DOI: 10.17816/KMJ2022-44

Structure of the drug treatment adherence in elderly patients with mild cognitive impairment and psychopathological symptoms

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Abstract

Background. The high prevalence of pre-dementia cognitive impairment in the elderly, their poor prognosis with a frequent transition to dementia, polymorbidity with somatic pathology determine the need for adequate correction of all somatic diseases. This increases the importance of treatment adherence.

Aim. To assess the structure of drug treatment adherence in elderly patients with mild cognitive impairment (MCI) and psychopathological symptoms.

Material and methods. An observational study of 264 patients diagnosed with mild cognitive impairment was conducted. The average age was 68.5±1.4 years. Of these, 17.6% were men, and 83.3% were women. The patients were divided into two groups: with psychopathological symptoms (main group, n=189) and without psychopathological symptoms (comparison group, n=75). Research methods used: clinical-psychopathological, psychometric, statistical by using Statistica 7 software for Windows OS. The Pearson's chi-squared test, the nonparametric Mann–Whitney U test, and the correlation analysis with calculation of Spearman's rank correlation coefficient (r) were used.

Results. The adherence (compliance) of the study participants in relation to general therapeutic recommendations is represented by social, emotional and behavioural compliance. The total score of general compliance in the main study group was 45.42±29.7, in the comparison group — 51.09±32.3 points (p=0.031). In the main group, half of the participants (49.7%) had a low total score of general compliance, less than half of the participants had an average total score, only 4.8% of the participants showed high compliance with therapeutic recommendations. Increased depression correlates with low overall, social and emotional competence (r=0.512). Severe agitation and aggression correlate with low behavioural and emotional competence (r=0.589). Statistically significant correlations were found between psychotic symptoms and low behavioural compliance (r=0.151 and r=0.145).

Conclusion. The overall medication compliance rates are lower in patients with affective and psychotic symptoms; an increase in the number of affective, psychotic, behavioural disorders in patients with mild cognitive impairment correlates with low overall, social, emotional and behavioural compliance.

Keywords: mild cognitive impairment, compliance, drug treatment adherence, adherence to therapy.

For citation: Kovtun OP, Sidenkova AP, Izmozherova NV, Serdyuk OV, Vikhareva AA, Melnik AA, Rezaikin AV. Structure of the drug treatment adherence in elderly patients with mild cognitive impairment and psychopathological symptoms. *Kazan Medical Journal.* 2022;103(1):44–53. DOI: 10.17816/KMJ2022-44.

Background

The vital senility of modern society determines the actively growing interest of researchers in cognitive impairment [1]. Moreover, the number of publications on this subject is increasing exponentially every year, following the increasing interest in dementia.

Currently, cognitive impairment of the advanced age is considered a phenomenologically manifested pathological aging of the brain [2]. This concept considers the mental manifestations of brain aging in the clinical continuum from the predementia stage to dementia. This approach highlights the significance of mild cognitive impairment given the high probability of its progression to dementia [1, 3].

The rate of dementia development in people with predementia cognitive disorders increases in the presence of comorbid pathologies, such as arterial hypertension, diabetes mellitus, hypercho-

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Received 25.06.2021; accepted 09.11.2021; published 15.02.2022.

lesterolemia, and hypovitaminosis D [4–6], which must be controlled and managed using appropriate therapy. Moreover, many patients with cognitive impairment have noncognitive psychopathological symptoms (such as affective, subpsychotic, and behavioral symptoms), which complicate the condition of patients with cognitive syndrome and worsen its prognosis, due to the comorbid relationships with somatic risk factors for dementia [7].

Meanwhile, psychopathological symptoms, which influence the parameters of psychosocial functioning, are often combined with a low readiness of patients to follow therapeutic recommendations, contributing to the acceleration of cognitive impairment [8], i.e., low adherence to therapy becomes an important independent factor that prevents the correction of cognitive impairment.

According to accumulating evidence, regular intake of statins, oral hypoglycemic drugs, and weight management reduce the probability of progression of predementia cognitive disorders to dementia in patients with type 2 diabetes mellitus and retinopathy, and timely correction of arterial hypertension in middle adulthood delays or stops cognitive impairment at an older age [9, 10]. It is for a good reason that the subject "Prevention and Reduction of the Risks of Dementia" was singled out by the experts of the World Health Organization as a priority field in the struggle against severe cognitive disorders ahead of the directions "Diagnostics, Development of Biomarkers, Monitoring of the Disease" and "Drug and other Treatment" [11, 12].

The efficiency of therapy for the control of risk factors for cognitive impairment depends not only on the pharmacological properties of the drug but also on patient compliance, as its indicators are low among patients with chronic somatic diseases [13]. According to some studies, the prevalence of noncompliance among older patients in the general medical network reaches 30%–60% [14, 15].

Until now, there is no common understanding of the phenomenon of "drug compliance." Some authors consider it as a quantitatively calculated and behaviorally implemented reflection of therapeutic interaction, considered through the lens of the individual and personal characteristics of the patient [16]. Another definition of compliance implies a certain internal space of the patient, within which we can suggest the coincidence of the patient's actions and medical recommendations [17].

Avedisova defined full compliance as "the midpoint on a wide continuum of the degree of adherence of patients to ongoing therapy (from complete or partial resistance to therapy to abuse of it), which is rather a desired goal…." "Non-compliance to treatment, that is, everything that is less than full compliance, has many different forms and needs to be carefully analyzed and studied" [13]. According to Mendelevich, drug compliance represents a complex structure that has sensory-emotional, logical, and behavioral components [18]. Regardless of the conceptual differences in approaches to the definition of drug compliance, the authors agreed that the formation of drug compliance is influenced by various factors, including psychopathological symptoms involved in the major psychopathological syndrome and cognitive impairment [8, 13, 16, 18].

Thus, the high prevalence of predementia disorders, their unfavorable prognosis with a high frequency of transition to dementia, and polymorbidity with somatic pathology, which is a proven risk factor for the development of dementia, necessitate adequate correction of all current diseases. This increases the importance of drug compliance and determines the need to study its structure and relationship with the mental state of patients.

Aim

The study aimed to assess the structure of drug compliance in older people with mild cognitive impairment and psychopathological symptoms

Materials and methods of research

We conducted an observational study of older patients (aged 60–75 years) who were under follow-up in 2016–2019 in the City Clinical Hospital No. 6 and Gerontological Center of the Sverdlovsk Regional Clinical Psychiatric Hospital (Yekaterinburg) and were diagnosed with mild cognitive impairment in accordance with the operational criteria for the syndrome of mild cognitive impairment. The International Classification of Diseases, the 10th revision (1992), does not comprise the heading "Mild cognitive impairment," while the heading "Mild cognitive impairment (F06.7)" is closest to it, suggesting the presence of a clear etiological central or systemic factor (infectious, traumatic, etc.).

The main study group and comparison group were formed based on the study aims and objectives. The main study group included patients with mild cognitive impairment syndrome who were identified to have psychopathological symptoms during the present examination. The comparison group included patients with mild cognitive impairment without psychopathological symptoms.

Gender and age characteristics of participants in the study groups are comparable (Table 1).

Clinical–psychopathological, psychometric, and statistical research methods were applied.

The Mini-Mental State Examination (MMSE) was used to assess cognitive status. The median final

Table 1. Gender and age of the study participants.

Study groups	Men		Women		Median age (percentile), years
	n	%	n	%	
Main, *n* = 189	30	15.9	159	84.1	69.0 (62.50 ± 73.00)
Comparison, *n* = 75	14	18.7	61	81.3	68.0 (61.00 ± 72.00)

Table 2. Frequency of noncognitive symptoms in patients with mild cognitive impairment syndrome in the study groups (results of completing the NPI questionnaire).

Psychopathological symptom	Study groups				Pearson's test χ^2
	Main		Comparison		
	n	%	n	%	
Delirium	68	36.0	0	0.0	0.000
Hallucinations	12	6.3	0	0.0	0.000
Agitation/aggression	48	25.4	0	0.0	0.000
Depression/dysphoria	77	40.7	0	0.0	0.000
Anxiety	89	47.1	0	0.0	0.000
Apathy/indifference	52	27.5	0	0.0	0.000
Irritability/mood instability	60	31.7	0	0.0	0.000
Sleep and nighttime behavior disorders	95	50.3	0	0.0	0.000
Appetite and eating disorder	68	36.0	0	0.0	0.000
Total	189		75		—

Note: NPI, Neuropsychiatric Inventory.

scores on the MMSE scale in the main and comparison groups were comparable (26.000 (26.000 ± 27.000) and 26.000 (26.000 ± 27.000); $p = 0.623$).

Psychopathological symptoms were assessed based on the results of the Neuropsychiatric Inventory (NPI). To assess compliance, the Compliance Level questionnaire was filled out, which enabled the identification of the general, social, behavioral, and emotional compliance of the patients [19].

Statistical data based on the results obtained were calculated using the Statistica 7 for Windows. Quantitative data are presented as median, 25th, and 75th percentiles. To assess significant differences in qualitative (parametric) indicators, Pearson's chi-squared test χ^2 was used. The nonparametric Mann–Whitney *t*-test was used to assess significant differences in quantitative indicators that do not follow a normal distribution. Fisher's exact method was used with the calculation of one- and two-tailed options. McNemar and Wilcoxon tests were used to assess significant differences in changes in paired indicators. Correlation analysis with the calculation of Spearman's correlation coefficients (*r*) enabled the identification of correlations between indicators. When comparing data, the significance of differences *p* between the study groups was determined. Differences were considered significant at $p < 0.05$.

The figures were made using Microsoft Excel and Microsoft Word.

At the planning stage of the study, an ethical review was conducted in the local ethics committee of the Ural State Medical University of the Ministry of Health of Russia (Protocol No. 3 dated November 27, 2015).

Results

The use of clinical–psychopathological and psychometric methods helped identify psychopathological symptoms in the main study group (Table 2).

Among patients of the main group, affective, psychotic, behavioral, and excitation subgroups were distinguished according to the leading psychopathological trait. All psychopathological symptoms in the main group were manifested subclinically, and their detection was possible through the use of the NPI questionnaire. The affective subgroup included subclinically manifested depression/dysphoria, anxiety, and apathy/indifference. The psychotic subgroup included delusional, hallucinatory–delusional, and hallucinatory syndromes, presented subclinically. The excitation cluster subgroup included disinhibition, agitation/verbal aggression, and irritability/mood instability. The behavioral cluster group included sleep and nighttime behavior disorder and appetite and eating disorders.

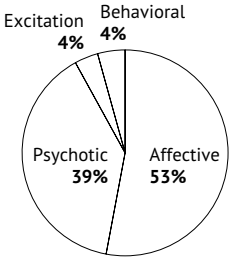

Fig. 1. Distribution of participants in the main group by non-cognitive subgroups

Such determination of psychopathological clusters is supported by several authors. A dimensional approach enables the assessment of the contribution of psychopathological disorders to the cognitive impairment changes over time. Herein, the names of psychopathological subgroups (affective, psychotic, behavioral, and excitation) are symbolic (Fig. 1).

The study patients were followed up on an outpatient basis, visited a doctor at least once every 12 months, and received therapeutic recommendations for the main (psychopathological) and concomitant (therapeutic) pathology.

Compliance levels of the study participants were represented by several components:

– Social compliance: patient's desire to comply with therapeutic recommendations and determined by the focus on social approval.

– Emotional compliance: readiness to comply with the recommendations because of increased sensibility and sensitivity.

– Behavioral compliance: desire to follow strictly the doctor's recommendations, aimed at overcoming the disease, perceived as an obstacle.

The total scores on general compliance were 45.42 ± 29.7 and 51.09 ± 32.3 points in the main study group and comparison group, respectively (p = 0.031). The calculation of extensive indicators of general compliance in the study groups helped identify patients with a low level of general compliance (0–40 points), medium level of general compliance (41–80 points), and high level of general compliance (81–120 points) (Fig. 2).

In the main study group, half of the participants had a low total score of overall compliance, less than half of the participants had a medium level of overall compliance, and only 4.8% showed high compliance with therapeutic recommendations. The overwhelming majority of the comparison group had a medium level of compliance. A low level of overall compliance was detected only in a third of cases. A high overall compliance was registered in 12.0% of cases, which was significantly higher than that in the main group (p = 0.041).

Patients with overall low compliance disagreed with the doctor's opinion regarding the diagnosis

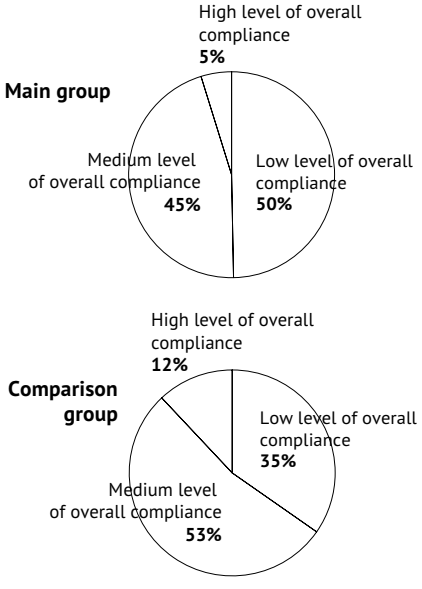

Fig. 2. Distribution of study participants by level of compliance.

and treatment of underlying and concomitant pathologies, doubted the recommendations, devalued them, tended to neglect some aspects of the recommended treatment, and indulged their desires, preferring not to make efforts to fulfill the medical recommendations.

Patients with a high total score of general compliance were ready to cope with the disease, focused on achieving recovery, followed conscientiously the doctor's recommendations, and followed the regimen.

Since compliance has multiple components, its social, emotional, and behavioral components were assessed in the study groups (Fig. 3). The total indicator was 0–15 points for a low indicator of compliance, 16–29 points for a medium indicator, and 30–40 points for a significantly pronounced indicator. The higher these indicators, the stronger, more stable, and deeper is the patient compliance.

In the main group, patients with low levels of all components of compliance (social, behavioral, and emotional components) were more common, and the emotional compliance of these patients was the most vulnerable. Moreover, the frequency of low, medium, and high compliance demonstrated significant differences (p = 0.031).

In the comparison group, more representatives had a high level of behavioral compliance than those with a medium one. Patients with a low level of social compliance were guided by their decisions, often canceled the recommended therapy, and interrupted it without consulting a doctor, and in any situation, they strove to have their opinion often contradicting the doctor's opinion.

A small number of study participants with a high level of social compliance strove for a trus-

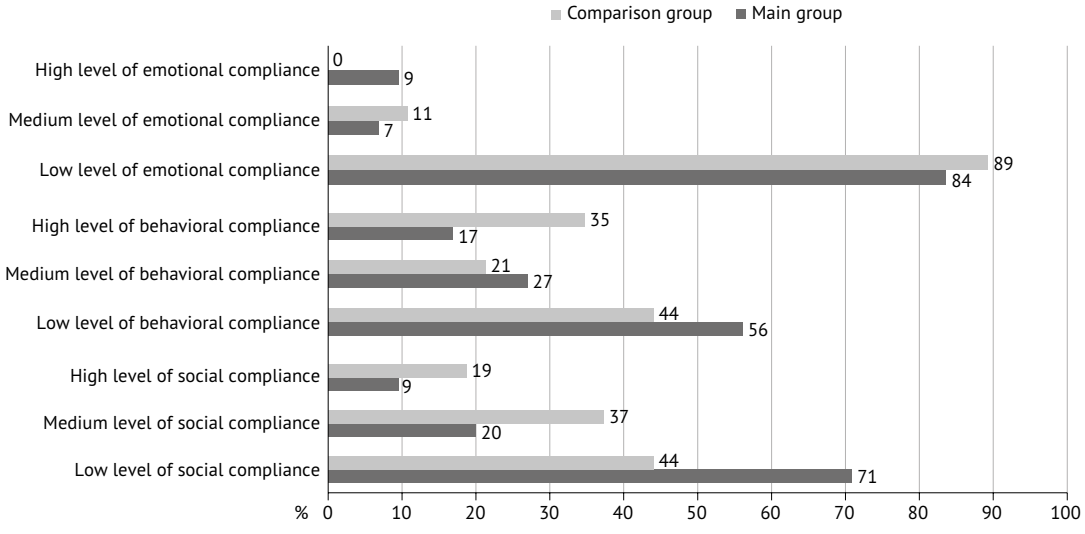

Fig. 3. Expressiveness of the structural components of compliance in the study groups.

ting relationship with the doctor, relied on his opinion, were dependent on him, and needed support. They were preoccupied with the impression they made on others, in particular on the doctor, whom they perceived as a significant person. They tended to consult with the doctor about concerns and doubts that arose in the course of treatment.

Patients with a low level of behavioral compliance preferred to act according to their desires, rather than make efforts to comply with medical requirements and recommendations. Those with a high level of behavioral compliance sought to comply strictly with medical recommendations aimed at overcoming the disease, perceived as an obstacle. They focused on achieving the goal in the disease situation, namely, recovery, and they followed conscientiously the doctor's recommendations, observed the regimen, and perceived the doctor as a colleague, hoping that together they can cure the disease.

Patients with a low level of emotional compliance focused on rational and logical ways to overcome the disease, often cast doubt upon medical recommendations, and tended to underestimate disease severity, while disregarding the possible consequences and complications. People with a high level of emotional compliance contributed to the treatment process in every possible way, while being unnecessarily worried about the consequences or possible failures of treatment, notifying the doctor about their experiences, and were inclined to visit the doctor frequently and consult about any changes in well-being.

The heterogeneity of the psychopathological structure of the main group determines the need for a comparative analysis of compliance among representatives of the affective, psychotic, behavioral subgroup, excitation subgroups (Table 3).

In the affective psychopathological subgroup, a vast majority of individuals had a low level of social, behavioral, and emotional compliance. The same tendency was detected in the psychotic subgroup. In the excitation subgroup, emotional compliance was represented only by a low level (100.0%), behavioral compliance of low and high levels has approximately equal rates, and social compliance was represented by all levels, with the highest frequency of low level. In the behavioral subgroup, social compliance in half shares was represented by moderate and high levels, a high level of behavioral compliance was more often revealed, and a low level of emotional compliance was more common (Table 4).

A comparative analysis of the median values of the total scores of compliance types showed a significant decrease in the indicators of social, behavioral, and emotional compliance in the affective psychopathological subgroup of the main group in comparison with the behavioral, excitation, and comparison groups. Patients of the psychotic subgroup had a significant decrease in social compliance in comparison with those of the behavioral, excitation, and comparison groups. Compliance indicators of behavioral subgroup exceeded similar indicators in all other psychopathological subgroups and comparison group, and as regards behavioral compliance parameters, the progression was significant. Analysis of different types of compliance in patients with noncognitive psychopathological symptoms showed their heterogeneity.

Correlation analysis was used to study the relationship between psychopathological symptoms as regards moderate cognitive impairment and the expressiveness of compliance. The exact Spearman

Table 3. Distribution of patients in the main study group according to the expressiveness of social, behavioral, and emotional compliance.

Compliance	Psychopathological subgroup							
	Affective		Psychotic		Excitation		Behavioral	
	n	%	n	%	n	%	n	%
Low level of social compliance	69	69.7	60	80	4	57.1	0	0
Medium level of social compliance	23	23.2	7	9.3	2	28.6	4	50.0
High level of social compliance	7	7.1	6	8	1	14.3	4	50.0
Low level of behavioral compliance	63	63.6	38	50.7	4	57.1	0	0
Medium level of behavioral compliance	24	24.2	25	33.3	0	0	3	37.5
High level of behavioral compliance	12	12.1	12	16	3	42.9	5	62.5
Low level of emotional compliance	73	73.7	69	92	7	100.0	7	87.5
Medium level of emotional compliance	9	9.1	3	4	0	0.0	1	12.5
High level of emotional compliance	17	17.2	1	1.3	0	0.0	0	0.0
Total	99		75		7		8	

Table 4. Expressiveness of social, behavioral, and emotional compliance in the psychopathological subgroups of the main group and comparison group (median).

Compliance	Psychopathological subgroup of the main group				Comparison group	p
	Affective	Psychotic	Excitation	Behavioral		
Social	10.0* (6.0 ± 18.0)	12.0* (8.9 ± 15.0)	15.0 (15.0 ± 40.0)	27.5 (23.0 ± 33.75)	18.0 (10.0 ± 25.0)	0.043
Behavioral	15.0* (9.0 ± 17.0)	15.0 (15.0 ± 26.1)	15.0 (15.0 ± 40.0)	32.000* (26.5 ± 35.0)	18.0 (7.0 ± 30.0)	0.039
Emotional	10.0* (8.0 ± 20.0)	12.0 (8.9 ± 14.0)	14.0 (12.0 ± 15.0)	12.0 (11.25 ± 14.0)	12.0 (10.0 ± 14.0)	0.047
Total	99	75	7	8	75	—

Note: *$p < 0.05$. Mann–Whitney test.

Table 5. Correlations of noncognitive psychopathological symptoms and compliance indicators (Spearman correlation coefficient).

Psychopathological symptom	Compliance indicators, r			
	General compliance	Social compliance	Behavioral compliance	Emotional compliance
Delusional ideas	0.032	0.023	0.153	–0.044
Hallucinations	0.097	0.101	0.147*	–0.067
Agitation/aggression	–0.331**	–0.229**	–0.589**	–0.468**
Low mood/dysphoria	–0.512**	–0.381**	–0.227**	–0.553**
Anxiety	–0.086	–0.265**	–0.166*	0.179
Apathy	–0.290**	–0.191*	–0.135	–0.395**
Irritability/mood instability	–0.347**	–0.423**	–0.287**	–0.467**
Disorder of appetite and eating behavior	0.102	0.089	0.112	0.078
Night sleep and nighttime behavior disorders	0.101	0.092	0.073	0.042

Note: $p < 0.001$; *Weak correlation; **Average correlation.

correlation coefficient was calculated for nonparametric indicators (Table 5).

Based on correlations, patients with low mood, agitation, and aggression and those affectively unstable are the least adherent to therapy in terms of overall compliance.

Discussion

This observational study of older patients with mild cognitive impairment syndrome and psychopathological disorders revealed differences in the rate of drug compliance in patients with and without psychopathological symptoms. The overall drug compliance rates were lower in patients with psychopathological symptoms, especially affective and psychotic symptoms. In the main group, patients with low levels of social, behavioral, and emotional compliance were more common, and the emotional compliance of these patients was the most vulnerable. In the affective and psychotic subgroups, the vast majority of patients had a low level of social, behavioral, and emotional compliance. They were registered significantly more often than among patients with a comparable cognitive status without psychopathological disorders.

An analysis of the completion of the Compliance Level questionnaire revealed the heterogeneity of the study groups with respect to compliance indicators and enabled the identification of subgroups with low, moderate, and high compliance. Statistical analysis confirmed that with a decrease in general, social, behavioral, and emotional compliance levels, the severity of psychopathological disorders increases, namely, agitation/aggression, mood depression/dysphoria, and irritability/mood instability. The increase in apathy correlates with low general, social, and emotional compliance. Anxiety intensity correlates with low behavioral and emotional compliance. Significant correlations were found between psychotic symptoms (delusions and hallucinations) and low behavioral compliance.

Conclusions

1. Drug compliance in older patients with predementia cognitive disorders has a heterogeneous structure.

2. The readiness of older patients with mild cognitive impairment to follow therapeutic recommendations for psychopharmacotherapy and somatic therapy is lower in patients with subclinical anxiety, depressive, and psychotic symptoms than in those with comparable cognitive impairment without psychoproductive symptoms.

3. The increase in affective, psychotic, and behavioral disorders in patients with mild cognitive impairment correlates with the low general, social, emotional, and behavioral compliance.

Author contributions. A.P.S. and N.V.I. developed the study design, took part in collecting the material, discussed the results, and wrote the article. O.V.S. and A.A.V. developed the study design, discussed the results, and wrote the article. A.A.M. and A.V.R. contributed to the collection of material, performed statistical data processing, discussed the results, and wrote the article.

Funding. The study had no external funding.

Conflict of interest. The authors declare no conflict of interest.

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