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Use of atypical antipsychotics in the treatment of patients with schizophrenia and drug addiction: A randomized control trial

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ABSTRACT

Objectives: Aim is to study of the therapeutic efficacy of atypical antipsychotics (aripiprazole and quetiapine) in comparison with haloperidol in cases of comorbidity of low-grade forms of schizophrenia and addiction. *Material and methods*: A randomized comparative study of these antipsychotic preparations was conducted during the period Feb-May 2021. We screened 90 men admitted to treatment in a narcological hospital. Of these, 54 (60%) patients those had a previously established diagnosis of schizophrenia, 36 (40%) did not. Patients by simple randomization were divided into three groups of 30 people each, in which the appropriate antipsychotic was prescribed: aripiprazole in dose up to 20 mg / day, quetiapine at a dose of up to 600 mg / day, haloperidol at a dose of up to 30 mg / day. *Results:* Intra-group analysis of the dependent variables on the ANSS, BPRS, VAS, PVN scales showed an appropriate significant difference in all groups in the dynamics of therapy. Intergroup analysis of independent variables showed significant correct differences between aripiprazole and haloperidol according to PANSS, BPRS to visit 4, according to VAS to visit 3, according to the PVI scale to visit 2. Intergroup analysis of independent variables showed significant differences between quetiapine and haloperidol by PANSS, VAS, and PVI scale - by visit 4. *Conclusion*: Based on the results of the correlation analysis, waters about the inextricable connection between psychopathological manifestations of schizophrenia and the syndrome of pathological attraction to psychoactive substances.

Keywords: schizophrenia, substance dependence syndrome, comorbidity, antipsychotics, aripiprazole, quetiapine.

1. INTRODUCTION

The problem of "double diagnosis" is widely discussed among researchers, since the combination of two diseases is called -not only differential diagnosis, but also therapeutic difficulties-, and also has enough poor prognosis for the

formation of high-quality remission (Scheller et al., 2004). The number of people suffering from combined forms of mental and drug addiction pathology (Bokhan & Semke, 2009), of greatest interest are the questions associated with comorbidity of dependence syndrome psychoactive substances (PAS) and schizophrenic diseases spectrum, such as low-grade forms of schizophrenia, schizotypal personality or unspecified new disorder.

There are epidemiological data indicating which, in almost half of the patients, giving diseases of the schizophrenic spectrum, in during life, disorders associated with the use of surfactants, about a third of them begin to abuse alcohol, about a quarter use drugs seal (Moggi, 2018). The use of surfactants increases the risk of developing schizophrenic process, (Eric, 2016) and patients with "double diagnosed" have an earlier age of onset schizophrenia (Green et al., 2004). Until now, any of them exists, “universal pathogenetic” to explain therelationship of endogenous psychoses and “dependence on surfactants”. One way or another, but mental illnesses are associated with an increased risk of developing PAS dependence syndrome (Sweden & Kevin, 2010). Some foreign studies have noted that patients who use more than three surfactants in combination, up to significantly more often suffer from schizophrenia and bipolar disorder in comparison with patients, including consuming one surfactant (Bhalla et al., 2017). In the population of patients with al-cog and cannabinoid addiction 3 times more often there are different forms of schizophrenia in comparison with people who do not use surfactants (Dixon, 1999). The use of cannabinoids by mentally ill people in the majority cases is associated with the early onset of schizophrenic proprocess and a higher risk of recurrence after the first psychotic episode (Linszen, 1994). The pre-the position that early stress sensitizationan increase in patients suffering from endogenous processes, leads to an increased risk of joining abuse of Surfactants in later life(Libuy et al., 2018).

Psychotic disorders caused by use of surfactants, such as amphetamines or cannabinoids, and are often considered as risk factors for the development of schizophrenia (Chiappelli et al., 2018). According to the meta-analysis carried out in period from 1990 to 2017, among patients suffering from diseases of the schizophrenic spectrum, 41.7% used use surfactants in forms from episodic use with harmful consequences to the developed addiction syndrome, while prohibited surfactants (such as opioids) are consumed are 27.5%, cannabis (legal in some countries for medical purposes) - 26.2%, alcohol - 24.3%, the share the remaining 22% are other surfactants (Bramness et al., 2012). Currently, there is an increase in the number of the prevalence of cases of combined use of non-how many surfactants. This trend has become noticeable since the early 2000s, when a number of Western European countries (Spain, France, Italy, Netherlands, and UK) began to report an increase in the use of non-how many surfactants and an increase in the number of deaths from the use of a combination of morphine, benzodiazepine, tranquilizers and alcohol. The same is observed in Russia pattern: epidemiological data of the last years indicate that the indicators of general morbidity with multi-substance dependence syndrome (F19, ICD-10) are growing. If the proportion of such patients in 2013 was 8.3%, then in 2014 it increased to 10.6%, in 2015 - up to 12.9%, and in 2016 it reached 15.8% (Green & Khokhar, 2018).

Research on psychotherapeutic and pharmacological logical treatment of patients with "dual diagnosis"so heterogeneous in characteristics of patients, methods of treatment, outcomes of diseases, which is hardly possible find two comparable works. Treatment results in general remain disappointing. The use of antipsychotics in patients with schizophrenia with comorbid alcohol dependence bridge (Kirzhanova, 2015), in patients with a "dual diagnosis", treating using atypical antipsychotics were the best results are obtained in terms of performance remission in comparison with patients receiving personal funds of this group. Some authors support point out that the success of the treatment of such patients is possible only when combining the traditional, adopted inpsychiatry therapy of endogenous psychosis and at the same time with her treatment of the syndrome of dependence on psychoactive substances (Ipser et al., 2015).

More and more data appear in the scientific literature that the use of antipsychotic drugs in patients with "dual diagnosis" allows you to effectively buy feast on psychopathological symptoms (Gouzoulis et al., 2015), reduce attraction to surfactants and the number of early relapses, and in the long term - to improve the quality of remissions (Potvin et al., 2006). In this case, the positive results of treatment are observed are given not only in patients with a "dual diagnosis", and in patients with various variants of the syndrome depending simplicity (Cuomo et al., 2018). It should be noted, that not all the obtained results are unambiguous, there are works in which the effectiveness of atypical antipsychotics is not supported statements (Mariani et al., 2014). The greatest research interest is there are two atypical antipsychotics - quetiapine, which are now widely used inpsychiatric practice, as they showed a high efficacy and safety in the treatment of not only mental medical diseases, but also addiction syndrome (George, 2016).

Quetiapine is an atypical antipsychotic with its own antidepressant action and favorable profile safety, has weak affinity for D1- and D2-receptors with high affinity for 5-HT2 receptors, to a certain extent blocks alpha-adrenergic. Aripiprazole is an atypical antipsychotic with unique pharmacological properties: partial agonist D2- and 5HT1a-receptors, affects 5-HT2-receptors, but use of presynaptic D2 autoreceptors, thus it can both increase and decrease the content dopamine in certain areas of the brain (Martinotti et al., 2016).

The purpose of this study is to study the effectiveness and safety of quetiapine and aripiprazole in comparison treatment with haloperidol in the treatment of patients with schizophrenic spectrum, occurring comorbidities with the disease of addiction.

2. MATERIAL AND METHODS

Preparations were conducted during the period Feb-May 2021. A total of 266 patients were examined in a narcological hospital. Of these, the study was whether 90 patients with an established diagnosis were included "Syndrome of dependence on several psychoactive substances (rubric F19 on ICD-10) ", aggravated by diseases of schizophrenic of the spectrum that needed treatment in a narcological hospital.

Study inclusion criteria: male gender; WHO-grow from 20 to 50 years old; previously installed or discovered schizophrenic disease during the examination spectrum (F20, 21); signatory informed agreement this for participation in the study, the use of atypical antipsychotic drugs (aripiprazole, quetiapine), consent to consult a psychiatrist.

The criteria for not including there was a pathological attraction to one surfactant; pathological attraction to gambling; acute somatic diseases or exacerbation of chronic forms of pathology; positive analysis RW, HIV; increasing ALT and AST in primary diagnosis more than 3 times from the upper limit of the norm. For a comprehensive assessment of medical, psychological the mental and social condition of persons suffering from drug dependence, we used the ASI (Addiction Severity Index) (Indave et al., 2016). To objectify data related to diagnostics some diseases of the schizophrenic spectrum, pronounced positive and negative symptoms, as well as for evaluating the therapeutic efficacy of drugs.

We used the following scales: BPRS (Brief Psychiatric Rating Scale) (Coffin et al., 2013), PANSS (Positive and Negative Schizophrenic Symptoms), where PANSS (P) is a positive syndrome scale. Mov, PANSS (N) - negative syndromes scale, PANSS (O) - scale of general psychopathology, the results of which expressed in points (Anne, 2014).

To objectify data related to dynamics psychopathological symptoms in the structure of the syndrome of dependence, we used a visual analog scale (VAS) and the scale of pathological attraction todrugs (PVN) (Pinkofsky et al., 2005). The safety of drugs was determined based on data on the development of adverse events (AE), serious adverse events (SAEs) or side reactions (PR), their manifestations, frequency and severity 3. The association of AE with a drug (MP) was assessed by Naranjo's algorithm 4. The degree of reliability of the connection "ЛС—AE "according to the Naranjo algorithm is considered as: definite, with 9 points or more; probable, with 5-8 points; possible, with 1-4 points; dubious, with 0 points or less (McLellan et al., 2008).

In the event of AEs, SAEs or PRs, the doctor registered his actions in the primary documentation, as well as filled in took the appropriate form 5. The total duration of the study was 21 days, which corresponds to the standard course of treatment in drug addiction hospital. Visit 0 corresponded to the 1-5th day inpatient treatment, included procedures screening, installation and confirmation of the "dual diagnosis for": syndrome of dependence on several PAS (F19) and schizophrenia paranoid, low-progressing type of course (F20) or schizotypal disorder (F21) (Table 1).

The relief of withdrawal symptoms was carried out by standard therapy, which did not differ in the groups, lasted the longevity was 4–5 days. On the 5th day, stationary treatment (i.e. after stopping the withdrawal syndrome) was randomized (visit 1) using random number generator, using the envelope method. Every-to the patient if he meets the inclusion criteria /exceptions were assigned a two-digit serial number from 01 to 90. All patients with "dual diagnosis" were separated into three groups (30 people each), depending on the use therapeutic agent. First-line patients the second group was prescribed aripiprazole (A) at a dose of up to 20 mg / day.

Table 1 study design

Visit	Visit 0	Visit 1	Visit 2	Visit 3	Visit 4
Days of treatment	1-5	5-9	10-14	15-20	>21

The patients of the second main group were prescribed quetiapine. (K) at a dose of up to 600 mg / day. Patients of the third control the groups were prescribed haloperidol (G) at a dose of up to 30 mg / day. The main target of therapy was a productive (affectivities and behavioral disorders) and negative symptoms of mental illness. The effectiveness and safety of the drugs used rats were assessed in dynamics - at visit 2 (10th day of chengyu), visit 3 (14th day), visit 4 (21st day). Along with the main drugs, patients receive whether tranquilizers and hypnotics. It was excluded when-changing any other psychotropic drugs. Wire or symptomatic therapy in order to correct disorders: arterial hypertension or hypotension, tachycardia, dyspeptic or other disorders. During the study, quantitative drugs included in the minimized standard dart therapy of withdrawal symptoms in the average daily dose: potassium chloride + sodium bicarbonate + sodiumchloride - 800 ml; bromo-dihydro-chloro-phenyl-benzodiazepine -4

mg; hop-antenic acid - 750 mg; tramadol - 300 mg; ketorolac - 90 mg; thiamine chloride - 100 mg; pyridoxine hydrochloride - 100 mg; ethyl-methyl-hydroxy-pyridine succinic acid - 375 mg, and post-withdrawal (subacute) state: in an average daily dose of diazepine - up to 4 mg; tofisopam - 150 mg. With statistical analysis of the volumes of drugs received in the groups compared or, no significant differences were obtained.

Statistical analysis

Each of 90 observations with held 15 variables. All variables were qualitative. The data obtained were analyzed bythe methods of descriptive, comparative statistics. Basic software for performing statistical analysis is the program IBM SPSS Statistics Ver.22, Python programming language Ver. 3.7, libraries SciPy, NumPy, Pandas. Checking the normality of the distribution studies were carried out using the Shapiro test. Ro-Wilk, and also used visual analysis of the distribution centimeters and quantile-quantile graphs. To identify intragroup differences in continuous data with normal distribution (p Shapiro-Wil-ka more than 0.05) used paired Student's t-test -the one for data that does not obey the law of normal distribution (p Shapiro-Wilk less than 0.05), used the Wilcoxon test. With intergroup comparisons of continuous data with a normal distribution unpaired Student's t-test was applied, in the case of when the data did not obey the law of normal determination, we used the one-sample Wilcoxon.

Correlation analysis of data with normal distribution division was performed according to Pearson's criterion. For data notobeying the law of normal distribution, used a nonparametric correlation coefficient Spearman. Connections were considered weak at $0.5 \geq p > 0.2$; Wednesday-them at $0.7 \geq p > 0.5$; strong at $0.9 \geq p > 0.7$.To estimate the mean values in three independent groups with a normal distribution of characteristics also used analysis of variance ANOVA.

Due to the problem of multiple comparisons (three groups) the calculation of the reliability index p was carried out afterthe following formula: $1–0.951 / 3 = 0.016952$. Selected parameters given in the tables have are the following designations: mean - mean, std - standard (root-mean-square) deviation, count – volume analyzed subgroup, p is the achieved level of knowledge importance.

Primary indicators of efficiency used data on the dynamics of symptoms according to BPRS and PANSS. The effectiveness of the investigational drugs was considered positive when reaching statistical reliability comparison with the reference drug at the time of visit 4 baseline (visit 1). The remaining criteria for the effectiveness of the drug are pure of patients (%) with the presence of adverse reactions to the background not carrying out therapy; number of patients (%), completely those who have undergone a study during therapy; the number of patients (%) who needed additional concomitant therapy were classified as secondary performance criteria.

3. RESULTS

Of the 90 patients included in the study, 22 patients were diagnosed with paranoid schizophrenia, low-progressive type of flow "(F20.01 – episodic flow type with a growing defect, F20.03 - episodic remitting type of flow); 68 patients -"Schizotypal disorder" (latent schizophrenia F21.1; pseudo neurotic (neurosis-like) schizophrenia F21.3; pseudo psychopathic (psychopathic) schizophrenia F21.4; "Symptom-poor" schizophrenia F21.5; schizotypal personality disorder (F21.8). Despite the different ciphers of diagnoses, the group was considered tripled in the total volume, since the number of observations with each individual variant of the schizophrenic pro the process was limited, and the clinical picture in all patients was very similar. All patients have a course of mental illness differed in relatively favorable, low predictive value type of flow, in the clinical picture predominant gave various options for depressive, sub depressive disorders, productive symptoms are most oftenis represented by overvalued, paranoid ideas,not reaching the level of delusion, but characteristic of schizophrenia process, deficiency symptoms are manifested was in the form of autism, isolation, emotional emasculation, a tendency to fruitless philosophizing, slippage and illogical judgments. Should note that negative symptoms were comparatively but shallow, it was hardly noticeable, and in patients with addiction syndrome was often behind the façade psychotogenic disorders resulting from chronic intoxication with surfactants.

Of the total sample, 54 (60%) patients had previously an established psychiatric diagnosis for which they were observed in the neuropsychiatric dispenser. Before the real hospitalization to psychiatric did not apply and did not have an established psychiatric of the clinical diagnosis in 36 (40%) patients, although the peculiarities clinical picture testified in favor of the presence mental illness, occurring comorbidly addiction disease. Data presented allow us to draw a disappointing conclusion that patients suffering from psychoactive substance dependence syndrome, chemical pathology occurs quite often, practical in 34% of cases, however, in a very large number of such patients (in our case - in 40% of screened patients, or 13.5% of all surveyed with the syndrome of depending on several psychoactive substances) mental illness remains unrecognized. This leads to the use of non-effective therapy regimens, which in turn leads to frequent recurrence, rapid social disintegration adaptation, and ultimately - early disability these patients.

Feature of the clinical picture of the narcological diseases occurring comorbidly with a schizophrenic process. Patients with a "dual diagnosis" are characterized by the following clinical and dynamic features of narcology medical disease: 1) early social maladjustment, as evidenced by the low numbers of workers (20%), high numbers of single, unmarried or relationships (80%); 2) a tendency to develop the so-called hospitalism, possibly associated with frequent recidivism and low quality of remissions, as evidenced byhospitalization rates are high during oneyears (42%); 3) the development of drug addiction inearly age - 21.2 ± 1.9 years; 4) the most common motive introduction to the use of surfactants - this is the so-called experiment (according to patients, "the scientific method use "), i.e. not to search for euphoria, but to study the effect of surfactants on the brain (39.9%) or "the desire to calm nod or cheer up "(that is, for the purpose of correcting their mental state (35.7%)); 5) uncharacteristic motivation for the introduction to the use of surfactants - "to join to the company "(7.1%); 6) the prevalence of high progression mentality of drug addiction (62%); 7) converting handling in the structure of withdrawal symptoms of psychopathology manifestations: sub depressive mood background, affective hesitation, ideas of self-blame and suspicionparanoia (68%); 8) the predominance in the structure of the syndrome of pathological drives of the ideational component (52%); 9) the pattern is surfactant consumption - chaotic, more than 2 surfactants (66.7%); more frequent combinations of surfactants in patients with "double diagnosis "are combinations of surfactants with anticholinergics, such as alcohol, psycho stimulants, anticholinergics (22.2%), alcohol, opioids, anticholinergics (15.2%) and psihost stimulants and anticholinergics (12.4%).

Dependent Variable Analysis, Intra-Group comparisons

Analysis of dependent variables according to BPRS, PANSS scales showed significant differences in three groups in dynamics therapy when comparing indicators to the periods of visits 1 and 4 (Table 2). Along with the positive dynamics of manifestations diseases of the schizophrenic spectrum underwent reduction and symptomatology of drug addiction, in particular, the syndrome of pathological attraction to surfactants (Table 3). The results obtained (Tables 2, 3) make it possible to determine make an unambiguous conclusion about the effectiveness of the application antipsychotic drugs used in treatment of patients with "dual diagnosis". However, the most of practical interest is information about the specificity of each drug, which can be seen use when making intergroup comparisons.

Table 2 Intragroup dynamics with the scales BPRS,PANSS

Group	Scale, visit	Mean±std	*p*	Criterion for calculating p
A	BPRS,B1	67,86±4,37	0,0001	Wilcoxon's criterion
	BPRS,B4	20,90±9,12		
	PANSSP,B1	20,86±2,15	0,0001	Wilcoxon's criterion
	PANSSP,B4	2,67±2,52		
	PANSSO,B1	33,52±3,63	0,0001	Paired Student's t-test
	PANSSO,B4	5,76±3,94		
K	BPRS,B1	68,40±4,79	0,0001	Also
	BPRS,B4	22,80±9,77		
	PANSSP,B1	20,20±3,97	0,0001	«»
	PANSSP,B4	3,35±3,00		
	PANSSO,B1	35,10±2,75	0,0001	«»
	PANSSO,B4	7,63±5,34		
Г	BPRS,B1	69,58±3,52	0,0001	«»
	BPRS,B4	27,89±8,94		
	PANSSP,B1	19,74±3,38	0,0001	«»
	PANSSP,B4	7,42±2,89		
	PANSSO,B1	34,47±4,71	0,0001	«»
	PANSSO,B4	12,84±2,89		

Note. Here and in table. 5-12: A - group receiving aripiprazole; K - the group receiving quetiapine; D - group receiving haloperidol; B - visits.

Table 3 Intragroup dynamics with the scales VAS, SACS

Group	Scale, visit	mean±std	*p*	Criterion for calculating p
A	ВАШ,В1	53,10±11,45	0,0001	Paired Student's t-test
	ВАШ,В4	12,86±5,38		
	ПВН,В1	21,81±3,22	0,0001	Also
	ПВН,В4	3,71±2,53		
К	ВАШ,В1	56,75±10,67	0,0001	«»
	ВАШ,В4	19,75±8,50		
	ПВН,В1	21,30±2,81	0,0001	«»
	ПВН,В4	6,40±3,42		
Г	ВАШ,В1	80,53±7,97	0,0001	Wilcoxon's criterion
	ВАШ,В4	39,74±7,35		
	ПВН,В1	22,47±3,19	0,0001	«»
	ПВН,В4	11,89±1,10		

Independent Variable Analysis, Intergroup comparisons

At the screening stage (visit 0) and randomization (visit 1) the groups did not differ from each other in terms of scale indicators, statistically significant differences between groups of were listed only at the end of the study (visit 4) (Table 4). Significant differences between group A and D received for visit 4 on the PANSS scale of general psychopathology (O): cf. meaning G = 12.84 ± 2.89; Wed meaning A = 5.76 ± 3.94; position active syndromes (P): cf. meaning G = 7.42 ± 2.89; Wed meaning A = 2.67 ± 2.52. By the time of visit, 4 were also received significant differences between groups on the BPRS scale: cf. meaning G = 27.89 ± 8.94; Wed meaning A = 20.9 ± 9.12 (figure 1).

Table 4 Aripiprazolevs Haloperidole: Intergroup analysis with the scales BPRS, PANSS

Scale, visit	Group A, mean±std	GroupD,mean±std	*p*	Criterion for calculating p
PANSSO,B1	33,52±3,63	34,47±4,71	0,4767	Odd Student's t-test
PANSSO,B4	5,76±3,94	12,84±2,89	0,0001	Mann-Whitney test
PANSSP,B1	20,86±2,15	19,74±3,38	0,1617	Also
PANSSP,B4	2,67±2,52	7,42±2,89	0,0001	«»
BPRS,B1	67,86±4,37	69,58±3,52	0,1810	Odd Student's t-test
BPRS,B4	20,90±9,12	27,89±8,94	0,0097	Mann-Whitney test

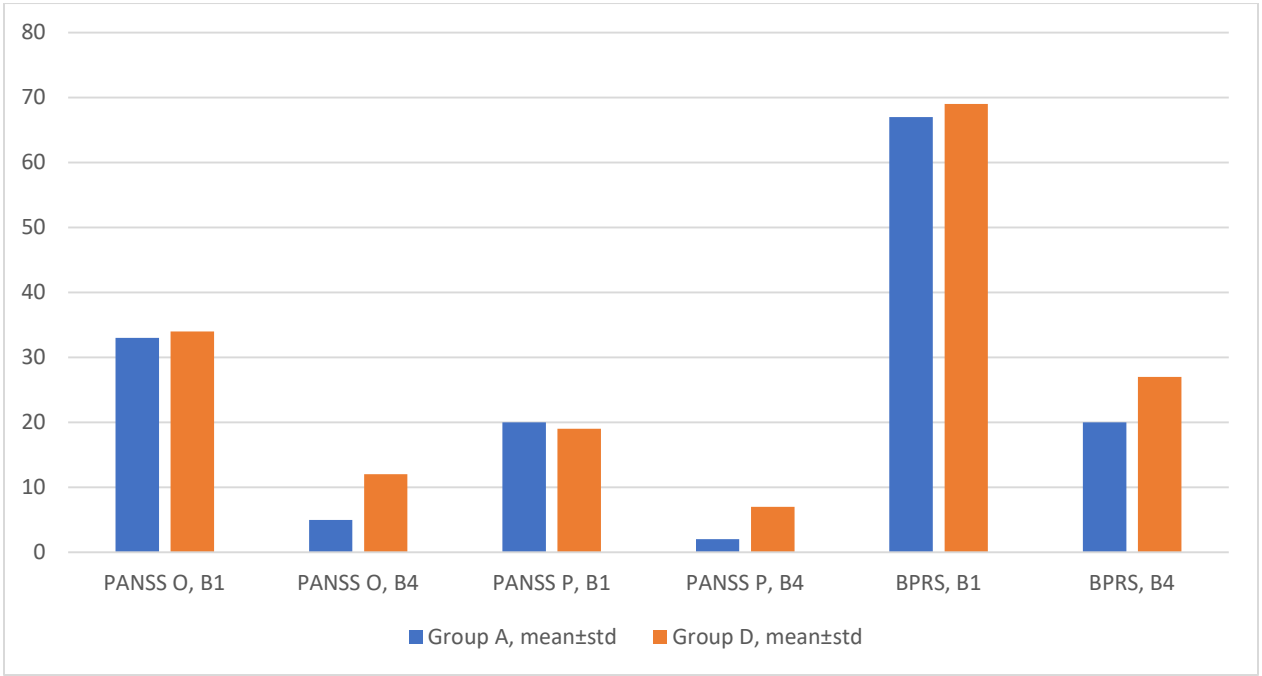

Figure 1 Aripiprazole vs Haloperidole: Intergroup analysis with the scales BPRS, PANSS

Significant differences in indicators of attraction scales were determined to the drug before the reduction of positive symptomatology, already by visit 2 (by PVN) or by visit 3. Intergroup comparison shows that aripiprazole is more effective than haloperidol in relation to the reduction of the syndrome of pathological attraction to drugs (PVN, YOUR): cf. meaning PVN-A 10.71 ± 1.19, cf. meaning PVN-G 17.79 ± 1.90; Wed meaning VASH-A 31.19 ± 10.24, cf. meaning VAS-G 53.16 ± 8.37 (Table 5).

Table 5 Aripiprazolevs Haloperidole: Intergroup analysis with the scales VAS, SACS

Scale, visit	Group A, mean±std	GroupD,mean±std	*p*	Criterion for calculating p
ПВН,В1	21,81±3,22	22,47±3,19	0,2223	Mann-Whitney test
ПВН,В2	10,71±1,19	17,79±1,90	0,0001	Also
ПВН,В4	3,71±2,53	11,89±1,10	0,0001	«»
ВАШ,В1	53,10±11,45	67,63±9,33	0,1850	«»
ВАШ,В3	31,19±10,24	53,16±8,37	0,0001	«»
ВАШ,В4	12,86±5,38	39,74±7,35	0,0001	«»

In the intergroup comparison of groups C and G, the indicators were some what different. On the PANSS scale, up to significant differences between these groups by visit 4: by scale of general psychopathology (O) cf. meaning G = 12.84 ± 2.89; Wed meaning K = 7.36 ± 5.34; positive syndromes (P) cf. meaning G = 7.42 ± 2.89; Wed meaning A = 3.35 ± 3.00. According to the BPRS scale, no true differences were obtained (Table 6). According to the indicator for drug craving scales (PVN, VAS) reliable differences were also identified by visit 4: cf. meaning PVN-K 6.40 ± 3.42, cf. meaning PVN-G 17.79 ± 1.90; Wed meaning YOUR-K 19.75 ± 8.50, cf. meaning VAS-G 39.74 ± 7.35 (Table 7).

Intergroup comparison of groups A and K showed that the two drugs are equally effective against the total psychopathological and positive symptoms of schizophrenic process (lack of reliable statistics the mental differences between the groups according to the PANSS scales, BPRS), but more pronounced statistically significant efficacy of aripiprazole versus quetiapine in relation to the syndrome of dependence (cf. 3.71 ± 2.53, cf. meaning PVN-K 6.40 ± 3.42; Wed meaning YOUR-A 12.86 ± 5.38, cf. meaning VAS-K 19.75 ± 8.50) (Table 8). With regard to the characteristics of clinical action aripiprazole was most effective in relieving ideational disorders (overvalued experiences, pa- early mood, a decrease in critical abilities, etc.) in the structure of the syndrome of pathological attraction to surfactants; quetiapine was most effective in relief of the affective component of the pathological attraction (depressive mood, anxiety, tense affect, etc.); haloperidol was the most effective active in the relief of behavioral disorders (aggressive this, psychopathic behavior, etc.) and ideological component of pathological attraction.

Table 6 Quetiapinevs Haloperidole: Intergroup analysis with the scales BPRS, PANSS

Scale, visit	Group K, mean±std	Group D, mean±std	*p*	Criterion for calculating p
PANSSO,B1	35,10±2,75	34,47±4,71	0,6127	Odd Student's t-test
PANSSO,B4	7,63±5,34	12,84±2,89	0,0029	Mann-Whitney test
PANSSP,B1	20,20±3,97	19,74±3,38	0,4215	Also
PANSSP,B4	3,35±3,00	7,42±2,89	0,0001	«»
BPRS,B1	68,40±4,79	69,58±3,52	0,3890	Odd Student's t-test
BPRS,B4	22,80±9,77	27,89±8,94	0,0983	«»

Table 7 Quetiapinevs Haloperidole: Intergroup analysis with the scales VAS, SACS

Scale, visit	Group K, mean±std	Group D, mean±std	*p*	Criterion for calculating p
ПВН,В1	21,30±2,81	22,47±3,19	0,0910	Mann-Whitney test
ПВН,В4	6,40±3,42	17,79±1,90	0,0001	Mann-Whitney test
ВАШ,В1	56,75±10,67	67,63±9,33	0,6760	Odd Student's t-test
ВАШ,В4	19,75±8,50	39,74±7,35	0,0001	Mann-Whitney test

Table 8 Aripiprazolevs Quetiapine: Intergroup analysis with the scales BPRS, PANSS,VAS, SACS

Scale, visit	Group A, mean±std	Group K, mean±std	*p*	Criterion for calculating p
PANSSO,B1	33,52±3,63	35,10±2,75	0,1265	Odd Student's t-test
PANSSO,B4	5,76±3,94	7,63±5,34	0,0383	Mann-Whitney test
PANSSP,B1	20,86±2,15	20,20±3,97	0,2599	Also
PANSSP,B4	2,67±2,52	3,35±3,00	0,2467	«»
BPRS,B1	67,86±4,37	68,40±4,79	0,7067	Odd Student's t-test
BPRS,B4	20,90±9,12	22,80±9,77	0,2691	Mann-Whitney test
ПВН,B1	21,81±3,22	21,30±2,81	0,2762	Also
ПВН,B4	3,71±2,53	6,40±3,42	0,0024	«»
ВАШ,B1	53,10±11,45	56,75±10,67	0,2976	Odd Student's t-test
ВАШ,B4	12,86±5,38	19,75±8,50	0,0034	Also

Correlation analysis

Correlation analysis was carried out on the general sample in order to demonstrate the tightness connections between signs concerning the manifestations of chemical and drug addiction diseases, in connection with which linear relationships were, identified between the scales PANSS, BPRS and scales VASH, PVN. Linear relationships were found at visit 1 between VAS and BPRS (rs = 0.8153 (95% CI 0.708; 0.886), n = 90, p <0.01), and at visit 4 between PVN and PANSS (general psycho pathology (O) (rs = 0.5823 (95% CI 0.712; 0.836), n = 90, p <0.01), positive symptoms (P) (rs = 0.5019 (95% CI 0.321; 0.661), n = 90, p <0.01)), between VAS and PANSS (total psychopathology (O) (rs = 0.5647 (95% CI 0.369; 0.721), n = 90, p <0.01), positive symptoms (P) (rs = 0.5697 (95% CI 0.583; 0.829), n = 90, p <0.01)) (Table 9).

The obtained strong and average correlations allow us to say that psychopathological sky symptoms of mental and drug addiction diseases are in a linear relationship: increase Correlation analysis was carried out on the general sample in order to demonstrate the tightness connections between signs concerning the manifestations of chemical and drug addiction diseases, in connection with which linear relationships were identified between the scales PANSS, BPRS and scales VASH, PVN. Linear relationships were found at visit 1 between VAS and BPRS (rs = 0.8153 (95% CI 0.708; 0.886), n = 90, p <0.01), and at visit 4 between PVN and PANSS (general psycho pathology (O) (rs = 0.5823 (95% CI 0.712; 0.836), n = 90, p <0.01), positive symptoms (P) (rs = 0.5019 (95% CI 0.321; 0.661), n = 90, p <0.01)), between VAS and PANSS (total psychopathology (O) (rs = 0.5647 (95% CI 0.369; 0.721), n = 90, p <0.01), positive symptoms (P) (rs = 0.5697 (95% CI 0.583; 0.829), n = 90, p <0.01)) (Table 9).

Table 9 Correlation analysis with the scales BPRS, PANSS and VAS, SACS

Scale, visit	YOUR,B1	YOUR,B4	PVN,B4
BPRS,B1	0,8153*		
PANSSO,B4		0,5647**	0,5823**
PANSSP,B4		0,5697**	0,5019**

Note. * - Pearson criterion; ** - Spearman's criterion.

The obtained strong and average correlations allow us to say that psychopathological sky symptoms of mental and drug addiction diseases are in a linear relationship: an increase in the manifestations of mental illness leads to an increase manifestation of the syndrome of pathological attraction, and its decrease leads to a decrease in the manifestations of the syndrome of pathological geological attraction.

Security Profile

Identified adverse and side effects (Table 10) were short-term, did not require the abolition of preparations or prescribing additional drugs. They identify-were only when questioning patients and passed on their own really. As can be seen from the presented data, the causal the investigative connection with taking the drug is doubtful in all manifestations except one (tremor), and clinical manifestations do not go beyond the priority manifestations withdrawal syndrome and post-withdrawal state. 16.7% of patients taking aripiprazole had revealed unfavorable PR. In the host group quetiapine, there were 26.4% of them; redox - 56.7%. The number of patients who completely passed the test follow-up on the background of therapy was as follows: aripiprazole - 83.3%, quetiapine - 73.6%, haloperidol - 43.3%.

Table 10 Supervise of Adverse Drug Reaction

Clinical manifestations	Goup A	Group K	Group D	Causal relationship
Tremor	1(3,3)	0	11(36,6)	Certain
Drowsiness	2(6,6)	4(13,3)	3(10)	Dubious
Increased anxiety	1(3,3)	0	0	Also
Headache	1(3,3)	0	1(3,3)	«»
Decrease in blood pressure	0	1(3,3)	0	«»
Dizziness	0	1(3,3)	0	«»
Xerostomia	0	1(3,3)	2(6,6)	«»

4. DISCUSSION

The results of the conducted randomized comparative study showed the following. Comorbid mental pathology of schizophrenic spectrum (mainly low-grade forms schizophrenia) in patients suffering from the syndrome of depending on the surfactant, it occurs quite often. In pro-in the study conducted the proportion of patients with double diagnosis" was 34% of these patients, slightly less than in half of the cases (in this study - in 40% of patients), the diagnosis of mental illness remained previously unrecognized. This situation can be associated with the fact that mental illness in such patients is erased, the clinical picture is dominated by de-oppressive and sub depressive disorders, overvalued, paranoid ideas that do not reach the level of delirium, which are very similar to the clinical manifestations of syn-core of addiction and can be seen in the structure attraction to psychoactive substances, withdrawal syndrome or mental de-gradation. Inherent in the schizophrenic process de- deficiency symptoms (autism, increasing isolation, emotional coldness, decreased energy potential) and specific disorders of laziness (reasonableness, slippage, illogicality of narrowing denim, etc.) are often not diagnosed by doctors. It leads to the use of ineffective therapy regimens, which in turn leads to frequent recurrence, rapid social maladjustment, and ultimately to early disability of these patients (Overall & Gorham, 1988).

Significant intragroup differences obtained on all scales in all groups, allow you to do one a significant conclusion about the effectiveness of antipsychotic remedies, both atypical and traditional, in the treatment of patients with "dual diagnosis". The resulting intergroup differences between atypical antipsychotics (aripiprazole, quetiapine) and a dietary agent (haloperidol) according to the PANSS scales, BPRS, VASH, PVN allow us to conclude that efficacy of atypical antipsychotics in relation to manifestations of the mental, and in relation to the manifestations drug addiction disease (Mosolov, 2011). Intergroup comparison of aripiprazole and quetiapine showed that the two drugs are equally effective against wearing the symptoms of the schizophrenic process (from-the absence of significant statistical differences between groups on the PANSS, BPRS scales), but aripiprazole ismore effective against the syndrome of pathological attraction to surfactants in comparison with quetiapine (reliable differences according to the PVN, VAS scales) (Huskisson, 1974).

The effectiveness of atypical antipsychotics in relation to manifestations of the schizophrenic process shows by the end of the 3rd week of treatment (visit 4), and in relation to manifestations of the syndrome of pathological attraction - to contuse of the 2nd week of therapy (visits 2 and 3). This data is sub-reaffirming the importance of long-term maintenance therapy antipsychotic drugs (Ivanets & Vinnikova, 2001). The obtained strong and average correlations allow us to say that psychopathological sky symptoms of mental and drug addiction diseases are in a linear relationship: increase manifestations of mental illness leads to increased manifestations of the syndrome of pathological attraction, and its decrease leads to a decrease in the manifestations of the syndrome of pathological geological attraction.

5. CONCLUSION

This result, in our opinion, is evidence testifies to the inextricable connection of psychopathological the phenomena of schizophrenia and the syndrome of pathological to surfactants. From this we can conclude that the drugs, used to stop the manifestations of mental diseases, are also effective in stopping syndrome of pathological attraction to surfactants. This is once again under-confirming that in situations of drug addiction, occurring comorbidly with mental endogenous pain, treatment tactics should be identical to treatment for endogenous disease.

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Author Contributions

Each author participated in the manuscript work & production.

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Conflict of Interest

The authors declare that there are no conflicts of interests.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval

The study was approved by the Medical Ethics Committee of KSUMC University (ethical approval number: REC-HSD -70/-2021).

Data and materials availability

All data associated with this study are present in the paper.

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