

The Factor of Autointoxication and Autoimmune Disorders in Some Mental Diseases and the Approach to Therapy

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Abstract

Introduction: The hypothesis of schizophrenia and some other mental disorders is not new. However, there is not enough convincing evidence of this hypothesis, including laboratory and instrumental studies. It is necessary to conduct a wide range of objective, including clinical studies and determine the approach to therapy.

Purpose: Identification of objective evidence of the presence of intoxication (autointoxication) and autoimmune disorders in the pathogenesis of schizophrenia and depressive disorders and the selection of an adequate method of treatment for these diseases.

Method: The study included inpatients and outpatients diagnosed with a depressive episode (severe and moderate severity) and schizophrenic spectrum diseases, according to the international classification of diseases of the 11th revision, who were treated from 2013 to 2018, using ECT (Efferent Combination Therapy) and antipsychotics.

Results and Conclusion: A depressive episode was diagnosed in 255 and schizophrenic spectrum diseases in 215 patients. Among the surveyed 225 women, 245 men aged 18 to 65 years. The results obtained showed the effectiveness of ECT (complete and incomplete remission) in 98% of the depressed and 86% of patients with schizophrenia.

Keywords: Efferent-Combination Therapy (ECT); Therapeutic Efficacy; Treatment of Patients with Depression and Schizophrenia

Introduction

Interest in the problem of the pathogenetic mechanisms of the emergence of some mental diseases, such as schizophrenia, depression and disorders similar to them, is quite large.

From the data of our early studies, as well as studies of other authors [5,7,18,23], it can be assumed that such diseases as endogenous origin of depression are closely related to the intoxication factor. Today, drug therapy for the above diseases remains the main method of treatment, but not always sufficiently effective and cost-effective for a large number of patients [8,11].

This is suggestive and a significant argument in support of the search for other pathogenetic mechanisms. The presence of an intoxication factor was noted by the earliest studies by E. Kraepelin, E. Bleuler. Based on these conceptual hypotheses, we tried to find out to what extent endogenous mental disorders are associated with intoxication (autointoxication) of the body. Indicators indicating the presence of an intoxication component are obvious. This is an accelerated work of the cardiovascular system, very often (in 90% of cases) the pulse of patients reached 110 - 125 beats/min. In addition, the presence of intoxication was manifested in the general status of patients - the absence of a pupillary reflex, nausea and other disorders of the gastrointestinal tract, decreased appetite, and sleep

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disorders. In addition to clinical symptoms, changes were noted in some laboratory and instrumental parameters: protein components of blood, immunological parameters (IgA, IgM, IgG), as well as electroencephalographic parameters (Table 1).

Examined group	Number of examined	Immunoglobulins		
		A	M	G
Schizophrenia (6A20) and delusional disorders (6A24)	55	2,04+0,047	1,22+0,0435	16,06+0,34B
		t = 5,9	t = 4,11	t = 10,16
		P 0,001	P 0,001	P 0,001
Schizoffective Disorders (6A21)	35	2,00+0,045	1,20+0,035	16,26+0,369
		t = 5,33	t = 3,61	t = 10,16
		P 0,001	P 0,001	P 0,001
Schizotypal Disorders (6A22)	30	2,16+0,131	1,28+0,097	15,41+0,876
		t = 3,25	t = 2,20	t = 3,65
		P 0,01	P 0,05	P 0,01
Control group	55	1,72+0,071	1,01+0,041	12,94+0,353
		t = 0,08	t = 1,11	t = 1,36
		Nedov.	Nedov.	Nedov.

Table 1: The content of immunoglobulins (in mg/ml) in the blood serum of patients with schizophrenia, the control group and other patients of the schizophrenic spectrum.

Thus, the relationship between the presence of intoxication and changes in the immune status of patients is visible. This inclines us towards the presence of intoxication factors that may be directly related to the disorder of the immunobiological status of the organism [6,8].

Aim of the Study

The aim of our study is to identify objective evidence of the presence of intoxication (autointoxication) in the pathogenesis of the most severe mental disorders and to select an adequate method of treating these diseases.

Materials and Methods

The study included a total of 470 patients (245 men and 225 women) aged 18 to 65 years (mean age 31 years) with moderate to severe mental symptoms, who were treated at the central railway hospital, at the M.O. Of the Republic of Azerbaijan and in the private clinic «Atlas». All medical institutions are located in the city of Baku. Schizophrenia: with primary attacks (95 people) and repeated attacks (120 people). Depressive disorders: primary episodes (155 people), repeated episodes (100 people). The examination of all patients was carried out from 2013 to 2018. The duration of the illness from the day of the onset of the illness ranged from 14 days to 6 months (on average 60 days).

The selection of patients in the studies was carried out on the basis of acute and subacute psychoses. The severity of depressive symptoms is not less than 17 points on the Hamilton scale (17 points).

The criterion for exclusion from the list was the absence of a psychological state. Suicidal tendencies in all patients accounted for 13% of all examined. Comorbid mental illnesses (generalized anxiety and obsessive-compulsive disorders, alcoholism, drug addiction, organic mental disorders) were excluded from the survey.

Hereditary burden of mental pathology in first-line relatives was noted in 100 patients, of whom schizophrenia in 61, with depression in 39.

In patients with schizophrenia, 98 belonged to the paranoid form, 12 to the catotonic form, and the remaining forms of schizophrenia, schizotypal, schizoaffective and delusional disorders were in 100 people.

Depending on the prevailing depressive affect, all episodes were divided into three groups: depression with a predominance of the affect of longing, anxiety and apathy, within which structural psychopathological analysis is carried out. In the structure of an acute psychotic state, perceptual disorders in the form of verbal pseudo-hallucinations, delusional relationships, persecution, and influence came to the fore. Among the leading psychopathological syndromes were hallucinatory-paranoid, paranoid, affective-paranoid, Kandinsky-Clerambo syndrome. Disorders of the associative process were represented by structural disorders of thinking in the form of resonance, paralogism, amorphousness, etc.

Patients suffering from schizophrenia and depression of moderate and severe severity were selected according to the criteria determined by the international classification of diseases of the 11th revision. (Table 2).

Patient group	Number of patients	%	Average age	18 to 40 years old				Average age	41 to 65 years old			
				Floor					Floor			
				Wives	%	Husband	%		Wives	%	Husband	%
Schizophrenia (6A20)	115	24,5	26	30	26,1	30	26,1	51	22	19,1	33	28,7
Diseases of the schizophrenic spectrum (6A21) including delusional disorders	100	21,3	28	18	18,0	39	39,0	50	20	20,0	23	23,0
Severe depression (6A71.4)	135	28,7	28	35	25,9	30	22,2	51	36	26,7	34	25,2
Moderate depression (6A71.1)	120	25,5	27	38	31,6	29	24,2	49	26	21,7	27	22,5
Total:	470	100	27	121	25,7	128	27,3	50	104	22,1	117	24,9

Table 2: Indicators of age and sex of patients with schizophrenia, schizophrenic spectrum and depression of various episodes of severity.

Patients were excluded from the list if the above diseases occurred in parallel with significant therapeutic, surgical and other diseases.

Efferent combination therapy (ECT) was carried out as a therapeutic measure. Results included improvements in psychological symptoms, interpersonal and social adjustment, quality of life, and participants’ satisfaction with both treatment and the way they received specialized care.

ECT is based on membrane plasmapheresis described in the literature [2,3,5,7,19]. Blood purification - detoxification therapy was carried out, as a rule, 3 sessions (at least 4 sessions) with an interval of 1-3 days with the use of ultraviolet blood irradiation in each session [2,3,5,8].

For membrane plasmapheresis, a PFM-800 plasma filter (Moscow, Russia) was used, and the Gambro AK-10 - 90 (Sweden) and Fresenius A 2008 C (Germany) devices were used to pump blood. For ultraviolet irradiation of blood - the device «Mustang» (Moscow, Russia), as well as intravascular disposable fiber optic guides (Moscow, Russia).

One day before the start of treatment, all patients underwent studies: electrocardiography, electroencephalography, ultrasound examination of the thyroid gland, clinical blood test, blood test for thyroid hormones (T3, T4, TSH), and the level of lithium in the blood. Also, in patients in both groups, blood saturation was determined, i.e. the partial pressure of oxygen in the cut was measured using a finger sensor. In all patients, the change in subjective data related to mood changes, the degree of communication with others, the adoption of more independent decisions in elementary everyday matters, a noticeable improvement in egoistic behavior, a dramatic decrease in the degree of stubbornness, the degree of reduction in anxiety, isolation, and a decrease in suffering from loneliness were assessed.

In all groups of patients, immediately before the sessions of plasmapheresis, an ECG study was repeated. For the purpose of demodulation, 1200 ml of liquid was injected intravenously: 0.9% sodium chloride solution (400 ml), Ringer's solution (400 ml), 5% glucose solution (400 ml). Systemic heparinization was also done (150 - 250 U/kg body weight). At each session, 30% of the circulating plasma volume was removed. By the end of the procedure, the residual effect of sodium citrate anticoagulant, the use of which is included in the method, was removed from all patients. In order to restore the volume of circulating plasma, all patients were repeatedly injected intravenously with 1200 ml of liquid: 0.9% sodium chloride solution (400 ml) + 10% calcium gluconate solution (10 ml), Ringer's solution (400 ml), 5% glucose solution (400 ml) + Panangin (10 ml) + 2% Riboxin solution (10 ml) + vitamin complex. Also, all patients were injected with cell protectors: Cartan (5 ml), Actovegin (2 ml), Essentiale (5 ml).

After this therapy, the next day, the autohemotherapy procedure began with the addition of 100mg of Eglonil's solution (ampoule) to the blood, 10 sessions in total. At the same time, patients received Anafranil (25 mg) as an intramuscular injection 2 times a day for 10 - 15 days. Then Agafranil was prescribed in the form of tablets of 25 - 50 mg 3-3 times a day. Patients with schizophrenia received psychotropic drugs adequate to the symptoms of psychopathology (Rispolept, Olenzapine, Clozapine). This therapy lasted for at least 3 - 6 months.

To normalize night sleep in the evenings, patients took Amitriptyllin (12.5 - 25 mg), Phenazepam (1 - 3 mg) and Corvalol (20 - 30 drops each), all three drugs at the same time. This combination in our practice normalized sleep for 7 - 9 hours.

Results and Discussion

As mentioned above, the priorities of the presence of a toxic origin of the schizophrenic process belong to E. Kraepelin. He linked the development of schizophrenia with autointoxication, due to the disruption of the functioning of the endocrine glands. Further attempts to detect any specific substances in the body of these patients were unsuccessful. His students decided to increase their efforts in studying the biochemical and immunological mechanisms of the pathogenesis of endogenous psychoses. This idea of the role of a toxic factor turned out to be quite fruitful and received experimental confirmation.

The impact of the so-called active biological factor on the cells of the nervous system in schizophrenic patients leads to the formation of autoantigens and autoantibodies, which in turn can damage brain tissue [5,14,16]. There is a relationship between the amount of these pathogenic substrates in the blood serum and the severity of the disease process. One should not overlook the fact that the roles of biogenic amines have been identified, which confirmed the hypothesis of the pathogenetic significance of metabolic disorders of the main mediators of the central nervous system - dopamine, serotonin, norepinephrine [1,4,20,21,32].

Despite the fact that to date, numerous data have been accumulated confirming the role of biological, including autointoxication and immunological factors in the origin of schizophrenia and other mental disorders, including depression, a single biogenetic concept of their essence has not yet been created [9,16,17,27,28,31].

Based on the foregoing, we conducted studies of the immunological, intoxication status of patients with schizophrenia and mental disorders similar to it, as well as patients suffering from depression [5,6,8].

The mechanism of action of ECT is different from that of many antipsychotics. This difference determines the significant features of the profile of its detoxification effects. The antipsychotic activity of ECT is undoubtedly explained by the inability to block dopamine (D₂) and serotonin (5-HT₂) receptors in the brain [12,15,29].

Cleansing the body of intoxicants and enhancing the immune status proves the high therapeutic activity of this method. Apparently, the powerful antipsychotic effect of ECT is associated with a certain combination of it with another pathogenetic mechanism, the study of which has yet to be studied (Figure 1).

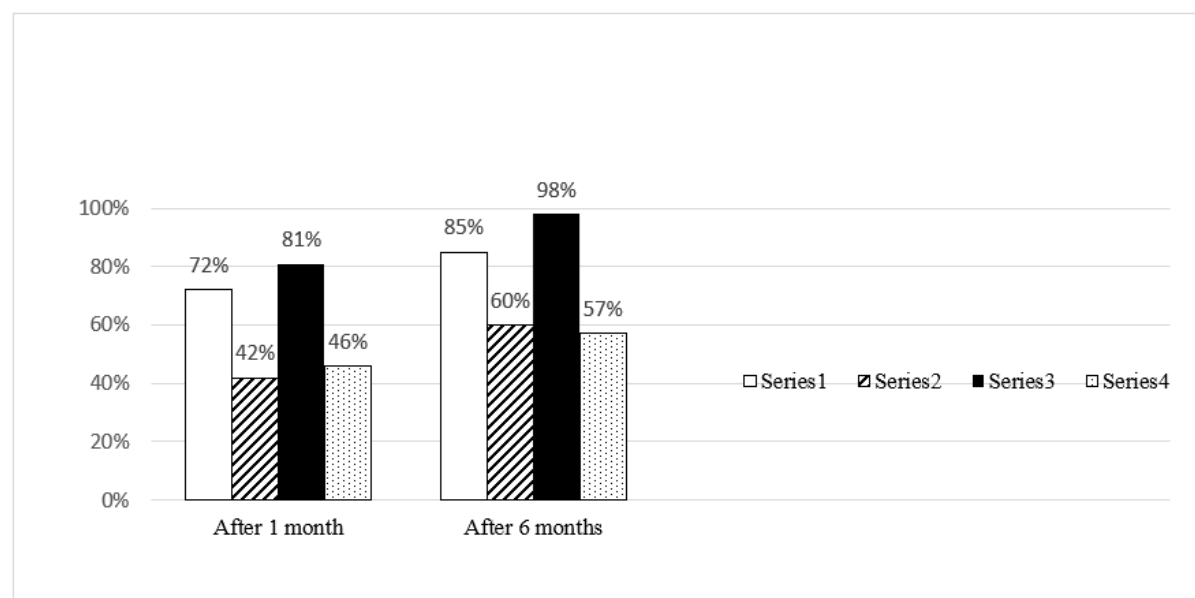


Figure 1: Therapeutic effect of ECT and antipsychotics in patients with schizophrenia and depression.

The antitoxic activity of ECT determines the possibility of its use in practical psychiatry for the treatment of various psychological disorders, where there is autointoxication and a decrease in the immune status of the body, and not only schizophrenia and depression.

The efficacy of antipsychotic drugs in the treatment of schizophrenia and depressive disorders has been studied in many studies: peerless, observational, placebo-controlled open and blind [13,22,25,30]. The value of these studies is to determine the effect of therapy on productive negative and cognitive disorders, aggression, suicidal behavior, and the frequency of recurrent exacerbations. The data of these studies usually give an idea of the overall effectiveness - the strength of the antipsychotic effect of these drugs, but do not allow to judge in detail the features of the profile of its pathogenetic activity. This gap needs to be filled with the results of well-designed comprehensive studies. Summarizing meta-analyzes and systematic reviews are of great importance in interpreting the results of individual studies.

The results of our studies indicate the high efficiency of ECT in the treatment of patients with depression, as well as schizophrenia, which occurs with a predominance of productive symptoms. The work published in the article summarizes the results of treatment of 450 patients suffering from depression and schizophrenia. They showed that ECT is highly effective compared to current antidepressant therapy.

Numerous studies have shown that along with general antipsychotic effects, ECT has a strong sedative effect. Its use leads to a significant and rapid weakening of psychomotor agitation, negativism and aggression, and to a greater extent than therapy with other atypical and typical antipsychotics [19,24,26]. This data is very important for practice. The listed symptoms are often found in the clinical picture of schizophrenia, especially in acute psychosis, and are accompanied by the refusal of patients from medical care, and their rapid elimination is the key to the success of further therapy. In our opinion, in terms of the severity of the sedative effect, ECT is comparable and even superior to traditional sedative antipsychotics with a powerful sedative effect (Chlorpromazine, Levomepromazine, etc.), which are still often used as the main means of symptomatic therapy of arousal state [8,16,24].

ECT reduces the risk of suicide. Presumably, this effect is due to a pronounced sedative effect. The results of a 2-year randomized study carried out by us in a large sample indicate that the number of suicides in patients taking ECT is lower than in patients treated with Olanzapine. At the same time, data were obtained on the weakening of the symptoms of depression in patients with schizophrenia and bipolar disorder during the treatment of ECT. However, for now, they need to be treated with caution, since rigorously planned independent studies are few and far between [30].

Our own observations indicate the high efficiency of ECT for the relief of acute attacks of continuous paranoid and sluggish forms of recurrent schizophrenia. Of particular interest are data on the effectiveness of treatment of the manifestation of the form of continuous paranoid schizophrenia (moderately progressive course with onset in adulthood). The use of ECT in this case, in contrast to therapy with other neuroleptics, leads to the formation of remissions of a fairly high quality, contributes to the transition of the course of the disease from continuous to conditionally paroxysmal.

There are interesting data on the effectiveness of ECT in the treatment of negative disorders. The results of many observations indicate that ECT therapy promotes activity and emotional revitalization of patients [5,10].

A number of studies are devoted to assessing the effectiveness of clozapine in the maintenance therapy of schizophrenia. The use of Clozapine at this stage of the disease leads to a further weakening of psychopathological symptoms. At the same time, the incidence of recurrent exacerbations with clozapine treatment is lower than with the use of traditional antipsychotics [19,24,26]. The results of our study show that after the weakening of the manifestations of psychosis in the paroxysmal and continuous course of schizophrenia, the condition of patients taking maintenance or continuous active clozapine therapy continues to slowly improve. The final formation of the structure of remission, the maximum recovery of social adaptation occurs six months or a year later (and even later) after the main manifestations of exacerbation and patients are discharged from the hospital, which indicates the rationality of long-term follow-up and maintenance therapy with Clozapine. Only in this case its efficiency is maximally high.

We carried out a comparative study of the effectiveness of ECT, risperidone, olanzapine [4]. Its results indicate a significant difference in the effectiveness of these atypical antipsychotics in the main forms and variants of the course of schizophrenia, different symptom complexes, at different stages of the endogenous process (exacerbation - remission, manifestation - active course - defect).

With exacerbations of moderately progressive paranoid schizophrenia and schizophrenia proceeding paroxysmal, the effectiveness of antipsychotics (the degree of weakening of productive disorders, the number of patients with a significant improvement in the condition, the rate of onset of the therapeutic effect) decreases in the following order: EKT → risperidone and olanzapine. In the treatment of exacerbations of sluggish schizophrenia, their effectiveness decreases in the order: clozapine → quetiapine → olanzapine → risperidone. During the period of remission in patients with schizophrenia, proceeding in a seizure manner, the effectiveness of therapy (the degree of weakening of psychopathological disorders) decreases in the following order: clozapine → olanzapine → risperidone.

The use of ECT to the greatest extent contributes to the «splitting» of productive symptoms (apathetic type of remission), and the structure of remissions is characterized by a lesser severity of negative disorders than when taking other atypical antipsychotics.

Conclusion

Thus, an analysis of the results of various studies shows that the spectrum of psychotropic activity of ECT is determined by pronounced incisive antipsychotic and powerful sedative effects, a wide range of specific antipsychotic action and, presumably, anti-negative effect. This spectrum of activity favorably distinguishes ECT from antipsychotics.

Considering the presence of autointoxication in the pathogenesis of depressive disorders, the use of efferent and immunostimulating therapy can be considered reasonable methods of treating depression, since this enhances the effect of active detoxification and relieves toxic stress. The ECT method can be introduced as a permanent complex of therapy for depressive disorders in cases of proven intoxication and ineffectiveness of traditional antidepressants.

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