# EFFICACY AND TOLERANCE OF PHARMACOTHERAPY WITH ANTIDEPRESSANTS IN NON-PSYCHOTIC DEPRESSIONS IN COMBINATION WITH CHRONIC BRAIN ISCHEMIA

**[1]Uskov Akram Ivanovich, [2]Sharapova Dilfuza Nematillayevna, [3]Turayev Bobir Temirpulotovich, [4]Shernazarov Farrux Farhod o‘g‘li**

[1]Siberian State Medical University, Russian Federation city of Tomsk
[2]Assistant of the department of psychiatry, medical psychology and narcology, Samarkand State Medical University, Samarkand, Republic of Uzbekistan
[3]Samarkand State Medical University Clinical ordenator in the direction of psychiatry
[4]608 group students of Samarkand State Medical University Faculty of Medicine

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***Abstract.*** *Depressions observed in various neurological disorders are an important medical problem. In the main forms of neurological pathology, the prevalence of depression is much higher. In most neurological nosologies, depression rates exceed 10%, with stroke (30%), pain syndromes (36% for back pain, 42% for tension headaches), and hereditary neurological disorders (Huntington – 30%, Wilson – Konovalov – up to 60%).*

***Keywords:*** *pharmacotherapy, antidepressant, non-psychotic depression, comorbid, brain ischemia.*

**Introduction.** Comorbidity of depression and neurological diseases (significantly higher than the population at the time of examination – 3,2%) indicates that depression is not only a "psychologically understandable" consequence of CNS severe disease (nozogenic Factor), but also determines complex pathogenetic connections with pathological processes with a biological basis [1-3].

In a number of neurological disease models, the presence of Affective Disorders has been shown to lead to further deterioration in quality of life (compared to patients with the same neurological pathology but without depression). Thus, comorbid depression in Parkinson's disease was found to cause a significant decrease in quality of life in all areas of the PDQ-29 survey. In addition, it is depression that predicts a decrease in quality of life relative to other factors – age, severity of motor signs and severity of cognitive disorders [4-7]. In epilepsy, depression predicts a decrease in quality of life rather than the localization or frequency of seizures of epileptic focus in the brain [8].

The presence of comorbid depression leads to a more severe course of the underlying disease, affects the severity of the underlying symptoms, increases the likelihood of complications and a negative outcome of neurological diseases. It is associated with specific symptoms of depression (e.g., a general decrease in motivation and adherence to treatment due to the severity of apathy) and completely undetermined neurobiological mechanisms, resulting in the majority of neurological disorders in joint depression being more severe than it [9-13]. The correctness of this pattern is confirmed for almost all major neurological diseases – Parkinsonism, stroke, epilepsy, dementia, multiple sclerosis, chronic pain syndromes. Depression itself, according to some data, plays a role predicting a less favorable course of Parkinson's disease, primarily accelerated

cognitive decline [14-16]. It has also been shown that depression in stroke is an independent risk factor for brain circulatory disorders, including recurrent [17-20]. According to Ohira et al., in the presence of depression (objectified on the Tsung scale), the likelihood of developing a subsequent stroke of any Genesis increases by 1.9 times, while ischemic stroke increases by 2,7 times [21]. The presence of post-vascular depression leads to a significant decrease in life expectancy, especially according to a large-scale study by Morris et al. [22], the likelihood of dying in depression over the next 10 years after an episode of circulatory disorders in the brain increases 3,4 times.

The most common immediate causes of death for patients with post-stroke depression are called recurrent ONMC and suicide [23]. In turn, comorbid depression in epilepsy increases the likelihood of developing side effects of antiepileptic drugs, makes frequent visits to doctors and leads to an increase in treatment costs [20]. The presence of comorbid depression in both Alzheimer's type dementia and vascular dementia increases the risk of death. For example, in Alzheimer's disease - 1.88 times (95% confidence interval– 1,12–3,18%) [21]. In multiple sclerosis, in cases of comorbid depression, cognitive disorders become more pronounced and the disease itself develops faster [22]. In cases of amyotrophic lateral sclerosis (ALS), depression reduces patients ' commitment to therapy and contributes to the Thera disorder of the pevtic alliance with doctors, which contributes to a more aggressive course of the disease [23].

The ratio of depression and chronic pain syndromes (back pain, tension headache, migraine) deserves a separate discussion. According to modern data, affective and pain disorders often coexist (table. 1) and common processes are involved in their pathogenesis (neuroplasticity disorders,

Lack of manifestation of trophic factors in the central nervous system, neuroinflammation, decreased branching of neurons) [24]. Depression and pain syndrome interact negatively to form a pathological "vicious circle". Thus, the presence of pain in the clinical picture of depression leads to difficulties in diagnosis and a late onset of adequate antidepressant therapy, while depression significantly worsens pain disorders and leads to a weakening of the response to therapy, poor daily life, greater risk of disability and less adherence to rehabilitation measures [25, 26].

As for the issues of the clinic and diagnosis of depression in some forms of neurological pathology, we note the following. Although many studies use the same diagnostic methods to diagnose depression in neurological patients, including scales/questionnaires formalized in other areas of medicine, as well as in psychiatric practice, depressive states in neurological pathology reveal some important clinical features [27-29]. For this reason, psychopathology and the depression clinic accompanying various neurological disorders are of great interest, primarily in the most common and/or disabled, such as stroke, Parkinson's disease, Huntington's chorea, etc.

As part of this publication, we will focus on the clinically most important options for combining neurological pathology and depression. It should be noted that regardless of the nosological affiliation of neurological suffering in Neurology, the clinical differentiation of depressions remains relevant for other areas of somatic medicine as well. It refers to isolation along with organic, nozogenic and endoform Affective Disorders [30-33].

Nosogenic depressions in neurological pathology are reactive conditions caused by a pronounced diagnosis, manifestation of the disease (for example, severe subjective painful symptoms of neurological pathology, difficult to control), as well as psychotraumatic (nosogenic) effect caused by the patient's data on prognosis and outcome (for example, high frequency). loss

of working capacity and disability, risk of death, etc.) [34]. The clinical picture of nosogenic depression is determined by the symptoms of the anxiety-hypochondria series: depression, pessimistic perception of the disease, hypertrophied assessment of its consequences, fear of repeated attacks of the disease, fear of death or impending disability [35]. The behavior of patients is accompanied by increased self-observation and registration of the smallest changes in well-being, often in combination with a mass of complaints that do not have a sufficient somatic basis (somatic, functional) [36]. Other components of depressive disorder include conversion ("lump in the throat" and tremors, numbness of the limbs in the form of "gloves" and "socks") and neurasthenic symptom complexes (in combination with increased fatigue, decreased activity, complaints of weakness, irritability, tears) [37].

The purpose of the study: was a comparative study of the efficacy and tolerance of antidepressant pharmacotherapy in patients with and without cerebrovascular disease with psychotic unipolar depression.

**Research materials and methods.** The study was conducted at SOPB's mental and Behavioral Disorders Treatment Unit. The study included patients diagnosed with ICD 10 (F3): one depressive episode or depressive episodic recurrent depressive disorder, aged 18 to 65, who signed informed consent. The main criteria for exclusion are: dementia, schizophrenia spectrum disorders, paroxysmal disorders, substance use, bipolar affective disorder, depressive disorders of the psychotic level, high suicide risk, chronic somatic disorders in the stage of severe decompensation.

Patients included in the study (90 people) underwent discontinuation therapy at moderate therapeutic doses (essitalopram 10-20 mg/s (N=30), paroxetine 30-60 mg/s (N=60)) with antidepressants for 4 weeks. All patients are divided into two groups: the first group (control) – patients with non – psychotic unipolar depression (N=48); the second group (primary) - patients with unipolar depression with cerebrovascular disease (N=42). 6 people in the second group (6,67%) refused to participate in the study due to adverse events (excluded from further analysis). To address this goal, the study used a clinical and psychopathological method; psychometric using standard quantized scales: Hamilton Depression Scale (HDRS-17), Beck Depression self-assessment scale (IBD,

Sheehan's social malpractice. Adverse events were recorded by the doctor (objective assessment) and patient (subjective assessment) at each visit on the uku side effect scale. Statistical analysis was carried out using the computer program "SPSS 17.0".

The average age of patients was 43,62±13,46 years, with female (86,67%, n= 78), higher / unfinished higher education individuals (80%, N=72) and unemployed (53,33%, N = 48) predominating. The proportion of married and single patients (50% each, N=45) was the same. The diagnosis of recurrent depressive disorder (56,67%, N=17) is somewhat more frequent than in "depressive episode" (43,33%, N=13). The condition of most patients was assessed as moderate (70%, N=21), rarely mild (23,33%, N=7) severity. The psychopathological structure of depressions is mainly represented by anxious (33,33%, N=30), less hysterical (23,33%, N=21) and apathetic (20%, N=18) depressions. Patients in the second group were dominated by hereditary severity of mental disorders compared to the first Group (2 groups -35,71% (15), 1 group – 6,25% (3)).

**Results and their discussion.** Remission (RM) has often been reported in control group patients (56.25% Group 1, 50% Group 2). Also, the first group was dominated by respondents

(HDRS≥ 50%, but >7 points (25%)), the second group by partial respondents (HDRS≥25%, but <50% (50%)). "Functional remission" (Frm) (less than 5 points on the Sheehan malfunctioning scale (Leon A. C., 1997)) in a group of patients with non-psychotic unipolar depression (50%) reported twice as many patients with cerebrovascular disease as the group with unipolar depression (25%).

The dynamics of the indicators of the HDRs-17 scale, IBD and Sheehan's social malfunctioning scale had similar trends, consisting of a faster rate of decline of the overall background indicators in the first group compared to the second group. At the same time, statistically reliable differences between the groups identified using the Mann-Whitney U test were found on the HDRs - 17 scale only in Weeks 2 and 3 of treatment (r<0,05) and on the Sheehan social malfunctioning scale in Week Four (R<0,05).

Adverse events identified by the physician were reported in 75 patients (89,29%). In total, 231 cases were reported through an objective assessment of adverse events, with an average of 2,75 for every 1 patient. Both groups were dominated by mental and vegetative adverse events, among which nausea complaints were most common (17,39% – Group 1, 16,13% – Group 2), concentration disorders (15,22% – Group 1, 22,58% – Group 2). At the same time, differences in spectrum were found between patients in two groups of adverse events across a number of symptoms. Thus, the first group was dominated by tension/anxiety (10,87%), decreased libido (10,87%), orgasm disorders (6,52%) and tension headaches (15,22%), the second by drowsiness/sedation (19,35%). Rare adverse events in both groups are asthenia/fatigue/increased fatigue (4,35%-Group 1, 6,45% – Group 2), decreased memory (6,52% – group 1, 6,45% - group 2) and tachycardia, sleep disorders and sleep duration, paresthesia, depression, which have only been reported in isolated cases.

According to the subjective assessment, adverse events were recorded more often – in 92,86% of patients. In the control group, objective assessment indicators outweigh subjective symptoms: impaired concentration (15,22% and 12,24%, respectively), drowsiness/sedation (8,7% and 4,08%, respectively), nausea / vomiting (17,39% and 14,29%, respectively) and decreased libido according to subjective - symptom (10,87% and 14,29%, respectively). In the second group, the frequency of detection of adverse events is a disorder of concentration (22,58% and 12,5%, respectively), which is higher by doctors in terms of symptoms compared to patients, while patients experience nausea/vomiting in the symptom (16,13% and 21,88%, respectively). The most unwanted events occurred in both therapy groups in the first week (38,33% -1 group, 37,8% -2 group). From the second week there was a tendency to reduce them.

**Conclusions.** The results of this study show a high frequency of clinical remission formation in combination with cerebrovascular disease (50%) in course therapy with antidepressants, both in patients with non-psychotic unipolar depression (56,25%) and in patients with non-psychotic unipolar depression related to information published locally. At the same time, in the second group of patients, the polarization of the results of therapy is taken into account, where one part of the patients has remission, and the other part has a very low effect – CRS.

The predominance of depressive severity in the control group relative to the main group is partly explained by the longer period of antidepressant titration. Therefore, a number of researchers can agree on the need to increase the deadlines required to achieve remission by 6-12 months standards for the treatment of depression in older people.

The results of the study of the tolerance of antidepressants confirm, first of all, a very high percentage of the prevalence of adverse events in the treatment of patients with non-psychotic depression. At the same time, for patients with non-psychotic unipolar depression and non-psychotic unipolar depression, in combination with cerebrovascular disease, general (nausea/vomiting, concentration disorders) and specific adverse events were identified.

Specific symptoms characteristic of the first group of patients were tension/anxiety, decreased libido, orgasm disorders and tension headaches, and drowsiness/sedation for the second. In this case, the dissociation between objective and subjective assessment was noted unpleasant phenomena. The good results of antidepressant treatment have helped to increase patients ' commitment to taking and taking antidepressants after the end of the study in both groups of therapy.

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