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Research Article

The Role of Buspirone in the Treatment of Patients with Paranoid Schizophrenia with Non-Suicidal Auto Aggression Who Have Had a Coronavirus Infection

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Summary

The relevance of this work is due to the insufficient number of modern studies on the treatment of patients with paranoid schizophrenia with non-suicidal autoaggressive actions or in short: "NSAA", who have had a coronavirus infection. The aim of the study was to study the role of buspirone in the complex therapy of patients with paranoid schizophrenia with NSAA who had a coronavirus infection.

Materials and research methods: 99 patients with paranoid schizophrenia meeting ICD-10 criteria were examined by a continuous, non-randomized clinical method. Fisher's test was used for statistical evaluation.

Results: It was established that the consequence of the coronavirus infection was an increase in the proportion of residual organic changes in the form of manifestations of the dysphoric syndrome, specific changes in the cognitive sphere, and the autonomic nervous system. The manifestations of dysphoria included an increase in the frequency of openly manifested aggression, anxiety, impulsivity, and the implementation of NSAA by the type of affective discharge. The structure of acquired cognitive impairments consisted of changes in thinking by the type of thoroughness, and rigidity of perseveration. Changes in the autonomic nervous system are presented in the form of diencephalic crises. Also, psychotic states not characteristic of the previously examined patients were noted, such as twilight stupefaction, delusional symptoms of Cappgras, Fregoli, and tactile hallucinosis. It has been established that the use of buspirone as part of complex therapy with neuroleptics, compared with monotherapy with neuroleptics, increases the effectiveness of therapy in relation to these clinical manifestations in the studied individuals.

Conclusion: The use of buspirone in combination with neuroleptic drugs increases the effectiveness of therapy in relation to the leading psychopathological manifestations in patients with paranoid schizophrenia with NSAA who have undergone coronavirus infection.

More Information

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Introduction

Coronavirus infection today is a serious clinical problem, the solution of which requires the use of an interdisciplinary approach. Despite unresolved questions regarding the pathogenesis of this infectious process, a number of studies suggest that SARS-CoV-2 enters the brain via the hematogenous route, or via the neuronal route through the nasal mucosa and olfactory nerve fibers. Coronavirus infection is a trigger for inflammatory and autoimmune processes, triggering the processes of change apoptosis and hypoxia of various parts of the brain [1-7].

Based on a number of studies, it can be argued that the implementation of the clinical effect of SARS-CoV-2 is the influence of the spike protein of the virus and the angiotensin-converting enzyme receptor 2, which is widely represented in neurons and microglia of cortical and subcortical formations. The wide presence in the central nervous system of such neurotransmitters as dopamine and serotonin makes them vulnerable to the destructive influence of SARS-CoV-2 [8]. The result is a change in the structure of psychopathological manifestations of patients with paranoid schizophrenia, which requires the selection of effective therapy, both in relation to the procedural disease and complications caused by the infectious process [9-18]. One of the options for solving this clinical problem is the use of adjuvant agents in regimens with the appointment of antipsychotics as first-line drugs for the treatment of patients with paranoid schizophrenia. A similar

adjuvant drug can be the use of buspirone in such patients, the main mechanism of action of which is to stimulate presynaptic serotonin 5-HT1A receptors of various localization. According to some researchers, this effect can be used in the treatment of negative disorders in schizophrenia [19-21]. At the same time, the question regarding the use of buspirone in the treatment of patients with paranoid schizophrenia with non-suicidal autoaggressive actions or in short: "NSAA" who have undergone coronavirus infection remains unexplored, making this study relevant.

Purpose of the study

Was to study the role of buspirone in the complex therapy of patients with paranoid schizophrenia with NSAA who had a coronavirus infection.

Materials and research methods

A 6-week study examined the efficacy of adjuvant use of buspirone in 99 patients with paranoid schizophrenia with NSAA who had a coronavirus infection. All surveyed were on inpatient compulsory treatment. All subjects were men aged 20 to 60 years. The average age of the subjects was 31.4 ± 1.0 years. The average duration of a procedural disease was 17.7 ± 1.7 years. Type of flow of the schizophrenic process: continuously - progressive. The inclusion criteria were: 1) compliance of the diagnosis of paranoid schizophrenia with the criteria of the ICD - 10th revision (F20.0); 2) a state of remission, with signs of an increasing procedural personality defect; 3) implementation of the NSAA by the surveyed; 4) verified past coronavirus infection not earlier than 6 months before inclusion in the study; 5) the course of the coronavirus infection corresponded to mild or moderate severity; 6) taking the drugs declared in the study no earlier than 6 months before inclusion in the study. Exclusion criteria were: 1) psychotic level of disorders prior to inclusion in the study; 2) severe course of coronavirus infection. The severity of the course of coronavirus infection was determined by the clinical guidelines for diagnosing coronavirus infection in force on the territory of the Russian Federation (*https://www.BMP_COVID-19_V16.pdf (minzdrav.gov.ru).* The assessment of the mental state of the survey was carried out by the clinical method at the time of inclusion in the study (day 1), then on the 21st and 42nd day of the study. A comparative analysis of the frequency of committed acts of non-suicidal auto-aggression was carried out for a period of 12 weeks before and after inclusion in the study. As part of the study, the main group and the comparison group were identified. The first group consisted of subjects who were on quetiapine monotherapy (24 people) and haloperidol monotherapy (22 people). The comparison group consisted of patients taking combination therapy: quetiapine + buspirone (27 people), as well as haloperidol + buspirone (26 people). The choice of antipsychotic drugs for the study was due to their most frequent use in practical work with this category of patients. Average daily doses were: quetiapine -665.6 ± 3.2 mg; haloperidol - 12.2 ± 0.3 mg; quetiapine + buspirone - 654.7 ± 2.9 mg + 57.4 ± 1.1 mg, and haloperidol + buspirone 9.4 ± 0.9 + 57.2 ± 1.3 mg, respectively. The assessment of the mental state of the survey was carried out by a clinical method at the time of inclusion in the study (1 week), then at 12 and 24 weeks of the study. The clinical efficacy of therapy was determined by a comparative analysis of the frequency of committed acts of non-suicidal auto-aggression for a period of 24 weeks before and after inclusion in the study. At the Scientific Center for Mental Health, Moscow, Russia (*https://www.ncpz.ru*).

Fisher's test was used for statistical evaluation. The structure of clinical and psychopathological manifestations in the pre-COVID period was determined by a persistent increase in negative disorders with periodic exacerbation of psychotic symptoms. The latter contained an element of protopathic anxiety, increasing psychomotor agitation and insomnia. Further, delusional ideas of persecution, a feeling of "mastery" of thoughts, a feeling of their accomplishment and openness to others joined. Hallucinatory experiences were auditory, had an imperative character. Among the negative procedural changes, apathy, abulia dominated, increased fatigue against which the patients developed mental disorders in the form of atactic closures, sperrungs. An additional background was a tendency to mood swings with a hypothymic tint, emotional coarsening. There was no criticism of his condition and attitude to treatment. NSAA were notable for their specific situational focus, such as strengthening hospital compliance requirements. Also, non-suicidal self-harm was distinguished by the presence of a preparatory period, during which it was possible to single out the stage of abstract ideas about the possibility of their commission; this was followed by a stage of thinking about the specific ways and timing of the implementation of the NSAA, including the collection of information on similar cases from other patients. Further, specific plans were supplemented by a volitional component, which was followed by the actual act of non-suicidal auto-aggression. The application of non-suicidal self-harm contributed to a sharp decrease in the relevance of the traumatic situation with a return to the usual level of social functioning over the next 3-4 days. The phenomenon of clinical pathomorphosis caused by the transferred infectious process manifested itself in the form of an increase in the frequency of dysphoric reactions in the form of a combination of anxiety with irritability, anger and increased impulsivity. Among the psychotic manifestations, the Kappgra symptom, the Fregoli symptom, and the phenomenon of tactile hallucinosis, which were not previously characteristic of the examined, were noted. Two patients have a syndrome of twilight confusion of consciousness with severe arousal, further developed tonic-clonic paroxysms. Psychotic experiences were accompanied by massive somato-vegetative manifestations of the type of diencephalic crises. Massive sweating, dizziness, diffuse headaches, subfebrile body temperature without signs of an inflammatory process

were noted. When the psychomotor excitation subsided, there were urges to urinate and defecate of an imperative nature. The development of negative disorders changed due to the appearance of previously uncharacteristic thinking disorders in the form of thoroughness, rigidity, and perseveration. Increased emotional coarsening, lack of initiative, narrowing the range of interests to the satisfaction of the simplest everyday issues. The NSAA themselves were also undergoing a change. The preparatory period was shortened due to the disappearance of the planning stage, as a result of which NSAA were applied impulsively, like an affective discharge, in fact, being a manifestation of the dysphoric syndrome. After an act of non-suicidal auto-aggression, a feeling of physical weakness, motor retardation developed, while maintaining an angry-irritable mood, difficulty in concentrating. The duration of this state was up to 7 days or more.

Research results

It was established that all the therapy regimens used had a positive effect on openly manifested aggression, differing in the degree of intensity and time of clinical response (Table N1). In the third week, such positive clinical changes in patients taking adjuvant therapy with buspirone took on a statistically significant character, and in cases of monotherapy remained at the level of positive trends. At the sixth week, the reduction in openly manifested aggression was statistically significant in all comparison groups, being more pronounced in individuals taking combination therapy.

Also, the treatment regimens used differed in the degree of clinical response in relation to impulsivity (Table N2). In the third week, such positive clinical changes in patients taking adjuvant therapy with buspirone took on a statistically significant character, and in cases of monotherapy remained at the level of positive trends. At the sixth week, the reduction in manifestations of impulsivity was statistically significant in all comparison groups, being more pronounced in individuals taking combination therapy.

Table N1: Comparative analysis of the effectiveness of therapy in the examined patients according to the scale of Yudovsky's openly manifested aggression.

International non-proprietary name of the drugs used	Stages of evaluation of therapy (in points)		
	1st day	21st day	42nd day
Quetiapine	14,2	9,7 F1.46)	6,1 F2.33)*
Quetiapine + Buspirone	14,5	6.3 F2.3)**	5,1 (F2.84)**
Haloperidol	14,7	8,4 F1.75)	5,6 (F2.63)**
Haloperidol + Buspirone	14,8	5,7 F2.6)**	4,7 (F3.15)**

*$p < 0,05$, **$p < 0,01$

Table N2: Comparative analysis of the effectiveness of therapy in the examined patients according to the Pluchek impulsivity scale.

International non-proprietary name of the drugs used	Stages of evaluation of therapy (in points)		
	1st day	21st day	42nd day
Quetiapine	50,9	39,2 (F1.3)	23,7 (F2.15)*
Quetiapine + Buspirone	51,4	29,1 (F1.77)*	20,1 (F2.56)**
Haloperidol	55,6	36,5 (F1.52)	21,3 (F2.61)**
Haloperidol + Buspirone	54,9	26,5 (F2.07)*	19,4 (F2.83)**

*$p < 0,05$, **$p < 0,01$

Table N3: Personal scale of manifestations of anxiety (J.Teylor).

International non-proprietary name of the drugs used	Stages of evaluation of therapy (in points)		
	1st day	21st day	42nd day
Quetiapine	46,4	32,4 (*F*1.43)	25,3 (*F*1.83)*
Quetiapine + Buspirone	46,3	24,1 (*F*1.92)*	21,4 (*F*2.16)**
Haloperidol	45,9	36,9 (*F*1.24)	25,2 (*F*1.82)*
Haloperidol + Buspirone	46,8	25,5 (*F*1.84)*	22,6 (*F*2.07)*

*$p < 0,05$, **$p < 0,01$

The treatment regimens used differed in the degree of influence on the level of anxiety (Table N3). In the third week, positive clinical changes in patients taking adjuvant therapy with buspirone took on a statistically significant character, and in cases of monotherapy remained at the level of positive trends. At the sixth week, the reduction of anxiety was statistically significant in all comparison groups, being more pronounced in patients taking combination therapy of quetiapine and buspirone.

Against the background of ongoing therapy, the frequency of NSAA in patients taking quetiapine was 3.8 cases in the retrospective period and 2.1 cases in the prospective period (F 1.81, $p < 0.05$). In patients taking haloperidol, this figure was 3.9 and 2.1 cases (F 1.86, $p < 0.05$); In patients who underwent combined treatment with quetiapine + buspirone, as well as haloperidol + buspirone, the dynamics of NAAA implementation was noted at the level of 3.6 and 1.7 cases (F 2.12, $p < 0.05$), and 3.8 and 2.0 (F 1.9, $p < 0.05$) cases, respectively.

Discussion

The results of a 6-week study indicate the ability of buspirone as an adjuvant to increase the effectiveness of therapy in the patients studied. It has been established that the selection of therapy for such patients should take into account the phenomena of clinical pathoformosis as a result of a coronavirus infection. In practice, this was manifested by an increase in the proportion of residual organic changes in the form of manifestations of dysphoric syndrome, cognitive impairment, and changes in the autonomic nervous system. The manifestations of dysphoria included an increase in the frequency of openly manifested aggression, anxiety, impulsivity, the implementation of NSAA by the type of affective discharge. The structure of acquired cognitive impairments consisted of changes in thinking by the type of thoroughness, rigidity of perseveration. Changes in the autonomic nervous system were presented in the form of diencephalic crises. Also, psychotic states not characteristic of the previously examined patients were noted, such as twilight stupefaction, delusional symptoms of Cappgras, Fregoli, tactile hallucinosis. At the same time, the question of the nosological affiliation of negative disorders noted at the clinical level in the form of increased emotional coarsening, lack of initiative, narrowing the circle of interests to satisfy the simplest everyday issues remains debatable. Verification of these conditions is possible with a more thorough clinical and follow-up analysis of

patients, as well as with their longitudinal observation in the future. The working hypothesis of the results obtained can be the polymodal effect of buspirone, which is realized mainly through the following mechanisms:

- 5-HT1A receptor agonism;

– Antagonism of D2 dopamine receptors;

- Antagonism of noradrenergic receptors.

To date, knowledge of the complex structure of the pathogenesis of schizophrenia raises doubts about the effectiveness of using buspirone as monotherapy in such patients. At the same time, this study showed that buspirone enhances the clinical effect of neuroleptics, which are the basic drugs in the treatment of this pathology. Moreover, the increase in the clinical effect with adjuvant use of buspirone concerned both first and second generation antipsychotics. A positive clinical response in relation to such psychopathological manifestations, which are aggressiveness, impulsivity, anxiety, and NSAA itself, with combined therapy with the use of buspirone, is realized more intensively and occurs earlier than with monotherapy with antipsychotics. The question of the effectiveness and tolerability of the use of buspirone when it is used for a longer time in such patients remains debatable. To a large extent, this depends on the degree of reversibility of residual organic changes in the central nervous system, which are complications of coronavirus infection. A promising method of therapy for such patients is a more active combination of buspirone with psychotropic drugs of different classes with different pharmacodynamic properties. For example, an increase in the effectiveness of therapy for psychomotor agitation is possible with the combined use of buspirone, neuroleptics and benzodiazepine derivatives (lorazepam, diazepam). To enhance the clinical response in the treatment of anxiety, dysphoria, diencephalic and convulsive paroxysms, as well as psychotic conditions associated with them, it is permissible to add both buspirone and anticonvulsants (carbamazepine, valproic acid, pregabalin) to the basic therapy with neuroleptics. These assumptions also require additional research.

Conclusion

Thus, it has been established that the use of buspirone in combination with neuroleptic drugs increases the effectiveness of therapy in relation to the leading psychopathological manifestations in patients with paranoid schizophrenia with NAAS who have undergone coronavirus infection.

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