Effects of Tenoten on Anxiety and Depression Disorders in Patients with Epilepsy

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The efficiency and safety of tenoten for anxiety and depression disorders in epileptics has been demonstrated. The drug does not change the incidence and severity of epileptic episodes, does not deteriorate the course of the underlying disease, and can be well combined with anticonvulsants. The results indicate the efficiency of tenoten used to arrest the anxio-depressive disorders in epilepsy.

Key Words: *tenoten; epilepsy; anxiety and depression disorders; ultralow antibody doses; S-100 protein*

Anxiety and depression are detected in 6-80% patients with epilepsy [5]. The incidence of episodes with anxio-depressive disorders varies from 3-9% in patients with controlled to 20-55% in patients with continuing attacks [4]. Up to 66% patients feel anxious between the episodes [8]. This variability is explained by a variety of epilepsy forms and its different severity, and differential diagnosis and adequate pathogenetic therapy remain a pressing problem in the majority of cases [3]. Moreover, the incidence of anxiety and depression between the attacks is higher in partial episodes than in generalized ones. This is explained by the fact that the aura (common partial episodes) includes various mental phenomena [7]. Other important factors are the types of episodes, location of the focus of pathological activity, long duration of disease, and early age of disease debut [5,6]. On the other hand, some antiepileptic drugs, used for a long time, are not free from side effects, such as mental changes, amnesia, depressions [1].

The regulatory disorders associated with dopamine, glutamate, and GABA play an important role in the development of anxio-depressive disorders. The GABA-ergic inhibitory systems, playing an important role in the development of anxiety and depression, attract special attention [7]. Tenoten (Materia Medica Holding), containing ultralow dose antibodies to S-100 protein, has exhibited GABA modulating effects and similarly as the neurotrophic factor, plays an important role in the regulation of energy and plastic metabolism in the CNS. High safety of the drug and the absence of side effects are worthy of note [2].

We studied the clinical efficiency and safety of tenoten in epileptic patients with anxio-depressive disorders.

MATERIALS AND METHODS

Twenty-five patients with epilepsy (7 men, 18 women) were examined. Twenty patients had local (partial) epilepsy: cryptogenic in 9 and symptomatic in 11. Five patients had a generalized disease. Depending on the type of the episodes, common partial attacks predominated in 2 cases, complex partial attacks in 4, common and complex attacks with secondary generalization predominated in 8 cases, and generalized episodes predominated in 10 cases. One patient with secondary generalized episodes developed a drug remission.

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Magnetic imaging of structural changes in 9 patients detected posttraumatic location-caused epilepsy in 2 patients, neuroinfection consequences in 1, hippocampal sclerosis in 1, perinatal disease consequences in 3, cysts in the frontal region in 1, and abnormalities in the ventricular system development in 2 patients. No focal changes in the brain matter were detected in the rest patients. According to EEG, 20 patients with location-caused epilepsy had equal presentation of the right and left foci.

Neuropsychological testing detected anxio-depressive disorders in all patients. The main complaints were sleep disorders (insomnia or difficult falling asleep), irritation, pessimistic evaluation of prospects for the future, anticipation of coming trouble, guilt ideas, low social activity, poor concentration, difficulties in decision making, *etc.*

All patients received anticonvulsants: 6 patients were treated with valproic acid (depakine chrono, convulex), 12 with carbamazepine (finlepsin retard), others received combinations of 2 drugs: topamax+difenin, 2 patients; depakine chrono+lamictal, 1 patient; depakine chrono+keppra, 1 patient; or finlepsin retard+depakine chrono, 1 patient.

Tenoten (2-month courses) was added to the treatment. The patients were divided into groups receiving different tenoten doses. Group 1 (8 patients) received tenoten in a dose of 1 tablet 3 times a day. Group 2 (9 patients) received 3 tablets 3 times a day. Group 3 (8 patients) received 4 tablets 3 times a day.

The efficiency of tenoten was evaluated by the time course of clinical symptoms; neuropsychological testing was carried out initially and after treatment in all patients. The following scales were used: Hospital Anxiety and Depression Scale (HADS), Hamilton Anxiety Rating Scale (HAM-A), questionnaire for depression evaluation developed by Center of Epidemiological Studies of USA (CES-D), and Pittsburg Sleep Quality Index (PSQI). The safety of therapy was evaluated by the incidence and duration of epileptic episodes and side effects.

RESULTS

Tenoten added to therapy of anxiety and depression disorders exhibited antianxiety and antidepressive effects. The majority of patients (69%) felt significantly better, sleep normalized, working capacity improved, as did the moods, emotional status, self-appreciation, *etc.*

Neuropsychological testing (HADS) showed initial isolated anxiety in 8 (32%) patients: in 2 in group 1, in 2 in group 2, and in 4 in group 3. Combined anxiety and depression disorders were detected in 17 (68%) patients. Subclinical manifestations of anxiety were found in 8 (32%) patients, of these, in 3 in group 1, in 2 in group 2, and in 3 in group 3. Clinically manifest anxiety was detected in 17 (86%) patients: in 5 in group 1, in 7 in group 2, and in 5 patients in group 3. Subclinical depression was detected in 7 (28%) patients: in 2 in group 1, in 2 in group 2, and in 3 in group 3. Clinically manifest symptoms of depression were detected in 10 (40%) patients: in 4 in group 1, in 5 in group 2, and in 1 (female) in group 3. After 2-month tenoten course, more pronounced changes were observed in groups 2 and 3. Evaluation of anxiety level showed a significant ($p<0.05$) reduction of the summary score from 12.4±3.4 (clinically

TABLE 1. Severity of Anxiety and Depression in Patients (HADS)

Group	Severity of depression/anxiety	Depression				Anxiety			
		initially		2 months		initially		2 months	
		abs.	%	abs.	%	abs.	%	abs.	%
Group 1 (*n*=8)	None (≤7 points)	2	25	2	25	–	–	–	–
	Subclinical (8-10 points)	2	25	2	25	3	37.5	4	50
	Clinically manifest (≥11 points)	4	50	4	50	5	62.5	4	50
Group 2 (*n*=9)	None (≤7 points)	2	22.2	3	33.3	–	–	9	100
	Subclinical (8-10 points)	2	22.2	6	66.7	2	22.2	–	–
	Clinically manifest (≥11 points)	5	55.6	–	–	7	77.8	–	–
Group 3 (*n*=8)	None (≤7 points)	4	50	5	62.5	–	–	7	87.5
	Subclinical (8-10 points)	3	37.5	2	25	3	37.5	1	12.5
	Clinically manifest (≥11 points)	1	12.5	1	12.5	5	62.5	–	–

TABLE 2. Time Course of PSQI Score in the Patients

Severity of sleep disorders	Group											
	1 (*n*=8)				2 (*n*=9)				3 (*n*=8)			
	initially		after 2 months		initially		after 2 months		initially		after 2 months	
	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%	abs.	%
Very bad sleep	–	–	–	–	2	22.3	–	–	4	50	–	
Rather bad sleep	2	25	3	37.5	7	77.8	–	–	2	25	–	–
Rather good sleep	6	75	5	62.5	–	–	6	66.7	2	25	6	75
Very good sleep	–	–	–	–	–	–	3	33.3	–	–	2	25

manifest anxiety) to 5.30±1.14 (no anxiety) and from 12.60±3.74 to 5.40±1.47, respectively. None of group 2 patients complained of anxiety. In group 3, only 1 patient exhibited subclinical anxiety, in the rest it was completely arrested during therapy. On the other hand, subclinical depression persisted in only 6 patients of group 2 after therapy was discontinued; in group 3 clinically manifest depression was detected in 1 patient and subclinical depression persisted in 2 (Table 1).

These results were confirmed by a significant ($p<0.05$) reduction of anxiety and depression in groups 2 and 3 according to the HAM-A scale and CES-D questionnaire. The summary HAM-A score reduced from 29.70±9.88 (anxious state) to 9.00±2.98 (anxiety symptoms) in group 2 and from 21.60±8.53 to 9.60±3.51 in group 3. The CES-D summary score reduced from 30.2±9.2 (manifest depression) to 22.30±4.25 (mild depressive disorder) and from 27.80±6.53 to 17.50±6.49 (no depression), respectively.

As high anxiety deteriorates the quality of sleep, the patients were tested by PSQI (Table 2). Symptoms of insomnia, difficult falling asleep, frequent awakening at night and early waking up were detected in each of the groups. The distribution by the intensity of insomniac disorders was as follows: very bad sleep in 6 (24%) patients, rather poor sleep in 11 (44%), and rather good in 8 (32%). After tenoten course no appreciable changes were detected in group 1, while in groups 2 and 3 sleep normalized in all patients.

Evaluation of tenoten safety in patients with epilepsy showed that the drug provoked no episodes during drug remission and did not increased their incidence during exacerbation. No side effects of tenoten were recorded.

Hence, our study demonstrated the efficiency of tenoten in anxiety and depression disorders in epileptic patients. Tenoten caused no changes in the incidence and severity of epileptic episodes, did not aggravate the course of the underlying disease, was well combined with anticonvulsants, all these allowing its wide use for combined therapy of this patient population.

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