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Problems of pain treatment in the elderly in primary care

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ABSTRACT

One of the most common reasons for patients reporting to their general practitioners is pain. With increasing age, these conditions become more common in the population and are more severe. In addition to the cause of pain, the clinical picture also includes comorbidities and medications taken for this reason, as well as psychophysiological changes that occur in the body with increasing age. With the aging of society, the problem of older people's pain is becoming a growing problem. The article presents data on the characteristics of pain among seniors, the principles of its treatment and describes the most common problems associated with pain therapy.

***Keywords*:** pain, pain treatment, elderly, seniors, primary care

1. INTRODUCTION

The treatment of pain in the elderly is a therapeutic process which may be associated with problems specific for this group. This is due to both the physiological changes occurring in the patients' body with increasing age, the multitude of concomitant diseases, other causes of pain, and the high heterogeneity of patients belonging to the group referred to as the old people.

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In Poland, 6.3 million people belong to this diverse group of people over 65 years old. According to the forecasts of the Polish Central Statistical Office, their number will increase, which means that practically every doctor will come across the problems of pain in elderly patients in their practice [1].

2. CHARACTERISTICS OF PAIN IN SENIORS

According to the World Health Organization (WHO), the group of seniors includes people over 65, but the same organization tends to shift the age limit down to 55 for the African population [2]. In most Western countries, a retired person is defined as senior, whose condition for granting retirement is, among others, reaching the age of 60-65 years depending on the country. A similar age limit is a condition for obtaining the possibility of using additional social programs for seniors. On the other hand, in the biological context old age begins at the time of andropause or menopause. Attention should also be paid to the patient's mental ("How old does the patient feel?") and social age (range of roles covered and quality of the patient's life) [3].

Almost 55% of seniors suffer from diseases that may be accompanied by the pain, i.e. neurological diseases, diabetes, cancer, vascular diseases (f.g. intermittent claudication), night pain in the lower extremities and the most common in this group of patients - musculoskeletal system diseases (primarily osteoarthritis and rheumatic diseases) [4, 5]. It may be aggravated by anxiety or depression often co-existing in these patients [6]. The frequency of chronic pain increases with age of patients and affects from about 42% to 55% of people over 85 [7, 8]. Women are affected more often than men, which results from differences in the incidence of some pain syndromes (e.g. rheumatoid arthritis, osteoarthritis or fibromyalgia) [8]. Research indicates that pain is more often felt by people whose work was associated with physical effort and is most often located in the area of joints, lumbar spine (so-called "low back pain") and lower limbs [4, 8].

Determining the level of pain in seniors is usually carried out using subjective tools also used in younger patients, i.e. *Numerical Rating Scale* (NRS) or *Visual Analogue Scale* (VAS). However, this assessment may be difficult for patients with advanced dementia that is associated with significant cognitive impairment. Therefore, to assess pain in these patients, attention should be paid to the observation of physical and verbal symptoms of pain. Symptoms of the pain may be: abnormal noises during breathing (loud breathing, moaning, sighing, howling), speech disorders (excessive talkativeness, "noisy", monotonic speech), facial expressions (frowns, grimaces, fast blinking, eyelid and tooth clenching, crying) and body (stiffness, increased tension, trample, changes in the moving) [9]. Determining the intensity of pain is necessary to determine the diagnostic and therapeutic process and the effectiveness of treatment. The average intensity of pain determined on the VAS scale in the study of the Polish senior population POLSENIOR was 6,22 [8].

3. PSYCHOPHYSIOLOGICAL CHANGES OCCURRING IN THE ELDERLY PEOPLE

With increasing age, there are many changes in the body that affect the course of treatment of the patient. These include, among others:

- Reduced cardiovascular efficiency - reduced cardiac output results in lower blood flow through the tissues, which is associated with poorer drug transport to target organs[10].
- Impaired liver function - a decrease in liver mass and a decrease in blood flow through it causes an increase in the concentrations of drugs, which are metabolized by the liver, an increase in their half-life and the need to reduce the dose by 1/3 – 1/2 compared to the dose used in younger patients [11].
- Impaired kidney function - reduction of kidney mass, reduction of kidney perfusion as a result of atherosclerotic changes and, above all, impairment of glomerular filtration rate (GFR) changes the renal clearance of drugs, which also affects their toxicity and forces them to reduce the doses of drugs used [12].
- Increased body fat and intercellular fluid content - volume of distribution and half-life of lipophilic drugs such as amitriptyline or lidocaine is increased [13].
- Reduced water and muscle tissue content - lower volume of distribution for water-soluble substances, such as morphine and other opioids, may cause increased blood levels of these drugs after a standard dose [13].
- Atrophic changes in the peripheral and central nervous system - there is a decrease in density of neuron endings, demyelination and degeneration of sensory fibers, and degenerative changes in the structure of the CNS and neurotransmitter systems, which causes an increase in the pain threshold [14].
- Reduced adaptability - patients may have problems with the implementation of complicated doctor's recommendations, such as splitting tablets in half or buying hard-to-reach drugs, which may disturb patient compliance. Moreover, cognitive, emotional or depression disorders may hinder the patient's contact with the doctor and thus disturb the proper assessment of pain [9].
- Weakness of mobility and manual capacity - increases the risk of falls that may cause injury, limits the patient's ability to perform independent exercises that can reduce the level of pain, and slows down the rate of rehabilitation performed by physiotherapists.

4. HOW TO TREAT PAIN IN THE ELDERLY?

Before starting to treat pain in an elderly patient, it should be remembered that the patient's expectations of complete relief of pain lasting for many years may be unrealistic. Therefore, it is necessary to inform him of this fact. According to experts from the American Geriatrics Society, the goal of treating pain in population of old people is to achieve an optimal and acceptable quality of life based on the balance of benefits and risks for the patient. It is important to choose the least invasive drug administration route (usually oral or topical) and choose the dosage to match the nature of the pain [15]. When choosing a drug for pharmacotherapy, you should be aware of the increased risk of side effects compared to younger patients, the risk of drug interactions and worse patients' compliance.

4. 1. Non-opioid analgesics

Paracetamol is the first-line drug for treating pain in the elderly. The drug works well in mild to moderate pain and its effects mainly affect the central nervous system. Although it is relatively safe and well tolerated, a dose of 3-4g paracetamol per day should not be exceeded,

taking into account its hepatotoxicity and side effects. The use of paracetamol at a dose greater than 9g per week in people treated with vitamin K antagonists (VKA) may cause an increase in the international normalized ratio (INR) [16].

One of the differences in the therapeutic process of pain in seniors is the issue of the use of nonsteroidal anti-inflammatory agents (NSAIDs). NSAIDs are not recommended for elderly patients, despite the fact that their effectiveness is similar to that of younger people. This is due to a much higher risk of side effects from the kidneys, the circulatory system, the gastrointestinal tract or the central nervous system. Indications for use of NSAIDs occur only when other therapeutic methods are ineffective and the benefits of treatment are greater than the risk of side effects. Despite this, NSAIDs are among the most commonly used drugs by patients. Every fourth older person among healthy, non-hospitalized people uses NSAIDs, because they are easily available as over-the-counter (OTC) drugs, which increases the incidence of side effects and adverse drug interactions [17]. Therefore, patients should be advised of the risks associated with independent attempts of pain therapy [18].

Gastrointestinal bleeding is the most common serious adverse reaction for NSAIDs. NSAIDs are mostly weak acids and can directly damage the gastric mucosa, in addition, by inhibiting the production of prostaglandins, they damage the protective barriers of the stomach and duodenum. To prevent this, the patient must use proton pump inhibitors (PPI) during treatment with NSAIDs to prevent bleeding. This is important because the risk of their occurrence increases with age: from 1% in people under 60, 3-4% in people over 60 to 9% in people over 60 with a documented history of bleeding, and using corticosteroids or INR-extending drugs [19,20]. Reducing the risk of bleeding can be achieved by selecting NSAIDs with a better gastrointestinal mucosal profile, such as selective or preferential cyclooxygenase 2 (COX-2) inhibitors or dexketoprofen and dexibuprofen [21-23].

An important disadvantage of NSAIDs is the negative effect on the cardiovascular system, which is characteristic for all drugs in this group except acetylsalicylic acid. It is associated with the inhibition of the synthesis of prostaglandins and prostacyclins with vasodilatory effect, a decrease in the effectiveness of treatment with acetylsalicylic acid, a decrease in sodium excretion and an increase in water retention (which causes an increased blood pressure and an increased risk of congestive heart failure) [24, 25]. If NSAIDs are needed to be used in a group of patients with a high risk of cardiovascular disease and a low risk of gastroenterological complications, ketoprofen and dexketoprofen appear to be applicable [23]. For example, diclofenac should not be used [26]. The antiaggregatory effect of NSAIDs means that the risk of bleeding increases and their duration increases [27]. Ketoprofen and dexketoprofen do not interact adversely with acetylsalicylic acid [23]. In patients with high gastroenterological and high cardiovascular risk, celecoxib with a proton pomp inhibitor should be preferred if necessary [23].

When choosing a drug from this group, it should be noted that the drug has a short biological half-life time. Drugs with a longer half-life are characterized by greater risk of causing nephrotoxicity. The mechanism of nephrotoxicity is to reduce kidney perfusion by inhibiting COX-1 [28]. Drugs with a longer biological half-life time are also more likely to cause dizziness, mood swings and perception disorders [29].

Despite this, in patients with localized pain (e.g. osteoarthritis), the first line treatment is the use of topical NSAID-containing agents, since their effectiveness is identical to that of oral agents, and the risk of side effects is significantly lower [30]. Corticosteroids may also be an alternative to oral nonsteroidal anti-inflammatory drugs [31].

4. 2. Opioid analgesics

Opioids find their use in the treatment of moderate to severe pain. When initiating opioid therapy, concomitant diseases should be taken into consideration - in particular liver and kidney failure. Impaired function of these organs causes accumulation of drugs or their metabolites, which increases the probability of side effects. Due to physiological changes occurring with increasing age, affecting both the liver and kidneys as well as the reduced water content in the body, the initial dose should be reduced by 25-50% compared to the dose in young people, and the interval between subsequent doses – extended [32]. Due to the greater sensitivity of the elderly to opioids, controlled-release drug forms should be chosen.

Frequency of constipation, which is one of the side effects of opioids, is higher in the elderly, so opioids should be chosen less often. Of the weak opioids, tramadol is the preferred drug, since codeine is more likely to induce constipation [33]. An important problem is the fact that the longer treatment with opioid analgesics is, the greater the risk of constipation and the lower the effectiveness of laxatives are. Implementation of prevention against defecation disorders and lifestyle or diet changes are often ineffective or impossible. An effective method of preventing constipation is the combination of an opioid with an opioid receptor antagonist (naloxone) [34].

Equally important side effect is the sedative effect, which is much more strongly expressed in the group of seniors - a preparation with lower potential for sedation is e.g. oxycodone [35].

Based on the consensus of pain management experts, five strong opioids have been distinguished from which one can choose a drug suitable for an elderly patient suffering from severe pain [36]:

- morphine, oxycodone, hydromorphone - their metabolites can accumulate in the event of kidney failure and result in toxic effects; in addition, morphine has more potential for causing constipation
- fentanyl - in kidney failure, the half-life and clearance of the drug may be increased
- buprenorphine - does not accumulate in the case of kidney failure, has a low risk of causing respiratory depression, immunological or endocrine disorders; in liver failure, its half-life is prolonged - however, its metabolites have little activity. It also has a direct antidepressant effect.

4. 3. Co-analgesics

When choosing a co-analgesic, attention should be paid to their numerous interactions and side effects. In the treatment of neuropathic pain, lidocaine is the drug of first choice [37]. Among antiepileptic drugs, pregabalin and gabapentin have the most favorable profile [15]. Of the antidepressants, duloxetine is mainly recommended. The use of tricyclic antidepressants (TCA) in the course of diabetic or herpes zoster neuropathy is associated with the occurrence of burdensome side effects including: dry mouth, constipation, arrhythmias, voiding disorders, double vision, cognitive impairment, orthostatic hypotension and excessive sedation [38]. These effects are less pronounced when medicines are taken before bedtime and the dose is increased gradually; reduced risk of their occurrence was observed for nortriptyline and desipramine. Due to possible cardiotoxic effects, the American Geriatric Society recommends using TCA in patients with cardiovascular diseases at doses below 100 mg per day and after ECG in people over 40 and does not recommend them for patients over 65 [15].

4. 4. Summary

Summarizing, the dosage of drugs should be reduced in older patients without renal or hepatic insufficiency [39]. In the presence of impaired renal function, the use of NSAIDs with a long half-life time (such as e.g. piroxicam, meloxicam or naproxen) should be discontinued due to their prolonged nephrotoxic effect. A safer choice will be drugs with a short half-life such as ketoprofen, ibuprofen and aceclofenac. Among the opioid drugs, the best choice will be fentanyl and oxycodone (the last - with monitoring the patient's condition), because the metabolites of morphine, tramadol or codeine accumulate in the body, which requires a reduction in doses and an increase in the interval between them [40].

Due to their age and the use of more drugs than younger patients, older people are at greater risk of drug-induced liver injury [41]. Therefore, the use of hepatotoxic paracetamol is not recommended in persons with hepatic impairment, and diclofenac, piroxicam and nimesulide from the NSAID group [40, 42]. Of the opioid drugs, morphine and alfentanil may be the best choice in this situation. Buprenorphine, often considered a safe opioid, in cases of impaired liver function, reaches its "ceiling effect" (a condition in which increasing the dose does not increase the effect of the drug, but only increases the toxicity) faster, hence it is necessary to use lower doses in such patients [43].

5. THE PROBLEM OF POLYPHARMACOTHERAPY IN THE TREATMENT OF PAIN

According to the Polish Central Statistical Office research from 2009, only every ninth elderly person declared that they do not experience long-term health problems and do not suffer from chronic diseases [44]. Almost 90% of seniors have at least one chronic disease. The most common geriatric health problems and their frequency are presented in Table 1.

Table 1. The frequency of occurrence of diseases in the elderly population [45].

CONDITION	FREQUENCY OF OCCURRENCE IN THE GROUP OF ELDERLY PEOPLE
Hypertension	81%
Hyperlipidemia	52,4%
Ischemic heart disease	37,9%
Diabetes	35,3%
Chronic kidney disease	31,2%
Atrial fibrillation	24,9%
Chronic obstructive pulmonary disease (COPD)	20,1%

Rheumatoid arthritis or osteoarthritis	23,3%
Hypothyroidism	19%
Depression	14%
Osteoporosis	6,7%
Prostate cancer	6,3%
Breast cancer	4,7%
Alzheimer disease	3%

Treatment of diseases, especially those occurring in one patient, may lead to the situation when the patient is taking several drugs at the same time [46]. There may be adverse pharmacokinetic and pharmacodynamic interactions between the various drugs. They may result in side effects whose risk increases proportionally with the number of medications taken and disproportionately when the patient is using polypharmacotherapy, i.e. taking more than five drugs [47, 48].

The most significant interactions between analgesics and other medications taken by patients are summarized in Table 2. It is stated that the incidence of adverse drug reactions in people over 65 is much higher compared to younger patients [49]. In this context, it is worth noting that people with chronic pain take statistically significantly more drugs than people who do not report pain [8].

Attention should be paid to antipyretics and anti-flu drugs taken by the patient independently, containing paracetamol or non-steroidal anti-inflammatory drugs. Using them during pain therapy may cause the daily doses to be exceeded, resulting in toxic effects. Moreover, the use of two different NSAIDs (and this can happen when the patient is using over-the-counter medications on his own) is a mistake, as this does not increase the effectiveness of the therapy, but only increases the risk of drug toxicity. The exception to this rule is treatment with two different NSAIDs when one is topically applied and the other is orally [50].

Table 2. Interactions between analgesics and other medications [51-58].

NON-OPIOID ANALGESICS		
analgesic	**drug that interacts with analgesic**	**effect of drug-drug interaction**
metamizole	phenothiazine neuroleptics (e.g. chlorpromazine, perphenazine, perazine)	risk of severe hypothermia
	ciclosporin, methotrexate	increased levels of cyclosporine and methotrexate and increased toxicity

paracetamol	CYP1A2 inhibitors (ciprofloxacin, erythromycin, fluvoxamine, ticlopidine)	increased concentration and half-life of paracetamol
	loop diuretics	decreased diuretic effect of loop diuretics
	barbiturates, carbamazepine	increased risk of hepatotoxicity
	acenocoumarol, warfarin	inhibited metabolism of warfarin and acenocoumarol; increased risk of bleeding
	oral hormonal contraception	reducted duration time of paracetamol
	glucosamine	reduced bioavailability of paracetamol
all NSAIDs	CYP2C9 inhibitors (fluoxetine, fluvoxamine, paroxetine, sertraline, amiodarone, anastrazole, ranitidine, clopidogrel, fluconazole)	prolonged half-life of NSAIDs
	CYP2C9 inductors (cyclophosphamide, ifosfamide, valproate)	shortened half-life of NSAIDs
	serotonin and serotonin/noradrenaline reuptake inhibitors (SSRI/ SNRI) (especially paroxetine, duloxetine, sertraline, fluoxetine)	increased risk of bleeding
	lithium	increased level of lithium in serum
	phenothiazine neuroleptics, hydroxyzine, doxepin, mianserin, diphenhydramine	attenuation of NSAIDs by anticholinergic effects of the listed drugs
	angiotensin converting enzyme inhibitors, loop diuretics, cyclosporine, tacrolimus, sirolimus, mycophenolate mofetil	increased risk of nephrotoxicity
	AT1 antagonists (sartans)	increased risk of nephrotoxicity, reduced hypotensive effect
	β-blockers	reduced β-blockers efficacy by inhibiting prostacyclin synthesis

	clonidine	decreased effectiveness of clonidine as a result of increased total peripheral vascular resistance
	spironolactone	significant increase in bleeding risk and hyperkalemia
	clopidogrel, prasugrel, ticagrelor	increased risk of bleeding
	dapagliflozin	increased dapagliflozin concentration
	metformin	reduction of renal metformin elimination and increased risk of acidosis in elderly patients
aceclofenac	ciprofloxacin, clarithromycin	inhibition of aceclofenac metabolism, increased risk of side effects
	carbamazepine, dexamethasone	acceleration of aceclofenac metabolism
	sulfasalazine	inhibition of sulfasalazine excretion, increased risk of gastrointestinal adverse reactions
acemetacine	triamterene	increased risk of nephrotoxicity
celecoxib	acetylsalicylic acid (ASA)	increased risk of bleeding
	metoprolol	inhibiting metoprolol metabolism; increased risk of hypotension and bradycardia
	propafenone	increased risk of arrhythmias
	fluconazole	increase in celecoxib concentration by approx. 50%
	cisplatin, carboplatin	increased risk of nephrotoxicity
	imatynib, sorafenib, erlotynib	increased toxicity risk
diclofenac	ASA	increased risk of bleeding
	dabigatran, rivaroxaban	increased risk of bleeding
	omeprazole	inhibition of diclofenac metabolism by omeprazole
	fentanyl, morphine	Inhibition of the metabolism of morphine and fentanyl, increased concentration of fentanyl and morphine and its metabolites
	imatynib, dasatynib	increased toxicity of imatinib and dasatinib
	sorafenib	inhibition of diclofenac metabolism, increased risk of nephrotoxicity
ibuprofen	rum	significant risk of kidney damage

	ASA	increased risk of bleeding
	imatynib, dasatynib, nilotynib	increased concentration of ibuprofen, increased risk of bleeding
indomethacin	ciprofloxacin	increased risk of nephrotoxicity and skin adverse reactions
	diazepam	dizziness
	haloperidol	severe increase in drowsiness
	triamterene	increased risk of nephrotoxicity
ketoprofen	metoclopramide, itopride	weakened effect of ketoprofen
meloxicam	atorvastatin	increased risk of hepatotoxicity
	loop diuretics, platinum derivatives	increased risk of nephrotoxicity
naproxen	ASA	increased risk of bleeding
OPIOID ANALGESICS		
all opioid analgesics	hypnotics, tricyclic antidepressants, benzodiazepines, neuroleptics, mianserin, mirtazapine, trazodone	synergistic depressive effect on the CNS and the risk of convulsions
	other opioids	increased risk of respiratory depression
buprenorphine	cholinolytic drugs	impaired salivation by cholinolytics may make it difficult to take the medicine by sublingual route
	zolpidem	inhibition of buprenorphine metabolism
dihydrocodeine	monoamine oxidase inhibitors (MAOIs)	increased risk of side effects
fentanyl	CYP3A4 inhibitors (e.g. SSRI, ciprofloxacin, norfloxacin, clarithromycin, erythromycin, fluconazole, ketoconazole, itraconazole, anastrazole, amlodipine, cizapride, diltiazem, methylprednisone, valproate, tamoxamil, clarithromycin	inhibition of fentanyl metabolism and increased risk of side effects

	clarithromycin	significant risk of respiratory depression
codeine	CYP2D6 inhibitors (e.g. metoclopramide, amitriptyline, bupropion, SSRI, venlafaxine, haloperidol, risperidone, lansoprazole, amiodarone, celecoxib, valproate) and CYP3A4	inhibition of codeine metabolism and increased risk of side effects
morphine	anticoagulants	increased anticoagulant effect
	ranitidine, oxazepam, lorazepam	inhibition of morphine metabolism and increased risk of side effects
	TCAs	increased morphine half-life and increased risk of side effects
	phenothiazine neuroleptics, antidepressants, NSAIDs	increased risk of myoclonus
	diclofenac, aceclofenac	inhibition of morphine metabolism and increased risk of side effects
	metoclopramide	increased morphine absorption from the gastrointestinal tract and increased its sedative effect
	fluoroquinolones	decreased bioavailability of fluoroquinolones during simultaneous use of both drugs
	gabapentin	increased gabapentin serum concentration
tapentadol	SSRIs	possibility of inducing serotonin syndrome
	naproxen	naproxen increases the area under the curve (AUC) of tapentadol, which potentiates the effects of tapentadol
tramadol	CYP2D6 inhibitors	inhibited formation of the active metabolite of tramadol and extended its half-life, which may result in decreased effect and increased risk of toxic effects
	SSRIs, SNRIs	increased risk of serotonin syndrome
	TCAs, SSRIs	increased risk of seizures, inhibition of tramadol metabolism
	carbamazepine	increased risk of an epilepsy
	metoclopramide	reduction of the analgesic effect of tramadol

	setrons, mirtazapine	the antagonistic effect of the substances reduces the effect of both tramadol and setrons and mirtazapine.
	antihypertensive drugs	risk of hypotension
CO-ANALGESICS		
duloxetine	benzodiazepines, opioids, antipsychotics, barbiturates, sedative antihistamines, alcohol	increased risk of side effects
	SSRIs, SNRIs, TCAs, triptans, tramadol, pethidine	risk of serotonin syndrome
	MAOIs	significant risk of serotonin syndrome; duloxetine should not be used during treatment and for 14 days after discontinuation
	CYP1A2 inhibitors (ciprofloxacin, erythromycin, fluvoxamine, ticlopidine)	prolonged duration of action of duloxetine
gabapentine	hypnotics	increased sleepiness and ataxia
	morphine	increased gabapentin serum concentration
pregabalin	lorazepam	increased effect of lorazepam

According to research by the Polish Public Opinion Research Center, over 40% of Poles are treated with herbal remedies. They are often considered to be a natural, harmless counterpart to drug treatment, apart from the fact that they contain various active substances that may interact with other medicines the patient is using. Patients' skipping them when answering the question about the drugs they take can lead to ineffective treatment as well as serious side effects. The list of herbal preparations that interact with analgesics is summarized in Table 3.

Table 3. Interactions between herbal preparations and analgesics [59-62].

HERBAL PRODUCTS		
herb	**analgesic that interacts with herbal medication**	**effect of drug-drug interaction**
garlic *Allium sativum*	NSAIDs, paracetamol	in combination with ASA, it may increase the anticoagulant effect; increased effect of paracetamol and NSAIDs

Hypericum	fentanyl, SSRIs	decreased efficacy of fentanyl, in combination with SSRI increased risk of serotonin syndrome
Echinacea purpurea	opioids	inhibition of opioid metabolism, do not use in patients receiving fentanyl
Ginkgo biloba	NSAIDs	in combination with ASA, it may increase the anticoagulant effect; increased effect of paracetamol and NSAIDs
milk thistle *Silybum marianum*	fentanyl, tramadol, codeine, NSAIDs	inhibiting the metabolism of analgesics and increasing their toxicity
dwarf palmetto *Sabal minor*	NSAIDs, paracetamol	in combination with ASA, it may increase the anticoagulant effect; increased effect of paracetamol and NSAIDs
golden root *Rhodiola rosea*	codeine, tramadol	increased risk of serotonin syndrome
willow *Salix*	NSAIDs	increased effect of NSAIDs
evening primrose *Oenothera*	NSAIDs	increased effect of NSAIDs
Ginseng	NSAIDS, corticosteroids, SSRIs, SNRIs	in combination with ASA may increase the anticoagulant effect; increased effect of paracetamol and NSAIDs; increased effect of corticosteroids; the combination of SSRI/SNRI and ginseng may cause serotonergic syndrome or change from the depression to mania.
cranberry *Vaccinium*	morphine, oxycodone	acceleration of renal elimination of morphine and oxycodone

6. CONCLUSIONS

The treatment of pain in elderly patients differs in many respects from the pain therapy of a younger patients. The main goal is to achieve an optimal quality of life for the patient. When choosing an analgesic, you should pay attention to all concomitant diseases, such as hypertension, gastric or duodenal ulcers, heart failure or arrhythmias, and in particular - impaired liver and kidney function. It is necessary to gather a full history of both drugs that were prescribed by the patient and the preparations that the patient takes by himself.

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