Tenoten in the Therapy of Anxious Disturbances in Patients with Essential Hypertension and Coronary Heart Disease

N. P. Vanchakova and A. P. Popov

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The study demonstrated high anxiolytic activity of tenoten, which was not inferior to the anxiolytic effect of grandaxin. The positive changes persisted after termination of treatment in the tenoten group (but not in grandaxin group). Tenoten can be recommended for the treatment of patients with cardiovascular diseases associated with neurotic disturbances.

Key Words: *tenoten; anxiolytic activity; autonomic hyperactivity; generalized anxiety disorders; anxiety level*

High incidence of anxiety disorders in patients with essential hypertension closes a vicious circle between anxiety and arterial hypertension. In light of this, correction of anxious states in these patients is an urgent problem. The possibilities of benzodiazepines and the spectrum of their activity in these patients are now unsatisfactory. We studied the efficiency of tenoten in patients with essential hypertension. Tenoten contained ultralow doses of affinity-purified antibodies to S-100 protein. Previous studies showed that tenoten applied for the treatment of neurotic and neurosis-like disorders was not inferior by its anxiolytic effect to standard benzodiazepines (diazepam and phenazepam). High safety and the absence of side effects were also reported.

In our simple open comparative randomized trial we compared clinical efficiency and safety of tenoten and tofisopam (grandaxin) in the treatment of anxious neurotic disorders in patients with cardiovascular diseases.

MATERIALS AND METHODS

The study was performed in Clinics of Propedeutics of Internal Diseases, I. P. Pavlov St. Petersburg State Medical University and included individuals (n=51) with pathological anxiety corresponding to ICD-10 criteria for generalized anxiety disorder (F 41.1) and mixed anxiety and depressive disorder (F 41.2) The integral anxiety level by Hamilton Depression Rating Scale was ≥20. The patients received no psychopharmacological preparations over 48 h before the study. All patients adequately assessed their state and signed informed consent for participation in the study. Patients with signs of severe depression, panic and obsessive-compulsive disorders, endogenous mental diseases, alcohol and drug abuse, and patients receiving psychotropic preparations were not included into the study. Exclusion criteria were hypersensitivity to any components of the test drugs.

Group 1 patients (n=31, mean age 49.3±7.0 years) received tenoten (1 tablet 3 times a day irrespective of meals, sublingually until complete dissolution, for 4 weeks). Group 2 patients (n=20, mean age 54.0±5.2 years) received tofisopam (grandaxin) in a dose of 100 mg/day (1 tablet (50 mg) 2 times a day) for 4 weeks.

The groups did not differ by somatic comorbidity and somatotropic therapy (Table 1).

Half of the patients in each group went through various stressful events in their live (illness of family members, death of elder relatives, dismissal, retirement, children grew up and leave the family, *etc.*).

Department of Psychiatry and Narcology, I. P. Pavlov St. Petersburg State Medical University; Psychosomatic Center of Central Hospital No. 122, St. Petersburg

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TABLE 1. Somatic Diseases and Somatotropic Therapy in Patients Included in the Study (%)

Parameter	Group 1	Group 2
Somatic diseases		
Essential hypertension (stages II and III), different degree of risk	100	100
CHD, various forms, rest and effort angina, different functional classes	51	50
Dyscirculatory encephalopathy (stage II)	0	2
Obesity (stage II)	17	20
Diabetes mellitus (type 1 and type 2)	17	20
Thyroid gland pathology	20.4	20
Chronic pyelonephritis	17	20
Chronic glomerulonephritis	3.4	5
Chronic nonspecific lung diseases	27.2	30
Cholelithiasis	6.8	5
Biliary dyskinesia	6.8	5
Chronic nonspecific ulcerative colitis	3.4	5
Rheumatism	6.8	10
Somatotropic therapy		
Hypothensive preparations (egilok, physiotens, estulic, normodipine, arifon, orientez)	100	100
Antianginal drugs (metaprolol, cardiget, betalok, nifedipine, nifecard, isoptin)	81.6	80
Diuretics (hypothiazide, lasix, arifon, losar)	88.45	90
Kavinton and nootropic drugs (without anxiolytic effects)	10.2	10
Hormones (L-thyroxine, insulin)	20.4	20
Desaggregants (aspirin, thromboASS®)	51	50

There were no significant differences between the groups by this parameter.

All patients were examined by a therapist in accordance with diagnostic standards for essential hypertension and CHD. The efficiency of therapy was evaluated by the dynamics of scores according to Hamilton scale and Clinical Global Impression scale, and by the dynamics of patient's somatic state after 1, 2, and 4 weeks of therapy and 4 weeks after withdrawal.

RESULTS

Parameters of anxiety rapidly decreased in the tenoten and grandaxin groups during the first week of therapy (Fig. 1) and then the symptoms continued to decrease slowly. In group 1 patients after 4-week therapy we observed a decrease in parameters of anxious mood (AM, by 79%), tension (by 83%), somatic sensory symptoms (by 66.7%), cardiovascular symptoms (by 85.8%), autonomic symptoms (by 81.2%) and parameters of behavior during examination (by 93%).

In group 2, similar but less pronounced changes were observed: parameters of AM, cardiovascular symptoms, behavior during examination decreased by

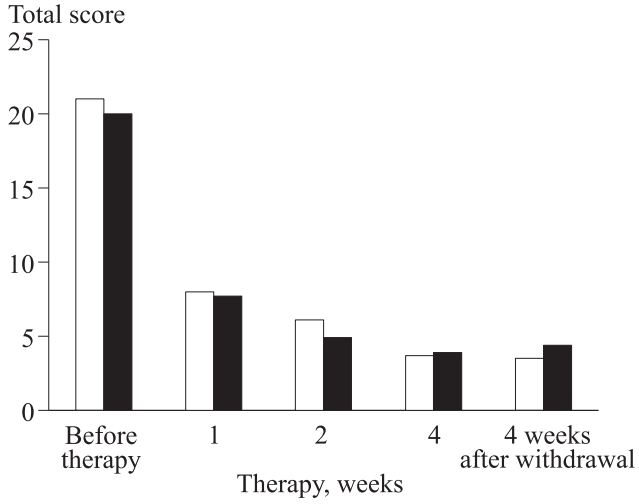

Fig. 1. Dynamics of anxiety according to Hamilton scale in tenoten (light bars) and grandaxin (dark bars) groups.

TABLE 2. Results of Patient Examination using Clinical Global Impression Scale

Preparation		Before treatment	Duration of treatment, weeks			
			1	2	4	4 weeks after withdrawal
Tenoten	Severity of the disease	2.74	1.93	1.07	1.05	1
	General improvement	0	2.24	2.29	1.44	1.39
Grandaxin	Severity of the disease	2.44	1.35	1.18	1	1.13
	General improvement	0	2.1	1.9	1.86	2.3

TABLE 3. Mean Blood Pressure and Heart Rate in Patients before and 4 Weeks after Treatment (*M*±*m*)

Parameter	Group 1		Group 2	
	before treatment	after treatment	before treatment	after treatment
Systolic blood pressure, mm Hg	161.5±18.5	122.0±5.0	155.4±10.0	130.60±3.44
Diastolic blood pressure, mm Hg	91.0±9.4	79.2±6.9	81.0±2.8	78.40±5.24
HR, bpm	61.5±17.4	69.7±4.4	70.6±6.9	72.0±5.8

70, 77, and 66%, respectively. Moreover, 4 weeks after completion of the treatment course, parameters of AM, tension, and behavior during examination tended to worsen in the grandaxin group, but not in the tenoten group.

Before the therapy, the disease severity according to Clinical Global Impression scale was comparable in both groups and corresponded to "borderline state"—"mild disease" range. This parameter gradually decreased during treatment; in group 1 it attained "normal, no illness" value by the end of therapy and remained at this level 4 weeks after withdrawal (Table 2).

In group 2 this parameter returned to normal by the end of the 4-week therapy, but tended to increase back after withdrawal. The dynamics of "general improvement" parameter revealed a clear-cut difference between the groups by the end of therapy: highly pronounced improvement was attained in group 1 patients and essential improvement in group 2. This difference remained 4 weeks after withdrawal.

Analysis of treatment compliance showed that 1 patient refused to participate in the trial in group 1 (he missed the last examination, 4 weeks after tenoten withdrawal). In group 2, two patients refused the therapy (on weeks 3 and 4, respectively). Moreover, 2 patients in this group dropped out 4 weeks after termination of treatment. Hence, treatment compliance was higher in group 1.

Thus, after 4-week complex treatment including cardiovascular drugs and the test preparation, blood pressure decreased and heart rate increased in both groups (Table 3).

No side effects of tenoten were noted. Combined administration of tenoten with the preparation prescribed for somatic diseases caused no undesirable events.

Thus, tenoten was comparable by its anxiolytic effect with standard benzodiazepine anxiolytic grandaxin. Tenoten treatment led to sustained improvement of emotional state (absence of anxiety). It should be noted that the tendency to improvement persisted for one month after drug withdrawal, which is an advantage of this preparation over grandaxin. The preparation was well tolerated, caused no side effects, and did not attenuate the effect of cardiovascular drugs. The compliance for tenoten treatment was higher than that for grandaxin. Tenoten can be recommended for the treatment of patients with cardiovascular diseases associated with neurotic disturbances.

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