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EVALUATION OF MEDICATION ADHERENCE IN PATIENTS WITH SCHIZOPHRENIA

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Medication adherence of schizophrenic patients is a growing public health problem. Non-adherence to medication has a negative impact on the course of illness resulting in relapses, rehospitalization, longer time to remission, suicide attempts, and drug abuse.

The article aims to determine the level of medication adherence and risk factors of non-adherence to the pharmacotherapy regimen in patients with schizophrenia.

Materials and methods. There was comparative study to evaluate the medication adherence in 40 patients with paranoid schizophrenia in department of psychiatry, psychotherapy, addictology and medical psychology at Donetsk National Medical University. The social-demographic and clinical-social factors were assessed by special social-demographic questionnaire. The clinical and psychopathological symptoms were measured by Positive and Negative Symptoms Scale (PANSS). The Medication Adherence was evaluated by Medical Adherence Rating Scale (MARS). The neuroleptic side effects were observed by Glasgow Antipsychotic Side Effect Scale (GASS).

Results. Young age of patients, male sex, professional and family dysfunction, substance abuse, productive, negative, neurocognitive psychopathological symptoms were associated with a low level of medication adherence. Typical oral antipsychotics of the first generation with neuroleptic adverse events (sedation, parkinsonism, akathisia, dyskinesia, dystonia, tachycardia, dry mouth, constipation, urinary retention, weight gain) were negatively associated with a low level of medication adherence in patients with schizophrenia.

Improving adherence to patients with schizophrenia may have a considerable positive impact on patients and society. This can be achieved by focusing on the identified multitude of factors driving nonadherence.

Keywords: schizophrenia, medication adherence, antipsychotic medication, neuroleptic side effects.

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ОЦІНКА ПРИХИЛЬНОСТІ ДО ЛІКУВАННЯ У ПАЦІЄНТІВ ІЗ ШИЗОФРЕНІЄЮ

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У роботі продемонстровані особливості прихильності до лікування у 40 пацієнтів, хворих на параноїдну шизофренію, та визначені основні фактори ризику недотримання режиму фармакотерапії. Показано, що молодий вік пацієнтів, чоловіча стать, професійна та сімейна дисфункція, зловживання психоактивними речовинами, продуктивні, негативні й нейрокогнітивні симптоми пов'язувалися з низьким рівнем прихильності до лікування. Зазначено, що прийом оральних антипсихотиків першої генерації з наявністю нейролептичних небажаних явищ (седація, паркінсонізм, акатизія, дискінезія, дистонія, тахікардія, сухість у роті, закрепи, затримання сечі, збільшення ваги) негативно корелював з низьким рівнем прихильності до лікування у пацієнтів, хворих на шизофренію.

Ключові слова: шизофренія, прихильність до лікування, антипсихотики, нейролептичні побічні ефекти.

Introduction

Schizophrenia is a widespread chronic mental disorder worldwide (more than 24 million people) with a wide range of psychopathological symptoms, such as positive (hallucinations, delusions, grandiosity, suspicion, hostility), negative (blunted affect, emotional detachment, apathy, social isolation), neurocognitive (impaired concentration, decreased short-term memory and information processing

speed, disorganization of thinking), affective (anxiety, tension, guilt, depression) and significant impairment of quality of life and social functioning (work and study, independence and autonomy, social activity, daily activities, interpersonal communication) [1–3].

In terms of global burden of disease (DALY), schizophrenia is one of the 20 most common causes of disability in the world, with significant economic costs that exceed \$150 billion per year in the United States alone. Schizophrenia reduces life expectancy and is associated with three to four times higher mortality due to the prevalence of risk factors (obesity, diabetes mellitus, metabolic syndrome, dyslipidemia, smoking), increased



suicide, poor health maintenance, and insufficient access to preventive medicine, care, and treatment compared to the general population [4].

The mainstay of pharmacological treatment of schizophrenia is the use of antipsychotic drugs. They are used to treat acute episodes of schizophrenia, supportive therapy, and to prevent relapse of the disease, i.e., preventive treatment. The use of modern antipsychotics in the treatment of schizophrenia can control the patient's mental state, is effective in alleviating positive and negative symptoms, reduces the likelihood of relapse, and improves quality of life and social functioning [5].

The patient's willingness to follow the doctor's recommendations, take medications (dose, frequency, duration), give up bad habits, and modify lifestyle is defined as medication adherence [6].

Patients with schizophrenia are considered adherent to treatment if they take more than 80% of the prescribed antipsychotics, partially adherent to treatment if they take only 50% of the medication, and non-adherent if they do not take any medication for a week [7].

According to the CATIE study [8], 74% of patients with schizophrenia discontinued antipsychotic treatment within 18 months. It was shown that 38% of patients left treatment due to their lack of effectiveness, 15% due to poor tolerability and safety, and 21% for other reasons.

In a prospective study assessing treatment adherence among patients with a first episode of schizophrenia, it was shown that one third of the subjects (35%) discontinued treatment within 6 months of starting therapy [9]. Another study involving male patients with schizophrenia, schizophrenia-like and schizoaffective disorders showed that 53.6% of them refused treatment during the first year of follow-up [10]. According to some authors, the rate of nonadherence to schizophrenia treatment is about 50%, ranging from 40% to 72% [11].

It has been proven that nonadherence to schizophrenia treatment increases the risk of relapse and re-hospitalization by almost five times [12]. It has been demonstrated that insufficient treatment adherence was associated with an increase in the frequency of involuntary hospitalization, slower recovery and longer stay in a psychiatric hospital, higher risk of suicide, substance abuse, poorer prognosis, and lower quality of life and social functioning [13].

According to some authors, the main reasons for nonadherence to treatment in patients with schizophrenia were insufficient criticism and awareness of the disease, negative attitudes toward medications, polypharmacy, current or past substance dependence, high cost of modern antipsychotics, poor relationships with the doctor, discharge from the hospital without an adequate follow-up plan, general fear of side effects, and the presence of concomitant neuroleptic adverse events and diseases [14]. At the same time, poor adherence to treatment among patients with schizophrenia was associated with cognitive, negative disorders, depression, lack of family support, low socioeconomic and demographic status of the patient [15].

Studies of treatment adherence and identification of risk factors for nonadherence to pharmacotherapy in schizophrenia are very relevant in modern psychiatry, aimed at improving patient awareness of the existing

mental illness and therapeutic tactics, forming motivational interest in treatment, acquiring skills for self-management of the therapy regimen, including acquiring a critical attitude towards the disease and willingness to adhere to the pharmacotherapy regimen.

The aim of the study is to determine the peculiarities of the level of adherence to treatment and risk factors for nonadherence to pharmacotherapy in patients with schizophrenia.

Material and methods

In 2024, a study was conducted at the Department of Psychiatry, Psychotherapy, Narcology and Medical Psychology of Donetsk National Medical University (Kropyvnytskyi) to assess adherence to treatment in 40 patients with schizophrenia after obtaining their written informed consent following the principles of the World Medical Association Code of Ethics (Declaration of Helsinki).

Study inclusion criteria:

1. Outpatients with a diagnosis of paranoid schizophrenia (F20.09-F20.00) according to ICD-10.
2. Age from 18 to 50 years.
3. Taking a stable dose of oral antipsychotics for at least 6 months.

Exclusion criteria for the study:

1. Acute psychotic state or exacerbation of schizophrenia.
2. Clinically significant negative and/or neurocognitive symptoms.
3. Criteria for substance dependence.
4. Clinically significant concomitant somatic and/or neurological diseases.
5. Active suicidal thoughts and/or suicidal behavior for 6 months.
6. Risk of harm to self or others.

The study involved 40 patients with paranoid schizophrenia with different types of course, among whom 22 patients (55%) were female and 18 (45%) were male. The average age of onset of the disease in the subjects was (21.3 ± 9.95) years, and the average duration of the mental disorder was (10.44 ± 10.13) years. The majority of patients (60%) had a low level of treatment adherence, 11 patients (27.5%) had a moderate level, and only 5 patients (12.5%) had a high level of treatment adherence.

To further identify risk factors for nonadherence to psychopharmacotherapy and the correlations between them, we grouped patients with high and moderate levels of adherence to treatment into the first group of the study. Patients with low levels of adherence were included in the second group.

The study used socio-demographic, clinical and social, clinical and psychopathological, and mathematical and statistical research methods.

In order to study socio-demographic and clinical-social features in patients with schizophrenia, the authors developed a semi-structured questionnaire that included socio-demographic (age, gender, education, professional employment, disability marital status) and clinical and social indicators (heredity of mental disorders, substance abuse, duration of mental disorder and antipsychotic use, history of somatic diseases, medication control, current

use of antipsychotic drugs (generation, frequency), side effects).

To identify and assess the severity of positive, negative, and general psychopathological symptoms in schizophrenia, the authors used the PANSS (Positive and Negative Syndrome Scale) [16], which included 30 items (7 items to determine the severity of positive symptoms, 7 items for negative symptoms, and 16 items to determine the severity of general psychopathological symptoms). Each item on the scale was scored separately from 1 to 7 points depending on the severity of the mental disorder.

The level of adherence to psychopharmacotherapy among patients with schizophrenia was assessed using the Medication Adherence Rating Scale [17], which included 10 items and determined the level of adherence to therapy (up to 5 points – low level, 5–7 points – medium (moderate) level, 8–10 points – high level).

The study of the presence and severity of adverse events associated with antipsychotics was assessed using the Glasgow Antipsychotic Side Effects Scale (GASS) [18]. This questionnaire included an assessment of 22 items depending on the frequency of side effects (never, once, several times, daily) and determined the level of distress for each item from 1 to 10 points.

The mathematical and statistical method of the study was performed using Microsoft Excel 2019 software. Quantitative mathematical changes are presented as mean (M) and standard deviation (SD), and the Mann-Whitney U test was used to analyze nonparametric statistical variables. A p value of less than 0.05 was considered statistically significant.

Results of the study

Young age of patients ($p<0.001$), male gender ($p<0.001$), disability ($p<0.05$), impaired professional ($p<0.05$) and

family functioning ($p<0.05$) were statistically significantly associated with low adherence to treatment when analyzing the socio-demographic characteristics of patients with schizophrenia (Table 1).

Table 2 demonstrates the statistical dependence of clinical, social and psychopathological features in patients with schizophrenia on different levels of their adherence to treatment.

The presence of a family history of psychiatric illness was associated with high and medium levels of adherence ($p<0.05$), while the absence of a family history of mental illness was significantly associated with low levels of adherence ($p<0.05$).

The history of substance abuse in patients with schizophrenia was a significant risk factor for poor adherence to pharmacotherapy ($p<0.001$).

Patients' self-administration of medications without supervision from an assistant (relatives, spouse) was significantly associated with low adherence ($p<0.001$). On the contrary, when the responsibility for taking the medication was assigned to the patient's assistant, adherence improved to moderate to high levels ($p<0.001$).

The use of conventional neuroleptics (first-generation antipsychotics) or their combination with other drugs was associated with poor adherence to pharmacotherapy compared with the use of atypical second-generation antipsychotics ($p<0.05$).

The frequency of antipsychotic use also influenced patient adherence to treatment. At the same time, an increase in the frequency of medication (two or three times a day) led to low adherence ($p<0.05$).

It is worth noting that more significant results in the productive ($p<0.05$), negative ($p<0.05$) subscales and the overall severity of schizophrenia on the PANSS scale were significantly associated with poor adherence to pharmacotherapy ($p<0.05$).

Table 1

Treatment adherence in patients with schizophrenia depending on socio-demographic characteristics

Socio-demographic indicators	First group (moderate and high level of adherence)	Second group (low level of adherence)	Total number
Age			
18–30 years	4 (40%)	6 (60%)	10 (100%)
31–40 years old	5 (20%)	20 (80%)**	25 (100%)
41–50 years old	4 (80%)	1 (20%)	5 (100%)
Gender:			
Female	17 (77.2%)	5 (22.7%)	22 (100%)
Male	4 (22.2%)	14 (77.8%)**	18 (100%)
Education:			
General secondary	5 (41.7%)	7 (58.3%)	12 (100%)
Professional	7 (46.7%)	8 (53.3%)	15 (100%)
Higher education	8 (61.5%)	5 (38.5%)	13 (100%)
Professional employment:			
Studying/working	4 (50%)	4 (50%)	8 (100%)
Not studying/not working	12 (37.5%)	20 (62.5%)*	32 (100%)
Disability:			
Presence of disability	14 (38.3%)	22 (68.7%)*	36 (100%)
Absence of disability	2 (50%)	2 (50%)	4 (100%)
Marital status:			
Married	6 (66.7%)	3 (33.3%)	9 (100%)
Single	10 (32.3%)	21 (67.7%)*	31 (100%)

Note: * – $p<0.05$; ** – $p<0.001$.

Table 2

Adherence to treatment in patients with schizophrenia depending on clinical, social, and psychopathological characteristics

Clinical, social, and psychopathological indicators	First group (moderate and high level of adherence)	The second group (low level of adherence)	Total number
Duration of mental disorder, years (M±SD)	10.47±10.11	10.31±10.06	
Duration of mental disorder treatment, years (M±SD)	10.36±9.95	9.45±9.54	
Family history of mental disorders:			
Present	8 (66.7%)*	4 (33.3%)	12 (100%)
Absent	11 (39.3%)	17 (60.7%)*	28 (100%)
History of substance abuse:			
Present	4 (26.7%)	11 (73.3%)**	15 (100%)
Absent	15 (60%)*	10 (40%)	25 (100%)
History of somatic diseases:			
Present	8 (57.1%)	6 (42.9%)	14 (100%)
Absent	12 (46.2%)	14 (53.8%)	26 (100%)
Control over medication intake:			
Takes medication independently	4 (21.1%)	15 (78.9%)**	19 (100%)
With the help of an assistant	15 (71.4%)**	6 (28.6%)	21 (100%)
Current medication use:			
Traditional neuroleptics	4 (40%)	6 (60%)*	10 (100%)
Atypical antipsychotics	12 (66.7%)*	6 (33.3%)	18 (100%)
Combination of antipsychotics	2 (16.7%)	10 (83.3%)*	12 (100%)
Frequency of medication intake:			
Once a day	16 (69.6%)*	7 (30.4%)	23 (100%)
Twice a day	4 (28.6%)	10 (71.4%)*	14 (100%)
Three times a day	1 (33.3%)	2 (66.7%)	3 (100%)
PANSS: positive subscale, (M±SD)	14.25±10.56	17.63±11.06*	
PANSS: negative subscale, (M±SD)	17.41±11.10	22.47±12.45*	
PANSS: general psychopathological subscale, (M±SD)	36.64±12.26	38.12±12.93	
PANSS: total disease severity score, (M±SD)	68.30±16.24	78.22±17.12*	

Note: * – p<0.05; ** – p<0.001.

The dependence of treatment adherence on the presence and severity of side effects while taking antipsychotic drugs is shown in Table 3.

Thus, an increase in the severity of some side effects associated with antipsychotics, namely excessive sedation, extrapyramidal symptoms (parkinsonism, akathisia, dyskinesia, dystonia), anticholinergic adverse events (tachycardia, dry mouth, constipation, urinary retention), weight gain, statistically significantly correlated with insufficient adherence to treatment (p<0.05).

In patients with moderate and high levels of adherence to pharmacotherapy, a lower overall score of severity of neuroleptic side effects according to the Glasgow scale was recorded (32.51±11.8, p<0.05).

Conclusions

One of the main problems in psychiatry is low adherence to pharmacotherapy in patients, which demonstrates a violation of consent to treatment, unwillingness to cooperate therapeutically and participate in long-term treatment and

Table 3

Adherence to treatment in patients with schizophrenia depending on the presence and severity of neuroleptic side effects according to the Glasgow Scale

№	Neuroleptic side effects	First group (moderate and high level of adherence)	Second group (low level of adherence)
1.	Excessive sedation	4.18±0.53	5.23±0.51*
2.	Cardiovascular adverse events	2.05±0.04	2.08±0.05
3.	Extrapyramidal adverse events	9.05±3.25	11.34±4.00*
4.	Anticholinergic adverse events	4.01±0.33	5.85±0.41*
5.	Gastrointestinal adverse events	1.15±0.01	1.49±0.01
6.	Genitourinary adverse events	2.01±0.02	2.09±0.05
7.	Symptoms of diabetes mellitus	1.05±0.08	1.07±0.39
8.	Hyperprolactinemia	8.05±3.43	8.65±3.50
9.	Weight gain	1.98±0.09	2.42±0.02*
10.	Total score on the Glasgow scale	32.51±11.8	40.22±12.4*

Note: 0–21 points – mild side effects, 22–42 points – moderate side effects, 43 points – severe neuroleptic side effects; * – p<0.05.

rehabilitation activities. Insufficient compliance and non-adherence to treatment in patients increases the likelihood of exacerbations and hospitalization, increases the risk of suicide and substance abuse.

The study demonstrated that the level of adherence to treatment in patients with schizophrenia is influenced by demographic (young age, male gender), social (professional and family maladjustment, history of substance abuse), economic (unemployment, disability) factors, clinical and psychopathological features of the disease (productive, negative, neurocognitive symptoms, schizophrenia pathomorphosis), and factors related to current treatment

(neuroleptic generation, form, quantity, and frequency of medication, duration of pharmacotherapy).

Low treatment adherence in patients with schizophrenia is characterized by side effects associated with antipsychotics, including excessive sedation, extrapyramidal and anticholinergic adverse events, weight gain, and metabolic endocrinological disorders.

Improving adherence to schizophrenia treatment can have a significant positive impact on patients and society as a whole. This can be achieved by focusing on the identification of multiple risk factors that lead to nonadherence to pharmacotherapy.

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