIDs are effective through cyclooxygenase (COX) enzyme; they inhibit prostaglandin synthesis from arachidonic acid. Although usage of selective COX2 inhibitors (celecoxib, rofecoxib) which are as effective as classical NSAIDs for pain control but less toxic on the gastric mucosa, has been recommended for a while as an alternative to classical NSAIDs, they were removed from the market after observing a small but significant increase in cardiovascular risk.

NSAIDs are especially suitable for short term usage in inflammatory conditions such as gout, calcium pyrophosphate arthropathy and acute exacerbations of rheumatic diseases. In addition, they can be used for acute mild to moderate pain like headaches or cramps. Do not make any addiction, and can be used oral, i.v. or i.m. way. A large number of NSAIDs in different level of anti-inflammatory activities are available on the market (ibuprofen, naproxen, sulindac, indomethacin, trilisat, ketorolac). They can be used as topical but however, the analgesic and anti-inflammatory activity of these forms are also topical.

High doses or continuously usage of NSAIDs should be avoided because of renal, gastrointestinal, hypertension, edema, side effects and

increasing the risk of bleeding in the elderly [4,38]. Gastrointestinal tract bleeding, renal function impairment and bleeding due to platelet dysfunction may occur. The usage of misoprostol, H2 blockers and proton pump inhibitors only reduce their side effects on the gastrointestinal tract, and partially effective. Drug interactions may be a problem. Their potential advantages are reducing inflammation, usage in cancer and bone pain, and can be added to assist other drugs. They do not have constipation, sedation and other CNS side effects. For these reasons, they can be used as a single agent or agent to help in moderate-to-severe pain.

Metamizole

Metamizole is prohibited in the United States and most European Union countries in the 1970s, due to its potential to cause agranulocytosis, a rare but fatal side effect. However, this effect is not unique to just metamizole and may be seen with many other analgesic (NSAIDs). Still used widely in many countries, including ours. Like acetaminophen, metamizole has no effect on platelets and gastrointestinal tract, and widely used in elderly patients. Analgesic strength of metamizole is higher than other non-opioids, and is the only non-opioid analgesic antipyretic, with spasmolytic activity. It has less toxicity than paracetamol in high doses. Caution should be taken in the use of parenteral; it may cause sudden hypotension [71].

Tramadol

It is classified as non-opioid analgesic in some sources, while others accepts as weak opioid agent [46]. However, it should not be considered as an alternative to the elderly that needs to use opioid drugs in any way. Analgesic mechanism is not fully understood. Does have mu receptor affinity in very low levels and this is far from being the reason of its analgesic effect. It should not be used among in elderly with drug abuse. Tolerance problem is low and dosage is suitable starting 50 mg every 12 hours.

Opioids

Opioids are the name of drugs that interact with opioid receptors in the body. There are a large number of opioid receptors in the brain and spinal cord.

Opioids act as an agonist on opioid receptors. This results in a reduction in the perception of pain. They are effective in relieving any kind of pain whatever the pathophysiology is. Opioids are very helpful to control pain in advanced disease states, particularly in the mild-to-severe pain [38]. Opioids have no ceiling effects. They provide relief in lower doses in elderly than used in young people, due to elongation in half-lives and changes in pharmacokinetics [72]. This applies both in cancer and postoperative pain [73]. However, in parallel with this, side effects are seen easier, often and with lower doses in the elderly.

The only contraindication to the use of opioids is the anaphylaxis against them. In real hypersensitivity, rash, wheezing, and edema occurs depending on release of histamine. Allergies are often against morphine derivatives. In this case, synthetic opioid that does not contain paint and preservatives can be used.

Opioids may cause cognitive impairment, respiratory depression, constipation, and nausea as side effects in the elderly. These side effects are dose-dependent. However, if opioid doses are carefully titrated to cut the pain, they rarely cause respiratory depression and iatrogenic death [38]. Furthermore, tolerance to these side effects except for constipation often occurs in few days, and patients often return to the previous cognitive status [71]. It should be told to the patient not to

use vehicle until tolerance develops, and warned to take more action against falls and other accidents. After the development of tolerance, patient's returns to former activities with better functionality as pain is relieved. Gastrointestinal side effects should be monitored. Constipation is an issue that should be taken into consideration when starting opioid drugs. Patients should be informed to increase fluid intake, continue activities and routine use of laxatives-stool softening agent. Fecal plug should be excluded if stimulant laxatives are going to be used. Suppositories and enema can be used to provide intestinal emptying. An important side effect during the use of opioids is nausea. Antinauseants like prochlorperazine and chlorpromazine, haloperidol, and antihistaminics can be used for nausea. However, it should be considered that most of these drugs have anticholinergic side effects like movement disorder and delirium, that limit their use in the elderly.

Opioid treatment should be started with low doses of morphine in the elderly that has not taken opioid before. The active metabolite of morphine, morphine 6-glucuronide is dependent on liver function and can accumulate in renal disorders.

All the physicians prescribing opioids should be aware of equivalent terms of expressions like "tolerance", "dependence" and "addiction" that may occur during opioid use or cutting it off. While tolerance and dependence are pharmacological problems, addiction is a behavioural problem. Tolerance means decrease in any effect of a drug with time. Tolerance against the side effects of opioids develops earlier than tolerance against pain relief. In the treatment of arthritis tolerance often has been suggested as not a significant problem [74]. Especially in recent years studies have been published suggesting that opioids to be effective in chronic non-cancer pain in the elderly (evidence Ib, IIb), and can be used with careful dose titration and monitoring tolerability [75,76]. Dependence is discomfortable side effects (withdrawn symptoms) of the drug when it is stopped abruptly (as well as the usage of beta-blockers and long-term steroid). It is difficult to estimate and depends on the duration of drug use, dose, and the type of opioid. Withdrawal symptoms that may develop after discontinuing of the drug in patients with opioid dependence include: loss of appetite, nausea, sweating, tachycardia, hypertension, fever. Autonomous crisis may occur. Not stopping the use of opioids suddenly, lowering doses slowly can eliminate this side effect. Clonidine can be used in severe autonomic side effects. In addiction, patients have irresistible desire to take the drug in order to feel psychological effects sensed with drug intake. They continue this despite the negative physical and social consequences. The fear of addiction is a significant barrier for restricting the use of opioids for pain management in the elderly [74]. However, the real dependency (addiction) is very rare when opioids are used for pain relief. Pseudoaddiction should not be confused with the real addiction. In this case, patients request increased doses because of an absence of sufficient analgesia. Fear of addiction and side effects should not preclude the use of opioids for pain control especially in patients with terminal pain.

Types of Opioid

There are many formulas that are in use. While the weak opioids are codeine, oxycodone, and according to some sources tramadol; morphine, hydromorphone, fentanyl, meperidine (pethidine hydrochloride) and methadone are strong opioid drugs.

Morphine has 'short' and 'long' effective forms as oral tablets. Liquid morphine's short-acting and immediate-release formulas can be used for 'breakthrough pain'.

Fentanyl, can be used i.v., patch and transmucosal. Transdermal

patch is ideal for elderly who has swallowing problems or cannot tolerate other opioids. Transdermal way may also cause sedation and constipation, but as the patient compliance is better, it is likely to give a better quality of life. Effect starts in 8-12 hours and continues up to 48-72 hours. In case of removing the patch, the effect continues because of the subcutaneous drug reservoir. Excessive heat can cause the medicine to run into the bloodstream more quickly. Due to these factors the use of transdermal fentanyl in the elderly should be made especially careful. Starting dose should never be higher than 25 ug/h in the elderly people who do not use an opioid before [10]. Oral transmucosal fentanyl citrate (Actiq[®]) is a fentanyl preparation which is presented with an applicator for patients to use rubbing to the oral mucosa. Drug is rapidly absorbed, shows rapid-acting and short-term effect. It can be used for breakthrough pain or before the procedures that may cause pain such as changing clothes. Analgesic effect starts within five minutes [77].

Levorfanol and methadone have longer duration of effect, but they are not ideal agents in the elderly because of the accumulation of the drug or risks of sedation. Meperidine is also not recommended for the control of chronic pain in the elderly [38]. Its metabolite is normeperidine, which accumulates in renal disorder, may cause CNS side effects such as seizures and delirium. Butorfanol, nalbuphine and pentazocine which have mixed agonist-antagonist effects, also have limited efficacy and may cause withdrawn symptoms in people who use pure agonist opioid drugs. Opioids which have mixed agonist-antagonist effects are not usually recommended for pain control in the elderly except buprenorphine [3,38,75].

Hydromorphone and oxycodone have tablets, liquid and suppository forms. As they are synthetic opioids, they can be used in patients who have true allergy against morphine; observed side effects associated with morphine metabolites, or have risk of accumulation of morphine metabolites because of renal dysfunction [38].

All opioids' (except buprenorphine) active forms and their metabolites' half-life are prolonged in the elderly and all age groups with impaired renal function. Doses should be reduced, longer dosing intervals should be given, and creatinine clearance should be monitored. Buprenorphine is also superior in terms of immunosuppressant effect associated with opioids. For these reasons it seems to be that buprenorphine should be the most preferred opioid in the elderly [75]. Opioids are also effective in neuropathic pain even if not as much as they are in nociceptive pain, and buprenorphine has also superiority in the treatment of neuropathic pain to other opioids [75]. However, it should be known that the respiratory depression is more common especially with this opioid, and should not be used in the elderly who have risks for it [75].

Opioids have also combination preparations available. Pain treatment can be achieved with fewer drugs with the combinations of acetaminophen-opioid or NSAID-opioid. However, when used combination forms with pure preparations, caution should be taken against unknowingly exceeding the maximum dose [10].

Adjuvant Drugs

Drugs that are not classified as an analgesic but may be useful in some painful conditions are called "adjuvant" (assistant) analgesics. Adjuvant drugs are used as primary painkillers in some special cases. In addition, they can also be used as combinations with opioid or non-opioid analgesics. These are antidepressants (amitriptyline, nortriptyline, desipramine), anxiolytics, anticonvulsants (clonazepam, phenytoin, carbamazepine, valproic acid, gabapentin),

corticosteroids (dexamethasone, prednisone), local anesthetics (lidocaine, capsaicin, prilocaine), bisphosphonates, NMDA receptor antagonists, neuroleptics, muscle relaxants (baclofen), antihistaminics, psychostimulants, and calcitonin [38,71]. Antidepressants and anticonvulsants can be used in neuropathic pain, corticosteroids in cerebral edema, bone metastases, neuropathic pain and nerve compressions, local anesthetics in localized pain and postherpetic neuralgia, bisphosphonates in bone metastases and Paget's disease, and calcitonin in bone pain. Adjuvant drugs should be also started with low doses and increased slowly in the elderly as with other drugs [38].

Antidepressants

The most commonly used adjuvant drugs for pain. Analgesic effects of tricyclics has been associated with inhibition of serotonin and norepinephrine reuptake in the brain. Nortriptyline and desipramine are preferred due to lower anticholinergic side effects in the elderly compared to amitriptyline. Anticholinergic side effects are mouth dryness, blurred vision, arrhythmias, orthostatic hypotension, urinary retention, constipation, and confusion. Selective serotonin reuptake inhibitors (SSRIs) have less side effects but most of them have no analgesic effect. The newer antidepressants which are selective serotonin-noradrenaline reuptake inhibitors, such as venlafaxine and duloxetine; or bupropion which is dopamine, serotonin and norepinephrine reuptake inhibitor, stands out as adjuvant analgesics in recent years with minimal side effect profiles and analgesic effects in the elderly [78-86]. However, there is no long-term information about their use as adjuvant analgesics.

Anticonvulsants

In this group, there are anticonvulsants such as clonazepam, phenytoin, carbamazepine, valproic acid and gabapentin. They are effective in neuropathic pain. However their side effects like sedation, confusion and tremor limits their use in the elderly. In this group there is another drug, lamotrigine which has no convincing evidence that it is effective in treating acute or chronic pain [87]. Gabapentin which is out in recent years is more reliable in terms of side effects. The main side effect is sedation like as other anticonvulsants. Starting with low dose and increasing progressively can reduce the risk of sedation. Effective doses are 900-3600 mg given 3 times a day. Pregabalin which is also put on the market in recent years also may be preferred because of the less complex titration chart and a lower side-effect profile.

Corticosteroids

They inhibit prostaglandin synthesis and reduce edema and are effective for neuropathic pain and pain in bone metastases. Problems like fluid overload, gastrointestinal side effects, hyperglycemia, delirium, withdrawn symptoms, osteoporosis, myopathy, and the skin changes are more serious and happens in lower doses in the elderly than younger [38].

Many vitamins and supplemented drugs except all of these drugs are used by patients for pain control. There are no studies showing their effectiveness. However, patients should be questioned about them especially to prevent possible harms.

Vitamin D

May be useful in some painful conditions in the elderly [10]. Because vitamin D deficiency is common in the elderly, and may be responsible for the deep musculoskeletal pain and pain with superficial light pressures.

Leflunomide and etnercept may be used in the treatment of pain associated with arthritis and in inflammatory arthritis, while intra-articular hyaluronan can be useful for osteoarthritis.

Anesthetics and Invasive Interventions for Pain Control in the Elderly

Anesthetic/interventional procedures that can be used for the treatment of pain in elderly individuals, and their proven benefits in elderly population and the usage limits should be known [88]. In situations where a continuous infusion is needed i.v way with pumps implanted, s.c, intrathecal and epidural injections can be made. Spinal opioid application can be used in acute perioperative pain and in chronic pain where pain control is not sufficient with other methods. External or internal implanted pumps, can make opioid more effective by acting directly to the spinal opioids receptors. In patients with localized (regional) pain, the pain may be temporarily stopped with neurolytic blockade. Sympathetic blockade can be made in visceral pain [38].

The role of multidisciplinary pain clinics in the treatment of elderly people with chronic pain and the situations in which elderly people should be directed to these clinics should be known [89,90]. Patients with chronic pain that is not controlled well should be directed to pain clinics.

As a result, although there are many disadvantages associated with aging, with appropriate approaches and an acceptable side-effect profile, effective pain control can be achieved in most elderly. The main rule is to start drugs with low doses and gradually increase them. Appropriate pain scales or logs may be helpful for the assessment of pain. But still, when it comes to pain, better professional training programs focused on the specific needs of the elderly, researches to guide clinical practice and better pain treatment strategies are needed. [56].

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