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**THE LEVEL OF ADHERENCE TO THE EXISTING INTERNATIONAL RECOMMENDATIONS FOR MEDICINAL THERAPY IN THE ELDERLY**

***Moroz V.A.***

*Department of Clinical Pharmacology and Clinical Pharmacy*

*The National University of Pharmacy, Kharkiv, Ukraine*

*vl\_moroz@yahoo.com*

**Abstract.** Taking into account the tendency towards ageing of the population all over the world, as well as the peculiarities of the course of various pathologies in elderly patients, the urgency of the problem of their rational pharmacotherapy should be recognized. Analyzed 150 inpatient case histories of patients over 65 years of age. In 73%, a preparation not recommended for the elderly was prescribed and in 57.1% - the wrong dosage. A high degree of polypragmasy was revealed.

**Keywords:** *polypragmasy, side effects of medications, elderly patients*

**Introduction:** At present, there is no doubt that the increase in life expectancy is the most significant achievement of medicine in recent decades. And, as is known from the literature, the proportion of elderly people in the general population of developed countries in recent decades is steadily increasing. Thus, in the USA, people over 65 years old make up 12%, and they consume about 30% of all medicines that are prescribed in this country. According to UN estimates, the proportion of people over the age of 65 over 2050 will reach 22% of the world population. Now by the number of elderly people Ukraine is ranked 11th in the world, and in the life expectancy only of 108th [1, 2]. Persons of the elderly, old age and senile age take an average of 17 medicines per year. It was established that in this category of patients, the incidence of drug-associated complications increases 2-fold in comparison with younger patients, and 7-fold in 70-year-olds [3]. However, the presence of concomitant diseases in this category of patients necessitates the use of several medicines at the same time, becoming the basis of polypragmasy. In this regard, the rational use of medicines in this contingent of patients is one of the urgent medical and social problems. At the same time, the objective analysis and evaluation of modern approaches to rational pharmacotherapy of the most common diseases in the elderly remain rather problematic.

**Aim:** The purpose of the work was to increase the rationality use of medicines in the elderly and old age.

**Materials and methods:** The histories of the disease were analyzed at 105 people (33 men and 72 women) over the age of 65 who were in inpatient treatment at the departments of the clinical base of the university. The analysis of disease histories was carried out using standardized international recommendations of the American Geriatric Association (AGA) 2015 [4]. They provided for the correlation of certain medicines to the categories: A) Which are not recommended for use or which should be avoided in the elderly; B) Potentially not recommended medicines, the use of which should be avoided in certain diseases and syndromes; C) Potentially dangerous medicines for the elderly, which should be used with caution. Identified the appointment of medicines, their dosage, the presence and degree of indications for the

prescription, as well as other aspects of rational use and the possibility of their replacement. Also, the conformity of the elements of the pharmacotherapy to the goals of treatment (the balance of indications/contraindications, the compliance of the dosage) and the risk of the interaction of medicines about the occurrence of adverse reactions according to the standardized index MAI (Medication Appropriateness Index) was also assessed [5].

**Results and discussion:** A total of 744 medicine assignments were recorded and 98 of them were correlated with the lists not recommended following the recommendations of the AGA. In the vast majority of cases, there was a high risk of adverse reactions to MAI. Thus, the prescribing of thioridazine, which is included in the B list (potentially dangerous medicines for elderly people to be used with caution), and has an average level of evidence and the highest strength of recommendations, has been found in 4 patients. The preparation has a relatively low affinity for dopamine receptors than other typical neuroleptics from the phenothiazine derivative group and therefore often causes the development of orthostatic hypotension or bradycardia. Other side effects include the frequent development of pigment retinopathy and corneal opacity, the risk of which sharply increases with a daily dose of 800 mg per day. But the most dangerous feature of thioridazine (as its analogue chlorpromazine) is to significantly increase the risk of arrhythmias, up to ventricular fibrillation and sudden death. The FDA recommends the use of thioridazine only in the ineffectiveness of any other neuroleptics. Spironolactone in a dose of more than 25 mg per day was prescribed in 9 patients of the examined contingent. At the same time, for elderly patients, he is included in list B of international recommendations (potentially not recommended medicines, the application of which should be avoided in certain diseases and syndromes). In particular, in larger doses, it can increase the activity of the renin-angiotensin system. This is one of the links in the pathogenesis of heart failure and directly stimulates the secretion of the antidiuretic hormone by the cells of the posterior pituitary gland. And, in turn, it dramatically reduces the excretion of water and increases its reabsorption in the distal renal tubules and thus greatly enhances water retention in the body. Also, it can cause common vasoconstriction. In a well-documented series of RALES trials, the combination of spironolactone 25 mg/day (but not more) with ACE inhibitors was safe and effective: the survival of patients with III-IV functional classes of heart failure increased by 30% and significantly decreased the need for hospitalization. And there was no significant hyperkalemia, which in elderly patients is associated with many side effects [3, 5].

Among the most commonly prescribed potentially not recommended medicines from list A in elderly patients, diclofenac (27 cases) and ketorolac (11 cases) have been observed, which in this category of patients significantly increase the probability of development of NSAIDs-gastropathy. At the same time, the literature states that the risk of developing gastrointestinal complications is directly related to age (up to 4 times more often), although the frequency of taking NSAIDs on various indicators also increases with age. According to Schellack N. [6], they receive from 20 to 40% of the elderly, and 6% of them - more than 9 months in a year or permanently. In this regard, it should be remembered that pain syndromes in the elderly are mostly caused by non-

inflammatory, and degenerative processes, in which NSAIDs have a limited effect. In this situation, the use of medicines from this group, having a reduced ulcerogenic activity (eg ibuprofen) or selective more justified. It is worth remembering that when using NSAIDs in the form of candles or parenterally unpleasant sensations from the upper gastrointestinal tract occur less often than when using tablet forms, but the risk of erosion and ulceration, in this case, is not reduced. The prescription of metoclopramide was detected in 9 patients. The medicine is also included in list A not recommended for the elderly due to known side effects - extrapyramidal disorders, including late dyskinesia. The risk of developing these undesirable reactions significantly increases with age [2, 7].

Digoxin is a daily dosage greater than 0.125 mg was also prescribed in 9 patients, which correlated with contraindications. In this case, it significantly increases its absorption in the intestine against the background of the overall weakening of its motor function in elderly patients. And in parallel, the content of the active free fraction of the medicine in blood plasma increases due to age-related albuminemia and the overall decrease in the amount of fluid in the body. The peculiarities of age-related pharmacokinetics also include the slowing of biotransformation in the liver and excretion by the kidneys. All this determines the rapid onset of glycoside intoxication. In this regard, in geriatric practice, reduced doses of cardiac glycosides in 1,5-2 times should be used [8].

Amiodarone, which was used in 7 patients, also has its peculiarities of use in geriatrics. His contraindications to using in these conditions have the highest level of evidence and the strength of the recommendations. And they are associated with a high risk of severe bradycardia, prolongation of the interval QT and stopping of the sinus node. The use of amiodarone is only allowed for the control of heart rate with a constant form of atrial fibrillation. Similar warnings in international recommendations also have some other antiarrhythmic medicines: dronedarone, procainamide, propafenone, quinidine, sotalol. However, amiodarone has a specific side effect, causing pulmonary toxicity (a cough, shortness of breath, pulmonary fibrosis) in 5-17% of patients. Moreover, the timing of its occurrence is directly related to the dose of the preparation. If the daily dose is 400 mg, then its manifestation is likely in 2 months, and at a dose of 200 mg the risk of development is high up to 2 years. Although, as most authors concede, amiodarone-induced pulmonary toxicity may occur at any time after the start of treatment. And the most vulnerable to its development are the elderly. If previously used low doses of amiodarone in an attempt to avoid toxicity, it is now believed that there is no safe dose for this medicine. In clinical trials, it was found that cardiovascular mortality was significantly higher in the early and remote period from the start of its intake compared with patients to whom amiodarone was not prescribed at all. In this regard, amiodarone is currently not used for prophylactic therapy in all patients with left ventricular dysfunction. An exception is its severe hypertrophy [9].

Amitriptyline, which was used in 5 patients of the investigated contingent, also has the highest levels of evidence and strength of recommendations (contraindications). Not recommended in elderly patients due to pronounced choline blocking effect and increased sedation leading to orthostatic hypotension. In these

conditions, rationally this medicine would be replaced by the related antidepressant doxepin in a dose of less than 6 mg per day.

The use of oral glucose-lowering glibenclamide (5 observations) should be avoided in the elderly, which is also included in the list of non-recommended medicines. The medicine has a low selectivity for the KATP channels of the pancreatic  $\beta$ -cells and affects the same channels of cardiomyocytes and smooth muscle cells in the blood vessels. In physiological conditions, these channels are closed. But in conditions of ischemia, they open, increases the outflow of potassium from cells, which is accompanied by a change in the membrane potential and a reduction in the time of repolarization. This is a protective mechanism for the heart muscle. Glibenclamide thus harms this mechanism of the cardiovascular system in cases of ischemia. Its application has a vasoconstrictive effect, decreases the coronary blood flow, increases the need for myocardial oxygen and reduces its electrical activity [9].

Receiving reserpine containing medicines (Normatens, 3 patients) creates conditions for the development of side effects from the central nervous system. Although the active substance belongs to the so-called "soft"  $\alpha$ -agonists of central action but has a high risk of side effects - bradycardia and orthostatic hypotension. Included in the recommendation of AGA for elderly patients on list A with maximum strength recommendations should not be used for routine treatment of arterial hypertension. Also, it is contraindicated in patients with creatinine clearance  $<30$  ml/min, which is especially relevant for the studied patient category. Similar contraindications have other medicines of this group (clonidine, guanabenz, guanfacine, methyl dopa).

Antimicrobial nitrofurantoin (3 cases of the prescription), which is commonly prescribed for urinary tract infections, also has a high potential for lung toxicity, has hepatotoxicity and can initiate peripheral neuropathy. Also included in list A with a maximum level of contraindications for elderly patients. The risk of side effects is particularly high with creatinine clearance below 30 ml/min. At the same time, its concentration in urine in this group of patients is not sufficient for the therapeutic effect [4, 10].

Atropine and promethazine, which were prescribed in three patients each, should also be avoided in the elderly due to their high anticholinergic potential. The recommendation has the maximum level of contraindications because of the high risk of patient's confusion, dry mouth, constipation and other serious side effects.

Thus, we detected the high frequency of prescribing of potentially unrecognized and dangerous elderly patient's medicines, which can lead to negative consequences, worsen the quality of life and increase mortality. It was almost three-quarters of all analyzed disease histories. Also, the balance of indications regarding the contraindications for the MAI index indicated an unreasonable risk of the use of some medicines in terms of their joint reception in about one-third of patients. Thus more than half of the patients were incorrect dosage (in diaries, lists of medicine prescriptions or recommendations at hospital discharge). Polypragmasy was observed in almost all cases (patients received at least 7 medicines). Doctors leaned toward

polypragmasy, trying to cure all the patient's disease immediately and prevent all possible complications.

### **Conclusions.**

1. According to the results of the analysis of the histories of the disease in 73% of cases, the use of medicines, which should be avoided for use in elderly patients, as well as potentially dangerous for them, is established.

2. The irrational use of medicines (compliance indications/contraindications) in elderly patients was 34.3%, and in 57.1% of cases, the dosage was uncorrected.

3. To increase the rationality of medicinal therapy in elderly patients, a thorough analysis of the pharmacotherapy is necessary, which necessitates participation in the medical process of a clinical pharmacist or clinical pharmacologist.

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