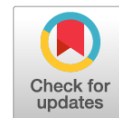


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Обзор факторов, влияющих на формирование ремиссии у наркологических больных

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АННОТАЦИЯ

Введение. Достижение устойчивой ремиссии пациентами с синдромом зависимости от психоактивных веществ — основной критерий качества наркологического лечения и приоритетная задача терапии. В статье проводится обзор факторов, влияющих на становление ремиссии у пациентов с психическими и поведенческими расстройствами, вызванными употреблением психоактивных веществ. Исследования за последние 15 лет рассматриваются по пяти основным группам факторов становления и срыва ремиссии: биологическим (пол, возраст, генетические параметры, органические поражения головного мозга и др.); наркологическим (течение заболевания, возраст первой пробы и др.); личностным и патопсихологическим (когнитивные нарушения, коморбидные психические расстройства, психологическая травма и др.); социальным (трудоустройство, семейная и социальная ситуация, социальная поддержка и др.) и терапевтическим (длительность и методы лечения, терапевтический альянс и др.).

Заключение. Существуют базовые, подтверждаемые от исследования к исследованию факторы благоприятного прогноза течения наркологических заболеваний: позднее начало заболевания, отсутствие сопутствующего синдрома зависимости тяжелого психического расстройства, вовлеченность в долгосрочные лечебно-реабилитационные программы, продолжающиеся и после формирования ремиссии.

Ключевые слова: наркологические заболевания; устойчивая ремиссия; срыв; рецидив; факторы

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Review of Factors Affecting Remission in Narcological Patients

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ABSTRACT

INTRODUCTION: Achievement of a sustained remission in patients with substance dependence syndrome is the main criterion of the quality of narcological treatment and a priority treatment task. The article presents a review of factors that influence remission in patients with mental and behavioral disorders resulting from use of psychoactive substances. Studies performed in the recent 15 years, consider the main five groups of factors for development and failure of remission: biological (gender, age, genetic parameters, organic lesions of the brain, etc.), narcological (course of the disease, age at the first use of a drug), personality and pathopsychological (cognitive disorders, comorbid mental disorders, mental trauma, etc.), social (employment, family and social situation, social support, etc.) and therapeutic factors (duration and methods of treatment, therapeutic alliance, etc.).

CONCLUSION: There are basic factors of favorable prognosis of the course of narcological diseases that are confirmed from study to study: late onset of the disease, absence of a comorbid dependence syndrome and of a severe mental disorder, involvement in long-term treatment and rehabilitation programs that continue after remission.

Keywords: *narcological diseases; sustained remission; failure; relapse; factors*

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LIST OF ABBREVIATIONS

AD — alcohol dependence (alcohol dependence syndrome)

PAS — psychoactive substance

INTRODUCTION

Achieving stable remission in patients with psychoactive substance (PAS) dependence syndrome is the main criterion of the quality of narcological treatment and the priority task of therapy. A meta-analysis of 21 prospective studies of dynamics of the substance dependence syndrome with a follow-up period not less than 3 years showed that up to 54.4% of patients of narcological profile achieved remission on average only after 17 years of follow-up [1]. These data reflect difficulties that patients face on the way to recovery, and emphasize the need for further effort for development of prevention and treatment methods that could make this way shorter and easier.

Remission in narcological patients is determined by a variety of factors: *biological* (gender, age, genetic parameters, organic lesions of the brain, etc.); *narcological* (course of the disease, progression rate, age of the first use of drug, type of use, etc.); *personal* and *pathopsychological* (personality traits, neuropsychological and cognitive-mnemonic disorders, comorbid mental diseases, mental trauma, etc.); *social* (employment, family and social situation, social support, etc.), *medical* and *rehabilitation* (duration and methods of treatment, therapeutic alliance, etc.) [2–6].

In this review, we will focus on the characteristics of the most striking and informative factors of the above identified groups.

Biological Factors of Remission

Sex and gender. Data on the influence of sex on the formation and quality of remissions are scarce and contradictory [7, 8], but in general there are no significant differences between men and women in the results of treatment [9]. There is some evidence that men have a higher risk of development of the disease and are much less likely to achieve remissions [7], the duration of which is also shorter than remissions in women [10]. As for *gender peculiarities*, the protective prognostic factor of stable remission was found to be the feminine type of gender in both men (53.5% of cases) and women (38.7% of cases), and the androgynous type in men (50% of cases) [11].

Age and ethnicity. Several large studies and meta-analyses have demonstrated a higher risk of relapse and

less persistent remission in young white adults [3, 12] compared to people of more mature age [2, 13].

Genetic predictors. In a double-blind placebo-controlled randomized study, it was found that the genes of the opiate and dopamine systems of the brain influence the stabilization of remission in patients with opiate dependence syndrome during treatment with subcutaneously implanted naltrexone [14]. In the course of study of the effectiveness of treatment of alcohol dependence (AD; syn.: *alcohol dependence syndrome*) with pregabalin, a number of genetic markers of long-term keeping of patients in the program and stabilization of remission were found; longer duration of remission before relapse was associated with the *LL DRD4 48 bp* variant (dopamine system), and a rapid relapse was associated with the *GG DRD2 Nco I rs6275* marker [15].

Specific disorders of the functional state of the brain. In the group of patients with unstable remission, reduced power of the θ - and α -rhythm is observed [16]. Significant predictors of a high risk of relapse were reduction in the volume of the right caudal and right rostral parts of the anterior cingulate cortex and of gray matter of the entire right frontal lobe [17] — areas responsible for cognitive and emotional control and self-regulation.

To identify patients with a high risk of relapse, **blood parameters** are used. In a prospective (6-month follow-up) study of 133 patients with AD after inpatient detoxification treatment, a greater risk of relapse, fewer sober days, greater daily tolerance and shorter periods of continuous abstinence from alcohol were found in patients with alanine aminotransferase/aspartate aminotransferase ratio > 1.00 and average corpuscular erythrocyte volume > 90.0 femtoliters [18]. In another study, alcohol-dependent patients who failed to achieve a stable remission, had a high concentration of testosterone in the first test (after detoxification). The authors conclude that it is possible to use testosterone for prognostic purposes to identify patients with a high risk of relapse after treatment [19].

Narcological Factors

The age of the beginning of alcohol consumption. Patients who started drinking alcohol over the age of 15 are more likely to achieve more stable remissions than people with an earlier start [13, 20]. In a Norwegian

study of patients with AD and antisocial personality disorder, an earlier age of alcoholic debut was a significant prognostic factor of early relapse and refusal of treatment [21]. However, in some studies [4], a younger age of onset, on the contrary, was associated with more stable remissions.

The factors that negatively affect the stabilization of remission and the achievement of long periods of sobriety traditionally include the **volume and frequency of PAS use** and the **severity of dependence** [2]. Thus, in one of the most famous prospective studies — The San Diego Prospective Study — stable remission in the long term was predicted by higher tolerance to alcohol and more rare use of it (each day of use reduced the chances of remission by 8%) [2]. However, there is evidence that a longer period of use of PAS before seeking treatment, and larger amounts of use in late middle age are associated with more stable remissions [4]. In a Swedish cohort study of 312 men whose history was traced within 50 years, significant factors in the formation of remission were episodes of *delirium tremens* in history and the presence of organic brain disorders [22].

The negative role of the **actualization of pathological attraction** in the relapse of narcological diseases is consistently found in various works [20, 23].

Personal (Psychological) Factors of Remission

Presence of psychopathology. It is believed that with increase in the severity of mental disorders comorbid to dependence syndrome, the probability of achieving remission in the long term period (up to 20 years) decreases [24, 25]. A number of authors described the influence of affective and anxiety disorders on stability of remission and the risk of relapse of narcological disorder. Patients, who practice self-treatment of symptoms of affective pathology with alcohol, showed absence of remission of dependence syndrome several years later in repeated examination [26]. A lower level of depression symptoms at the beginning of treatment was associated with the achievement of stable remission in repeated evaluation after 2 years in 1,453 men of middle age — veterans of military operations [27].

Among comorbid disorders preventing formation of sustained remission, the role of asocial personality disorder and combined dependence on other PAS is consistently emphasized. In a twin study of a cohort of twins (n = 1,769) born between 1939 to 1957 and served in the US Armed Forces, the risk factor of the onset of AD and unstable remission was high expression of symptoms of antisocial personality disorder and drug addiction, despite the fact that panic, generalized anxiety, posttraumatic disorders accelerated formation of remission [28]. It is interesting that patients with

comorbid nicotine dependence are consistently having a rather low percent of remission [17, 28], and the remission of nicotine dependence in itself within the previous year significantly reduces the probability of relapse of drug addiction [3]. On the other hand, in some works, the mentioned disorders had a lower influence on parameters of remission than injuring experience in history, higher level of prolactin and early start of PAS use [21].

In a 6-month prospective study of 150 patients with AD and opioid dependence syndrome and sleep disorders [29], data were obtained about a nine-fold higher risk of relapse or exclusion of **patients with low quality of sleep** from the study, with this, the maximal risk of relapse was noted in participants who were falling asleep after midnight.

Premorbid personality traits are another important factor in the formation of sustained remissions in narcological patients. In the above twin study, the main protective factors were such personality traits as *conformity* and *conscientiousness* [28]. The occurrence of relapse of drug-related diseases is often associated with *Impulsivity* — a characteristic feature of antisocial and borderline personality disorders which often accompany addictions [30]. A systematic review of the literature, which included 25 studies of various parameters of impulsivity in dependent patients, demonstrated the leading role of disorders of inhibition control, devaluation of delayed rewards and impulsive taking decisions in patients' ability to achieve sustained sobriety during and after treatment [31]. Failure of remission and actualization of attraction are associated with such personality traits as *search for novelty* and *impulsivity* associated with lack of planning, and the relationship between these traits and relapse is mediated by the presence of attraction [32].

Psycho-traumatic experience in childhood and adulthood is also noted among the pathopsychological factors of relapse and the absence of long-term remissions. Patients (55.4%) who terminate treatment prematurely have a greater traumatic burden, and do not differ in socio-demographic parameters and treatment terms from those who remain in the program [33]. In another study of women with narcological disorders with 1-year follow-up, it was shown that patients without experience of violence in childhood formed better remissions and demonstrated better treatment results in a number of parameters compared with victims of violence [34].

Considering other significant psychological factors of the formation of long-term and sustained remissions in patients with a narcological profile, it is necessary to mention a higher level of *self-efficiency* [35], a greater variety of *positive stress-coping strategies* [23], *safe attachment style* [36], etc.

Social factors of remission formation

Various researchers consistently note the role of social and family status in the formation of remission [2].

Low socio-economic status is considered one of the main predictors of relapse [30]. People with a lower level of education are more likely to demonstrate a worse outcome of drug-related diseases [2, 23], and each year of higher education increases the probability of forming a sustained remission by 16% [2]. The duration of education less than 15 years is associated with relapse, greater severity of alcohol consumption, the total number of months of harmful use (> 100 standard portions of alcohol per month) and the age of the onset of alcohol use [17]. Similar data on the protective role of a higher level of education in preventing the recurrence of AD (but, apparently, not other dependencies [3]) were obtained in other studies [25]. On the other hand, higher education did not play a favorable role in the Swedish cohort study, and the best remissions were achieved by blue-collar workers engaged in physical labor [22], which is confirmed by other epidemiological studies [3]. Stressful events related to professional status (job loss, job search for more than 1 month, conflict with a boss/colleague, change of job or job responsibilities, financial crisis, bankruptcy, inability to pay bills, problems with the law) had the expected negative impact on the severity of drug use and the stability of remission [3]. Among the professional factors that potentiate the relapse of PAS addiction, besides unemployment and job loss, there are also long and hard work, the necessity to spend a long time driving, dissatisfaction with professional activities, professional failures and the availability of opiates in the workplace [37].

The **factors of family status** that influence formation of remission, include, in the opinion of most researchers, stability of family (marital) relations and the presence of children [25], while factors that potentiated relapse of addiction, included divorces, positive heredity for narcological diseases, death of parents and partners, family discrimination, etc. [37], especially if these 'family' distressing events occurred in the year preceding the relapse.

The **role of negative social surrounding** is also noted [30]: addicted and problematic friends and colleagues, availability of PAS, rejection by friends, death of husband (wife) [37]. Positive factors include refusal co-dependent relations with PAS co-users, birth of child, new marriage, friendly support and treatment [38].

Therapeutic Factors

Based on the data of cohort long studies of AD in Sweden and the USA, stable remission was observed 10 times more often in those who *received treatment* [2, 22]. The duration of remission is directly related with such parameters as the number of treatment attempts, the completion of a full course of inpatient treatment, duration of treatment, participation in self-assistance groups [4, 23, 39]. Especially important for further stabilization and maintenance of sustained remission is duration and intensity of treatment prescribed in the first turning of the patient for help [35]. Patients receiving short-term treatment (2–4 months), have a higher risk of relapse in comparison with those undergoing long-term treatment (> 6 months) irrespective of duration of stay in the program [39]. In a cross-sectional study of sustained remission in patients with opiate dependence (552 participants at the age from 20 to 60) it was found that the main factor in maintaining sustained remission was visiting groups of Anonymous Drug Addicts (adjusted odds ratio 3.28; $p < 0.001$) [4]. Visiting 12-step programs and other mutual assistance groups upon completion of treatment in the rehabilitation center are associated with sustained remission by other studies as well. Besides, protective factors also include monitoring of drug use in the post-rehabilitation period and completion of the treatment program, while duration of treatment, the type of drug and age did not influence stability of remission [8]. A therapeutic alliance between a doctor and a patient is also reported to increase the likelihood of sustained remission [40].

CONCLUSION

As it follows from the presented material, the main difficulties of verification of relatively stable biological parameters and factors voluntarily regulated already in the course of formation of remission as reliable predictors of the future stable remission, are associated with diverse contingent of studied patients and different understanding of such concepts as 'failure', 'relapse', 'remission', 'recovery'.

Nevertheless, there are basic factors of favorable prognosis of the course of dependence, that are confirmed from study to study: late onset of the disease, absence of comorbid severe mental disorder, involvement in long-term medical and rehabilitation programs that continue after the remission has been established.

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