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Чему эпидемия COVID-19 научила психиатров?

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АННОТАЦИЯ

Статья посвящена анализу психопатологических последствий эпидемии COVID-19. Особо подчёркнут факт повышенной летальности от COVID-19 больных шизофренией и аффективными расстройствами. Сделан вывод о том, что на это влияло нерациональное использование антипсихотиков, способствовавших появлению у пациентов сахарного диабета и избыточной массы тела.

Ключевые слова: COVID-19, шизофрения, психические расстройства, психофармакотерапия, рациональное использование антипсихотиков и антидепрессантов.

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What did the COVID-19 epidemic learn psychiatrists?

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ABSTRACT

The article is devoted to the analysis of the psychopathological consequences of the COVID-19 epidemic. Particular emphasis is placed on assessing the fact of increased mortality from COVID-19 in patients with schizophrenia and affective disorders. It is concluded that this was influenced by the irrational use of antipsychotics, which contributed to the appearance of diabetes and overweight in patients.

Keywords: COVID-19, schizophrenia, mental disorders, psychopharmacotherapy, rational use of antipsychotics and antidepressants.

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The acute period of the COVID-19 pandemic demonstrated that, in addition to serious somatic (pulmonological, cardiovascular, etc.) complications and an attendant high mortality rate, the increased incidence of mental and behavioral disorders has become a significant problem [1–10]. Anxiety disorders, delirium, and insomnia are the conditions most frequently tracked. At the late stages of the new coronavirus infection, asthenia, increased fatigue, and cognitive impairment were detected [1, 4, 11–14]. Furthermore, the incidence of increased manifestations, failures of remission, and exacerbations were registered in patients who previously had psychopathologies, such as schizophrenia, bipolar affective disorder, and neurotic and organic mental disorders [7, 15–19].

that the related prevalence has been somewhat uneven across regions of the world.

Many of the short-term and long-term psychopathological effects of COVID-19 could be predicted based on the already-known patterns of transformation of mental functions during periods of viral infections. In particular, the development of so-called exogenous mental reactions in the form of asthenia, delirium, and cognitive impairment was already expected. It was not surprising that 9 months after the ingress of infection, one-fifth of patients (19%) continued to have these symptoms. Factors such as being of the female gender, at a younger age, medical history, depression, and the number of acute symptoms of COVID-19 have been seen to be associated with increased fatigue (Fig. 1) [12].

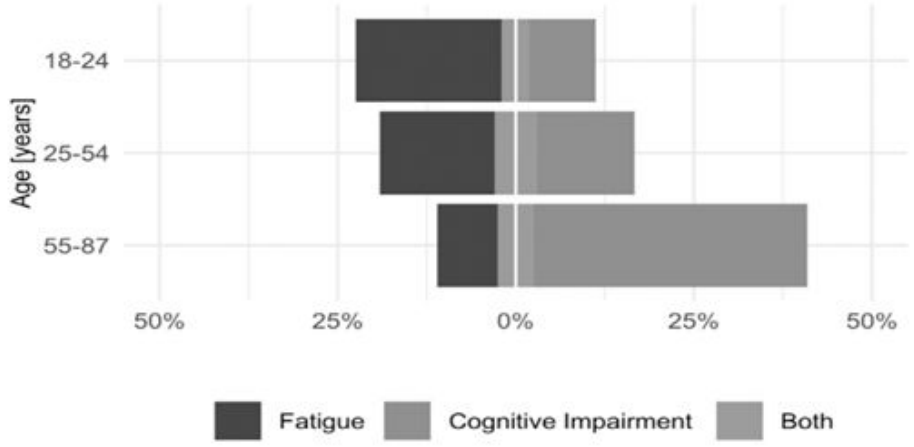

Fig. 1. Persistence of clinically significant fatigue and cognitive impairment 9 months after COVID-19 [12].

Following the acute period of the pandemic, the statistics indicated a significant increase (by 25.6%) in the prevalence of anxiety disorders across the world among 76.2 million people. The number of patients with a major depressive disorder increased from 38.7 to 49.4 million [20]. The largest growth (by 38.7%) was recorded in the Americas and South Africa, while in the Russian Federation, the increase was over 25%. During the pandemic, studies were conducted that have shown a risk of developing Alzheimer's disease and other forms of dementia in people who have had COVID-19 [13, 21].

The work "Long-Term Mental Health Consequences of COVID-19: a Systematic Review" [20] summarized the data on the impact of a novel coronavirus infection on mental health and concluded

However, psychiatrists found some unexpected effects that needed to be analyzed. It seemed logical to seek clear evidence that patients infected with SARS-CoV-2 might develop a significant cognitive impairment [standardized mean difference –0.41 (95% confidence interval –0.55; –0.27)], regardless of the stage of pathology and the age of the patients. However, another factor turned out to be unpredictable, as there was no clear relationship between the severity of the infection and the resultant degree of neurocognitive deficit [13].

The evidence that, in psychiatric patients, COVID-19 was much more severe, and had more pronounced negative consequences, also turned out to be scientifically perplexing. The prevalence of schizophrenia among 7,341 Korean patients with

Table 1. The mortality rate resulting from COVID-19 among mentally ill patients and in the group without mental disorders [24]

SARS-Cov-2-positive	Mortality rate, n (%)
All patients (n = 7003)	822 (11.7)
Schizophrenia spectrum disorders (n = 46)	12 (26.1)
Mood disorders (n = 374)	80 (21.4)
Anxiety disorders (n = 234)	29 (12.4)

COVID-19 was shown to be 3.6%, which increased the historic national prevalence rate for schizophrenia in Korea by more than five times (0.66%). The prevalence of schizophrenia in the case of severe COVID-19 was even higher, amounting to 5.4% [22]. Among 50,750 patients hospitalized with COVID-19 in France, the prevalence of schizophrenia was 1.6%, which was 60% higher than in the general population [16]. In addition, the presence of schizophrenia was found to be the second-largest risk factor for death from COVID-19 [23] and COVID-19 infection had a significant impact on the ultimate recovery and psychological well-being of patients with schizophrenia.

The comparative data on mortality deriving from a new coronavirus infection in patients with various mental disorders turned out to be even more shocking. The mortality rate was more than two times higher in the group of patients with schizophrenia, and almost two times higher in the group of patients with affective disorders, compared with the group of patients with no psychiatric history (Table 1). However, at the same time, the mortality rate of patients with anxiety disorders did not differ from the control group.

In connection with the data obtained during the research, psychiatrists turned to the analysis of the mutual influence of viral infections and psychopathological disorders, especially in terms of schizophrenia. Their attention was drawn to the historically viral concept of schizophrenia [25], and to the work by Menninger "Influenza and Schizophrenia: Analysis of Post-Influenza Dementia Praecox in 1918 and Five Years Later" [26]. The viral theory of schizophrenia assumed that the key factor in the induction of this pathology is a prenatal viral infection (i.e., retroviruses and viruses of the herpes family) [27, 28].

At a novel stage in the development of psychiatry, it was suggested that influenza has several pathogenic pathways in both the prenatal and postnatal periods, which thereby increased the risk of schizophrenia [29].

However, more current studies have shown that the incidence of a primary psychiatric diagnosis (including schizophrenia) between the week 2 and the month 3 after recovery was 5.8%, and the occurrence of any psychopathological symptoms after COVID-19 was approximately two times more common than was found with influenza or other acute respiratory infections. Thus, the implication was that the new coronavirus infection turned out to be more pathogenic for the psyche than other viral infections.

In this regard, the question arose about the mechanisms of the particular impact of COVID-19 on mentally disabled patients. Behavioral, somatic (comorbid), and pharmacotherapeutic factors were among the groups of factors that worsened the prognosis of the underlying disease during the pandemic. The first group included risky behavior and ignoring the danger of COVID-19, the poor financial situation of patients and the inability to purchase personal protective equipment, the refusal of vaccination, and a delusional interpretation of the pandemic. The second group included diabetes mellitus, obesity, hypertension, and chronic obstructive pulmonary disease, which was registered in patients with mental disorders, and the group 3 included the use of psychopharmacotherapy [30–34].

It has been suggested that the most significant contribution to the development of the severe course of COVID-19 and the mortality of patients with schizophrenia is made by a high level of comorbidity with diseases, in particular hypertension, diabetes mellitus, and chronic obstructive pulmonary disease. It was, therefore, proposed to change the therapeutic approaches to schizophrenia radically [35] due to the significance of the iatrogenic pathway of deterioration in the health of mentally disabled patients.

It is known that many psychotropic drugs can affect somatic health indicators negatively. Thus, for example, carbamazepine, valproates, and several antipsychotics can suppress the activity of myelocytes, increasing hypovolemia and electrolyte disorders; benzodiazepines can cause a decrease in

Table 2. Risk of developing diabetes mellitus and weight gain with the use of various antipsychotics [37]

	Risk of weight gain	Risk of diabetes mellitus	D_2- dopamine	$5HT_{2c}$- serotonin	$5HT_{1a}$- serotonin	M_3- muscarinic	α_2- Adrenergic	Hi- histamine
Role in body weight regulation			√	√				√
Role in insulin secretion			√		√	√	√	
First-generation antipsychotics								
Chlorpromazine	+++	+++	++++	++++	+	++++	+	++++
Perphenazine	+	+	++++	++++	+	+	+	+++
Haloperidol	++	+	++++	++	–	+	+	+/–
Second-generation antipsychotics								
Clozapine	+++	+++	+++	+++	++	+++	++	+++
Olanzapine	+++	+++	+	+++	+	+++	+	+++
Quetiapine	++	++	+	+	+	+	+++	++
Risperidone	++	++	+++	++++	++	–	++++	++
Ziprasidone	+	+	+++	++++	++++	–	++	+
Aripiprazole	+	+	++++	+++	++++	–	++	+
Paliperidone	++	+	+++	++++	+	–	+++	++
Lurasidone	+	+	++++	++	++++	–	N/A	–

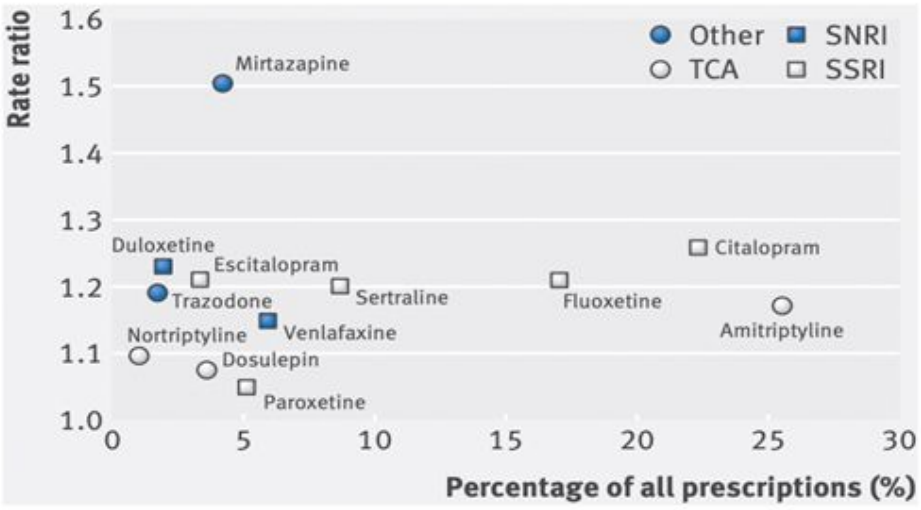

Fig. 2. The risk of becoming overweight when using various antidepressants [41].

muscle tone, increasing myasthenia and inhibiting respiratory function, and thereby increasing the risk of pneumonia; and central anticholinergic drugs (trihexyphenidyl, biperiden, etc.) increase the risk of pneumonia in older patients by between 1.6 and 2.5 times [4].

Such an analysis led to the conclusion that it is necessary to focus on the safety of drugs used in the treatment of patients with schizophrenia, especially on the appropriate use of antipsychotics [36]. The risk of developing two of the most important factors that aggravate the course and prognosis of COVID-19 (diabetes mellitus and weight gain) is known to vary when different antipsychotics are used (Table 2). The lowest risk was found for ziprasidone, aripiprazole, lurasidone, and paliperidone, and the highest risk was revealed for chlorpromazine, clozapine, and olanzapine [37].

The risk of diabetes mellitus when using antidepressants is not the same either, as it is 1.25 when

using selective serotonin reuptake inhibitors, 1.33 when using other antidepressants, 1.65 when using tricyclic antidepressants, and 1.82 with their combined use [38]. Long-term use of antidepressants increases the risk of type 2 diabetes mellitus in a timing- and dosing-dependent manner [38–40].

A comparative study of the risk assessment of becoming overweight when using antidepressants showed that mirtazapine and citalopram are among the most risky (Fig. 2) [41].

Another paradoxical psychopharmacological fact that emerged during the COVID-19 pandemic was the information that the use of certain antidepressants in those patients without signs of mental disorders can lead to the prevention of severe COVID-19 and reduce the attendant mortality rate. Based on the results of a scientific analysis of 15 randomized clinical trials of some 290,950 patients, this conclusion was found to be proven [38]. Fluvoxamine was among such antidepressants [42]. In addition, psychiatric hospital patients who took antidepressants were found to have a reduced risk of contamination with COVID-19. This led scientists to conclude that antidepressants could be an important weapon in the struggle against COVID-19 [33].

Thus, what psychiatrists learned from the analysis of findings from the COVID-19 pandemic enables us to draw the following conclusions:

1) Mentally disabled patients represent one of the most vulnerable groups in terms of mortality and complications from COVID-19 and other viral infections

2) It was noted that the use of psychopharmacological agents made a significant contribution to alleviating the negative consequences of COVID-19 in mentally disabled patients

3) Special attention should be paid to the safety criteria of psychopharmacotherapy

4) Some antidepressants are effective in treating COVID-19.

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