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Initiation of Pharmacotherapy as a Risk Factor of Falling in Older Patients

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Abstract—The paper presents literary and original data on the problems of falling for elderly patients. The relationship between the occurrence of a fall and the initiation of drug therapy with a known negative effect on the risk of falling is considered. Data on the frequency and structure of falls by patients with cardiovascular diseases over the age of 75 who received treatment at a multidisciplinary hospital are presented. The data analysis showed a tendency of fall prevalence: a fall was observed in 33.8% of patients in the first 5 days of the hospital stay. This may be associated with a high drug burden and the prescription of new drugs to the patient. The study noted that the therapy was chosen on the first day. Additional drugs were often prescribed, which led to the polypharmacy state. Analysis of individual groups of drugs allowed reliable confirmation of the relationship between the prescription of drugs that increase the fall risk and occurrence in relation to the ophthalmic form of β-blockers ($p = 0.04$). Polypharmacy as a risk factor of falling in gerontological patients, which was described in the scientific literature, also confirmed the negative effect in our study. Thus, patients who are newly administered drugs known to have negative effect on fall development can be attributed to the risk group for falling.

Keywords: elderly and senile age, drug-induced falls, initiation of pharmacotherapy, drugs that increase the risk of falling, antihypertensive drugs, psychoactive drugs, antiglaucoma drugs, risk factors of falling

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INTRODUCTION

The problem of drug-induced falls is mainly typical for patients in economically developed countries, which have an increasing proportion of the population of older age groups. They are burdened by a large number of comorbid diseases and are forced to take a large number of drugs, which, as a result, increases the probability of the development an adverse drug reaction [16]. Recent publications on the problem of falling in elderly and senile patients have noted the effect of pharmacotherapy initiation or prescribing new drugs on the increased risk of falls along with the polypharmacy factor (the simultaneous administration of five or more drugs), was noted in recent publications on the problem of falling in elderly and senile patients, [5, 10]. Thus, a number of studies on drug-induced falls showed that the administration of new drugs that increase the patient's risk of falling (fall-risk increasing drug, FRID) increased the probability of a fall in the first days of the administration as compared with the long-term adminstration of drugs from the FRID group [4, 11, 15].

In a cohort study evaluating six-year antihypertensive treatment in 906000 older people living in Norway, it was found that falls with the development of a trauma were more frequent with the use of loop diuretics in new users. A patient prescribed drugs for the first time or as an addition to the basic treatment is classified a new user [13].

A study by D.A. Butt et al. confirms this dependence, and it turned out to be especially high for thiazide diuretics, ACE inhibitors, angiotensin-II receptor blockers, calcium channel blockers, β-blockers during the first 14 days of the administration; the risk remains up to 45 days [5].

G. Corrao et al. in their study also noted an increased vulnerability of elderly patients upon the initiation of therapy with loop diuretics and α-blockers in terms of the risk of falling and the development of a traumatic fracture of the femoral neck; this dependence was observed for the first 30 days [6].

The goal of the work is to study the effect of the prescription of new drugs to senile patients on the fre-

Table 1. Demographic and pharmacological parameters in elderly patients with cardiovascular diseases who experienced a fall in the hospital

Parameter	160 persons	
	men, $n = 31$	women, $n = 129$
Average age, years old	86.27 ± 5.73	87.318 ± 4.99
Number of diseases	8.89 ± 2.60	8.50 ± 2.21
Charlson Comorbidity Index, points	9.4 ± 1.9	9.7 ± 2.3
Average number of drugs received, pcs.	9.36 ± 1.87	9.6 ± 2.7
Average number of drugs that increase the risk of falling, pcs.	1.05 ± 0.94	1.27 ± 0.97

quency of falls under polypharmacy at a multidisciplinary hospital.

MATERIALS AND METHODS

The analyzed sample contained 966 patients over the age of 75 years with cardiovascular diseases (CVDs) who received treatment in the cardiology department of the Hospital of War Veterans No. 2 (Moscow) for the period 2011–2017 (Table 1). The time of the fall, the type of injury, the therapy received, and its possible correlation with fall development were evaluated. Pharmaceutical agents included in the Guidance Sheet of FRID, which was recommended by the British Geriatric Society in 2014, were classified as FRID. It allows drugs to be ranked by the degree of the negative effect on falls into high risk (red level), moderate risk (amber level), and possible cause (yellow level). According to the this classification, FRIDs are represented by two subgroups with respect to the main mechanism of influence on falls: psychoactive drugs that depress the central nervous system with slower reactions, excessive sedation, and the possible development of orthostatic hypotension and drugs that affect hemodynamics with a possible negative effect on the work of the heart and a decrease in vascular tone, which indirectly leads to the development of orthostatic hypotension [1, 7, 14]. Statistical processing was performed with the IBM SPSS Statistics package, version 20.

It is necessary to pay attention to the fact that, as a rule, in-patients at a hospital received ineffective therapy during outpatient treatment; thus new drugs must be selected and prescribed. In our analysis of the data, which included complete information about the patient (gender, age, diagnosis, fall anamnesis, cause of hospitalization, previously received drugs), laboratory and instrumental examination data, and received pharmacotherapy, we found that patients showed severe polymorbidity, which naturally leads to forced polypharmacy (Table 1). In addition, it should be noted that patients who noted a fall in the anamnesis were not included in this study. Although 172 cases of falling were detected, the fall in 12 cases was a consequence of the development of an acute cardiovascular event (acute myocardial infarction, pulmonary embolism, cerebral blood flow acute disturbances); therefore, the data of these patients were not included in the further drug audit.

Thus, a comprehensive assessment and audit of drug therapy was carried out for 160 patients who suffered falls during hospitalization to the inpatient facility. In the analysis of the effect of a certain group of drugs on the initiation of falls, these patients were divided into two groups: those who received specified pharmacotherapy and those who did not. In the case of the absence of the drug in the treatment sheet, this case was added to the control group; if it was present, the case was added to the main group. A main group and control group were formed for each drug. The initiation was assessed with survival analysis via the construction of Kaplan–Mayer curves performed in the SPSS Statistic program, version 20.0.

RESULTS AND DISCUSSION

Our study examined 160 cases of falls, 87 of which were complicated by the development of a trauma. Most of the injuries sustained during the fall were bruises, hematomas, and abrasions of the soft tissues of the head, trunk, and limbs (48 cases), which did not lead to a serious deterioration in the state of health. The development of nosebleeds was noted in two cases, and hemorrhage in the eye was revealed in one patient. In two patients, the falls led to the development of posttraumatic pneumonia. Most of the falls resulted in concomitant injuries, e.g., when a hematoma of the soft tissues of the head was accompanied by a bruise or abrasion of the chest region of the trunk. The most serious consequences of the falls were the development of bruised and scalped wounds in 7 patients, dislocations in 4, bone fractures in 19, closed traumatic brain injury in 1 patient, and joint injuries in 4. Our study found two cases of a fall in elderly patients (women) that resulted in fatal outcomes: a fall with a femoral neck fracture in one patient and a fall with fractures of the nasal bones, closed traumatic brain injury, and internal bleeding in the other.

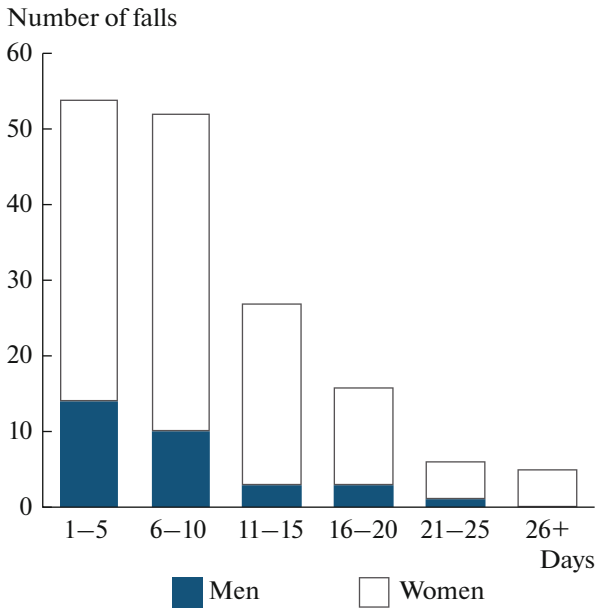

Fig. 1. Falls by elderly patients in the hospital with respect to the day of stay.

An interesting fact is that falls occurred in the daytime in 70% of women, while men experienced falling mainly at night.

It was noted that falls in patients developed mainly on the first day of hospitalization, which can apparently be explained by a more aggressive therapy due to the desire to achieve the most pronounced clinical improvement. Figure 1 shows the data on the time frames of falls in senile patients with cardiovascular diseases.

Analyzing the study material, we pointed out a larger number of falls in the first 10 days of hospitalization, with a subsequent decrease in fall frequency at longer time periods of up to 21 days. The most common fall cause reported by patients in our study was dizziness (42%), darkening in the eyes (34%), and leg weakness (8%). During the fall, medical personnel recorded bradycardia in 20%, hypotension in 15%, hypoglycemia in 5%, and retardation/confusion of consciousness in 20%.

In a drug audit to detect drugs from the red group (with a high fall risk), we obtained the following values as a percentage when comparing patient cohorts by fall times (Fig. 2). In addition, we noted that bromine preparations, the ingestion of proton pump inhibitors, and parenteral magnesium salts, which do not belong to the red group of the FRID classification, were new drugs for patients; however, these drugs could increase the probability of undesirable drug reactions due to drug interactions [14].

Our assessment of the effect of drugs from the red group (with high risk of developing falls) on fall initiation compared the groups of patients receiving the drug and all patients who did not have this drug on the treatment sheet (control group) (Table 2).

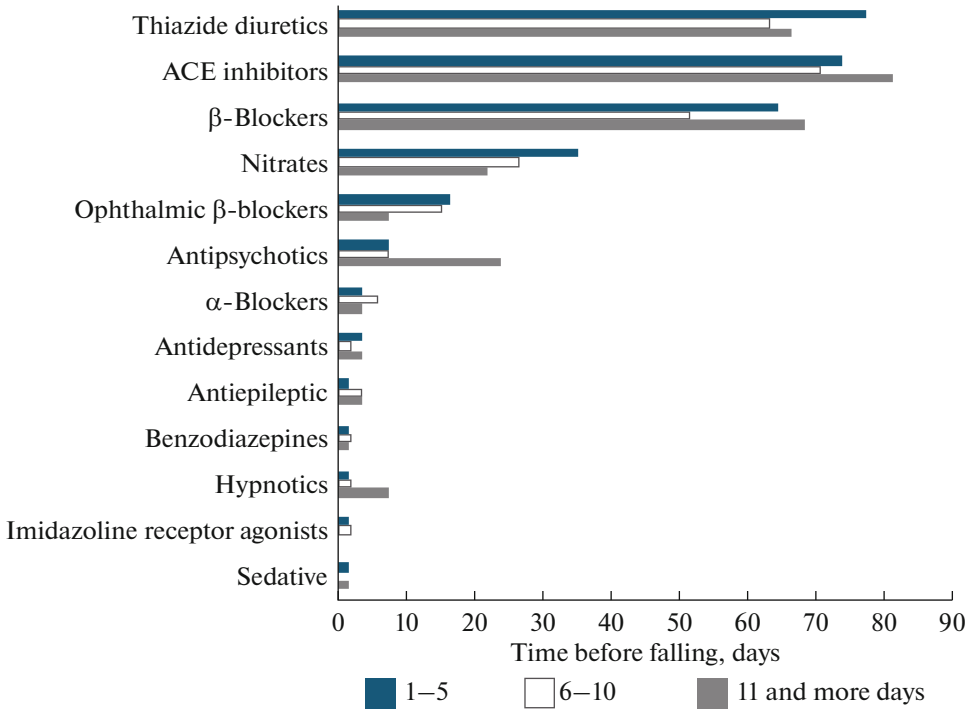

Fig. 2. Drugs prescribed to patients from the red category according to the FRID classification with respect to the day of hospital stay.

Table 2. Effect of drug groups on the fall risk in elderly patients

Drug group	Average time before falling in patients to which the drug was prescribed, days (95% CI)	Average time before falling in the control group, days (95% CI)	Log Rank (Mantel—Cox), p
Antidepressants	9.8 (2.46–17.14)	9.16 (8.06–10.27)	0.79
β-Blockers	9.1 (7.81–10.52)	9.21 (7.37–11.05)	0.91
Ophthalmic β-blockers	6.67 (4.76–8.57)	9.56 (8.35–10.77)	0.04
Benzodiazepines	8.0 (0–16.54)	9.2 (8.1–10.31)	0.8
α-Blockers	9.43 (4.97–13.89)	9.17 (8.05–10.29)	0.96
Imidazoline receptor agonists	5.5 (2.56–8.44)	9.23 (8.13–10.33)	0.29
Antipsychotics	9.9 (6.83–13.04)	9.1 (7.94–10.27)	0.7
Nitrates	7.96 (6.01–9.9)	9.66 (8.36–10.97)	0.19
Antiepileptic	9.2 (4.67–13.73)	9.18 (8.06–10.3)	0.98
Sedative	7.5 (0.64–14.36)	9.2 (8.1–10.3)	0.68
Hypnotics	11.17 (6.74–15.6)	9.1 (7.98–10.22)	0.57
Thiazide diuretics	8.95 (7.55–10.33)	9.71 (8.09–11.4)	0.63
ACE inhibitors	9.5 (8.17–10.81)	8.18 (6.45–9.92)	0.27

The analysis results did not reliably confirm the contribution of FRIDs to the patients' falling frequency; nevertheless, according to our data, ophthalmic β-blockers ($p = 0.04$) were the most reliable fall initiators. The effect of β-blockers on fall risk is shown in Fig. 3, from which it can be seen that all patients prescribed this group of drugs fell significantly earlier than patients who did not receive the drugs from this pharmacological group.

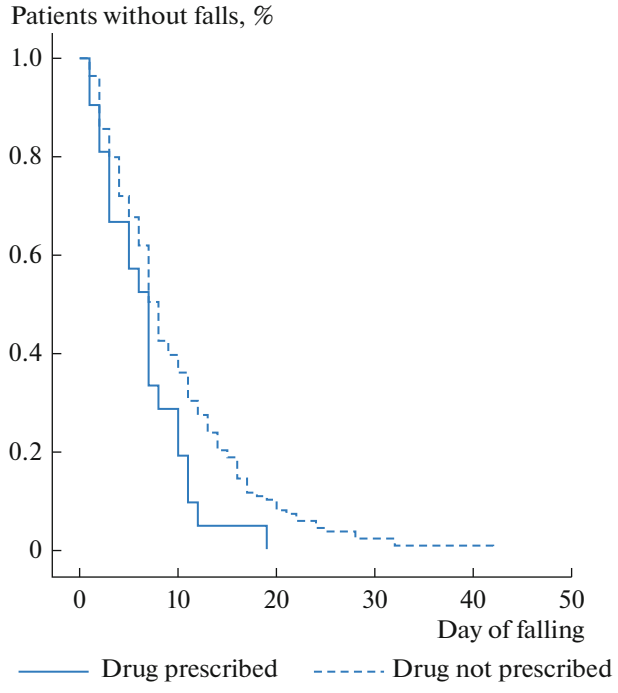

Fig. 3. Effect of therapy initiation with ophthalmic β-blockers on the increase in fall risk. Statistical method: Kaplan–Mayer curves. Lines of survival functions indicate patient groups with respect to the prescription of these drugs.

Thus, the higher fall frequency in the first days of hospitalization can be explained not so much by the influence of individual groups of drugs but by the prescription of the entire complex of pharmacotherapeutic treatment and polypharmacy, which increases the probability of the development of an adverse drug reaction.

Given the importance of the problem of falling in elderly and senile people, health regulatory authorities and geriatric societies of different countries are forming strategies and algorithms for its prevention. A pharmacological audit to reduce the number of prescribed drugs or to cancel and/or reduce the dosage of FRIDs, especially psychoactive drugs, is included in all programs for the prevention and prophylaxis of falls [8, 11, 12].

The All-Russia Scientific and Methodological Gerontological Center proposed that the prescribed therapy for older patients should be evaluated as part of fall prevention, especially in the presence of the syndrome of senile asthenia, which burdens the state [2].

Patient-oriented approaches that recommend treatment individualization must necessarily take into account the peculiarities of pharmacotherapy in the elderly by considering changes in pharmacokinetic and pharmacodynamic parameters, as well as the risk of an adverse drug reaction during initialization in new users [3].

Citing the materials of the American Geriatrics Society/British Geriatrics Society guidelines, L.V. Moncada et al. recommend a regular therapy audit for older patients that includes not only patients with an increased risk of falling (fallers) as the target audience, but also

patients in older age groups during the annual medical examination within the Medicare program [9].

CONCLUSIONS

Our study confirmed the effect of polypharmacy and the use of the ophthalmic form of β-blockers on fall risk, which coincides with the literature data. Psychoactive and antihypertensive drugs (nitrates, thiazide diuretics, ACE inhibitors, β-blockers) also showed a negative effect (trend), but the data were unreliable. The study revealed and confirmed that polypharmacy is of key importance in fall development for senile patients.

Thus, based on the results, we suggest that doctors of medical organizations who are prescribing new drugs to patients with polypharmacy should start with the minimum doses and proceed under the close supervision of medical personnel.

COMPLIANCE WITH ETHICAL STANDARDS

Conflict of interest. The authors declare that they have no conflict of interest.

Statement of compliance with standards of research involving humans as subjects. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants involved in the study.

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