Research progress on polydrug-associated falls in the elderly

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***Abstract:** Falls are the leading cause of injury and death in the elderly, and medication is one of the important adjustable factors causing falls in the elderly. It is of great significance to explore the relationship between polypharmacy and falls in the elderly. This article systematically reviews the relevant literature from three aspects: the types of polypharmacy in the elderly, the harm of polypharmacy to falls, and the management of polypharmacy, in order to provide a theoretical basis for the safe medication management of the elderly, improve the drug safety of the elderly, and reduce the occurrence of drug-related falls.*

***Keywords:** Senior citizen; polypharmacy; Fall; prophylaxis*

1. Introduction

A fall is an unexpected fall to the ground or lower, and excludes external violence, loss of consciousness, hemiplegia and other intervention factors [1]. The annual fall rate of the elderly over 65 years old in China is about 30% [2]. Falls have become the leading cause of injury death for the elderly [3], and the occurrence of falls will not only cause a series of physical and psychological hazards to the elderly, but also bring huge economic burden to families and society. According to research data, China's annual medical expenses caused by falls are at least 5 billion yuan [4]. Falls in older adults are primarily influenced by physiological, sick, environmental, pharmacological, and psychological factors, of which medication is a potentially important and modifiable risk factor [5]. According to a cross-sectional study based on Medicare, the incidence of falls in people who did not use drugs was 5.42%, and the incidence of falls after medication was as high as 10.29%, which was 4.87% higher than that of people who did not take drugs [6].There is no consensus on the definition of polypharmacy, which is generally defined as the use of five or more conventional drugs per day, mainly including over-the-counter drugs, prescription drugs, Chinese herbal medicines, and health supplements [7]. Polypharmacy is prevalent in older adults because of the large number of underlying diseases, and it is also an important drug factor that causes falls in older adults [8]. Falls have become an important patient safety topic for medical workers, and a large number of scholars at home and abroad have conducted research on the influencing factors and interventions of falls, but there are few reports on the elderly as the key population, and the main factors of falls caused by multiple drugs are few. Therefore, it is particularly important to further clarify the relationship between falls and polypharmacy in the elderly. In order to provide a reference for the later research and development of fall prevention management measures.

2. Types of drugs related to falls

Older patients are at increased risk of falls when they cause side effects such as orthostatic hypotension, sedation, lethargy, confusion, unsteady pace, and cognitive impairment [8]. According to the 17th edition of "New Edition of Pharmacology", the types of drugs that may cause falls are mainly divided into 6 categories, including drugs acting on the central nervous system, drugs acting on the cardiovascular system, drugs acting on the digestive system, drugs acting on the urinary and reproductive systems, hormones and related drugs, and drugs that mainly affect allergic reactions and immune function. Among them, drugs that significantly induce falls in the elderly include anti-central nervous system drugs and multi-drug therapy [3].

2.1 Anti-central nervous system drugs

2.1.1 Antipsychotics

Antipsychotic drugs generally refer to drugs that can pass through the blood-brain barrier and directly act on the central nervous system, and adverse reactions such as tardive dyskinesia, dizziness, cognitive impairment, and orthostatic hypotension may occur during the process of taking them, which may increase the risk of falls [10]. It mainly includes typical and atypical drugs, typical drugs are (chlorpromazine, thioridazine, flufenazine, haloperidol, trifluoperazine, etc.); Atypical agents are (quetiapine, clozapine, risperidone, olanzapine). Studies [11] found that 85.75% of the elderly have antipsychotic drugs at home. Tan Zhaohui et al. [12] studied the effects of hypotensive, hypoglycemic, anti-inflammatory and analgesic, psychotropic drugs on falls in the elderly, and the results showed that the OR of psychotropic drugs was 2.04, indicating that the risk was relatively large. Li Liuxiang et al. [13] conducted a retrospective cause analysis of 80 hospitalized patients who had falls, of which the age group of fall was 65-74 years old, and 9 cases of falls caused by taking antipsychotic drugs, accounting for 11.25%. Therefore, for patients who take antipsychotic drugs for a long time, doctors should start with a small dose and gradually increase the dose. Nursing staff should strengthen the health guidance of the control caregiver (name of the drug, dosage, side effects and symptoms), familiarize them with the symptoms related to easy falls and the time of occurrence, and call the medical staff as soon as symptoms appear.

2.1.2 Antidepressants

Depression is one of the most common problems in the elderly, with an overall prevalence of 11%~57% [14]. Common antidepressants include selective serotonin (5-HT) reuptake inhibitors (SSRIs), selective 5-HT and norepinephrine (NE) reuptake inhibitors (SNRIs), tricyclic antidepressants, and newer antidepressants. Common adverse reactions include gastrointestinal reactions, orthostatic hypotension, dizziness, sedation, and confusion [15]. Carvalho et al. [16] studied the use of venlafaxine and olanzapine in the elderly, resulting in an incidence of orthostatic hypotension of 50% and 7%, respectively. Liu Qing et al. [17] analyzed the results of the survey results of 4696 elderly people in a community and showed that the tricyclic antidepressants among antidepressants had an OR 2 for the first fall of the elderly. 2 indicated that the harm was greater, and the selective 5-HT reuptake blocker had an OR of 3.1 for falls and repeated falls in the elderly. Prompt medical staff to carry out first aid education measures for patients and their families to identify adverse reactions in a timely manner. If patients and family members are informed that orthostatic hypotension occurs when taking this drug, bed rest should be taken as much as possible to reduce activity. If orthostatic hypotension has occurred, lie down on the ground immediately for protection, and then notify medical staff in time. Although the above two studies have reported the occurrence of falls caused by taking antidepressants, there are no specific measures such as optimizing drug dosage and timing, and preventing adverse reactions, and a lot of research and exploration on the above issues are needed in the future to provide clinical reference with high-quality research results.

2.1.3 Antiepileptic drugs

Antiepileptic drugs have been reported in 9 percent of older adults in nursing homes [18]. Affected by age, drugs are metabolized slowly in the body, and the efficacy of drugs also changes, which also amplifies adverse reactions such as drug sedation, ataxia, dizziness, confusion and blurred vision, and fractures, thereby increasing the probability of falls [19]. Clinically, antiepileptic drugs are divided into traditional antiepileptic drugs (such as phenobarbital, benzodiazepines, phenytoin, carbamazepine and valproic acid) and new antiepileptic drugs (such as oxcarbazepine, lamotrigine, topiramate and levetiracetam). Ensrud et al. [20] evaluated the use of central nervous system medications in 8127 women aged 65 years and older, with a 28% incidence of one fall and an 11% incidence of two or repeated falls. Masud et al. [21] studied the correlation between central nervous system drugs and falls in 4696 men aged 60~75, and found that the OR values of single falls and repeated falls of antiepileptic drug users were 2.6 and 2.8, respectively. The above studies have proved that anti-epileptic drugs can increase the probability of falls through multiple perspectives such as large samples, different genders, and different drug types, but the disadvantage is that there is no in-depth study of how to reduce the risk of falls caused by anti-epileptic drugs, such as long-term use of antiepileptic drugs patients should be informed that there may be osteoporosis and fracture risk, bone density should be regularly monitored, and osteoporosis should be prevented. In addition, there are no large-sample studies reported in China, and the randomized controlled experimental research of large samples will be a direction in the future.

2.1.4 Sedative-hypnotic drugs

The study found [22], 58.01% of the elderly had experienced taking sedative hypnotic drugs. In 2011, the former Ministry of Health issued the "Technical Guidelines for Fall Intervention in the Elderly", which confirmed that long-term use of sedative-hypnotic drugs increases the risk of falls [23]. Commonly used sedative hypnotics include four major classes, namely barbiturates, benzodiazepines (BDZ) and non-benzodiazepines, and a new class of hypnotics. After taking it, 67.8% of the population experienced drowsiness, fatigue, dizziness, and 23.2% of the population produced adverse reactions such as gait instability and balance disorders, which caused the elderly to lose attention and lead to falls [24]. Lin Jianyu et al. [25] showed that the incidence of adverse events of falls in elderly patients taking sedative hypnotic drugs was 12.5‰, which was higher than that of 1.3‰ without sedative hypnotics, and the common time period of falls was 24:00-6:00, and the most common occurrence places were bedside and bathroom. Neutel et al. reported [26] that the risk of falls was highest after two weeks of taking benzodiazepines. Perry et al. [27] followed older adults for one year, and the highest risk of fall with a first use of benzodiazepines was 11.4. For patients with insomnia, psychological and behavioral interventions should be preferred and pharmacotherapy considered second. Patients should also be advised to take it after bedtime. The downside is that the effectiveness of specific cycles that lead to an increased risk of falls needs to be further demonstrated.

2.2 Multimedication

There is no consensus on the definition of polypharmacy, which is generally defined as the use of five or more conventional drugs per day, mainly including over-the-counter drugs, prescription drugs, Chinese herbal medicines, and health supplements [7]. A survey of 13,869 cases of prescription drug use among the elderly over 65 years old (1988-2010) showed that the proportion of patients using polypharmacy increased from 12.8% to 39.0% [28], and Wang Ru et al. [29] showed that among the elderly medication, the combination of polypharmacy with higher frequency was hypertension + coronary heart disease (4.00%) and hypertension + coronary heart disease + diabetes (1.13%). In clinical practice, doctors and pharmacists should use drugs rationally and appropriately based on evidence-based prescriptions and conduct drug monitoring, and the elderly should clarify the types of polypharmacy to identify and prevent adverse reactions caused by polypharmacy.2 Hazards of polypharmacy for falls.

3. Hazards of polypharmacy for falls

Polypharmacy is associated with an increased risk of falls, mainly because polypharmacy significantly affects the absorption, distribution, metabolism, and excretion of drugs in the human body. A study by a domestic scholar [30] showed that polypharmacy was closely associated with adverse outcomes in the elderly, including side effects and an increased risk of falls, hospitalization, and death. At the same time, a study [31] showed that the risk of cardiovascular disease death increased by 2.45 times in the elderly who used polypharmacy, mainly because of the increased risk of drug interactions and drug-disease interactions, which in turn caused a series of adverse drug reactions, posing a huge threat to the health of the elderly. With the deepening of research, some scholars have proposed that the essence of polypharmacy in the elderly is due to their own multiple chronic disease states, which will produce complex pathophysiological changes in the body [32]. Some acute or chronic diseases, such as osteoporosis, diabetes mellitus, urinary incontinence, and cardiovascular disease, are also risk factors for falls [33,34]. The reason for this is that it can cause cardiocerebral ischemia, which can induce angina, dizziness, and amaurosis that can lead to falls [35]. Therefore, prospective and interventional studies are warranted to elucidate the causal relationship between polypharmacy, comorbidities, and falls. Polypharmacy involves complex drug combinations and drug interactions, and further research and detailed standardized evaluation of polypharmacy are required.

4. Precautions for drug-related falls

4.1 Reasonably select tools to accurately assess the risk of falling

Studies have suggested that fall risk assessment should be performed on an annual basis for older adults over 65 years of age [36], and from the perspective of the assessment process, all older adults should be screened for fall risk, asked whether they have fallen history, gait, and balance problems in

the past 12 months, and for each patient who has fallen, impaired balance, or difficulty walking, gait, balance, and mobility should be assessed on a professional assessment scale; Take more than 5 types of medications). In the absence of these conditions, a multifactorial fall risk assessment is performed, which includes a history of drug use, falls, associated diseases, physical function and structure, environmental factors, balance, gait, ability to perform daily living, footwear, cognition, and neurologic function [37]. After the above evaluation, if the patient has any drug-related fall factors, appropriate preventive management measures should be taken according to the use of the drug to reduce the fall.

4.2 Establish an effective drug management program to reduce drug harm

Huang et al. [38] established a project management team based on project management thinking (establishing the project name, project team members, setting project management target values, conducting feasibility analysis, formulating plans and specific implementation steps), and effectively reduced drug-related fall adverse events in hospitalized elderly patients. It has been suggested by researchers [39] that physicians should reduce polypharmacy when treating various diseases, and should start with the lowest dose of drugs as much as possible. Zhang Qi et al. [40] carried out drug management by clinical pharmacists in 36 patients, including the establishment of clinical pharmacists, improving the professional skills and level of clinical pharmacists, participating in ward rounds, monitoring various adverse reactions, and strengthening outpatient prescription intervention, and the total incidence of irrational drug prescription after intervention was reduced compared with that of the control group. Medication guidance for fall prevention can also be strengthened for older adults, such as those taking sedatives and sleeping pills, who are awake before going outside [41]. The above-mentioned drug management has been carried out from multiple perspectives such as hospital evaluation, doctor adjustment, clinical pharmacist supervision, and medication guidance for the elderly, and has achieved results to varying degrees. However, assessment, adjustment, supervision, guidance, etc., can only be used as part of a comprehensive pharmacological intervention. In the future, it is necessary to optimize the drug regimen for different drug patients and establish the optimal drug regimen.

4.3 Implement health education and raise awareness of fall prevention

BLarsson et al. [42] demonstrated that regular health education for older adults is effective in reducing the risk of falls. According to the Guidelines for Fall Intervention for the Elderly at Home (Care) [43], the elderly should strengthen their dietary nutrition, appropriately supplement vitamin D with 15 μg (600 IU) per day, and tolerate a maximum intake of 50 μg (2000 IU) per day to prevent osteoporosis and prevent falls. For those who are taking the above medicines, they can affix a fall prevention label on the medicine box. Through the popularization of knowledge, negative case presentation, video push, psychological counseling, etc., health education interventions are carried out for the elderly and their families, to identify their own factors of fall risk, and to master daily medication (dose, frequency, sequence, adverse reactions) and other methods, so as to enhance the self-confidence of the elderly, thereby improving their awareness of fall prevention and giving full play to their self-efficacy[44-46]. Feng et al.[47] integrated virtual technology into home dialysis management, and provided training forms (rhythm boxing, bear children chasing me, happy volleyball, dodgeball, and game ellipsis), suggesting that VR can give full play to the subjective initiative of patients, stimulate patients' interest and motivation in training, and reduce the risk of falls.

5. Conclusion

At present, there are few studies on drug-related fall intervention in the elderly in China, and the following problems were found during the implementation of this study: there are fewer multicenter large-sample drug-related fall studies. The existing drug-related studies have a small sample size and unclear effective management measures, and a large-scale multi-center cohort study on drug-related fall risk for the elderly population in China is needed in the future. Secondly, there is a lack of recognized, highly reliable and universal tools, although there are some assessment models and scales for the risk of falling in the elderly, but from the perspective of operability, simple and easy to operate, accurate and time-consuming assessment of the scale needs further research and discussion; Finally, the intensity and scope of outpatient and community-based interventions need to be strengthened. It is suggested that in addition to regularly carrying out publicity and education on the knowledge of fall prevention for the elderly, outpatient clinics and communities can also combine emerging technologies

such as virtual technology to enhance the awareness of the elderly or strengthen supervision, so as to improve their own compliance.

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