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Experience in the Use of an Immunomodulator in the Complex Treatment of Patients with Resistant Forms of Paranoid Schizophrenia

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ABSTRACT

The problem of therapeutic (medical) resistance is quite complex and relevant. The emergence of new antipsychotic drugs, as well as special methods designed to affect resistance, the number of patients who do not respond to drugs remains constant and is 30%.

Introduction. Therapeutic (medical) resistance in some cases determines the tendency for the development and change of psychopathological syndromes and the course of mental illness [1], which in turn leads to the need to develop anti-resistance measures. The problem of polyprogmasia in the treatment of mental disorders also remains relevant. In most cases, half of patients take two or more medications [2-4]. Using combined therapy, psychiatrists seek to increase the effectiveness of treatment, stop painful manifestations, sometimes forgetting that the main problem when using several drugs can not only develop potentially dangerous interactions of drugs, but also increase the risk of developing extrapyramidal complications [5-8]. In the last decade, various methods of increasing the effectiveness of anti-resistance therapy in a more favorable direction have been tested. Studies show that when the maintenance dose of the drug drops significantly, the risk of developing side effects decreases and the therapeutic effect is maintained [9, 10]. According to statistics, the number of patients with schizophrenia is increasing every year. Therefore, the problem of the formation of therapeutically resistant cases of paranoid schizophrenia, the study of the mechanisms of development and effective methods of overcoming resistance to treatment remains relevant. In a large proportion of patients with Paranoid schizophrenia, a change in the immunobiological reactivity of the body is one of the main reasons for the development of therapeutic resistance. Data on a decrease in the functional activity of blood t-lymphocytes in schizophrenia has been confirmed in many studies. This suggests the need for the use of immunostimulating drugs in the complex treatment of paranoid schizophrenia and the development of scientifically based immunocorrectional methods to

overcome resistance to psychotropic drugs in patients [11-13].

Modern epidemiological studies found that in patients with somatic diseases in the Russian Federation, the prevalence of schizophrenia is much higher than in the population and is 6.2% compared to 1% of the total population [14].

Through numerous studies, it was found that not only the biological theory of the appearance of schizophrenia, the concept of hereditary and constitutional dependence, autointoxication, but also serious disorders of the immune system prevail, which served as the basis for the use of immunoactive drugs [15].

Disorders in the immune system are one of the predisposing factors for the development of pyoderma, a wide and common group of skin infections that account for one-third of all skin pathologies. It includes a variety of clinical manifestations, courses, and prognostic disorders that can occur spontaneously and complicate other dermatoses [16].

To date, pyoderma is one of the most common dermatoses, ranging from 17% to 43% in the general structure of skin pathology [17]. According to the researchers, the prevalence of pyoderma in patients with mental and behavioral disorders is 17.3% [18]. At the same time, in general, the problem of schizophrenia in patients with a general medical network and pyoderma remains insufficiently developed. In the popular literature, work has hardly been presented in which the problem of pyoderma pharmacotherapy in patients with schizophrenia can be systematically studied. In this regard, it is advisable to consider the possibility of using immunotropic drugs in the treatment scheme of these patients. High rates of pyoderma in patients with schizophrenia, often with a chronic, repeated malignant course, resistance of individual clinical forms to therapy, the development of invapidizing complications determine the relevance of the problem and determine the need to study these diseases more deeply in order to improve their treatment methods [19-21].

Schizophrenia is characterized by a chronic course, the functional state is constantly worsened, repeated and repeated more often hospitalization, decreased quality of life and, as a rule, it is accompanied by significant psychosocial misalignment of patients, social barriers and communication difficulties [22]. Each exacerbation worsens the chances of cognitive and social functioning of patients aggravates the prognosis of the disease, increases the risk of resistance to therapy; this is due to increased neurodegenerative changes in the brain [23]. With each relapse of the disease, the patient's chances of returning to the previous level of work are reduced [24].

One of the conditions of a favorable prognosis of the disease is timely and effective treatment [25]. Of particular importance for patients with schizophrenia is long-term supportive therapy aimed at forming high-quality remission and preventing recurrence of the disease [26]. The quality of remission is associated both with effective symptom control and (to a greater extent) with the effectiveness of exposure to negative and affective symptoms of the disease. An important factor in providing supportive therapy is the commitment of patients to treatment, which largely depends on the tolerance (safety) and effectiveness of psychopharmacotherapy [27-29].

Thus, according to the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, higher rates of therapeutic response and tolerance profiles of the drug are associated with lower levels of therapy discontinuation [30].

There is an opinion that a large percentage of patients with schizophrenia spectrum disorders can be treated in a public setting, without being separated from the usual social environment [31-35], which is primarily determined by the nature of antipsychotic therapy.

Despite the remarkable advances in the treatment of schizophrenia in recent years, the range of

therapeutic resistance in schizophrenia ranges from 5 to 60%.

In recent decades, the proposed options for differential indications for the use of antipsychotic agents based on the clinical and psychopathological structure of diseases have certain limitations due to different tolerances [36-38].

A number of studies have shown that, unlike classical antipsychotics, the absence or negligible severity of adverse events, and the maintenance of subjective well-being in treatment with atypical antipsychotics help improve patient compatibility and quality of life. In addition, one of the advantages of atypical antipsychotics is a certain dose range [39-44].

Paliperidone (Invega) is an atypical antipsychotic developed by Janssen Pharmaceuticals that has been shown to be effective and safe in clinical trials involving more than 1,600 patients from 23 countries. Invega is the first oral antipsychotic, providing the same and constant level of drug substance concentration without sharp fluctuations due to the special supply of the active substance to the body – controlled release of Paliperidone for 24 hours. Paliperidone is an active metabolite of risperidone and is characterized by an innovative system of osmotic controlled release of the drug [45-50].

Indication for the use of the drug Invega schizophrenia both in the period of exacerbation and in the stage of prevention of recurrence of schizophrenia [51]. The therapeutic strategy in all observations is aimed at stopping and controlling positive and negative symptoms and ensuring the social functioning of patients [52-57].

Thus, Invega was successfully used as a stop and anti-relapse therapy in a 48-year-old patient. In the patient was admitted to a day hospital in connection with an exacerbation of the condition in the form of psychomotor arousal, phenomena of mental and physical automatism, ideas of dramatization. Inve was prescribed at a dose of 6 mg,and then the dose was up to 12 mg per day, in the first 3 days – in combination with intramuscular phenazepam. The patient tolerated the therapy satisfactorily; no additional appointments of correctors were required. The mental state stabilized against the background of taking Invegi at a dose of 12 mg per day. A complete state of medical remission was achieved through 2,5 months of therapy. The patient was sent to inve care therapy at a dose of 9 mg per day, against the background of which the adherence to therapy increased and had a stable remission for 3 years. There was a clear flattening of negative symptoms, an increase in patient activity. During this period, he completed hairdressing courses and got a job. An improvement in microsocial adaptation, an expansion of the social circle was noted [58-60].

The effectiveness of invegui against relapse also indicates a case of treatment for a 37-year-old patient who has alcohol abuse and stopped taking medication shortly after discharge from the hospital, which is accompanied by an increase in hallucinatory-paranoid symptoms with suboneuroid events. 35 mg of majeptyl per day and 100 mg of azaleptin per day therapy did not allow the Prevention of annual regospitalization. The patient was characterized by conflict, antisocial tendencies. As of 2009, Group III disability is associated with the development of an apatoabular defect, a personality change of the schizophrenic type. The therapy was changed to solian 400 mg / day, Convulex 600 mg / day, azaleptin 12.5 mg / day. The situation remained unstable. In August 2009, inve was prescribed 6 mg/day, depakin 900 mg / day, azaleptin 25 mg. against the background of this therapy, there was no exacerbation of symptoms, the patient's behavior was regulated, including stopping alcoholism. The patient found a job, began to regularly visit the HDPE, strictly adhered to the supportive therapy regimen, no adverse events were recorded. Family relations were restored [61-64]. The mental state remains stable. This experience of using Invega demonstrated the possibility of taking it as part of combined therapy with good tolerance and no drug interaction. At the same time, the choice of psychotropic agents was carried out taking into account the structure of psychopathological symptom complexes.

Suppressing and support therapy with Invega, which combines a strong antipsychotic effect with good tolerance and the absence of behavioral toxicity phenomena, allows for a significant optimization of the prognosis of patients with schizophrenia. The following observations confirm that inve can be successfully used in patients at high risk of developing side effects with poor tolerance of neuroleptic therapy [65-67].

The purpose of the study: to develop a new method of complex treatment of resistant forms of paranoid schizophrenia, including psychotropic and immunostimulating effects.

Materials and methods. The case was based on a study that found 80 men with schizophrenia undergoing mandatory treatment in a specialized type inpatient hospital under intensive surveillance for more than a year. Regardless of the nature of the preliminary data (results of clinical-psychopathological and clinical-catamnestic studies, medical history, conclusion of forensic psychiatric examination, court decisions, archival materials, results of direct observation of patients), diagnostic criteria were used to identify paranoid schizophrenia in accordance with the diagnostic criteria of ICD-10.

Other criteria for inclusion in the study:

- Patients with a correct diagnosis for a sufficient period of time (1-2 years) from 20 to 60 years, combined psychopharmacotherapy, including in an expanded form;
- Informed voluntary consent of the examined person (excluding persons who are incapacitated).

Exclusion criteria:

- presence of severe somatic and neurological symptoms;
- substance dependence.700

Research methods:

1. Clinical-psychopathological;
2. Clinico-catamnestic;
3. Immunological;
4. Experimental-psychological;
5. Statistic.

Research results. In the process of work, immunological blood tests were performed on all patients before and after the use of immunostimulating therapy, where the functional activity of t-cell and humoral immune connections was determined. It has been found that the number of T-lymphocytes, t-aids, and t-suppressors in patients with schizophrenia does not differ from these indicators in the immunogram of a generally mentally healthy person.

Differences were found in the classification of a general group of patients with Paranoid schizophrenia into subgroups based on the course of effective symptomatology. Thus, in the first subgroup (57 patients), at the stage of assessing the state of immunity before the appointment of immunostimulating therapy, an increase in the number of t-AIDS and a decrease in the number of t-suppressors were found in patients with a constant type of disease. A decrease in the total number of T-lymphocytes was found in patients with low progressive schizophrenia in the second subgroup (23 patients). It was also noted that the number of killer cells in all small groups of patients did not differ from that of healthy patients.

The study found that the highest levels of interleukin - 1B (il - 1B) were associated with increased psychotic symptoms in patients with schizophrenia (92% of those tested) and interleukin - 6 (il-6) and interleukin -2 (il-2) were associated with increased severity of hallucinatory-paranoid symptoms and resistance to therapy. (85%).Also, with long-term treatment with psychotropic drugs (more than 5 years), the number of T-suppressors in patients decreased significantly (60% of those tested).

All patients are prescribed the immunostimulating drug "BESTIM" in a solution of 100 mcg in 1 ml of water for intramuscular injection 1 time a day. The course of treatment is 5 injections. After the course of immunostimulating therapy, the following results were obtained: an increase in the number of t-suppressors was recorded compared to the initial level – 88,75 % (71 patients) 3,75 % (3 patients) - the indicators did not change; 7,5% (6 patients) due to the development of side effects (nausea, dizziness), immunostimulating therapy was not possible). When assessing mental state during the study, positive dynamics were noted with a decrease in acute effective symptoms in 82,5% of subjects, excluding cases of side effects of immunostimulating therapy. In 8 patients, despite the prognostically favorable course of the disease and combined therapy, it was impossible to achieve a therapeutic effect, we are not talking about complications, but about endogenous affective, affective-paranoid and hallucinatornoparanoid attacks, which cannot be stopped even with intensive therapy. These patients make up a small percentage of therapeutic resistance cases-10% of all cases of resistance.

Conclusions. The study of immune status indicators proved that one of the reasons for the decrease in the effectiveness of psychopharmacotherapy is a change in the immunological reactivity of patients under the influence of psychotropic drugs, and the complex treatment of resistant forms of paranoid schizophrenia, including psychotropic and immunostimulating effects, provided the basis for drawing conclusions about the return of immune system disorders in, in combination with basic antipsychotic therapy, not only the normalization of immunological indicators in patients, but in some cases their mental state improves.

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