

Serum Ciliary Neurotrophic Factor Concentration as a Potential Biomarker of Efficacy of Citicoline Pharmacotherapy of Temporal-Lobe Epilepsy in Women



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Abstract

One of the poorly understood aspects of the pathogenesis of neuropsychiatric diseases, including epilepsy, is the role of glia and neuron–glia interactions despite the recent findings that show their principal importance in the functioning of the central nervous system [1]. During last decades the most efforts of investigators were focused on impairments in neuronal functions, whereas the status of brain glia cells has not been adequately considered [2]. Role of neurotrophic factors is poorly understood in pathogenesis of epilepsy. Ciliary neurotrophic factor (CNTF) is neurotrophic cytokine from interleukin-6-family. CNTF is released (secreted) by astrocytes; it stimulates the survival of neurons. The aim of the study was to analyze relationship between CNTF concentration in serum of patients with temporal-lobe epilepsy and severity of disease under the treatment of nootropic drug citicoline.

Material and Methods

36 women with temporal-lobe epilepsy were enrolled in the study. Patients were divided into three groups (G1, G2, G3) depending on severity of disease: slowly progressing (G1), moderately progressing (G2), and progressing (G3) courses of disease. Each group included 12 patients selected randomly. Clinical profile of disease, as well as the inclusion and exclusion criteria were described previously [3]. Investigation was performed in accordance with the permission of the local ethical committee of Moscow Research Institute of Psychiatry (N 19/8,27.11.2017). Control group consisted of 35 healthy women. 500 mg of citicoline was injected i/m daily for 5 days on the background of antiepileptic treatment. CNTF concentration in blood serum was assessed by ELISA method using Uniplan analyzer (Russia) and RsD systems (United States) [3]. The Mann–Whitney U-test was used for the comparison of small groups. The difference was considered significant at $p < 0.05$.

Results and Discussion

At the beginning of study CNTF concentration in accordance with severity of disease was significantly ($p < 0.001$) higher: 14.3; 18.9 and 32.1pg/mL in G1, G2 and G3 groups, respectively, in comparison with control level (3.4pg/mL of serum). A comparison between different types of epilepsy course demonstrated statistically significant ($p < 0.05$) differences in the CNTF level:

2.24-fold between the G3 and G1 groups, 1.7-fold between the G3 and G2 groups, and 1.32-fold between the G2 and G1 groups. After citicoline treatment CNTF concentration significantly decreased by 1.7 (8.3pg); 1.5 (12.6pg) and 1.3 (24.4pg) times in G1, G2 and G3 groups, respectively, in comparison with the level before treatment (14.3; 18.9 and 32.1pg/mL, respectively), and these changes in CNTF concentration were followed by the improvement of clinical status of patients. Aggravation of clinical manifestation is accompanied by increase in CNTF levels in serum of patients with epilepsy. A more severe epileptic process is accompanied by more intensive production of CNTF in the brain. However, CNTF does not exhibit neuroprotective action. We hypothesize that CNTF is generated in response to pathological process, but immediately leaks into blood through damaged blood–brain barrier and does not exhibit neuroprotective action [3,4]. Citicoline is a natural endogenous compound with nootropic properties. It is an intermediate metabolite in phosphatidilcholine synthesis. The latter is one of the most important structural components of biological membranes. Decrease of CNTF concentration in serum after citicoline treatment points out on repair of blood–brain barrier function and tendency to normalization of metabolic processes.

Conclusion

Results of our investigation point out that serum CNTF concentration can be considered as a potential biological marker of

the efficacy of citicoline treatment of patients with temporal-lobe epilepsy.

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