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Abstract

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THERAPY OF PATIENTS WITH ANXIETY DISORDERS AND METABOLIC SYNDROME X

Objective of the research: to investigate the efficacy and safety of Afobazole in the treatment of adult patients with anxiety disorders and metabolic syndrome X.

Material and methods of research. The study included 60 adult patients (18–65 years) (36 men, 24 women), whose clinical picture revealed mild and moderate forms of neurotic disorders observed in the therapeutic hospital and outpatient service. The main group (30 people) and control group (30 people) formed on the basis of representativeness by gender and age ($\chi 2emp < \chi 2krit$, $p \leq 0.01$). The sample consisted of patients who signed a written informed consent to participate in the study. The average age of the patients in the control group was 44.81 ± 2.17, in the main group – 45.13 ± 2.34 ($p < 0.01$); the average age of onset of mental disorders in the main group was 33.2 ± 3.1 years; in the control group it was 34.1 ± 3.4 years ($p < 0.05$); the average duration of psychopathological symptoms in the main group was 5.6 ± 0.6 months, in the control group – 5.8 ± 0.3 months ($p < 0.05$). The duration of treatment equaled 1 month of active therapy (later, the patients were transferred to maintenance therapy outside this study). Afobazole containing 0.01 g of active substance per tablet was used for treatment. The drug was prescribed 3 times a day (morning, afternoon and evening); the dose of the drug was increased: 1–1–2 (number of tablets per administration).

Research results. There were changes in psychometric scaling, i.e. a significant decrease in state (by 57.2 and 42.9%; $p \leq 0.001$) and trait (by 23.8 and 23.3%; $p \leq 0, 01$) anxiety on the Spielberger–Khanin scale in the main and control groups at the end of treatment. In all groups of patients, we noted complete recovery (38.4%) or a significant improvement (37.9%); for most patients with mild manifestations, complete recovery was observed in 92% of cases. Among patients with moderate manifestations, a good response was recorded in 75% of cases; for the rest, moderate and minimal effects were observed, respectively. The changes in the severity as compared with baseline values were significantly positive ($p < 0.05$) already after 7 days of Afobazole therapy; similar changes were noted in the indicators of the overall effectiveness of therapy. No positive changes after Afobazole therapy were observed in 3.3% of cases, deterioration was registered in 3.3% of cases, while in the control group these values were 6.6% and 3.3%, respectively. The changes in somatic indicators also had positive trends

in the control and main groups – SBP reduced by 11.0% and 18.0%, respectively ($p \leq 0.05$); DBP – by 4.4% and 14.9% ($p \leq 0.05$).

Conclusion. The therapeutic effect of Afobazole is the reduction of viscero-vegetative manifestations of anxiety disorders, including relief of breathing, normalization of blood pressure and heart rate, reduction of muscle tension and pain, sweating and dizziness.

Keywords: metabolic syndrome, mental disorders, tranquilizers, Spielberger-Khanin scale, Afobazole.

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Резюме

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ТЕРАПІЯ ПАЦІЄНТІВ З ТРИВОЖНИМИ РОЗЛАДАМИ ТА МЕТАБОЛІЧНИМ СИНДРОМОМ Х

Мета роботи: дослідити ефективність і безпеку препарату Афобазолу при терапії дорослих пацієнтів з тривожними розладами та метаболічним синдромом Х.

Матеріал та методи дослідження. В дослідження включені 60 пацієнтів зрілого віку (18–65 років) (36 чоловіків, 24 жінки), у клінічній картині яких виявлялися легкі та помірні форми невротичних розладів, що спостерігаються в умовах терапевтичного стаціонару й амбулаторної служби. Основна (30 осіб) та контрольна (30 осіб) групи сформовані з урахуванням репрезентативності за статтю та віком ($\chi 2$емп < $\chi 2$крит, $p \leq 0,01$). Вибірку склали пацієнти, що дали добровільну письмову інформовану згоду на участь у дослідженні.

Середній вік обстежених контрольної групи склав 44,81 ± 2,17, основної групи – 45,13 ± 2,34 ($p < 0,01$); середній вік початку психічних розладів відповідно в основній групі – 33,2 ± 3,1 року, в контрольній – 34,1 ± 3,4 року ($p < 0,05$); середня тривалість психопатологічної симптоматики в основній групі склала 5,6 ± 0,6 місяця, в контрольній – 5,8 ± 0,3 місяця ($p < 0,05$). Стан пацієнтів верифіковано згідно з відповідними критеріями за МКХ-10. Як в основній, так і в контрольній групі переважали пацієнти з розладами адаптації з соматичними симптомами та органічними непсихотичними розладами. Тривалість лікування склала 1 місяць активної терапії (надалі хворі переводилися на підтримуючу терапію вже поза межами цього дослідження). Для лікування використовували препарат Афобазол, що містить у таблетці 0,01 г діючої речовини. Препарат призначали 3 рази на день (вранці, вдень і ввечері); використовувалося збільшення дози препарату до 1–1–2 (кількість таблеток на прийом).

Результати дослідження. В основній та контрольній групах наприкінці лікування відмічено динаміку показників психометричного шкалування у вигляді суттєвого зниження показників реактивної (на 57,2 і 42,9 %; $p \leq 0,001$) та особистісної (на 23,8 і 23,3 %; $p \leq 0,01$) тривоги за шкалою Спілбергера-Ханіна.

В усій групі пацієнтів нами відмічено повний вихід з хворобливого стану (38,4 %) або значне поліпшення (37,9 %) причому для більшості пацієнтів з легкими проявами повний вихід

з стану був відмічений в 92 % випадків. Серед пацієнтів з помірними проявами хороший ефект зафіксовано у 75 % випадків, у решти відповідно спостерігались помірний та мінімальний ефекти. Динаміка тяжкості стану пацієнтів порівняно зі скринінгом була достовірно позитивною ($p < 0,05$) також вже с 7-го дня терапії Афобазолом; подібні зміни були відзначені у показниках загальної ефективності терапії. Відсутність позитивних змін на терапії Афобазолом відмічено у 3,3 %, погіршення – у 3,3 %. У контрольній групі – 6,6 та 3,3 % відповідно. Динаміка соматичних показників також мала позитивні тенденції в контрольній та основній групах: редукція склала відповідно: САТ – 11,0 і 18,0 % ($p \leq 0,05$); ДАТ – 4,4 і 14,9 % ($p \leq 0,05$).

Висновок. Особливістю терапевтичної дії Афобазолу є редукція вісцеро-вегетативних проявів тривожних розладів, у тому числі полегшення дихання, нормалізація показників артеріального тиску та пульсу, зменшення напруження та болю у м'язах, пітливості та запаморочення.

Ключові слова: метаболічний синдром, психічні розлади, транквілізатори, шкала Спілбергера-Ханіна, Афобазол.

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Introduction/Вступ

Metabolic syndrome X (MSX) is a heterogeneous state, the set of components of which is due to psycho-social, metabolic and pathophysiological relationships [1, 3, 4, 5]. In recent years, there has been a pathomorphosis of mental disorders in various somatic and endocrine diseases [2, 6]. Naturally, despite of the nosological affiliation of its somatic components, in the correction of anxiety disorders secondary to metabolic syndrome, priority is given to tranquilizers that have a complex anxiolytic, hypnotic, vegetative-stabilizing and central muscle relaxant effect, and therefore affect almost all pathogenetic links. In clinical practice, doctors prefer "day" tranquilizers without significant hypnotic effect, which is convenient to use on an outpatient basis. Such drugs include Alprazolam (Xanax), Medazepam (Rudotel), Oxazepam (Nozepam, Tazepam), Tofizopam (Grandaxin), Lorazepam (Lorafen), and Afobazole.

Afobazole, which is not a benzodiazepine receptor agonist, is chemically related to mercaptobenzimidazole derivatives. The action of the drug is based on the inhibition of membrane-dependent changes in the GABA receptor, which reduces its availability to the corresponding ligand. Afobazole is a short-acting drug: the elimination half-life and time to reach the maximum concentration is about an hour, and the retention of the drug in the body is from one to two hours.

Materials and methods. A 4-week study of the efficacy and safety of Afobazole drug for the treatment of adult patients with anxiety disorders within the metabolic syndrome X has been performed.

The study included 60 adult patients (aged 18–65 years) (36 men, 24 women), whose clinical picture revealed mild and moderate forms of neurotic disorders observed in the therapeutic hospital and outpatient service.

The main (30 people) and control (30 people) groups were formed by taking into account the representativeness by sex and age ($\chi 2emp < \chi 2crit$, $p \leq 0.01$). The sample consisted of patients who gave voluntary written informed consent to participate in the study.

The average age of the patients in the control group was 44.81 ± 2.17, in the main group – 45.13 ± 2.34 ($p < 0.01$); the average age of onset of mental disorders in the main group was 33.2 ± 3.1 years; in the control group it was 34.1 ± 3.4 years ($p < 0.05$); the average duration of psycho-pathological symptoms in the main group was 5.6 ± 0.6 months, in the control group – 5.8 ± 0.3 months ($p < 0.05$). The condition of the patients was verified according to the relevant ICD-10 criteria. Both in the main and in the control group, patients with adaptation disorders with somatic symptoms and organic non-psychotic disorders predominated.

This syndromic distribution into non-metabolic syndrome X (NMSX) group and MSX group was due to the fact that against the background of long-term chronic MSX, stabilization of neurotic symptoms was observed, as well as further development and complication of the pathological syndrome, and formation of nosologically defined mental disorders.

The study was conducted in accordance with the requirements of the protocol using possible optimal doses of the drug. The duration of treatment was 1 month of active therapy (later patients were transferred to maintenance therapy outside this study). Afobazole containing 0.01g of active substance in a tablet was used for treatment. The drug was prescribed 3 times a day (morning, afternoon and evening); the dose of the drug was increased: 1–1–2 (number of tablets per administration).

The final results of treatment were evaluated according to standard criteria of effectiveness: indicators of "marked improvement" or "improvement" in CGI; 50% reduction in HAM-A scales, as well as the dynamics of physical data. The analysis of the results of the study also took into account the following indicators: the severity of the overall therapeutic effect (% of CGI respondents); the timing of the therapeutic effect; doses of the drug, against which there was an improvement; total frequency of side effects; the most frequently registered side effects; quality of life of patients and treatment background.

Research results. Psychometric study data confirm a number of targeted psychopathological phenomena for patients with NMSX and MSX. The number of people with a high level of state anxiety on the Spielberger-Khanin scale is twice as high in patients with NMSX (57.35%) than in patients with MSX (26.36%) ($\varphi^* = 2.2$, $p = 0.014$), and four times greater than in healthy individuals (13.36%) ($\varphi^* = 1.8$, $p = 0.035$).

Pronounced trait anxiety is more common in patients with MSX. The distribution of high scores of state and trait anxiety shows that in the process MSX formation in the absence of clearly defined somatic pathology (hypertension, diabetes, coronary heart disease, etc.), there is a high level of psychological discomfort at the state rather than trait level. State anxiety as a result of subjective response to emotions of tension, anxiety, concern with the corresponding activation of the sympathoadrenal system, contributes to the further development of metabolic syndrome. The presence of a somatic disease in a patient with metabolic syndrome increases trait anxiety (fears about the state of health, the future) and partially deactivates current events in his imagination.

Complaints of overweight and high blood pressure took the leading place, which were further objectified: BMI was 30.2 ± 2.7 for the main group; for control group – 28.7 ± 4.4; waist circumference respectively, 98.4 ± 3.3 and 97.6 ± 3.6 cm; systolic blood pressure – 138.6 ± 5.7; 144.3 ± 6.8 mm Hg; diastolic blood pressure – 81.4 ± 5.1; 87.7 ± 5.4 mm Hg.

The treatment was completed by 55 patients, including 28 patients in the main group and 27 patients in the control group. The therapeutic effect of Afobazole in our study was detected fairly quickly. Already at the end of the first week of therapy, there was a reduction in anxiety in the form of a decrease in irritability, anxiety and some deactualization of fears and bad feelings. Patients also reported improved sleep, greater ability to relax, and decreased anxiety, fear, and tearfulness. A feature of the therapeutic effect of Afobazole was a significant reduction by the 7th day of treatment of a significant number of viscero-vegetative manifestations of anxiety disorders: patients noted relief of breathing, more stable with a tendency to normalize blood pressure and pulse, reduced tension and muscle pain, reduced or lack of dry mouth, sweating and dizziness, reduced need for food. In addition, patients noted an improvement in performance by improving the quality of cognitive functions (attention, memory).

In the main and control groups at the end of treatment, changes in psychometric scaling were noted, i.e. significant decrease in state (by 57.2 and 42.9%; $p \leq 0.001$) and trait (by 23.8 and 23.3%; $p \leq 0.01$) anxiety by the Spielberger-Khanin scale.

In the whole group of patients, we noted a complete recovery from the disease (38.4%) or a significant improvement (37.9%) and for most patients with mild manifestations, complete recovery was observed in 92% of cases. Among patients with moderate manifestations, a good response was recorded in 75% of cases; for the rest, moderate and minimal effects were observed, respectively. The changes in the severity as compared with baseline values were significantly positive ($p < 0.05$) already after 7 days of Afobazole therapy; similar changes were noted in the indicators of the overall effectiveness of therapy. No positive changes after Afobazole therapy were observed in 3.3% of cases, deterioration was registered in 3.3% of cases, while in the control group these values were 6.6% and 3.3%, respectively. The changes in somatic indicators also had positive trends in the control and main groups – SBP reduced by 11.0% and 18.0%, respectively ($p \leq 0.05$); DBP – by 4.4% and 14.9% ($p \leq 0.05$); the decrease in BMI and waist circumference was within the statistical error.

We also conducted a comparative analysis of the effectiveness of Afobazole treatment for anxiety disorders of different syndromic structure. It is especially advisable to prescribe Afobazole to patients with such personality traits as anxious thoughtfulness, insecurity, increased vulnerability and emotional lability, low stress resistance. Throughout the treatment period, we monitored the side effects of Afobazole; they were registered in 7 patients (23.3%). Most of them were recorded at the beginning of treatment (mostly in the first week); they were mild and did not require additional correction or changes in therapy; in most cases they were transient and resolved during the course of treatment. The spectrum of recorded side effects was represented by: headache (10.0%), tremor (6.7%), dry mouth (3.3%), and increased irritability (3.3%).

No adverse effects for the cardiovascular, bronchopulmonary and endocrine systems were observed. Indicators of laboratory tests were within normal range. According to our observations, Afobazole provided high compliance and did not show a negative impact on the course of somatic pathology within the metabolic syndrome. Afobazole did not show any clinically significant interactions with drugs used to treat the somatic component of metabolic syndrome.

Conclusions/Висновки

1. An open parallel group actively controlled post-marketing study confirmed the effectiveness and safety of Afobazole in the treatment of adult patients with anxiety disorders and metabolic syndrome X.

2. The most significant predictors of Afobazole therapy are represented by anxious thoughtfulness, insecurity, increased vulnerability and emotional lability, low stress resistance.

3. Afobazole provided high compliance and high quality of life of patients; it did not show a negative impact on the course of somatic pathology within the metabolic syndrome. The therapeutic effect of Afobazole lies in the reduction of viscero-vegetative manifestations of anxiety disorders, including relief of breathing, normalization of blood pressure and heart rate, reduction of muscle tension and pain, sweating and dizziness.

4. Side effects of Afobazole were registered mainly at the beginning of therapy, were transient and did not lead to discontinuation of treatment.

5. Afobazole should be used in complementary inpatient and outpatient monotherapy for psychosomatic patients leading an active lifestyle in an aggressive stressful environment.

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Conflict of interest/Конфлікт інтересів

The authors declare no conflict of interest.

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