Review

https://doi.org/10.23934/2223-9022-2021-10-4-719-727

Self-Poisoning with Antihypertensive Drugs: Clinical, Psychological and Sociodemographic Factors and General Approaches to Prevention

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ABSTRACT The study of the clinical group of patients with self-poisoning with antihypertensive drugs is an urgent complex task due to its heterogeneity, high comorbidity of somatic and mental (depressive) disorders, as well as combination of a number of unfavorable social and environmental stress factors. In the present review, based on identifying the relatively specific psychological and sociodemographic groups, and risk factors of self-poisoning antihypertensive drugs the necessity of clinical-psychological support of patients with self-poisoning. General principles of suicide prevention among the groups most at risk in the primary care network formulated.

Keywords: self-poisoning with antihypertensive drugs, risk factors, prevention of depressive disorders and suicidal behavior

For citation Pugovkina OD, Kholmogorova AB, Pockhveriya MM, Sukhodolova GN. Self-Poisoning With Antihypertensive Drugs: Clinical, Psychological and Sociodemographic Factors and General Approaches to Prevention. *Russian Sklifosovsky Journal of Emergency Medical Care*. 2021;10(4):719–727. https://doi.org/10.23934/2223-9022-2021-10-4-719-727 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study has no sponsorship

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INTRODUCTION

The problem of self-poisoning with antihypertensive drugs and their prevention is becoming relevant due to the prevalence of cardiovascular diseases, which often involve the regular use of antihypertensive drugs. Although it is not of an acute epidemiological nature (5% of all poisonings), due to its interdisciplinary status, it highlights many aspects of medical, psychological and social support for a large group of patients, primarily those with cardiovascular diseases and, more broadly, the elderly age with severe somatic and mental disorders. The relevance and practical significance of the analysis of socio-demographic and clinical factors of self-poisoning by antihypertensive drugs is determined by the sufficient prevalence of this type of self-poisoning and the large number of risk groups. According to statistics, moderate, severe, and extremely severe acute poisonings with antihypertensive drugs account for 5% of all poisonings and 10–11% of drug poisonings [1, 2]. Mortality is up to 6.5% [3].

It should also be noted that a significant part of antihypertensive drugs is included in the List of vital and essential drugs and is widely available to the population [3, 4].

Prescribed antihypertensive drugs are taken by a large contingent of patients, since arterial hypertension is one of the most common diseases of the cardiovascular system. According to Russian epidemiological studies, only among men under the age of 65, the incidence of this disease is 49%, and among women - 40%. At the same time, about 42% of men and 62% of women take drugs to lower blood pressure [5], while both accidental and intentional violations of the dosage and frequency of taking antihypertensive drugs are often encountered, which leads to acute poisoning.

The problem of the intentional use of prescribed course drugs or, more broadly, OTC drugs for the purpose of self-poisoning has long been discussed in medicine [1, 6, 7]. In some cases, taking antihypertensive drugs is a type of suicidal behavior, that is, self-poisoning is not a violation of the prescribed regimen, but acts as a suicide method [1, 8].

The main place among antihypertensive drugs is occupied by drugs belonging to the groups of β-blockers, slow calcium channel blockers and angiotensin-converting enzyme inhibitors. Some of them, especially in combination with cholesterol-lowering drugs, are associated with an increased risk of developing depressive disorders [8]. In the context of the problem of self-poisoning as a form of suicidal behavior, it is important to take into account these risk mechanisms.

The aim of the study was to identify the socio-demographic and psychological characteristics of patients with self-poisoning with antihypertensive drugs based on the systematization of empirical data and the identification of common prevention targets.

1. THE PROBLEM OF SYSTEMATIZATION OF EMPIRICAL DATA AND APPROACHES TO THE STUDY OF SELF-POISONING BY ANTIHYPERTENSIVE DRUGS

When trying to identify the characteristics of the target group of patients with self-poisoning with antihypertensive drugs, a number of objective and methodological problems of study arise. These patients represent a heterogeneous group and rarely become the target sample for a systematic study of risk factors for self-poisoning by this particular group of drugs. The subject of study is mainly various aspects of medical rehabilitation measures and general principles for the admission and management of patients with acute self-poisoning, which are determined by the nature of pathological processes - rapid and progressive development (for example, [4, 9–11]).

The available epidemiological and clinical-psychological studies are devoted to the study of broader issues: comparative statistics of different methods of suicide [12-14], the prevalence of depressive disorders among patients with severe somatic diseases [15-18], problems of medical and social support for elderly and senile people [12, 19, 20]. In each of these areas, patients with self-poisoning with antihypertensive drugs do not occupy the first positions in terms of morbidity and mortality, but their number is a stable proportion.

With limited sample sizes, individual studies have to deal with very heterogeneous data. For example, the age of patients included in studies of self-poisoning with antihypertensive drugs ranges from 18 to 87 years. Some studies pre-limit the age range of patients with self-poisoning [19, 21–24] to advanced age. Together with the shift in the sample by the average age, this also shifts the focus of the study, since factors associated with the age and social situation of older patients acquire a greater share. In connection with such heterogeneity, the descriptions of the socio-demographic profile of patients with self-poisoning [4, 13] available in the literature, for example, require additional data for a meaningful interpretation.

Regardless of age, women predominate among patients with self-poisoning by antihypertensive drugs (from 65 to 78% in different studies) [4, 13, 19]. All studies draw attention to concomitant mental disorders (about 80%, mainly depression) and somatic diseases (about 60%), which are themselves associated with the risk of occurrence and chronicity of depression and suicidal risk [8]. A number of patients have a comorbid diagnosis of alcohol misuse. Thus, the characteristics of the samples and inclusion criteria largely determine the results, and the limitation of most of the available works is the inability to separate the specifics associated with the age, gender, and clinical status of the patient from the specifics associated with the drug used for self-poisoning.

We also note the heterogeneity of the structure of the episode of self-poisoning when using the same antihypertensive drugs. Situations of self-poisoning include intentional suicide attempts, cases of overdose or violation of the frequency of taking a regularly taken drug, as well as accidental drug use.

Such a complex overlay of research samples makes it difficult to interpret the results.

Thus, the following can serve as grounds for systematizing the available empirical data: 1) age characteristics of patients with suicidal attempts; 2) clinical and psychological characteristics of patients taking antihypertensive drugs according to indications; 3) pharmacological properties of some drugs that have an antihypertensive effect, increasing the risk of developing depressive disorders (β -blockers). The structure of the episode of self-poisoning (deliberate or accidental intake of drugs) also needs to be taken into account.

In this regard, the main part of the review is devoted to the factors of intentional self-poisoning, or suicidal risk factors among the main risk groups, and then the factors of accidental poisoning by antihypertensive drugs will be analyzed. In conclusion, the general principles of prevention and medical, psychological and social support of patients with self-poisoning by antihypertensive drugs are formulated.

2. CLINICAL AND PSYCHOLOGICAL CHARACTERISTICS OF PATIENTS TAKING ANTIHYPERTENSIVE DRUGS ACCORDING TO INDICATIONS

2.1 Clinical characteristics; combination of cardiovascular and anxiety-depressive disorders

The literature has accumulated a significant amount of data on risk factors for suicidal behavior in various types of chronic or severe somatic pathology, including oncological, cardiovascular, neurological, mental diseases, lung and kidney diseases, diabetes mellitus, epilepsy, AIDS, and others [16, 17]. In these studies, suicidal behavior includes various forms - hanging, falling from a height, self-poisoning with analgesics, psychotropic, antihypertensive and other drugs. Types of suicidal behavior are almost never singled out as a variable for analysis, and the focus of research affects the specifics of the clinical picture, factors associated with treatment, prognosis, the presence of pain, etc.

The most common factors of suicidal behavior in severe somatic pathology are social inequality, unemployment, loneliness, demoralization, a sense of burden on oneself and others, pain syndrome, dissatisfaction with everyday help, concomitant mental disorders, primarily depression.

The group of self-poisoning with antihypertensive and antiarrhythmic drugs is distinguished only in the study of suicidal behavior in patients with cardiovascular diseases. In this group, the frequency of using these drugs for the purpose of self-poisoning is about 12-14%, which is the second place after psychotropic drugs [1, 16, 25].

Studies indicate the highest, compared with other diseases, association of cardiovascular pathology with mental disorders [15], although a direct link between cardiovascular diseases and suicide is not so unambiguously confirmed [26]. The risk of suicidal behavior also increases with drug-lowering cholesterol levels (in men) [8].

M.S. Umansky et al. (2017) analyzes the relationship between suicide and cardiovascular disease. While precise statistics are not available, it is indicated that cardiovascular disease may be the leading cause of suicide (21.6% of men and 34.4% of women). Suicidal risk is primarily increased by anxiety and depressive disorders, which determine suicidal ideas in every tenth patient with cardiac ischemia. It is important to note a direct correlation between depression and reduced adherence to therapy, which in some cases may also indicate suicidal activity [26–28].

As objective statistics, the authors of [26] use data on cardiotropic drugs used for self-poisoning. Cardiovascular drugs (especially antihypertensive and antiarrhythmic drugs) are consistently ranked second after psychotropic drugs in the structure of drugs used for suicide. Moreover, studies conducted in different regions of the country give very similar figures: Nizhny Novgorod - 12.6%, Tyumen - 13.5%. From this, a conclusion is drawn about the high prevalence of suicidal moods among cardiac patients, which, however, are not recorded [15, 26, 27].

The problem of high comorbidity of cardiovascular and anxiety-depressive disorders is studied in different aspects: epidemiological data, pathogenetic mechanisms of the relationship of disorders, a complex of psychosocial factors, the role of stress in the development of the disease. The patterns identified in large clinical groups of patients with cardiovascular and comorbid anxiety-depressive disorders seem to be essential for understanding the factors of intentional self-poisoning by antihypertensive drugs.

Thus, in epidemiological studies of comorbidity, it is noted that among patients with cardiovascular disorders, clinical depression is detected in 17–27% [29, 30]; about a third of patients (14-45%) are diagnosed with depression during their stay in the hospital and immediately after discharge [31]; after 3–4 months, depressive states are detected in up to 33% of patients [32].

It has been established that depression and cardiovascular diseases have a two-way relationship: there is an increased risk of cardiovascular disorders in patients with depression [15]. Thus, depression increases the risk of cardiovascular diseases by an average of 1.5 times (depending on the specific diagnosis) [15] and significantly worsens the course of the disease, even compared with a combination of several chronic diseases [33]. Symptoms of depression increase the risk of recurrent acute conditions associated with cardiovascular pathology [34]. Among the factors linking depression and cardiovascular disease, there are both behavioral (passivity, inactivity, late seeking help and low treatment adherence) and physiological (inflammatory cytokine processes and increased platelet activity). An important role is assigned to psychological distress, which often acts as a mediator between behavioral aspects and environmental influences, on the one hand, and the activation of the pathogenetic mechanisms of the disease, on the other [15].

Thus, it is possible to emphasize the role of timely detection of symptoms of depression, both directly for correcting the emotional state and for strengthening compliance in the treatment of the underlying disorder and preventing the negative impact of depression on the course of the disease.

The development of depressive symptoms immediately after the patient's acquaintance with the diagnosis is considered as a variant of an acute reaction to stress. Heading F43.8 in the ICD-10 describes nosogenic anxiety and depressive reactions that occur in connection with a somatic disease (ICD-10, 1998). Foreign authors [31] propose to specifically consider the diagnosis of post-traumatic stress disorder in relation to patients with cardiovascular diseases and distinguish the so-called post-traumatic stress syndrome induced by a cardiac disease (CDI-PTSD). In addition to these two diagnostic categories for depressive states that occur against the background of a somatic disease, a special “demoralization syndrome” is distinguished [35]. This is due to the fact that the complex of symptoms that occurs in patients may not fully meet the criteria for a depressive episode, but still require consideration in therapy and support.

Thus, in relation to intentional hypotensive self-poisoning, from the data presented, the role of timely detection of symptoms of anxiety and depressive disorders, which are a very common and often underestimated factor in the course of cardiovascular disorders, should be emphasized. It can be emphasized that affective disorders can act as a predisposing factor in relation to cardiovascular pathology, and can occur at different stages of the disease (manifesto, familiarization with the diagnosis, in the delayed period of the disease). Therefore, it makes sense to supplement the routine prescription of antihypertensive drugs with screening for the risk of developing symptoms of depression and suicidal behavior. A particular indication of the need for such screening or specialized consultation may be low adherence to treatment in patients.

2.2 Psychological characteristics: personality pattern of the cardiometabolic risk group

Cardiovascular diseases are distinguished by a high contribution of psychological and other environmental factors - about 2/3 of the cardiometabolic risk factors are related to the patient's lifestyle. Despite the fact that the personal profile and the profile of the emotional response of patients with arterial hypertension (let us recall that these patients are about 12-14% of patients with intentional self-poisoning with antihypertensive drugs) are quite well studied, the results of these clinical and psychological studies are little implemented in the practice of supporting patients in the primary health care network [16, 29, 36].

The profile of emotional response manifests itself in symptoms of anxiety, depression, interpersonal sensitivity, loneliness and hopelessness, difficulties in cognitive processing of stress (rumination), magical thinking, and some others [15, 28, 36, 37].

The main individual psychological factors that contribute to the chronicity of emotional disorders and the emergence of suicidal risk in patients with cardiovascular diseases include the following:

ruminations are repetitive cyclical thoughts about feelings, thoughts and problems that are fruitless, unproductive and crowd out other constructive mental processes aimed at real resolution of life problems. The tendency to constantly analyze oneself and one's problems is accompanied by a feeling of grief and hopelessness [38, 39];

anxiety - chains of negatively charged and relatively uncontrollable thoughts and images, which, like ruminations, are an example of persistent negative thinking, however, "restless" thoughts are more often focused on catastrophic images of the future, while ruminative thoughts focus on the past [38, 40, 41];

demoralization - capitulation to the need to process the stress of the disease, a persistent inability to cope with powerlessness, helplessness, a sense of incompetence associated with the loss of meaning and purpose in life [35];

hopelessness is a negative attitude towards one's own future, which is expressed in the absence of a life perspective and the loss of the meaning of searching for this perspective. This characteristic is one of the most important predictors of suicide [40, 42].

The psychosocial characteristics of the profile of patients with cardiovascular disorders include chronic stress, lack of social support, and lack of social integration [36]. As a result of summarizing numerous studies, complex personality profiles were identified that are typical for the cardiometabolic risk group and are known under the names of type "*A*" personalities ("hurry sickness" is a motor-emotional complex that includes an energetic style of behavior, aggressiveness, impatience, and a mood to achieve a goal) and type "*D*" (tendency to experience negative emotions, neuroticism combined with a tendency to restrain the expression of feelings and social distancing).

It should be noted that various types of compact and effective interventions (psychoeducational and short-term psychotherapeutic programs) aimed at identifying and correcting these traits have been developed to date [40]. Examples are metacognitive training for depressed patients [43], mindfulness -based stress reduction (*MBSR*) cognitive-behavioral psychotherapy as the basis for stress reduction [44].

These interventions can be used as target-oriented means of preventing self-poisoning by antihypertensive drugs both in the group of patients taking them as prescribed, and in other risk groups, which will be discussed below.

2.3 Socio-demographic characteristics and social stressors

The analysis of the age distribution of persons with self-poisoning by antihypertensive drugs gives a contradictory picture. On the one hand, as mentioned above, some of the studies that can be used for analysis limit the age range of patients with self-poisoning to older age as an inclusion criterion [19, 21–24]. This is partly due to epidemiological data: self-poisoning is the most common type of suicidal behavior in the elderly and accounts for about 20% of all completed suicides [12, 19]. Researchers pay attention to the combination, on the one hand, of the presence of a number of somatic and / or mental disorders as sources of pain and suffering, and on the other hand, access to drugs prescribed for course administration to control symptoms.

At the same time, it should be noted that both in the 90s and today, suicidal behavior in elderly patients remains the least studied, which indirectly confirms the relevance of separating self-poisoning with antihypertensive drugs into a separate area of research, despite the fact that, in terms of frequency of use in intentional self-poisoning, antihypertensive drugs are significantly inferior to psychotropic drugs (benzodiazepines and antidepressants) [19].

In the study of elderly patients, factors of loneliness, isolation, symptoms of real or perceived helplessness, social isolation, and latent protracted family conflicts are generally singled out as factors of suicidal behavior [19].

In separate naturalistic studies, several more characteristics of suicidal behavior in old age have been identified. It is noted that about 60% of patients who committed intentional self-poisoning with drugs prescribed for course intake suffered from chronic physical problem, 80% had a history of chronic depressive disorder, while only a third of them sought psychiatric advice. These data indicate the role of chronic stress in connection with somatic pathology and pain syndrome [12, 19].

In the group of women, a certain calendar pattern was identified: significantly more often suicidal attempts were made in the winter months (January, February, March) and on certain days of the week (Mondays, Fridays). There were no such patterns in the group of men. About half of the patients were married, 30% were widowers, 8% were divorced, and 14% had never been married. The age of patients included in the study was 65–91 years [19].

However, the age of patients who commit self-poisoning with antihypertensive drugs is not limited to the elderly and senile. In statistics and studies, there are patients from 15 to 91 years old. Moreover, an analysis of the distribution by age shows that elderly and senile people make up no more than 30% in different years. The largest group (about 50%) is made up of persons aged 30 to 60 years, and it is important to note the increase in the proportion of patients under 20 years of age from 5.2% in 2010 to 8.3% in 2014 [4]. Thus, the problematic tendency of the growth of self-poisoning by drugs acting on the cardiovascular system among people of working age is emphasized [4].

Studies of psychosocial risk factors for suicidal behavior, regardless of age, are culturally specific. For example, in India, the most significant are unemployment, lack of education, stressful events within the last 6 months, somatic disorders and pain syndrome [45]. Western European and American studies emphasize the

contribution of family status (disturbances in the family system), early loss of parents, the presence of a mental disorder, suicide in the family history, high levels of life stress and stress in the interpersonal sphere.

In the context of this review, the results of one of the recent studies of suicidal experiences in patients with hypertension are important, in which it was shown that it is psychological distress that mediates the relationship of other psychosocial factors (gender, economic and marital status, substance misuse, etc.) with suicidal intentions and behavior [25].

Thus, with regard to self-poisoning with antihypertensive drugs, we can conclude about the role of psychological distress and the lack of psychological means of its constructive processing. These factors mediate the contribution of heterogeneous socio-demographic, psychosocial characteristics, the content of patients' life stress and can be targets for prevention and comprehensive support.

3. PHARMACOLOGICAL PROPERTIES OF SOME ANTIHYPERTENSIVE DRUGS THAT INCREASE THE RISK OF DEVELOPING DEPRESSIVE DISORDERS

Several studies have shown that some antihypertensive drugs may increase the risk of suicide [8]. One large study in the 1990s analyzed 58 529 patients receiving antihypertensive and antiarrhythmic therapy (β-blockers, calcium channel blockers, angiotensin inhibitors). It was shown that in the group of patients taking β-blockers, the risk of suicide was higher than in the population. It was also noted that the risk of suicide increased in the first 12 months after the start of therapy and within a year after the interruption of therapy. The risk of suicide was lower with drugs with low lipid solubility compared with drugs with medium and high lipid solubility [8].

The use of individual drugs in routine practice is analyzed. It has been shown, for example, that propranolol (prescribed to normalize the work of the heart muscle and has hypotensive, antianginal and antiarrhythmic effects) in case of overdose leads to rapid and pronounced disorders, and therefore it is not recommended to prescribe it in specific risk groups (for example, anxious patients who interpret their sensations catastrophically and risk overdosing) [46]. Reports on individual clinical cases are important, which indicate the need for screening the emotional state of patients when prescribing antihypertensive therapy. There are case reports in the literature that show that antihypertensive drugs are dangerous not only in terms of overdose (intentional or accidental), but also in terms of the risk of intense development of affective disorders. For example, *Ullrich et al*. [47] reported a case of a severe depressive episode and a suicide attempt in a 43-year-old female patient after 4 weeks of taking a combination of valsatran and hydrochlorothiazide as antihypertensive therapy. It is noted that the episode of depression resolved spontaneously without additional treatment within 10 days after discontinuation of antihypertensive therapy.

CONCLUSION

Research prospects. Principles of prevention and comprehensive support of patients with self-poisoning by antihypertensive drugs

Summarizing the results of the review, we should return to the idea that a heterogeneous group of patients with self-poisoning with antihypertensive drugs is a challenge for interdisciplinary study and identification of specific prevention targets. However, for both intentional and accidental self-poisoning, a number of provisions can be formulated regarding the prevention of suicidal behavior and the optimization of comprehensive patient support.

With regard to accidental self-poisoning with antihypertensive drugs, violations of dosages and frequency of administration in the primary medical network, psychoeducational work, the development of psychohygiene skills, accurate and accurate interpretation of physical symptoms, strengthening compliance and adherence to treatment, taking into account the cognitive characteristics of the contingent recommended for course antihypertensive therapy, are important.

In relation to all risk groups of self-poisoning with antihypertensive drugs, there is a significant contribution of psychosocial factors and the role of psychological distress, which mediates the relationship between stressful life circumstances and the activation of suicidal behavior. In addition, in relation to all major risk groups (elderly patients, patients with cardiovascular and comorbid anxiety-depressive disorders), there are insufficient detection and accounting of symptoms of affective disorders and signs of suicidal risk.

It has been shown that patients with intentional self-poisoning, compared with those who use more brutal forms of suicidal behavior, are distinguished by a greater number of external signs that can be used to predict suicidal risk. These patients show clear symptoms of depression, or at least marked changes in mood compared to normal. One can track a decrease in interest in ordinary activities, individual episodes of reckless, atypical

actions, as well as steps to plan and search for means of poisoning [48; 49]. These data highlight the role of the primary health care network in identifying the risk of suicidal behavior; training primary care staff to detect depression and suicidal ideation is one of the few scientifically proven effective elements of prevention [50].

Approaches to the prevention of suicidal behavior traditionally emphasize the role of adequate treatment of the underlying disease, understanding by this the quality of everyday care in the broad sense of the word: timely diagnosis, informed consent, a team approach to managing a patient with the involvement of mental health professionals and relatives of the patient [50]. It is noted that the staff of medical institutions is not sufficiently aware, vigilant and focused on identifying emotional disorders and suicidal risk [50, 37]. The tendency of the medicalization of the therapeutic environment to the detriment of establishing therapeutic relationships and increasing the compliance of patients, as well as the underestimation of the potential of interdisciplinary interaction of specialists, is emphasized.

Supporting the patient after an episode of self-poisoning also plays an important role, including correct algorithms for discussing the diagnosis, psychoeducation, screening and monitoring of depression and substance misuse, psychorehabilitation measures for the patient's family [51], doctors involved in the management of the patient, and other possible witnesses [16 , fifty].

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Received on 01/27/2021

Review completed on 02/10/2021

Accepted on 06/29/2021