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Clinical-dynamic features of affective disorders comorbid with alcohol dependence

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Abstract: *Introduction***:** The comorbidity of affective disorders (AD) and alcohol dependence (AlcD) worsens the prognosis and efficacy of therapy, exacerbates non-compliance in patients, and lowers their level of social adjustment. *Objective***:** To study the influence of AlcD on the clinical-dynamic characteristics of AD. *Material and Methods:* Two groups of patients were examined and compared based on the Affective States Department of Mental Health Research Institute (Tomsk, Russia). The study group included 32 patients with AD and comorbid AlcD, and the comparison group included 31 AD patients without comorbid addictive pathology. The groups were matched on sex, age, and AD, without any statistically significant ($\alpha = 0.05$) differences in those variables. The Clinical Global Impression scale (CGI), the Hamilton Depression Rating Scale (HDRS-17), the Hamilton Anxiety Rating Scale (HARS), and the Social Adaptation Self-evaluation Scale (SASS) were used. *Results:* Compared to the group without comorbidity, the group of patients with comorbid AD and AlcD had more frequent suicide attempts in their medical history, a higher level of anxiety according to HARS, more severe disorders according to CGI-S, and more impairment of social adaptation according to SASS. Patients with recurrent depressive disorder (RDD) and bipolar disorder (BD) also experienced a larger number of affective episodes per year. *Conclusion:* AlcD comorbid with AD affects clinical-dynamic indicators and levels of social adjustment in patients.

Keywords: alcohol; affective disorders; concurrent disorders

Introduction

In recent decades, many studies have been devoted to researching comorbidity in mental health disorders (Kessler et al., 2015). Both epidemiological and clinical studies have revealed a high level of comorbidity of affective disorders (AD) with other mental disorders (Kessler et al, 2011; Merikangas et al., 2011). Alcohol dependence (AlcD) is considered the most prevalent comorbid pathology with AD, along with anxiety disorders and personality disorders (Boschloo et al., 2011; Nabavi et al., 2015; Perugi et al., 2013). The prevalence of AlcD among patients with AD is several times that of the general population.

According to data from Schuch and colleagues (2014), AlcD develops more frequently in men with AD, while anxiety disorders are a more frequent comorbid pathology in women with AD. The risk of developing AlcD among people with bipolar disorder (BD) is six to seven times higher than in the general population (Mosolov et al., 2008). Patients with AD quite frequently use alcohol to alleviate symptoms of depression and anxiety (Crum et al., 2013; Terra et al., 2006). In patients with addictive pathology, the frequency of mood disorders is also high. According to the data collected from specialized institutions of eight European countries, 43.2% of patients with AlcD (n = 1,767) between the ages of 18 and 64 also suffered from depression (Rehm et al., 2015). Affective disorders and alcohol dependence each heighten the risk for development of the other, but some research suggests this pattern may occur only in males (Bulloch et al., 2012).

Many studies have attempted to find pathogenic interactions in the comorbidity of AlcD and AD. Results from these efforts have demonstrated a commonality of genetic factors in the development of both disorders (Katz & Kravitz, 1996), specifically involvement of the same neurohumoral mechanisms into the pathogenesis. Personality traits such as alexithymia and social anxiety appear to be common psychological factors of alcoholism and depression (Cristal, 2000). But this issue is not yet solved.

Alcohol dependence can develop before and after the development of AD. Mood disorders manifest earlier and more frequently, and alcohol dependence develops after affective disorder. The comorbidity of AD and AlcD makes it difficult to differentiate pre-existing AlcD from symptomatic alcohol use resulting from AD. For instance, depressive disorders can be difficult to distinguish from secondary depression due to intoxication with ethanol, or from depression caused by the social implications of an individual's alcoholism. The most significant differential criterion of primary depression is the manifestation of a depressive disorder before the development of alcoholism.

The comorbidity of AD with AlcD is characterized by more frequent repetition of depressive episodes, a greater number of suicide attempts, greater degree of inadaptation, and worsened prognosis (Cardoso et al., 2008; Simhandl et al., 2016). Data in the literature concerning the effects of comorbid alcoholism on the efficiency of anti-depressant treatment for

depressive disorders are varied. Some authors report no effect of alcoholism on the treatment of depression with anti-depressants (Hashimoto et al., 2015), whereas others do find such effects (Iovieno et al., 2011). Abuse of alcohol also complicates collaboration between the physician and the patient by lowering patient compliance.

Objectives

The objectives of this study are (1) to analyze cases of comorbidity of affective disorders with alcohol dependence, (2) to assess the influence of alcohol dependence on the clinical-dynamic characteristics of affective disorders (in particular, the age of onset of AD, syndromal variant of depression, indices of suicidal behavior of patients, frequency of affective episodes per year in bipolar disorder and recurrent depressive disorder, level of depression according to HDRS-17, anxiety according to HARS, and severity of the disease according to CGI-S), and (3) to determine the level of social adaptation among these patients.

Material and methods

A total of 63 patients with AD (20 women and 43 men) were recruited based on the Affective States Department of Mental Health Research Institute, Tomsk, Russia). All were of Slavic nationality.

Table 1

Socio-demographic characteristics of the studied patients

Characteristics	Proportion (*n*)
Sex	
Female	31.7% (*n* = 20)
Male	68.3% (*n* = 43)
Marital status	
Married	61.9% (*n* = 39)
Single	11.1% (*n* = 7)
Divorced	14.3% (*n* = 9)
Widowed	12.7% (*n* = 8)
Level of education	
Secondary	19.1% (*n* = 12)

Secondary vocational	20.6% (*n* = 13)
Sigher	60.3% (*n* = 38)
Professional status	
Employed	52.4% (*n* = 33)
Unemployed	33.3% (*n* = 21)
Unemployed due to mental pathology	14.3% (*n* = 9)

The median age of female patients was 45.5 years, and the interquartile range (IQR) was 21 [35; 56]. For males, the median age was 38 years, and the IQR was 26 [31; 57]. Depending on AD, patients in the study were divided as follows: BD with current depressive episode (19%, *n* = 12), recurrent depressive disorder (RDD) with current depressive episode (42.9%, *n* = 27), depressive episode (DE; 27%, *n* = 17), and dysthymia (11.1%, *n* = 7).

Criteria of inclusion for patients in the study included giving informed consent, being between 18 and 65 years of age, and diagnosis according to ICD-10 of one of: (1) depressive episode, (2) dysthymia, (3) recurrent depressive disorder, or (4) bipolar disorder with current depressive episode. Criteria of exclusion were diagnosis of severe cognitive impairment/dementia and/or severe or decompensated somatic or neurologic diseases.

The primary research methods we used in this study were statistical, psychometric, and clinical-psychopathological (the record chart of formalized description of the patient was filled in). We assessed the severity of disease with the Clinical Global Expression scale–Severity (CGI-S), level of depression with the Hamilton Depression Rating Scale (HDRS-17), and level of anxiety with the Hamilton Anxiety Rating Scale (HARS).

The quality of life and social functioning of patients was assessed with the Social Adaptation Self-evaluation Scale (SASS), developed in 1997 by Bosc, Dubini, and Polin. The questions included in this scale are designed to assess level of social functioning and life satisfaction in various domains (e.g., work, intrafamily relations and relations outside the family, leisure, etc.).

To study the influence of comorbid alcohol dependence on the clinical-dynamic characteristics of AD, the patients were divided into two groups. The main group included 32 AD patients with comorbid AlcD (9 women and 23 men), with a median age of 44.5 years [36; 51.5]. Affective disorders included BD (25%, *n* = 8), RDD (40.6%, *n* = 13), DE (28.1%, *n* = 9), and dysthymia (6.3%, *n* = 2; Fig. 1). The median duration of alcohol

dependence in patients was 8 years [3.5; 11]. In 59.4% of cases (n = 19), patients in a state of depression changed their manner of alcohol use, in that they began to drink alone. Basic motives of alcohol use during development of depressive symptoms cited by patients included (1) to distract from painful/gloomy thoughts, (2) to stifle a feeling of anguish, (3) to "escape" their problems, and (4) to cope with anxiety or insomnia.

The comparison group included 31 AD patients without any comorbid addictive pathology (11 women and 20 men), with a median age of 45 years [32; 52]. This group's affective disorders comprised BD (12.9%, n = 4), RDD (45.2%, n = 14), DE (25.8%, n = 8), and dysthymia (16.1%, n = 5; Fig. 1). The groups were matched on sex, age, and distribution of AD so that there were no statistically significant differences in proportion between groups.

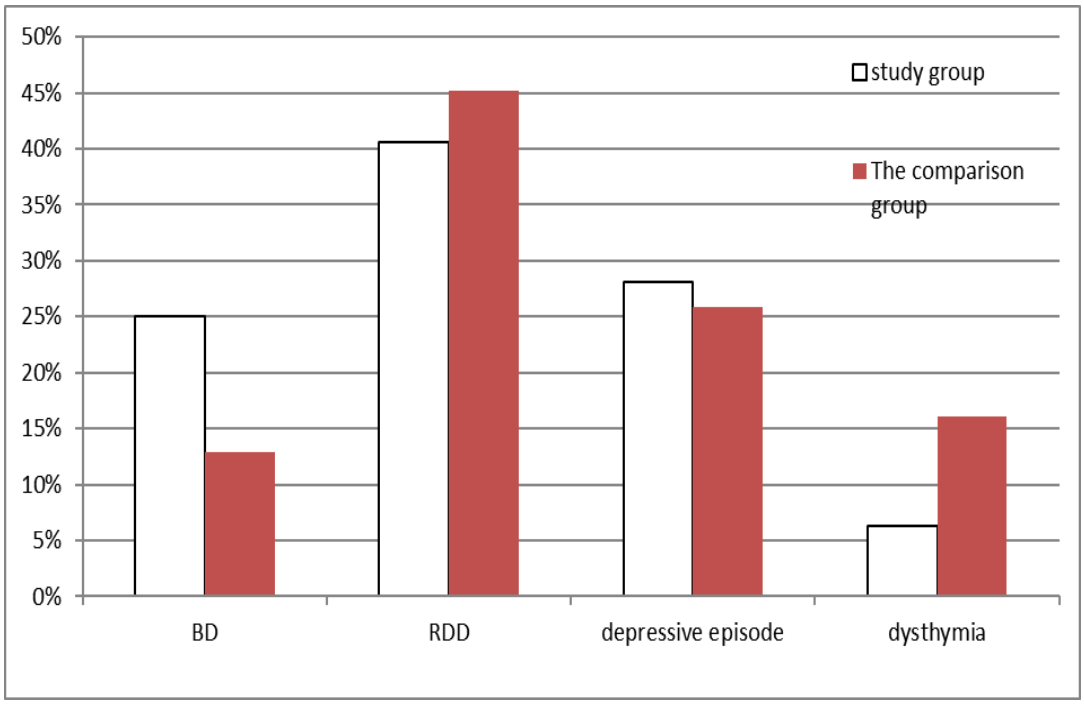

Figure 1. Distribution of affective disorders in compared groups.

Comparative assessment between the groups was conducted for the following characteristics of AD: Age of onset of AD, syndromal variant of depression, indicators of suicidal behavior, number of affective episodes per year (in BD and RDD), level of depression (according to HDRS-17), level of anxiety (according to HARS), and severity of the disease (according to CGI-S). The level of social adaptation in patients was also assessed (according to SASS), as well as the chronology of development of AD and alcohol dependence.

Statistical data analysis was conducted with the Statistical program for Windows (Version 8.0). Index score distributions were tested for normality with the Shapiro-Wilk W-test. For quantitative indices that did not meet the assumption of normal distribution, comparisons between groups were assessed for statistical significance with the Mann-Whitney U test (α=0.05). The Chi-Squared test for independence was used to assess differences in frequency of symptoms between the groups (α=0.05).

Results

The median age of onset of AD in the main group was 28.5 years [20; 39.5], and in the comparison group it was 30 years [26; 40]. The distribution of patients in the studied groups depending on the leading syndrome of depression is presented in Table 2. There were no statistically significant intergroup differences in the syndromal structure of depression.

Table 2
Distribution of patients in the main and control groups, depending on the syndromal variant of depression

Syndromal variants of depression	Main group		Comparison group	
	Abs.	%	Abs.	%
Anxiety	12	37.5	9	29.1
Dysphoric	13	40.6	8	25.8
Hypochondriac	3	9.3	4	12.9
Conversion	2	6.3	5	16.1
Adynamic	2	6.3	5	16.1
Total	**32**	**100**	**31**	**100**

We conducted a comparative assessment of two indicators of suicidal behavior: availability of suicidal thoughts in the current episode and suicide attempts in the anamnesis. The incidence of availability of suicidal thoughts in their current state did not significantly differ between groups. In the main group, suicidal thoughts were available in the clinical picture in 65.6% of cases (n = 21), and in 48.4% of cases (n = 15) in the comparison group. For patients of the main group, suicidal thoughts became the most painful in the context of withdrawal syndrome and acquired a frequently obsessive character.

The analysis of anamnestic and follow-up data showed significantly more frequent incidence of suicide attempts in the anamnesis of patients in the main group (25%) than in the comparison group (6.5%), $p < 0.05$. Regarding the rise of suicidal ideation in the main group, contributing factors included not only painful

depressive experiences, but also psycho-traumatic circumstances that were frequently social consequences of alcoholism.

The main group also presented significantly more affective episodes per year in patients diagnosed with RDD and BD than the comparison group: 1.5 [0.9; 2.0] and 0.9 [0.7; 1.6] respectively, $U = 200$, $Z = 2.509$, $p = 0.012$. According to the HDRS-17, the severity of depressive symptoms was not significantly different between the two groups (Table 3).

Table 3

Severity of depression and anxiety symptoms

Scale	Main group, *n* (%)			Comparison group, *n* (%)		
	Mild	Moderate	Severe	Mild	Moderate	Severe
HDRS-17	2 (6.3)	22 (68.7)	8 (25)	4 (12.9)	23 (74.2)	4 (12.9)
HARS	1 (3.1)	9 (28.1)	22 (68.8)*	1 (3.2)	17 (54.9)	13 (41.9)*

Note: * indicates a statistically significant difference between groups at the 0.05 level.

Scoring according to HARS showed that there were more patients with a "severe" level of anxiety in the main group than in the comparison group, $\chi^2 (1) = 4.58$, $p = 0.03$. The analysis also revealed that diagnoses of a severe disorder (CGI-S = 6 points) occurred more frequently in the main group (34.4%) than in the comparison group (12.9%), $\chi^2 (1) = 4.00$, $p = 0.04$).

Depending on the total score obtained from the SASS, participants were divided into 3 subgroups: Those with poor social adaptation (from 0 to 22 points), those with complicated social adaptation (from 22 to 35 points), and those with good social adaptation (from 35 to 52 points). In both the main group and the comparison group, the greatest number of patients had complicated social adaptation (Table 4).

Table 4

Distribution of patients with different levels of social adaptation in the studied groups

Adaptation sub-group	Main group, *n* (%)	Comparison group, *n* (%)
Poor social adaptation	6 (18.7)	3 (9.7)
Complicated social adaptation	23 (71.9)	17 (54.8)
Good social adaptation	3 (9.4)	11 (35.5) #

Note: * indicates a statistically significant difference between groups at the 0.05 level.

According to the SASS, there were fewer patients with good social adaptation in the main group (9.4%) than in the comparison group (35.5%), χ^2 (1) = 4.79, p = 0.03. Assessment of the chronology of the onset of comorbid disorders in the main group showed that AD preceded the development of AlcD in 75% of cases (n = 24).

Discussion

It is noteworthy that in patients with AD, both with comorbidity of AlcD and without, anxiety and dysphoric variants of depression presented in more than half of the cases (Table 2). According to epidemiological and clinical studies, the prevalence of full-blown anxiety disorders in patients with both AD and AlcD is high (Merikangas & Pato, 2009; Nabavi et al., 2015; Terra et al., 2006). While patients with anxiety disorders were not included in our sample, the available symptoms of anxiety were an integral part of the clinical picture of AD and AlcD. Furthermore, assessment of the severity of anxiety in groups revealed a higher level of anxiety in patients with a combination of AD and AlcD than in patients who had AD without comorbid AlcD.

The age of onset if AD did not significantly differ between patients with and without comorbidity of AlcD, although data exists in the literature that supports the manifestation of AD that is comorbid with other mental disorders at a younger age (Joslyn et al., 2016). Our previous studies have also indicated an earlier age of patients at the onset of depressive disorders comorbid with anxiety disorders than patients with depressive disorders without a comorbid pathology (see Vasilieva, 2010).

According to current knowledge, AD and AlcD are often accompanied by suicidal behavior (Morin et al., 2013; Orui et al., 2011), and the comorbidity of these disorders leads to an even greater risk of suicide (Oquendo et al., 2010). Our data on suicide attempts in the anamnesis support the hypothesis that the comorbidity of AlcD and AD increases the risk of suicidal behavior in patients.

The indices presented in Table 4 are in line with data in previous research on the negative effects of AD and AlcD on the social adaptation of patients. The combination of these disorders leads to a more pronounced decrease in this indicator.

In most of the patients studied, AD preceded the development of AlcD, which is consistent with the literature (Crum et al., 2015; Zimmermann, 2003). At the same time, a group of authors indicates that alcohol abuse occurs more often prior to the manifestation of AD, but not AlcD (Falk, Yi, & Hilton, 2008).

Conclusions

The results of our study show that in AD with comorbid AlcD, there are more frequent exacerbations of affective pathology and higher levels of

anxiety, disease severity, and risk of suicidal behavior than with AD alone. Patients with this comorbidity also have lower levels of social adaptation than patients with AD alone. In most cases, AlcD develops in the context of pre-existing AD. Supported by the above data, it is possible to draw the conclusion that AlcD comorbid with AD has a negative effect on the clinical-dynamic indices and level of social adaptation in patients.

Ethics statement

Ethical approval for the study was received from the research team's university's ethics committee, and complied with the Declaration of Helsinki (Approval number № 129/4.2020).

Conflict of Interest

There is no conflict of interest.

Availability of data and materials

Data will be made available upon reasonable request.

Funding source

None.

Authors' contributions

All authors significantly contributed to the preparation of this manuscript.

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