

## INTOXICATION PSYCHOSES CAUSED BY COMBINED DRUG USE

Ibragimova Muazam Holdorovna

Assistant of the department of psychiatry, medical psychology and narcology, Samarkand State Medical University, Samarkand, Republic of Uzbekistan

Shamshiyeva Zohida Saloxiddin qizi

Samarkand State Medical University Faculty of medicine №1,  
516-Group student, Samarkand, Republic of Uzbekistan.

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**Abstract.** *In recent years, there has been a trend in all developed countries of the world for the rapid spread of the combined consumption of psychoactive substances, the market of which is increasingly expanding due to the emergence of new synthetic drugs and drugs. Cases of the appearance of intoxicating psychoses as a result of the combined use of psychoactive substances of various pharmacological groups have become significantly more frequent, they are practically not found in the mono-consumption of classical opioids, and rarely occur with an overdose of natural cannabinoids.*

**Key words:** *synthetic drugs, drugs, psychoactive substances psychoses, classical opioid cannabinoid.*

## ИНТОКСИКАЦИОННЫЕ ПСИХОЗЫ, ВЫЗВАННЫЕ СОЧЕТАННЫМ УПОТРЕБЛЕНИЕМ НАРКОТИКОВ

**Аннотация.** *В последние годы во всех развитых странах мира наметилась тенденция быстрого распространения комбинированного потребления психоактивных веществ, рынок которых все больше расширяется за счет появления новых синтетических наркотиков и наркотиков. Значительно участились случаи появления интоксикационных психозов в результате сочетанного применения психоактивных веществ различных фармакологических групп, они практически не встречаются при монопотреблении классических опиоидов и редко возникают при передозировке натуральных каннабиноидов.*

**Ключевые слова:** *синтетические наркотики, наркотики, психоактивные вещества, психозы, классические опиоиды каннабиноиды.*

**Introduction.** The clinical features of such psychoses have not been sufficiently studied, and measures to stop them have been poorly developed, a number of researchers [1] argue that the use of synthetic drugs is currently at the epidemic level, and the real level of their abuse can be assessed only indirectly – with the appearance of somatic complications and psychotic diseases. Thus, in particular, clinical observations show that people who consume synthetic catinones are more likely to develop psychotic disorders when exposed to surfactants than those who use "conventional" drugs, whose clinical manifestations have symptoms typical of schizophrenia [2-4]. At the same time, issues related to the prevalence of schizophrenia-like psychotic disorders in consumers of synthetic catinones and the possibility of transforming them into disorders of the schizophrenia spectrum have not been fully studied. Currently, great attention is paid to the biochemical mechanisms of synthetic athinones, the acute toxic effect of their intake, the description of individual clinical cases of acute poisoning, etc. in some studies, they have been combined with other designer drugs, notably synthetic cannabinoids (spaysami.) [5-6]. There are

separate studies in which, on the contrary, mental disorders that occur during the reception of various groups of "designer drugs" are compared, but such works are of a special nature [7].

**The purpose of the study:** analysis of the phenomenological properties of psychotic disorders of consumers of synthetic catinones based on the results of modern research.

**The results and their discussion** are general data on psychotic disorders in those who take synthetic catinones. M. V. Prilutskaya and S. N. Molchanov, reviewing world literary data on publications devoted to the clinical aspects of designer drugs, found that the greatest number of health problems of users of these substances were associated with mental disorders – 64,4%. Often there were psychotic symptoms, as well as signs of darkening and mind suppression. At the same time, problems with the cardiovascular system came second with a frequency of about 17% [8]. In this regard, it should be noted that the presence of psychopathological symptoms in the reception of "traditional" psychostimulants was previously noted, but was mainly characterized as a complication of intoxication or withdrawal syndrome [9]. According to the European network for drug emergencies (Euro-DEN), the incidence rate of psychotic disorders caused by taking surfactants and leading to hospitalization is 6,3%. From the group of synthetic catinones, the following were noted: methylene dioxypirovaleron (MDPV) (27,3% of observations), mephedrone (5,7%) and methedrone (3,3%).

Thus, the ability of drugs to cause psychotic disorders differs significantly not only in substances of different groups, but also in one of them, in particular, in the group of synthetic catinones [10]. Taking catinones (in the study they were "natural catinones") was one of the first to focus on the possibility of causing the development of hallucinatory-delusional symptoms, J. Giannini and S. Castellani [11]. According to the literature, the most common acute psychopathological diseases after the adoption of SC are: anxiety, fear, symptoms of depersonalization and derealization, dysphoria, panic attacks, depressive disorders, acute paranoid reaction, sleep disorders, hallucinatory and illusory disorders, catatonic symptomatology, suicidal thoughts and actions, and convulsive seizures. It is noted that these acute psychotic disorders, as a rule, develop through the nose 0,5–2 hours after smoking or inhaling synthetic catinones and(or) immediately after intravenous administration [12].

In most sources, intoxication the appearance of psychotic disorders is indicated not only in the presence of addiction, but also with a single dose of SC [13]. However, risk factors for their occurrence are: genetic predisposition, history of opioid drug use and brain damage, intravenous and high-dose SK, experience of use, severity of addiction, early age of abuse, joint psychiatric disorders and high levels of anxiety [14]. V. D. Mendelevich noted that despite the fact that the frequency of intoxication psychotic disorders is associated with the duration and frequency of drug use, in some cases it is determined by individual sensitivity ("weakness"), since even one-time SK intake in a number of people leads to the development of psychotic diseases. In his opinion, the predisposing factors of their development were: injection or inhalation methods, repeated use in a short time, addiction, history of psychotic episodes, use along with other surfactants, long-term sleep disorders [15]. Examining clinical manifestations caused by drug use, the designer notes that intoxication is superior to withdrawal symptoms (24% to 76%) of psychotic disorders (54% to 76%). 46%) [16]. In this case, psychotic disorders usually develop within 2 weeks after drug use (according to the diagnostic categories ICD-10, F15.5x meets the criteria. "mental and behavioral

disorders caused by taking psychostimulants. Psychotic disorder"). Several clinical variants of such diseases have been noted in modern literature: polymorphic (45-91%), schizophrenia-like (up to 55%), mostly delusional (3,3-6%), Mostly hallucinatory (1,7–3,3%) [16]. Many publications emphasize the superiority of polymorphic psychotic disorders over isolated hallucinatory or delusional disorders. In addition, polymorphic intoxication psychotic disorders have been noted to contain symptomatology of the "endogenous" register, allowing them to be identified as schizophrenia-like psychotic disorders (F15.50) according to ICD-10. It has also been noted that these psychotic disorders are usually characterized by a longer and more severe course, and in some cases can develop into a disorder of the Schizophrenia Spectrum [17]. Psychotic disorders similar to schizophrenia as a result of taking synthetic catinones. In modern literature, there has been a significant increase in publications about the relationship between the increase in psychotic disorders similar to schizophrenia and the intake of certain surfactants from the mid-90s of the last century [18]. Thus, in Japan, cases have been described in which such disorders resulting from the intake of methamphetamines lasting up to 3 years, auditory hallucinations, imaginary ideas of a percutaneous nature, ideator automatism and spontaneous psychotic relapses (flashbacks) occur after a psychotic state [19]. Nevertheless, it has been noted that psychotic disorders resulting from "traditional "drug use are easily characterized by schizophrenia, as psychotic disorders are" moderate " and more suited to classical intoxication psychoses. V. D. Mendelevich studied the clinical picture of intoxication psychotic disorders, noting that the appearance of new synthetic surfactants has made the intoxication sixic diseases clinic more acute and diverse, which complicates their differential diagnosis with schizophrenia [20].

In modern literature, the most common clinical manifestations of psychotic disorders similar to schizophrenia are: affective-medial derealization and depersonalization, persecutor delirium, structural thinking disorder (elements of resonance, sperrung, mentism, disorder), senestopathic disorders, verbal and visual pseudogallusions, mental syndromes ("openness" and "mind reading").) and physical automatism, imaginary ideas of superpowers, catatonic symptoms [21]. For Example, V. Colley et al. one described catatonic arousal in a 19-year-old patient, replaced by waxy stiffness and immobility after taking a suspended mephedron within 3 days [22]. In The Study, N. M. Catatonic arousal was reported in 18% of patients with draluk acute intoxication psychotic disorder [23]. Initially, cases were recorded in which the manifesto of psychotic disorder occurred according to the exogenous type, and later the clinical picture had a clear "endogenous color" (the emergence of imaginary ideas of exposure and pseudogallusions), with a change in personality deficit [24]. In rare cases, gebephrenic arousal has been noted, as well as paraphrenization of delusional ideas [25]. In turn, some authors argue that in such cases the manifestation of mental automatism syndrome (experience of "extraordinary work of the brain", the phenomenon of "collective reading of thoughts" and "openness of thoughts", verbal and visual pseudogallusions) is unstable, has a short-term character and decreases at the end of an acute psychotic state [26].

A. A. Andrusenko, after studying 12 patients with schizophrenia-like psychotic disorders caused by taking SC, found that patients are characterized by syntonicity, no deficiency changes, initial changes in drug-type personality, symptoms of early organic brain damage, infantilism, and deviant behavior in adulthood. The beginning of the psychotic effect between these individuals, as

a rule, was acute, and at the same time there was a clear connection with the reception of SK, the secondary unopened nature of delirium, psychotic disorders had a long-lasting, oscillating character, but ended with a complete recovery (return to the "original" painful level). The other group consisted of 8 patients who were the first psychotic episode of undifferentiated schizophrenia associated with taking PAV (primarily  $\alpha$ -PVP). In this group of patients on the premorbid, manifestations of schizotypal diathesis, mild cognitive and negative disorders were identified, there was no direct causal relationship with intoxication. At the same time, psychotic disorders were characterized by the gradual expansion and complication of psychotic disorders, the absence of criticism, the beginning of subacute with the incompatibility of influence on the topic of delirium. Characteristic procedural changes in personality were also noted during the period of resolving the psychotic state [27-30]. In turn, I. V. Dubatova et al., examined 158 male patients on HDPE in a psychotic condition associated with the administration of designer drugs (catinones and "spices") and identified two groups of patients. The first group consisted of patients of the psychotic "exogenous" (45%), and the second group of patients of the "endogenous" (55%) type. In the first group, the severity of clinical manifestations and the duration of psychosis were clearly related to the dynamics of intoxication. In 73,6% of cases, psychotic conditions were stopped within 24 hours, and the rest within 2-3 days. The second group was formed from the very beginning by patients whose clinical picture included a combination of Affective and characteristic "schizophrenia" symptoms and often manifested by the consistent development of Affective-oneiroid attack. Thus, in 74% of patients with psychotic disorders similar to schizophrenia, the stage of Affective-delusional derealization and depersonalization was recorded with dramatization, false recognition, delusional disorders, affective and psychomotor disorders [31-33].

In 26% of patients with psychotic disorders similar to schizophrenia, the development of psychosis has reached the stage of delusional-fantastic derealization of self-awareness, disorientation, polar affective fluctuations, fantasy-fantastic perception of the environment, depersonalization with catatonic inclusions. In this group of patients, psychotic conditions, as a rule, took a long-term course (up to 4-6 weeks.) and intensive psychopharmacotherapy with antipsychotic drugs, and in some cases electroconvulsive and insulinomatous therapy were required. At the same time, there was no parallel between the reality of intoxication and the dynamics of mental disorder [34-37].

Recurrence of psychotic disorders similar to schizophrenia was mainly associated with the recovery of intoxication, but in 8% of patients they occurred autochthonically. The authors observed a large hereditary severity of mental and Narcological disorders in patients whose psychotic disorders have a clear schizophrenia-like clinical picture. It was also noted that psychotic disorders appeared in a certain group of patients independent, from the presence or absence of addiction syndrome [38]. Mental Disorders at the stage of formation of remission and in the postabstinent period. The study shows that 80% of psychotic disorders caused by taking synthetic cannabinoids and catinones persisted within a week, another 8% for 2 weeks, and 12% of patients for several months. At the same time, there is a tendency to complicate psychopathological structure, which often led to a revision of the diagnosis [39]. In turn, O. S. Yukov found that the duration of long-lasting psychoses in SK intake was an average of 2-3 months [40]. Many sources

indicate that after the cessation of psychotic disorder, critical response to the past condition does not occur immediately, and some patients retain a residual delusional interpretation even after discharge from the hospital. At the same time, partial amnesia of painful experiences was noted [41].

A. V. Pokrovskaya et al. patients dependent on synthetic psychostimulants experience schizophrenia-like symptoms during the postabstinent period, such as: hypomanic conditions, relationships, damage, harassment, as well as specific thinking disorders in the form of disorders, shifts, inconsistencies, resonances. Also, these individuals are characterized by the presence of individual signs of psychoorganic syndrome: a decrease in mental processes, a weakening of memory and attention, impoverishment of the emotional sphere, lability of influence, a decrease in mental activity, a decrease in criticism, etc. [42-45]. In turn, I. V. Pyatayeva et al. it is noted that in the postpsychotic period, thought disorders such as resonance, diversity, slippage occur in 90% of patients receiving synthetic catinones (before psychiatric hospitalization) [46]. Some researchers suggest that a number of patients addicted to "designer drugs" have hallucinogenic-persistent perceptual disorders (HPPDS), otherwise known as "flashbacks". Often such phenomena are observed at the stage of formation of remission and are very poorly stopped by antipsychotics [47]. It is noted that before the appearance of "designer drugs", these symptoms were mainly associated with the intake of hallucinogens (LSD, psilocybin, mescaline) and, in rare cases, psychostimulants [48]. Clinical manifestations, as a rule, include visual perception: geometric pseudogallusions, halos, light flashes, micropsies, subsequent images, etc [49]. Possibility of transition to schizophrenia and differential diagnostic criteria. Speaking about the similarity of psychotic disorders in the reception of synthetic catinones and effective symptoms in schizophrenia, many authors note that the totality of the pathogenetic mechanisms of the development of these mental disorders is associated with the dopaminergic neurotransmitter system.

It should be noted that most modern neurobiological theories come from the study of the effects of surfactants on neurotransmitters. The initial serotonin model was formed in the process of studying the effects of LSD on the human body, with amphetamines giving rise to the dopamine theory, the ketamine-glutamate model [50]. It is noted that dopamine-active surfactants (including SK) mainly affect effective symptoms and glutamate-active, in addition to affecting effective symptoms, has negative and cognitive effects [51]. The results of modern studies show that in schizophrenia, both systems are impaired, and these disorders are correlated [52]. It has been argued that the dopaminergic psychosis model is more typical of schizophrenia because drugs acting on D2 receptors are able to effectively suppress psychotic disorders [53]. In a study of methamphetamine psychotic structures, it was noted that early psychosis may be associated with the risk of more severe psychotic states due to the sensitivity and development of "dopaminergic hypersensitivity", especially in "vulnerable" people (with excessive expression and sensitivity of the DRD2 dopamine receptor) [54]. It is known that before the spread of modern "designer drugs", cannabinoids were considered the main trigger of intoxication of schizophrenia [55]. Thus, the average risk of psychotic disorder resulting from cannabinoid use becoming schizophrenia was 34%, while amphetamines were 22%, as the risk of psychotic disorder in cannabinoid abuse is very low– 0,5–5,0% [56]. M. S. K. Starzer et al. A study of psychotic disorders triggered by PAV



(n=6788) found that in 26% of patients, within the 20 years following the recording of these disorders, it had become schizophrenia, with about half of them within 5 years. The largest conversion rate to schizophrenia and bipolar disorder was cannabinoids – 47%, amphetamines – 32.3%. Also, their research shows that the likelihood of such a change is significantly higher in the younger (16-25 years old) [57]. However, there are publications showing that increasing the population's cannabinoid intake does not increase the proportion of schizophrenia in this population [58]. In his study I. V. Dubatova et al. intoxication compared patients with "schizoform" psychotic disorders and patients with normal endogenous schizoaffective disorders, and found that those who consume psychoactive substances with schizoaffective structures lacked the specifics of the clinical picture of psychopathological disorders. True, psychotic disorders caused by the use of surfactants were reduced by 1-2 weeks, there was less hereditary weight, and relapses occurred only with drug rehabilitation [59]. Similarities between psychostimulants and psychotic disorders caused by schizophrenia have previously been noted by other researchers [60]. At the same time, psychotic disorders caused by taking met differ from schizophrenia in that, first of all, visual and tactile hallucinations are often noted, and in rare cases, symptoms of negative symptoms: impaired thinking, decency, emotional detachment, blurred effect, etc., what can be used in differential diagnosis [61]. In the diagnosis of "endogenous" and "exogenous" psychotic disorders, many authors play a key role in the fact of taking surfactants before they appear [62]. However, the prevalence of "pure" cases of "endogenous" diseases is not so significant, as patients with schizophrenia often abuse drugs [63]. Up to 60% of all patients with schizophrenia have been recorded abusing Pav [64]. And here, G. A. Fastovtsov and S. N. According to oskolokova, an important issue: at what stage of the "endogenous" violation there were "exogenous" symptoms as a result of the intake of surfactants [65]. In addition, there is evidence in modern literature that psychopathological disorders caused by SC uptake persist even after the immediate effects of surfactants have ended, i.e. sometimes there is no direct parallelism

the effects and dynamics of psychotic disorder that allow this disorder to be reclassified as "endogenous" [66]. In addition to the lack of parallelism with drunkenness, G. A. Fastovtsov and S. N. According to Oskolokova, "exogenous" psychotic diseases caused by the use of SC are not characterized by a clear sequence of syndromes, which is characteristic of "endogenous" diseases, which can serve as one of the criteria for their differential diagnosis. Also, in their opinion, in the differential diagnosis of exogenous and comorbid psychotic diseases, the "response to therapy", that is, the "main response" to antipsychotic therapy, can help. In addition, they suggest that the picture of schizophrenia has undergone patomorphosis in recent decades, masked behind neurosis-like and psychopatho-like manifestations, which can further complicate diagnosis, including differential [67-70]. One of the important criteria for differential diagnosis is proposed to use the duration and tolerance of psychotic symptoms [71]. According to the 10th revised International Classification of diseases (ICD-10), the duration of hallucinatory-delusional symptoms should be more than 10 days, but less than 6 months. If it lasts more than 6 months, it is preferable to make a diagnosis from the categories of schizophrenia, schizotypal and delusional disorders [72]. The presence of psychotic disorders in long-term (more than 6 months) surfactant consumers makes it possible to speculate that they can be converted into a disorder of the Schizophrenia Spectrum. It is no coincidence that in recent years the scientific community has been discussing the issue of

introducing a separate category into ICD-11 – "psychotic disorder under the influence of surfactants", since these diseases do not always correspond to the traditional criteria of schizophrenia: these patients are critical of their condition, delusional disorders are mainly associated with incorrect perception.. and the onset of psychotic diseases, as a rule, is associated with the consumption of acute and surfactants. Also, with these disorders, visual perception deceptions often prevail, patients experience more aggressive behavior, suicidal thoughts are more common, and affective symptoms are observed [73-76]. However, factors that contribute to the transformation of the psychotic disorder of intoxication into schizophrenia are also distinguished: the absence of criticism of its condition, low premorbid function, the presence of schizotypal personality traits and the history of psychotic disorders in relatives [77-79]. Thus, the initial conclusion can be made that high rates of transformation can be associated both with the development of psychotic disorders and with misdiagnosis. In many ways, the inaccuracy of diagnosing schizophrenia in patients with long-term intoxication psychotic disorder can be attributed to the premorbidity of psychotic disorder and its debut itself, as well as an insufficient amount of catamnestic information. Affective Disorders in patients receiving synthetic catinones. Disturbances in the emotional sphere are characteristic of dependence on all surfactants, including psychostimulants [80]. Affective Disorders often dominate the clinical picture of removal symptoms, and are also an integral part of pathological attraction to surfactants. Often the formation of permanent remissions is hindered by disorders in the affective area of patients [81].

However, there is little research on the structure and phenomenological properties of Affective Disorders in SK consumers. This may be due to the fact that the attention of individual researchers is often directed to the diagnosis and description of hallucinatory-delusional symptoms, as well as the fact that Affective Disorders in the reception of SC did not differ significantly from other psychostimulants. There are many studies devoted to the study of SC consumer suicide behavior. Over the past few years, more than 70 works have been published on the connection of the use of SK with suicide [82]. At the same time, a characteristic feature of Affective Disorders in patients taking synthetic catinones: a connection with drug use, uncertainty of structure, weak differentiation, daily mood swings and lack of viability of the effect. Depressive disorders resulting from the intake of synthetic catinones and cannabinoids during the Postabstinent period are mainly represented by dysphoric type – 53%, apathetic – 27%, to a lesser extent – sad variant (20%). At the same time, high levels of anxiety are identified in 23% of patients and it is noted that affective disorders are directly related to PVN [83]. O. N. According to Patrikeyeva et al. in patients taking synthetic drugs (catinones and spices), the 3-6 month depression rate during remission ("vigilance") is not statistically different from the depression rate of healthy people, and is statistically significantly less than the 6 month remission. The anxiety level was statistically much higher than that of healthy individuals, and it remained virtually unchanged by the "vigilance period" (equally high as in the 3-6 month period., and for over 6 months.) [84]. At the same time, there are separate studies showing that "depression predisposition" is higher in SC-dependent patients (without indicating a "period of vigilance") than in healthy people [85]. D. A. Lyubchenko et al. their work emphasizes that for patients using SC, the presence of signs of subclinical depression and anxiety is common: emotional imbalance, tension, inner restlessness, decreased mood, joyslessness, "the tendency to see everything through black

glasses", etc. The main clinical picture of Affective Disorders in these patients, in their opinion, is depression, the second most common anxiety disorder (social phobia, panic attacks, obsessive – compulsive disorders). However, it has not been determined at what stage of treatment these patients were in [86]. M. L. Rohlina described ephedrone and primary addiction, noting that affective disorders such as clinically apparent dysphoria or sluggish-apatetic depression came to the fore after overcoming acute removal disorders [87]. A. R. Asadullin's study mentioned 30.8% of the occurrence of "suicide depressions" during the withdrawal period, 41% of patients had at least one history of attempted suicide, and 59% of them recorded suicidal thoughts [88]. In general, according to domestic and foreign literature, the proportion of patients receiving synthetic catinones with suicidal behavior ranges from 26% to 73% [89, 90]. A. R. Asadullin's study argues that suicide thought often arose during the withdrawal period, with suicide-related death being the second most common cause of death in SC-dependent [91]. A number of researchers, on the contrary, argue that the main reason for the suicide of such patients, on the contrary, is hallucinatory-delusional symptomatology during psychotic disorders of intoxication [92]. There is also evidence that an important prognostic sign of suicidal behavior of individuals receiving SC is of constant concern both during the removal of surfactants and during the period of "long-term withdrawal" [93]. O. N. According to Patrikeyeva et al., patients with a remission duration of more than 6 months have a higher risk of suicide (3-6 months) than those with a lower risk of suicide.) and in healthy people, which is related to their level of depression. At the same time, the risk of suicide in patients with a " duration of consciousness " of 3-6 months did not differ from healthy people [94].

**Conclusion** thus, the following preliminary conclusions can be drawn based on a review of the published data. Currently, the literature contains a detailed description of psychopathological diseases that develop with systematic and episodic reception of SC, highlighting their high comorbidity with a violation of the Schizophrenia Spectrum. At the same time, little is known about the catamnesis of patients with psychotic disorders, as well as the results of the treatment and rehabilitation of this group of patients. Issues such as the spread and causes of psychotic disorders similar to schizophrenia, their conversion to schizophrenia and, accordingly, differential diagnosis between them are still not well understood.

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