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Drugs increase the risk of suicide in the elderly

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Abstract

Introduction and objective: The purpose of this paper is a systematic review of articles and research in the context of drugs used and suicide in elderly patients

Materials and methods: A non-systematic review of the scientific literature was carried out according to the following keywords: opioids, beta-blockers, levodopa, benzodiazepines, risk of suicide, the elderly. PubMed was searched and 51 articles published up to 2022 were analysed.

Description of the state of knowledge: Suicide in the elderly may be much more frequent than in the younger population. In addition to factors such as mental illness, dementia, deteriorating health, or problems with adapting to old age, the impact of chronic and reliever medications in this age group should also be considered. The greatest challenge of pharmacotherapy in the elderly is polypharmacy, drug interactions, different metabolism, pharmacokinetics and pharmacodynamics of the drugs used, as well as the side effects appearing in chronic therapy. In elderly patients, strong groups of drugs such as benzodiazepines and opioids are used extensively and sometimes too often. These drugs can cause addiction and overdose. Prescribing benzodiazepines alone carries a high risk of suicide. On the other hand, opioids often lead to addiction and abuse of these drugs, which may be associated with the development of respiratory depression. According to estimates by the Centres for Disease Control and Prevention (CDC), suicide accounts for approximately 7% of all opioid overdose deaths. Therapy should be carefully selected with regard to the use of other medications, drug interactions, and possible dependence and drug abuse by patients.

Summary: The use of some classes of drugs in the elderly requires increased vigilance and control in the context of depression and episodes of suicide attempts. Drugs such as B blockers, digitalis glycosides, NSAIDs, opioids, ACEIs, calcium channel blockers, corticosteroids, diuretics, levodopa, and benzodiazepines can cause symptoms of depression. Older people are more susceptible to side effects of drugs, for example because of polypharmacy and the chronicity of treatment.

Key words: opioids, beta-blockers, levodopa, benzodiazepines, risk of suicide, the elderly

Introduction

Suicide is a serious global problem that affects all age groups, including the elderly [1,3]. WHO reports that more than 700,000 people die from suicide worldwide each year. [2]. Suicides among the elderly may be more frequent than in other age groups, and for example in Korea these rates are up to three times higher [3,4]. The reasons that lead the elderly to attempt suicide may be related to aging stressors, such as deteriorating health or problems with adapting to the aging process [5]. One of the most important risk factors for suicide are mental diseases, especially depression, anxiety and bipolar disorder [4,6]. Multi-disease patients are particularly prone to depression due to a reduced standard of living and the use of drugs that can cause depression symptoms such as B-blockers, digitalis glycosides, NSAIDs, opioids, ACEI, Calcium Channel Blockers, Corticosteroids, diuretics, Levodopa, benzodiazepines and others [7,8].

Material and methods

An unsystematic review of the scientific literature was carried out according to the following keywords: opioids, beta blockers, levodopa, benzodiazepines, risk of suicide, elderly people. The PubMed database was searched and 51 articles published up to 2022 were analysed. Review, quantitative and qualitative studies were included in the analysis. The criteria for qualifying the records for the review were: the title, the content of the abstract and the topic related to the risk of suicide in the elderly associated with the use of drugs.

Benzodiazepines

Benzodiazepines (BZD) have an anxiolytic, hypnotic, sedative, centrally muscle relaxant and anticonvulsant effect. Due to their properties this drugs are widely used in the treatment of panic attacks, anxiety disorders and sleep disorders. These states are characteristic for the elderly. BZD are one of the most prescribed classes of psychotropic drugs in USA [13,14]

The use of benzodiazepines is significantly higher in the elderly compared to younger adults. [9] Moreover use of them in clinical practice has a number of advantages such as efficacy, speed and versatility. While safety is considered the greatest asset of BZD, it can induce cognitive side effects such as asthenia and most importantly abuse and addiction. [10,11] Older people are more likely to experience BZD side effects than younger people because of their increased sensitivity to BZD and impaired metabolism [12].

Several studies have shown that, in relation to the elderly, BZD was prescribed more often by a primary care physician than by psychiatrists. This is often the reason for delayed administration of the first psychopharmacological treatment appropriate to patients factual state. Therefore it can lead to an increase in the duration of untreated conditions such as depression and anxiety disorders. [13]

Prescribing benzodiazepines alone carries a high risk of suicide, even when they are not used as a suicide measure. The mechanism by which prescribed benzodiazepines are associated with suicide in the elderly population is unclear. BZG use was noticeably more frequent in the suicide group than in the group that did not commit suicide. [15]

Long-term use of benzodiazepines in the elderly population is a serious public health problem. BZD is an important clinical tool, and while it can rapidly alleviate anxiety, clinicians should be aware of concerns about suicide risk, abuse, and addiction . BZG should be discharged at the lowest possible dose for the shortest possible period. [16] In many patients in the elderly population, BZD should be withdrawn and therapeutic strategies other than BZD should be considered for the management of anxiety and insomnia in these patients. [17] Suicidal tendencies should be screened in regard to elderly patients who were engaged in or at risk for prescription medication misuse. [9]

Opioids

Opioids are drugs that are used to control pain. Their mechanism of action is based on binding to opioid receptors in the central nervous system and the subsequent reduction of pain signal transmission to the brain. Opioids also bind to receptors in the gastrointestinal tract and respiratory system, therefore, apart from treating pain, they are also used to treat diarrhoea and cough [18].

Opioids are used to treat patients with severe, chronic pain that does not respond to other therapies. Unfortunately, opioid use carries risks for patients, including abuse, dependence, and overdose deaths. Mortality from opioid use is higher in middle-aged people with a history of substance abuse and comorbid mental illnesses [19].

A potentially life-threatening side effect of opioids is respiratory depression. The main cause of death is cardiac arrest with hypoxia and hypocapnia. The μ -opioid receptors located in the central nervous system on respiratory neurons participate in the mechanism of respiratory depression [20].

Opioid overdose mortality in the United States continues to increase. Unfortunately, it is difficult to precisely determine what percentage of them are suicidal. According to estimates by the Centres for Disease Control and Prevention (CDC), suicides account for approximately 7% of all opioid overdose deaths. Opioids may lead to the occurrence of opioid use disorder (OUD) and thus cause abnormalities in the course of mental processes, including the reward system [21].

Q. Vu et al. conducted a study in 2010-2013 to record cases of opioid overdose in hospitalized patients, based on orders for naloxone, which is a pure opioid antagonist. Among the checks on age information, gender, data checks, and opioid collection, inflammation control, comorbidities, and the use of depressants on the nerve centre. Among the significant risk factors associated with opioid overdose, distinguished above 65 years, staying in the ICU, disorders, disorders, concomitant heart disease and drugs depressing the main nervous system. [22]

The study by Sinyor et al. Investigated all suicides with or without opioid poisoning in Toronto in 1998-2015. The study confirmed that opioids are the main contributor to suicide in Toronto [23].

Oliva et al. Conducted a study to investigate the relationship between opioid discontinuation, treatment duration, and death from overdose or suicide in 1,394,102 Veterans Health Administration patients. There were 2,887 deaths due to overdose or suicide. It was observed that patients were more likely to die from overdose or suicide after the end of opioid treatment, and the risk was proportional to the time of taking the drug before its discontinuation [24].

In a study conducted by Karbakhsh et al. to present the poisoning pattern in the older Tehran population (60 years and older), it was shown that of all patients with acute poisoning who stayed in the emergency department of a hospital over a 6-month period, 32.4% were a suicide attempt. Opioids accounted for 54.02% of the substances that led to poisoning. Opioids were also the main factor responsible for deaths [25].

A study by Olie et al. Aimed to determine whether elderly people (over 65 years of age) with a history of suicide attempts have a higher rate of pain medication use compared to patients with depression and control group. It was shown that the consumption of opioids was higher in the groups with a previous suicide attempt and depression. It is believed that suicidal susceptibility in this group may be associated with an increased sensitivity to pain [26].

In a study by Schepis et al. on a group of patients 50 years of age and older ($n = 17,608$), it was shown that prescription opioid abuse was associated with suicidal ideation in elderly people in the United States [27].

Parkinson's drugs

Parkinson's disease (PD) is one of the most common chronic neurodegenerative diseases in the elderly and occurs in about 5% of people over 85 years of age. PD is characterized by a progressive loss of dopaminergic (DA-ergic) neurons in the Substantia Nigra (SN) in the midbrain [28]. Patients with PD usually show resting tremor, stiffness, bradykinesias and a bent posture. PD may also be associated with neurobehavioral disorders (depression, anxiety) [29], cognitive disorders (dementia) and autonomic disorders (e. g. orthostasis and hyperhidrosis) [30].

Dopaminergic agonists (dopamine precursors) such as levodopa are the gold standard in Parkinson's disease [31]. This drug was approved by the U. S. Food and Drug Administration in 1970. It is absorbed by the intestine via active transporters of large neutral amino acids (LNAA), transported to the brain and converted into dopamine [32]. Levodopa is usually used in combination with a DOPA decarboxylase inhibitor such as carbidopa. This adjuvant prevents the peripheral degradation of levodopa and thus increases the bioavailability of levodopa. [33] It reduces the frequency and intensity of motor symptoms caused by dopamine deficiency. It is a so-called dopamine replacement therapy (DRT) [34]. It can also be used in restless legs syndrome [31].

Long-term use of levodopa may result in serious adverse reactions such as orthostatic hypotension, hallucinations and impulse control disorders (including pathological gambling, compulsive eating, compulsive shopping and hypersexuality) [31,35]. One way to reduce these effects is to stop DRT therapy. However, cases of dopamine agonist withdrawal syndrome (DAWS) with symptoms such as anxiety, panic attacks, dysphoria, depression, agitation, irritability, suicidal ideation, fatigue, orthostatic hypotension, nausea, vomiting, sweating, generalised pain and drug hunger have been reported. [31,34] These symptoms lead to significant strain or impairment of social/occupational function and may lead to suicide [34].

Levodopa is not the only medicine for Parkinson's disease that may be associated with an increased risk of suicide. Three treatment modes were compared: deep hypothalamic stimulation (STN-DBS), subcutaneous apomorphine in combination with oral levodopa and duodenal levodopa. A long-term infusion of apomorphine has been shown to be associated with impaired impulse control and STN-DBS may lead to behavioural changes leading to suicide attempts. The greatest benefit and least side effects were from the use of duodenal levodopa [36].

The severity of side effects depends on how levodopa is used. A newer treatment method, the gastro-resistant levodopa/carbidopa gel (LCIG), which can be administered directly into the fasting intestine, provides

continuous dopaminergic stimulation. There is also a lower incidence of adverse reactions compared to oral administration. However, there are also other challenges, such as invasive procedures with percutaneous endoscopic gastrostomy and surgical and postoperative complications. There are also problems with the pump and the hose. In addition, polyneuropathies and vitamin deficiency may occur. [37]

An association between the severity of the side effects of levodopa was found when a test that differentiates PD from atypical Parkinsonism (Acute Levodopa Challenge, ALC) was used. In atypical Parkinsonism, the incidence of adverse reactions may be up to twice as high as the typical formulation. During ALC, nausea, vomiting, confusion, drowsiness, dizziness and general malaise may be observed [38].

B-blockers

B-blockers are commonly used drugs among the elderly in the treatment of hypertension, arrhythmias, heart failure or in secondary prevention of myocardial infarction [39,40]. Side effects related to the central nervous system resulting from the use of β -blockers include: poor sleep, fatigue, hallucinations and depression [41]. The lipophilicity of β -blockers influences their passage through the blood-brain barrier, β -blockers with high lipophilicity, such as metoprolol, are easier to pass than β -blockers with low lipophilicity, eg atenolol [42].

In 1967, there was described the first possible relationship between β -blockers and depression in patients who took propranolol [43]. There are several studies on the influence of propranolol on the occurrence of depression in the available literature, some indicate an increased incidence of depression in patients taking propranolol [44,45], while other studies have not shown the depressant effect of β -blockers [46,47].

The mechanism of the influence of β -blockers on mood is not fully understood, but it has been suggested that it may be due to decreased β -adrenergic transmission in the central nervous system. Other studies suggest blocking serotonergic receptors by β -blockers, while propranolol has a greater affinity for serotonin receptors than atenolol [48]. Studies have shown increased prescription of antidepressants to patients taking β -blockers, which was more common in patients taking propranolol [49].

Two observational studies have been conducted to investigate the relationship of β -blockers with the risk of suicide. One of these studies showed an association of lipophilic β -blockers with suicide. On the other hand, the second one, which included various classes of drugs used in cardiovascular diseases, did not show a significant relationship between β -blockers and the risk of suicide [50, 51]. Due to the limited number of studies and inconclusive results, more research is needed to better understand the relationship of β -blockers with the risk of suicide in the elderly.

Summary

Suicide in the elderly may be more frequent than in other age groups, and is associated with multiple morbidity, a lowered standard of living, and the use of medications that can induce symptoms of depression.

Due to the emergence of depression in old age, panic attacks, anxiety disorders and sleep disorders, benzodiazepines are used. Studies have shown that elderly people were more likely to experience side effects from this class of drugs and were associated with a higher risk of suicide.

Chronic diseases are also accompanied by pain. One of the most frequently used groups of drugs in the treatment of pain, but also in the treatment of diarrhoea and cough, are opioids. The mortality after opioid overdose in the United States is constantly increasing, some of the overdose patients are elderly people after suicide attempts. Opioid consumption was shown to be higher in groups with prior suicide attempt and depression.

Parkinson's disease is one of the most common neurodegenerative diseases. When used in the treatment of PD, levodopa in long-term therapy may cause serious side effects such as postural hypotension, hallucinations and impulse control disorders, and may lead to suicide. The above information suggests that suicidal thoughts may be due both to the use of levodopa (mainly orally) and to Parkinson's disease itself.

Beta-blockers are commonly used drugs among the elderly in the treatment of cardiovascular diseases. One of the side effects of B-blockers can be depression. This compound is especially exhibited by propranolol. The mechanism of the influence of beta-blockers on mood is not fully understood, but it has been suggested that it may be due to a reduction in beta-adrenergic transmission in the central nervous system. Due to inconclusive results, more research is needed.

Particular care should be taken when treating elderly, multi-disease patients with comorbid depression, bearing in mind the possible side effects of drugs, such as worsening mood or an increased risk of suicide. If possible, choose drugs from a different group, devoid of these side effects.

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