# Experience of daytime anxiolytics administration in the therapeutic practice of anxiety in patients with neurological disorders.

**Zhusupova A.S., Tautanova R.S., Kalinichenko Z.K., Smagul N.B.**

Functional neurotic disorders, psycho-vegetative disorders remain the subject of discussion to this day, there is still no consensus on definitions of these conditions. In clinical practice, various terms have been used, such as “neurosis” [1], “vegetative dystonia”, “vegetative neurosis”, “neurocirculatory dystonia” [2], “psychosomatic disorder” [3], etc. In ICD-10, the term “somatoform disorders” is used which was adopted in the third and further in the fourth revision of the classification by the American Psychiatric Association which meant somatic disorders with no organic basis. [4] Intrinsic relation and between somatics and psychics discussed in the times of ancient medicine. At present, the objective reality of modern life, leading to psycho-emotional overstrain of people requires an improvement in the assessments of psychopathological manifestations and methods for correcting them.

Anxiety is among the most common non-specific phenomena that are included in the structure of both psychopathological and various somatic disorders [5]. Anxiety is a sense of danger arising spontaneously in anticipation of uncertain situations [6]. At the same time, emotional upheaval always manifests in a degree absolutely incommensurable with the actual danger from these objects and situations. From 10 to 26% of women and from 5 to 12% of men throughout the world experience anxiety and depression [7,8]. Treatment of anxiety states requires the use of specific medicamentous therapy. An effective method of psychoemotional disorders correction with anxiety syndrome is the use of adequate anxiolytic. One of these medicinal products is Gidazepam – daytime tranquillizer of the benzodiazepine series – which has an original spectrum of pharmacological activity, combines anxiolytic effect with activating and antidepressant components with low severity of adverse events and low toxicity, as well as no hypnotic effect [9].

We have worked to assess the effectiveness of Gidazepam in the treatment of neurological patients with neurotic mixed anxiety-depressive disorders that meet the criteria of ICD-10.

## Material and methods

The trial included patients with various neurological diseases having an increased anxiety level, sleep disturbance, panic attack. Patients were monitored in the neurological hospital and the neurologist's office of the district outpatient department. The paper was based on the results of a clinical trial conducted by questionnaire survey before and after treatment, as well as the results of a general clinical laboratory assessment to exclude the adverse effects of drug administration.

*Clinical trial*. The trial involved 20 patients with complaints of anxiety and agitation, psychogenic headaches, panic attacks, sleep disturbance. Of these, out of the outpatient

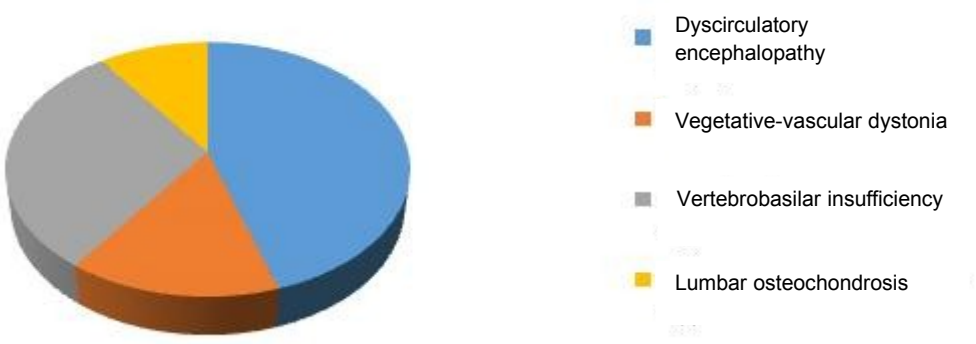
visit – 11 patients, from the neurological hospital – 9 patients which is a percentage of 55% and 45%, respectively. By gender, the group was divided as follows: 5 men (22.2%), 15 women (77.8%). Mean age of patients was 50.9 years (46.8 years among men, 52.1 years among women) and ranged from 24 to 77 years. By ethnicity, representatives of the Asian population were 38.9%, and Slavs were 61.1%. (Table 1)

**Table 1.** Disposition of subjects by age, gender, type of surveillance.

| **Value** | **Age** | | | **Sex** | | **Type of surveillance** | |
|---|---|---|---|---|---|---|---|
| | Young | Median | Elderly | Male | Female | Outpatient | Hospital |
| Absolute | 6 | 8 | 6 | 5 | 15 | 11 | 9 |
| Percentage | 30% | 40% | 30% | 22,2% | 77,8% | 55% | 45% |

The trial found that 66.7% are married, and 33.3% were unmarried people, widows and single people. 44.44% of the subjects have a secondary education, 66.56% graduated higher education institutions. The majority of patients in the trial population were 38.9% pensioners, 33.4% employed people, and 27.7% unemployed.

Among trial subjects, patients diagnosed with dyscirculatory encephalopathy (chronic cerebral ischemia) were 44.4%, vertebrobasilar insufficiency in 27.7%, vegetative dysfunction in 16.7%, lumbar osteochondrosis in 11.2%.




Picture 1. Disposition of group according to diagnoses

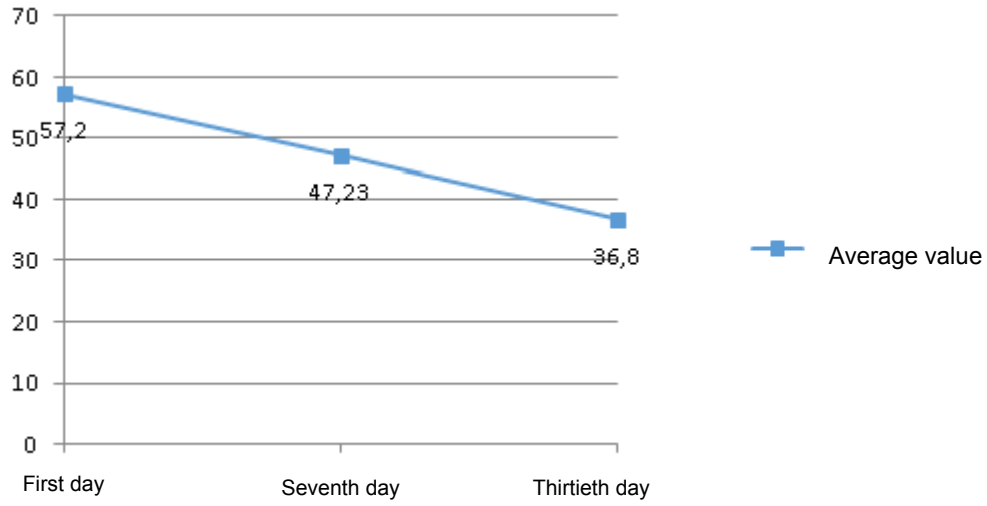
To evaluate the anxiety level, State-Trait Anxiety Inventory by Spielberger Ch.D. And Hanin Y.L., as well as Hospital Anxiety and Depression Scale (HADS) were used. Evaluation method for state and trait anxiety by Ch.D. Spielberger and Y.L.Hanin (State-Trait Anxiety Inventory) determines the anxiety level based on the self-assessment scale (severe, moderate, mild anxiety). Hospital Anxiety and Depression Scale (HADS) was developed in 1983. (Zigmond A.S, Snaith R.P.) The scale contains 14 questions: seven for determining the anxiety symptoms and seven for assessing the depression level. This is one of the most concise, but at the same time effective scales for determining depression. The total time for filling the printed version of the text and counting scores is 2 to 5 minutes. HADS focuses on non-somatic symptoms, so it can be used to diagnose depression in people experiencing significant physical health problems.

Gidazepam – a tranquilizer with anxiolytic action – which is a benzodiazepine derivative, was chosen as therapy. It combines anxiolytic and activating effect with antidepressant properties while possessing extremely low toxicity and a minimum of adverse effects. The drug acts as a selective anxiolytic and daytime tranquilizer. It differs from other benzodiazepines by its activating and mild muscle relaxant effects. The dosage in this trial was 20 mg 2 times per day. Treatment course duration was 30 days. All trial subjects were questioned before taking Gidazepam, on the 7th day of drug administration and at the end of the treatment course.

Laboratory examination included determination of the ALT and AST levels before and after the end of the treatment course. These indicators are selected taking into account the pharmacokinetic properties and adverse effects of the drug.

**Trial outcomes and discussion.**

According to State-Trait Anxiety Inventory, a score of 45 or more is characterized by severe anxiety, the range from 31 to 44 scores corresponds to a moderate anxiety, and less than 30 scores corresponds to mild anxiety. During the initial questionnaire survey, 100% of patients experienced severe anxiety, the average score was 57.2. During the secondary questionnaire survey, severe anxiety was noted in 66.7% of the subjects, the average score decreased to 47.23 which still corresponded to severe anxiety level. During the final assessment, only 11.1% of patients remained anxious, and the remaining 88.9% had a moderate anxiety level. At the end of the trial according to State-Trait Anxiety Inventory, the median value was 36.8 scores.




Picture 2. The median value of anxiety level according to State-Trait Anxiety Inventory and dynamics over time during therapy

In disposition of subjects by gender, the severe anxiety level was noted among both men and women. The average value in the initial questionnaire according to trait anxiety scale was 59.25 scores in men and 56.8 scores in women and was 37.7 scores and 36.5 scores, respectively, by the end of the therapy course. Over the period of monitoring, the male subgroup demonstrates a decrease in anxiety level from severe to moderate in 100% of cases. Results among women are less univocal and a positive trend can be noted in 85.71% of the subjects. At the same time, indicators of increased anxiety, despite therapy, remains in 14.29%.

According to age, the group was divided as follows: 27.8% of young people, 33.4% of middle, 27.8% of elderly and 11% of senile age. The average values in different age groups and their changes during therapy are presented in Table 2.

**Table 2.** The median value of anxiety level according to State-Trait Anxiety Inventory in various age groups

| Therapy day | Average value, scores | | | |
|---|---|---|---|---|
| | Young age | Middle age | Elderly age | Senile age |
| Day 1 | 57.2 | 59.6 | 56.6 | 52 |
| Day 7 | 47.8 | 49 | 44.8 | 46.5 |
| Day 30 | 38.4 | 36.3 | 37 | 33.5 |

Severe anxiety level was recorded in all subjects (100%) in percentage, regardless of age. On day 7, in 20% of young people anxiety decreased to moderate level. Middle-aged patients in 83.3% of cases remained a severe anxiety level. 60% of elderly people showed a positive trend in the form of a decrease in anxiety to moderate level. Requestioning revealed that 50% of senile-aged people remained increased anxiety.

After delivery of therapy, the moderate anxiety level was recorded in 100% of the young and 100% of the elderly. The remaining subgroups also show positive trend. Middle-aged patients in 16.7% of cases did not respond to therapy and remained with increased anxiety, and in 83.3% it decreased. The anxiety level after therapy decreased to moderate in 80% of the elderly, but in 20% it remained at severe level.

Representatives of the Asian population demonstrate severe anxiety during initial questionnaire and the average indicator is 57.14 scores which decreases after the end of Gidazepam administration to 38.85 scores. However, despite such a significant decrease in the average value after the drug administration, 14.29% of respondents still have an increased anxiety.

All participants of Slavic origin are also included in the trial due to increased anxiety. The average value according to State-Trait Anxiety Inventory before treatment was at the level of 57.36 scores, and decreased to 35.45 scores. Of the representatives of the Slavic population, the anxiety level decreased from severe to moderate in 90.90% of respondents, and in 10.10% the indicators demonstrate an increased anxiety.

The trial involved 66.67% of unmarried and 33.3% single participants. The average value according to State-Trait Anxiety Inventory before taking Gidazepam in people in marriage

bonds was 58.91 scores, and in the lonely group was 54 scores while regardless of the marital status, all patients had the severe anxiety level. By day 7 of the treatment, the severe anxiety level was detected in 66.67%, moderate was in 33.33% in both subgroups. However, after the end of Gidazepam therapy, the moderate anxiety level was recorded in 100% of single people, and in the subgroup of those who were married, the 16.67% had a severe anxiety level, and in 83.33% of the observed subjects decreased to moderate level. And despite the initial difference between single and married by day 30 of observation, the average value almost became the same, decreased to 36.6 and 36.8 scores, respectively.

Also, during assessment of anxiety level the patient employment was taken into account. Thus, among those participating in the survey there were 33.3% of employed, 27.7% of unemployed, 38.9% of pensioners. The average value of the anxiety level according to State-Trait Anxiety Inventory among unemployed was 60.2 scores, among employed the average was 56.5 scores and among pensioners 55.8 scores which decreased during requestioning to 47.8 scores, 49 scores and 45.2 scores, respectively. In the final questionnaire, the average value of anxiety decreased among the employees to 38.3 scores, among pensioners the indicator was 35.8 scores and among the unemployed - 35.6 scores.

Similarly, as in groups formed on other grounds, regardless of social employment, all trial participants in the initial questionnaire according to State-Trait Anxiety Inventory demonstrate an increased anxiety level. During requestioning, the severe anxiety level was remained in 83.3% of employed, 80% of unemployed persons and 42.8% of pensioners. After the end of therapy, all patients without permanent employment had the moderate anxiety level. However, 16.7% of employed and 14.3% of people who are on well-deserved rest, are still experiencing increased anxiety.

Depending on the diagnosis, the group was divided into 4 subgroups (DEP, vertebrobasilar insufficiency, lumbar osteochondrosis, vegetative-vascular dysfunction). The mean values and their change during Gidazepam therapy in patients with different neurological diagnoses are shown in Table 3.

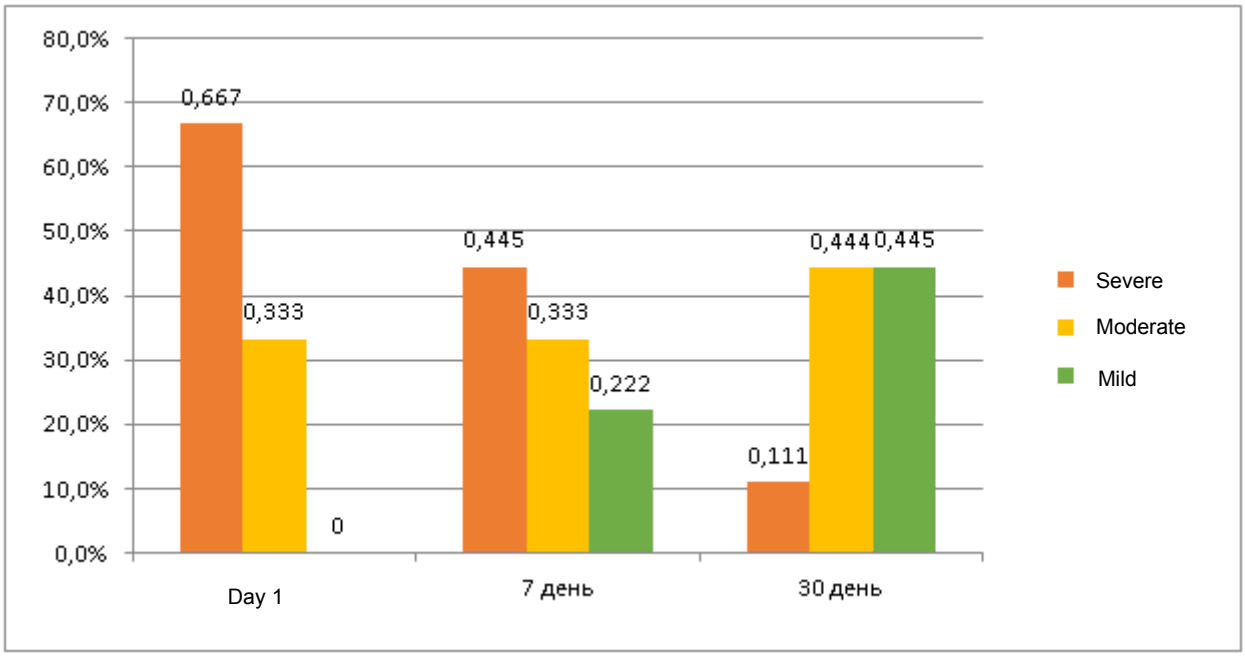
**Table 3.** The mean values and their dynamics depending on the diagnosis according to State-Trait Anxiety Inventory

| Observation Day | Mean value | | | |
|---|---|---|---|---|
| | DEP | VSD | VBI | LO |
| Day 1 | 57.5 | 53.67 | 59 | 57.5 |
| Day 7 | 45.5 | 42.67 | 52 | 49 |
| Day 30 | 34.87 | 36 | 38.8 | 40.5 |

During conversion the questionnaire results into percentages, it can be seen that in the subjects with DEP, the indicators decreased at day 7 in 50%, and by the end of the therapy 87.5% of patients experience the moderate anxiety level. The fastest effect of Gidazepam is observed in subjects with vegetative system dysfunction since a decrease in anxiety from severe to moderate is observed in 66.67% on day 7 of therapy. People suffering from lumbar osteochondrosis, at the end of treatment with anxiolytics responded

positively in 100% of cases. However, participants with diagnosis of vertebrobasilar insufficiency, despite taking the drug, experience increased anxiety in 20% of cases.

During questionnaire of patients according to Hospital Anxiety and Depression Scale (HADS) before taking the drug, clinically significant anxiety was detected in 66.7% of the subjects, and subclinical anxiety was recorded in 33.3%. It should be noted that the total scores more than 11, characterize clinically apparent anxiety/depression, the range from 8 to 10 scores is subclinical anxiety/depression, and the total of 0-7 scores characterizes the normal or decreased level of anxiety/depression. The average score at the baseline according to the HADS scale for anxiety and depression was 12.6 scores and 8.4 scores, respectively. At 7th day of treatment during questionnaire the group was divided according to the anxiety level as follows: 44.5% - severe, 33.3% - moderate, 22.2% - mild. After the end of Gidazepam administration, mild anxiety level was recorded in 44.5% of subjects, moderate in 44.4% and only 11.1% of subjects had clinically apparent anxiety.




Picture 3. Anxiety level according to HADS scale and its change over the period of monitoring.

In disposition of trial population by gender, the average indicators for men in the initial questionnaire are 15.5 scores, for women - 11.7 scores. Before treatment, 100% of men had clinically apparent anxiety, by the 7th day, increased anxiety persisted in 75%, and in 25% subclinical anxiety was noted. After Gidazepam administration, 50% of respondents demonstrate moderate anxiety level, 25% – normal level. However, 25% of the subjects did not respond to therapy. Clinically apparent anxiety before treatment was recorded in 57.14% of women, subclinical anxiety in 42.86% of women. One week after administration, 35.71% of women had an increased anxiety level, 35.71% – moderate level, 28.58% – mild anxiety. After 30 days of treatment, 50% of women do not report anxiety symptoms, according to the HADS questionnaire, in 42.86% of subjects anxiety level decreased to moderate. At the same time, 7.14% of women did not respond to therapy and still demonstrated clinically apparent anxiety.

When questioning young patients before treatment, according to HADS, 80% of subjects noted severe anxiety level and 20% – moderate. During requestioning, on the day 7 of treatment, indicators changed as follows: 60% - severe anxiety, 20% - moderate anxiety, 20% - mild anxiety. After Gidazepam administration, in 60% of subjects anxiety level

decreased to moderate, and 40% noted mild anxiety. Questioning in the middle-aged group revealed an increased anxiety level in 66.7%, and 33.3% in patients with moderate anxiety. After the end of therapy with anxiolytics, clinically apparent anxiety persisted in 16.7%, the moderate anxiety was noted in 50% of respondents. 33.3% responded positively to treatment, mild anxiety level was noted in these subjects.

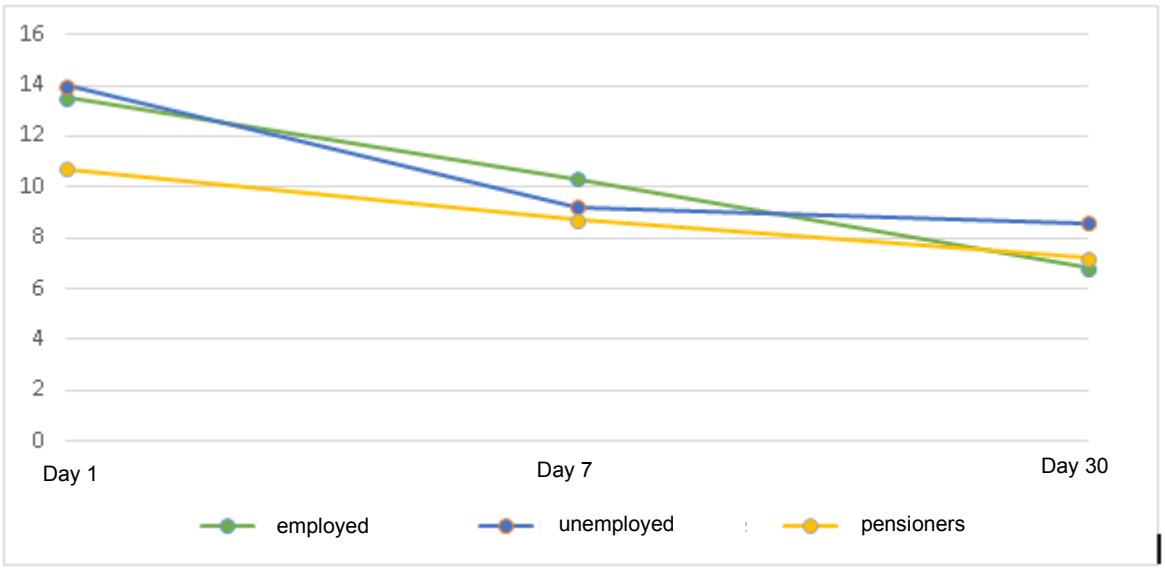
Before initiating therapy, 60% of elderly patients had severe anxiety, and 40% – moderate. On the thirtieth day of follow-up after requestioning according to HADS, clinically apparent anxiety was noted in 20% of subjects, subclinical - 40%, and 40% with a mild anxiety level. During initial questioning, 50% of senile-aged subjects demonstrated severe anxiety level and 50% – moderate. Positive trend was noted in 100% of cases, anxiety level decreased to mild.

Table 4. Dynamics of average values according to HADS in various age groups.

| Observation Day | Mean value | | | |
|---|---|---|---|---|
| | Young age | Middle age | Elderly age | Senile age |
| Day 1 | 13 | 13.3 | 11.6 | 11.5 |
| Day 7 | 11 | 9.1 | 9.6 | 8.5 |
| Day 30 | 7.4 | 7.6 | 7.8 | 6.5 |

Dividing the trial population by ethnic origin to Asians and Slavs, the average indicators for the initial questioning according to HADS were at the level of 13.28 and 12.09 scores, respectively. In the setting of antianxiety drug Gidazepam administration, by the 30th day of monitoring, the average value in the Asian population decreased to 7 scores, and in Slavic – to 7.8 scores. At the same time, in the Asian subgroup, prior to treatment, the severe anxiety level was detected in 71.43%, and moderate in 28.57% of respondents. Slavs with clinically severe anxiety were 63.64%, subclinical anxiety - 36.36%. After the end of anxiolytic therapy, anxiety remained in 14.29% of Asians and 9.10% of Slavs. Anxiety decreased to moderate level in 28.57% of the Asian population and in 54.55% of people of Slavic origin. A decrease in anxiety level to normal is observed in 42.86% of Asians and 36.36% of Slavs.

When calculating the anxiety level according to HADS scale in subgroups with different employment, the highest average value was recorded in unemployed group – 14 scores with a slight difference in the employed subgroup - 13.5 scores. In people who are on well-deserved rest, the average value was 10.5 scores, which corresponds to the moderate anxiety. At the end of the 30-day treatment of anxiolytics, the average value of anxiety among the employed decreased to 6.8 scores, pensioners 7.2 scores, and in unemployed persons to 8.6 scores. Dynamic pattern in the average values in the subgroups is clearly shown in Picture 4.



Picture 4. Dynamics of average anxiety values according to HADS scale depending on employment.

In percentage terms, questionnaire results according to HADS demonstrate clinically apparent anxiety in 83.3% of employees, 80% of unemployed and 42.8% of pensioners. Subclinical anxiety was recorded in 16.7% of employed, 20% of unemployed and 57.2% of pensioners. After Gidazepam administration on day 30, questionnaire results revealed the following: severe anxiety persisted in 20% of unemployed and in 14.3% of pensioners. Moderate anxiety level was observed in 50% of employed patients, in 60% of unemployed and in 28.6% of pensioners. Positive respond to therapy gave 50% of employed, 58.1% of pensioners and 20% of unemployed subjects, and their anxiety level decreased to the normal.

When the group was divided according to diagnoses, the average values according to HADS in patients with DEP and sleep disorders varied from 12 scores in the initial questioning to 7.75 scores after the end of therapy. During monitoring, in patients with VSD, the average anxiety was 12.6 scores before treatment and 6.6 scores after treatment with Gidazepam. The average anxiety among trial subjects with VBI decreased from 12.8 scores to 8 scores before and after treatment, respectively. In patients undergoing treatment for osteochondrosis, the average value of the results of the initial questionnaire was 14 scores, which decreased to 6.5 scores during therapy.

Percentages of anxiety level according to HADS depending on the diagnosis are shown in the diagram in Figure 4.

| Diagnosis | Severe anxiety level, % | | | Moderate anxiety level, % | | | No anxiety, % | | |
|---|---|---|---|---|---|---|---|---|---|
| | Day 1 | Day 7 | Day 30 | Day 1 | Day 7 | Day 30 | Day 1 | Day 7 | Day 30 |
| DEP | 62.5 | 37.5 | 12.5 | 37.5 | 37.5 | 50 | 0 | 0 | 0 |
| VSD | 66.67 | 33.33 | 0 | 33.33 | 33.33 | 33.33 | 0 | 33.33 | 66.67 |
| VBI | 60 | 60 | 20 | 40 | 20 | 40 | 0 | 20 | 40 |
| Osteochondrosis | 100 | 50 | 0 | 0 | 50 | 50 | 0 | 0 | 50 |

*Laboratory examination.* This examination included the determination of ALT and AST levels. Elevated liver function tests and liver failure are contraindications to use of Gidazepam. Given this factor, transaminases level was determined for all patients before and after treatment. The average values were ALT 17.9 U/L, AST 18.98 U/L and ALT 15.0 U/L, AST 16.8 U/L on the first and 30th day of therapy, respectively.

Thus, the results of our trial on the effectiveness of Gidazepam in neurological patients with anxiety have led to the conclusion that women, middle-aged patients, patients of Slavic origin, pensioners and married are most susceptible to anxiety disorders. Patients diagnosed with dyscirculatory encephalopathy and vertebrobasilar insufficiency are more anxious than subjects with other diagnoses. However, according to the data from State-Trait Anxiety Inventory, HADS scale, the highest positive effect of therapy and a decrease in anxiety to an average in 80% of cases and more were noted in these groups of patients. The trial showed a trend to reduce the anxiety level in patients with neurological diseases while taking Gidazepam; these patients noted sleep normalization, mood improvement, increased performance efficiency, decreased the number of dizziness episodes and panic

attacks with anxiety and fear. According to the State-Trait Anxiety Inventory, the majority of patients experience a decrease in anxiety level from severe to moderate, but others continued to have increased anxiety despite the treatment. At the same time, the results of questionnaire according to HADS scale demonstrate a decrease in anxiety level to moderate, and often to normal.

In conclusion, it should be emphasized that special attention should be paid to identifying the causes of anxiety and their timely correction with the use of modern multitargeted drugs taking into account the individual characteristics of the patient which will increase the effectiveness of associated diseases management.

**References:**


1.Thiele W., Munch Med Wschr 1958; 100: 149: 1918-1923

2. Makolkin V.I., Abbakumov S.A. Sapozhnikova A.A. Neurocirculatory dystonia: Clinic, diagnosis, treatment. Cheboksary, 1995

3. Uexeckull T.V., Kohle R. Psychosomatische Medizin (3 Aifl.) H.Th. Von Uexeckull Munchen – Wien – Baltimore 1986; 489- 501)

4.Diagnostic and statistical manual of mental disorders /Am.Psych.Assoc. – 4th ed. – Washington, 1994. – 886 c.

5. Pollack M.H. Optimizing pharmacotherapy of generalized anxiety disorder to achieve remission // J. Clin. Psychiatry.— 2001.— Vol. 62, Suppl. 19.— P. 20–25.

6. Maser J.D., Cloninger C.R. Comorbidity in Anxiety and Depression. Washington DC 1990

7. Hidalgo R.B., Barnet S.D., Davidson J.R. Social anxiety disorder in review: two decades of progress // Int. J. Neuropsychopharmacol.— 2001.— Vol. 4, № 3.— P. 279–298.

8. Wayne A.M., Dyukova G.M., Vorbieva O.V., Danilov A.B. Panic attacks. St. Petersburg, 1997.)

9. Andronati S.A., Voronina T.A., Golovenko N.Ya. et al. Gidazepam / Ed.-in-chief Andronati S.A. - K.: Naukova Dumka, 1992. — 200 p.