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DYNAMICS OF CLINICAL AND PSYCHOPATHOLOGICAL CHARACTERISTICS IN PATIENTS WITH NEGATIVE SYMPTOMS OF SCHIZOPHRENIA

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In the study 252 patients with negative symptoms of schizophrenia were examined: 83 patients with a first psychotic episode, 88 patients with schizophrenia in a state of exacerbation, and 81 patients with schizophrenia in a state of remission. The study of the clinical-psychopathological structure of patients with negative symptoms in schizophrenia at different stages of the disease included the analysis of the distribution of patients according to the severity of forms, the type of course and manifestations of schizophrenia, the duration and progression of the disease, the number of relapses, hospitalizations and the duration of episodes, and the presence of leading symptom complexes in the examined patients.

Key words: patients with schizophrenia, negative symptoms, clinical characteristics, clinical and anamnestic analysis, first psychotic episode, schizophrenia in a state of exacerbation, schizophrenia in a state of remission.

Н.О. Марута, Ю.А. Кушнір, В.В. Огоренко, В.І. Заворотний ДИНАМІКА КЛІНІКО-ПСИХОПАТОЛОГІЧНИХ ХАРАКТЕРИСТИК У ПАЦІЄНТІВ З НЕГАТИВНИМИ СИМПТОМАМИ ПРИ ШИЗОФРЕНІЇ

У дослідженні взяли участь 252 пацієнта з негативною симптоматикою при шизофренії: 83 пацієнта з першим психотичним епізодом, 88 пацієнтів з шизофренією в стані загострення та 81 пацієнт з шизофренією у стані ремісії. Вивчення клініко-психопатологічної структури у пацієнтів з негативними симптомами при шизофренії на різних етапах захворювання включало в себе аналіз розподілу пацієнтів за вираженістю форм, типом перебігу та проявів шизофренії, тривалістю і прогресивністю захворювання, кількістю рецидивів, госпіталізацій та тривалістю епізодів та наявністю провідних симптомокомплексів у досліджуваних.

Ключові слова: хворі на шизофренію, негативні симптоми, клінічні характеристики, клініко-анамнестичний аналіз, перший психотичний епізод, шизофренія у стані загострення, шизофренія у стані ремісії.

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The prevalence of schizophrenia in the world is from 0.3 to 1.4 % [9]. Negative symptoms (NS) are considered as core psychopathological or core symptoms in schizophrenia [2, 9]. Current epidemiological data on the prevalence of negative disorders indicate that these disorders are registered in 90 % of patients with schizophrenia [4]. For around 20–30 % of these patients, several characteristic domains of NS are manifested, that indicate an increased risk of chronicity of symptoms and an unfavorable outcome of the disease [5]. Most often, NS are not recognized, and primary NS do not respond or respond poorly to available types of therapy [7].

Schizophrenia, which occurs especially with negative disorders, entails serious financial costs for patients, their relatives, and the economy as a whole, making the disease one of the "most expensive" mental disorders [5, 6]. Since NS are associated with adverse functioning and outcome of schizophrenia, their recognition, correct assessment and treatment are extremely important [11]. However, the process of developing innovative treatment methods has been quite slow until now, and NS still represent an unsolved problem in the treatment of people suffering from schizophrenia [7, 11]. The clinical-psychopathological analysis of the NS structure and severity in patients with schizophrenia is essential for the diagnosis of the disease and is also directly related to treatment and rehabilitation. Therefore, the investigation of the peculiarities of clinical and anamnestic characteristics in patients with NS in schizophrenia is relevant and determines the purpose of this study.

The purpose of the study was to determine the features of clinical and anamnestic data in patients with schizophrenia for establishing determinants associated with negative symptoms at different stages of the pathological process development.

Material and methods. The study was carried out on the basis of SI the Institute of Neurology, Psychiatry and Narcology at the National Academy of Medical Sciences of Ukraine. In this study, 252 patients with NS in schizophrenia totally were examined, including 83 patients with the first psychotic

episode (group I), 88 patients with schizophrenia in a state of exacerbation (group II) and 81 patients with schizophrenia in a state of remission (group III). Patients were given full information about the study, in accordance with the principles of the Helsinki Declaration of Human Rights, the Council of Europe Convention on Human Rights and Biomedicine, relevant laws of Ukraine and international acts, and they were asked to sign an informed consent for participation in the study, which was approved by the ethics committee. The study used a comprehensive approach, consisting in the use of clinical-psychopathological, psychometric (PANSS scale) and statistical study methods. Statistical data processing was used to determine the mean values of quantitative parameters, their standard errors (in $M \pm m$ format), the reliability of differences (Fisher's exact method and Fisher's angular transformation). For each gradation of the diagnostic criterion, its contribution to the diagnosis was determined: Kullback's measure of informativeness (MI) was calculated and diagnostic (prognostic) coefficients (DC) were calculated. Statistical processing of the results was carried out using Excel-2010 and STATISTICA 6.1.

Results of the study and their discussion. The study of the clinical and psychopathological structure in patients with negative symptoms of schizophrenia at different stages of the disease included analysis of the distribution of patients by severity of forms, type of course and manifestations of schizophrenia, duration and progression of the disease, number of relapses, hospitalizations and duration of episodes.

Females predominated among all examined patients with NS in schizophrenia (59 % of 252). There was predomination of 20–29 years old persons (67 % of 83, $p=0.0001$) in the group I, of 30–49 years old persons (87 % of 88, $p=0.049$) % in the group II, and 30–39 years old (41 % of 81) and 50–60 years old (26 % of 81, $p=0.0001$) ones in the group III. Among the patients of group I, individuals with secondary education (32 % of 83, $p=0.028$), and in groups II and III, individuals with special secondary education (34 % of 88, $p=0.048$, and 58 % of 81, $p=0.0001$, respectively) predominated. Unmarried persons predominated in group I (76 % of 88, $p=0.0001$), and divorced persons in groups II and III (52 % of 88, $p=0.0001$, and 58 % of 81, $p=0.0001$, respectively).

An analysis of the distribution of patients with NS in schizophrenia according to the form of schizophrenia showed that in group I of patients, 25 % of 83 patients had a simple form of schizophrenia, 19 % of 83 had undifferentiated schizophrenia, 18 % of 83 had a hebephrenic form of schizophrenia, 16 % of 83 had a paranoid form of schizophrenia, and 11 % of 83 have residual and catatonic forms of schizophrenia. In 40 % of 88 patients of group II, residual schizophrenia, in 21 % of 88 persons paranoid schizophrenia, and in 15 % of 88 patients simple and hebephrenic schizophrenia were recorded. In group III, 37 % of 81 patients were diagnosed with a residual form of schizophrenia, 25 % of 81 – with simple schizophrenia, 16 % of 81 – with hebephrenic schizophrenia, and 11 % of 81 – with paranoid schizophrenia. A statistical analysis of the distribution of patients with NS in schizophrenia showed that among patients of group I there were more individuals with an undifferentiated form of schizophrenia as compared with patients of groups II and III ($p=0.017$, $DC=3.84$, $MI=0.22$, and $p=0.008$, $DC=4.95$, $MI=0.32$, respectively), while among the patients of the groups II and III there were more people with a residual form of schizophrenia ($p=0.0001$, $DC=5.64$, $MI=0.82$, and $p=0.0001$, $DC=5.33$, $MI=0.77$, respectively). It should also be noted, that among patients with NS in schizophrenia in the remission stage, there were more people with a simple form of schizophrenia as compared with the patients with NS in schizophrenia in a state of exacerbation ($p=0.042$, $DC=2.23$, $MI=0.11$).

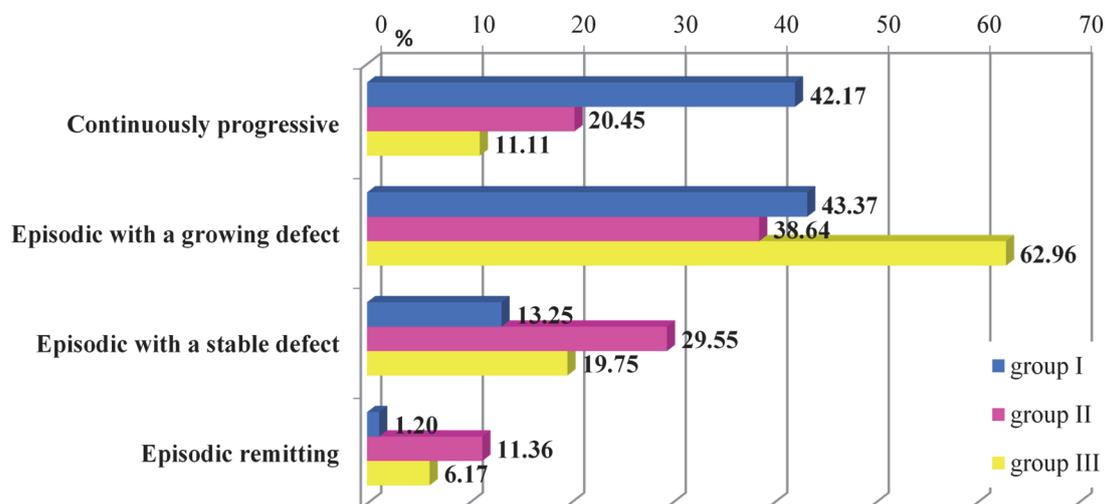


Fig. 1. Distribution of patients with NS in schizophrenia according to the type of course of the disease.

According to the type of the course of the disease, patients with NS in schizophrenia were distributed as follows: in the majority of patients of group I, an episodic course with an increasing defect (43 % of 83) and a continuously progressive course (42 % of 83) was detected, in 13 % of 83 patients, an episodic course with a stable defect was recorded. In group II, 39 % of 88 patients had an episodic course with an increasing defect, 29 % of 88 had an episodic course with a stable defect, 20 % of 88 patients had a continuously progressive course, and 11 % of 88 had an episodic remitting course. Most of the patients of group III had an episodic course with an increasing defect (63 % of 81), 20 % of 81 had an episodic course with a stable defect, and 11 % of 81 had a continuously progressive course of the disease. A comparison of the results made it possible to establish that the continuously progressive course of the disease was more characteristic for patients of group I in comparison with groups II and III ($p=0.001$, $D=3.14$, $MI=0.84$, and $p=0.0001$, $DC=5.79$, $MI=0.90$, respectively) (Fig. 1).

Episodic course with a growing defect was more pronounced among patients of group III as compared with patients of groups I and II ($p=0.005$, $DC=1.62$, $MI=0.16$ and $p=0.001$, $DC=2.12$, $MI=0.26$, respectively). The episodic course with a stable defect was more pronounced among patients of group II in comparison with groups I and III ($p=0.005$, $DC=3.48$, $MI=0.28$, and $p=0.049$, $DC=1.75$, $MI=0.09$, respectively). The episodic remitting course prevailed among patients of group II in comparison with group I ($p=0.006$, $DC=9.75$, $MI=0.50$).

An analysis of the duration of the disease among patients with NS in schizophrenia allowed us to establish that all patients of group I (100 % of 83) had a duration of the disease of 1–3 years. In 39 % of 88 patients of the group II, the duration of the disease was 4–6 years, in 35 % of 88 patients – 7–9 years, and in 17 % of 88 – 10–12 years. In the vast majority of patients of group III, the duration of the disease was 10–12 years (52 % of 81), in 25 % of 81 patients – 7–9 years, in 12 % of 81 – 13–15 years, and in 10 % of 81 – 4–6 years. Mathematical analysis of the results made it possible to prove that group I differed from other patients with NS in schizophrenia by the short duration of the disease (1–3 years) ($p=0.0001$). Patients of group II differed from other patients with NS in schizophrenia by the predominance of individuals with a disease duration of 4–6 years ($p=0.0001$, $DC=5.92$, $MI=0.85$) and 7–9 years ($p=0.044$, $DC=1.54$, $MI=0.08$). Patients with a disease duration of 10–12 years predominated in group III ($p=0.0001$, $DC=4.83$, $MI=0.84$).

According to the time of occurrence of negative symptoms, the patients were distributed as follows: in the group I patients, in most cases, the onset of negative symptoms was observed in the initial period (37 % of 83) or in puberty (23 % of 83) (Table 1).

Table 1

Distribution of patients with NS in schizophrenia by the time of onset of negative symptoms

| Name of indicators | group I (n=83) | | group II (n=88) | | group III (n=81) | |
|---|----------------|------------|-----------------|------------|------------------|------------|
| | Abs. | %±σ | Abs. | %±σ | Abs. | %±σ |
| In puberty | 19 | 22.89±2.45 | 6 | 6.82±0.76 | 9 | 11.11±1.31 |
| In the initial period | 31 | 37.35±3.61 | 34 | 38.64±3.48 | 22 | 27.16±2.90 |
| During the manifestation of the disease | 18 | 21.69±2.34 | 12 | 13.64±1.46 | 10 | 12.35±1.44 |
| In remission | 15 | 18.07±1.99 | 36 | 40.91±3.61 | 40 | 49.38±4.39 |

In 22 % of 83 patients of group I, the onset of negative symptoms occurred during the period of manifestation, and in 18 % of 83 patients, it was in a state of remission. In patients of group II, for the vast majority of patients, the onset of negative symptoms was observed in the state of remission (41 % of 88) and in the initial period (39 % of 88), and in 14 % of 88 patients, NS occurred during the period of disease manifestation. In the majority of patients of group III, negative symptoms appeared during the period of remission (49 % of 81), in 27 % of 81 persons – in the initial period, in 12 % of 81 – in the period of manifestation of the disease, and in 11 % of 81 – in puberty of age.

At the same time, it was established that there were more patients with the onset of negative symptoms at the age of puberty among patients of group I ($p=0.002$, $DC=5.26$, $MI=0.42$, and $p=0.023$, $DC=3.14$, $MI=0.18$, respectively), while the increase in negative symptoms in remission was observed more often among patients of the groups II and III ($p=0.0001$, $DC=3.55$, $MI=0.41$, and $p=0.0001$, $DC=4.37$, $MI=0.68$, respectively). It should be noted, that the onset of NS in the initial period occurred more often among patients of group II as compared with group III ($p=0.038$, $DC=1.53$, $MI=0.09$).

The distribution of patients with NS in schizophrenia according to the number of relapses showed that in most patients of group I, the number of relapses was “from 1 to 2” (96 % of 83). In 56 % of 88 patients of the group II, the number of relapses was equal to “more than 5”, and in 41 % of 88 – “from 3 to 5” (Fig. 2). In most patients of the group III, the number of relapses was “more than 5” (65 % of 81), and in 34 % of 81 patients – “from 3 to 5”.

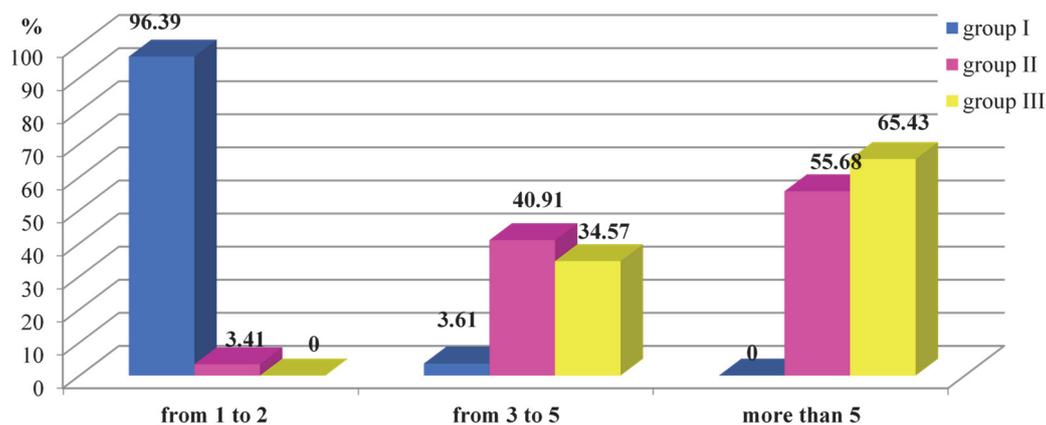


Fig. 2. Distribution of patients with NS in schizophrenia by the number of relapses.

The mathematical analysis revealed that a smaller number of relapses was more typical for patients of group I as compared with groups II and III ($p=0.0001$, $DC=14.51$, $MI=6.75$ and $p=0.0001$, respectively), while the number of relapses “from 3 to 5” was more frequent for these groups ($p=0.0001$, $DC=10.54$, $MI=1.97$, and $p=0.0001$, $DC=9.81$, $MI=1.52$, respectively), as well as “more than 5” ($p=0.0001$ and $p=0.0001$, respectively).

In the majority of patients of group I, the duration of the current episode was “up to 6 months” (55 % of 83), in 22 % of 83 patients the current episode lasted “up to 3 months”, in 17 % of 83 patients – “up to a year” (Fig. 3).

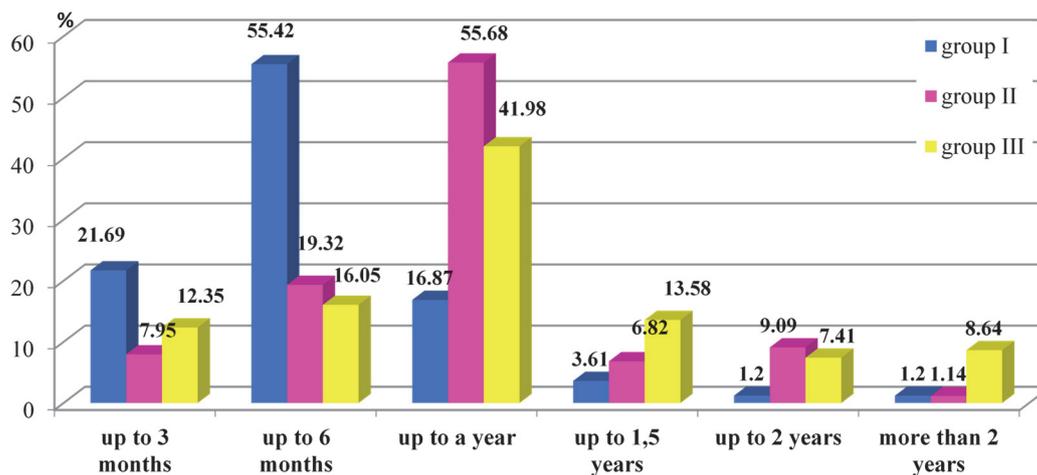


Fig. 3. Distribution of patients with NS in schizophrenia by the duration of the current episode

In the majority of patients of group II, the duration of the current episode was “up to a year” (55 % of 88) and in 19 % of 88 – “up to 6 months”. In a significant number of patients of group III, the current episode lasted up to a year (42 % of 81), in 16 % of 81 – up to 6 months, in 13 % of 83 – up to one and a half years, and in 12 % of 83 – up to 3 months. A comparison between the 3 groups allowed us to establish that the current episode in patients of group I lasted more often up to 6 months ($p=0.0001$, $DC=4.58$, $MI=0.83$ and $p=0.0001$, $DC=5.38$, $MI=1.06$ respectively) and up to 3 months ($p=0.007$, $DC=4.36$, $MI=0.30$ and $p=0.048$, $DC=2.45$, $MI=0.11$ respectively) as compared with groups II and III, in which the current episode more often lasted up to a year ($p=0.0001$, $DC=5.19$, $MI=1.01$, and $p=0.0001$, $DC=3.96$, $MI=0.50$, respectively). At the same time, patients of the group III differed by a larger number of persons with a duration of the current episode up to 1.5 years as compared with the group I ($p=0.017$, $DC=5.75$, $MI=0.29$). Patients of the group II differed from patients of the group III by the predominance of persons with the duration of the current episode up to a year ($p=0.025$, $DC=1.23$, $MI=0.08$).

Patients of the group I were hospitalized more than once a year in 41 % of 83 cases, 31 % of 83 patients were hospitalized once a year, and 28 % of 83 patients were hospitalized less than once a year (Fig. 4a). In the group II, 45 % of 88 patients visited a hospital more than once a year, 42 % of 88 patients – less than once a year, and 12 % of 88 patients were hospitalized once a year. In the group III, 47 % of 81 patients were hospitalized more than once a year, 31 % of 81 – once a year, and 22 % of 81 patients were hospitalized less than once a year.

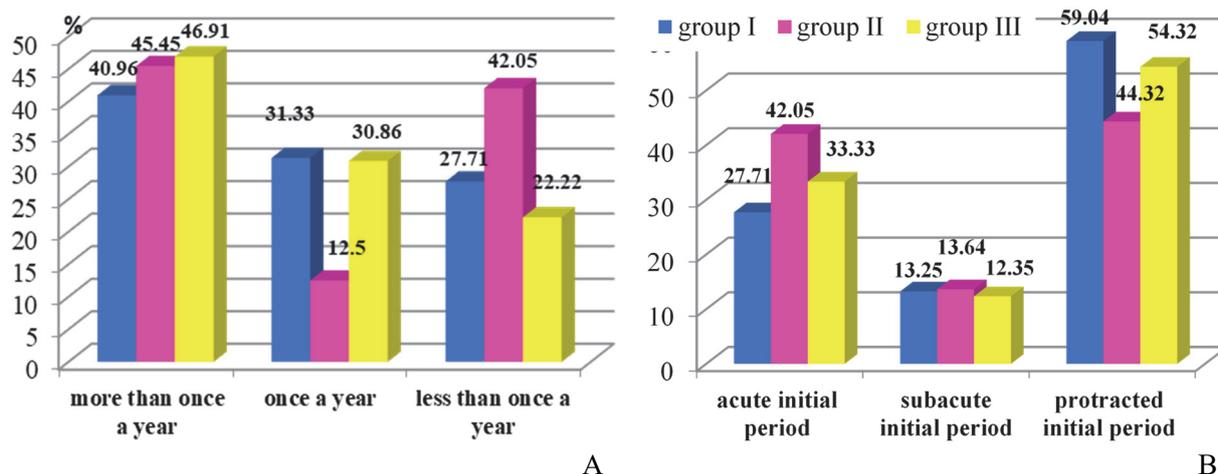


Fig. 4. Distribution of patients with NS in schizophrenia. A – Distribution of patients with NS in schizophrenia by the number of hospitalizations. B – Distribution of patients with NS in schizophrenia according to the characteristics of the initial period.

As a result of the statistical analysis, it was proved that patients with NS in schizophrenia were hospitalized more often than once a year, but patients of group II differed by a larger number of patients who were hospitalized less than once a year in comparison with groups I and III ($p=0.019$, $DC=1.81$, $MI=0.13$, and $p=0.003$, $DC=2.77$, $MI=0.27$, respectively), while among the patients of groups I and III there were more persons who were hospitalized once a year ($p=0.002$, $DC=3.99$, $MI=0.38$, and $p=0.002$, $DC=3.93$, $MI=0.36$, respectively). The features of the initial period among patients with NS in schizophrenia were analyzed (Fig. 4b).

Thus, it was revealed that the majority of patients of group I had a protracted initial period (59 % of 83), 28 % of 83 patients had an acute onset, and 13 % of 83 had a subacute onset. A significant number of patients of group II had a protracted (44 % of 88) and acute (42 % of 88) initial period, and 14 % of 88 had a subacute period. Most group III patients had a prolonged onset (54 % of 81), 33 % of 81 had an acute onset, and 12 % of 81 had a subacute initial period. As a result of the mathematical comparison of the groups, it was determined that the protracted onset was more frequent among the patients of group I ($p=0.019$, $DC=1.25$, $MI=0.09$), while the acute onset was more frequent among the patients of group II ($p=0.019$, $DC=1.81$, $MI=0.13$).

The data of modern scientific literature on the clinical and anamnestic characteristics of patients with NS in schizophrenia are fragmentary and do not take into account differences depending on the stage of development of the pathological process [1, 2, 6]. The data obtained by us differ in their complexity, taking into account the features of schizophrenia and the negative symptoms associated with them. As a result of the study, clinical and dynamic factors in NS in schizophrenia were determined, which included an analysis of the distribution of patients according to the severity of forms, type of course and manifestations of schizophrenia, duration and progression of the disease, the number of relapses, hospitalizations and duration of episodes, and the presence of leading symptom complexes in the subjects. The obtained data are consistent with the studies of other authors, who emphasize that the presence of negative symptoms in schizophrenia is closely related to the protracted initial period and the episodic course of schizophrenia [3, 10].

Conclusions

1. Most patients with the first psychotic episode (group I) were characterized by: the predominance of simple and undifferentiated forms of schizophrenia; a long initial period; the predominance of an episodic course with a growing defect and a continuously progredient course; the onset of negative symptoms in the initial period and in puberty; the duration of the current episode from 3 to 6 months; the duration of the disease of 1–3 years; the number of relapses “from 1 to 2”; the number of hospitalizations of 1 time per year.

2. The majority of patients with NS in schizophrenia in a state of exacerbation (group II) were characterized by: the predominance of the residual form of schizophrenia; the appearance of negative symptoms in the initial period and in remission; the duration of the current episode of up to 1 year; the duration of the disease of 4–6 years and 7–9 years; the number of relapses “from 3 to 5” and “more than 5”; the number of hospitalizations of less than 1 time per year; the predominance of an episodic course with a stable defect and episodically remitting course; protracted and acute initial period.

3. The majority of patients with NS in schizophrenia in a state of remission (group III) were characterized by: a predominance of residual and simple forms of schizophrenia; the appearance of negative symptoms in a state of remission; the predominance of an episodic course with a growing defect; a long initial period; the duration of the current episode of up to a year and up to 1.5 years; the duration of the disease of 10–12 years; the number of relapses “from 3 to 5”; the number of hospitalizations of 1 time per year.

The obtained data can be used to establish diagnostic criteria for patients with NS in schizophrenia, depending on the dynamics of the disease.

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