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Research Article

Citicoline Treatment is Followed by Decrease of Ciliary Neurotrophic Factor Concentration in Blood Serum in Women with Temporal-Lobe Epilepsy

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Abstract

Ciliary neurotrophic factor (CNTF) is a 22-kDa cytokine belonging to the interleukin Il-6 family and expresses in glial cells. It plays an important role in neuroprotection. Citicoline is a natural endogenous compound with nootropic properties. The aim of the study was to investigate the relation between the severity of the disease and CNTF concentration in blood serum of women with temporal-lobe epilepsy under the treatment of nootropic drug citicoline.

CNTF concentration in blood serum of patients before the treatment increased in dependence of the severity of the disease: 14.34, 18.90 and 32.10 pg/mL of serum in G1, G2 and G3 groups, respectively, in comparison with healthy persons (3.4pg/mL of serum) ($p=0.001$). Inclusion of nootropic drug citicoline in the antiepileptic treatment process resulted in significant decrease of CNTF concentration in blood serum by 1.7, (8.31), 1.5 (12.59) and 1.3 (24.45 pg/mL of serum) times in G1, G2 and G3 groups, respectively ($p< 0.05$), in comparison with the level before treatment. It may be hypothesized that ciliary neurotrophic factor generated in response to pathological process in the brain is immediately released into the blood through a damaged blood–brain barrier. Decrease of CNTF concentration in blood serum after citicoline treatment points out on the tendency to restoration of blood–brain barrier function and to normalization of metabolic processes.

Keywords: Epilepsy; Ciliary neurotrophic factor; Citicoline; Biomarker

Abbreviations

CNTF: Ciliary Neurotrophic Factor; G1: Slowly Progressing Epilepsy Group; G2: Moderately Progressing Epilepsy Group; G3: Progressing Epilepsy Group

Introduction

Epilepsy is a severe neuropsychiatric disease that requires complicated therapy, although it may often be resistant to antiepileptic drugs, that results in decreased professional abilities, social limitations, and a drastic decrease in the quality of life of patients. All of these issues demand a thorough investigation of epilepsy pathogenesis in order to reveal biomarkers, find new molecular targets, and develop new therapeutic approaches [1,2].

The role of glia and neuron–glia interactions is one of the poorly investigated aspects of the pathogenesis of neuropsychiatric diseases, including epilepsy. Recent findings clearly indicate on the important role of glial cells in the functioning of the central nervous system [3].

Ciliary neurotrophic factor (CNTF) is a 22-kDa cytokine belonging to the interleukin Il-6 family and is mainly expresses in glial cells of the central and peripheral nervous systems. CNTF plays an important role in the regulation of neuronal development, neuroprotection and may also influence cognitive processes [4].

Neuroprotective potential of CNTF has been established in several models of acute neuronal death and neurodegenerative diseases [4]. CNTF concentration rapidly increases after traumatic or ischemic damage to the CNS.

CNTF have recently been implicated in the pathogenesis of certain common neurodegenerative disorders, including epilepsy [2,4,5].

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. It possesses a wide spectrum of action: contributes for the recovery of damaged cell membranes, inhibits phospholipase activity, antioxidant properties, etc [6].

The aim of the study was to investigate the relation between the severity of the disease and CNTF concentration in blood serum of patients with temporal-lobe epilepsy under the treatment of nootropic drug citicoline.

Subjects and Methods

There were investigated 36 women with temporal-lobe epilepsy. Depending on the severity of disease all patients were divided on three groups: slowly progressing (G1), moderately progressing (G2), and progressing (G3) courses of disease. Clinical picture, the inclusion and exclusion criteria and antiepileptic therapy were described previously [7].

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Each group included 12 patients who were selected randomly. The control group consisted of 35 healthy women aged 18–49 years.

The study was performed in accordance with Helsinki Declaration and the permission of the local ethical committee of Moscow Research Institute of Psychiatry (N 19/8, 27.11.2017).

500mg 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 Human CNTF Quantikine ELISA Kit (RsD systems, USA).

The Mann–Whitney U-test was used for the comparison of small groups. The difference was considered significant at $p< 0.05$.

Results

In the study has been revealed that CNTF concentration in blood serum in patients before the treatment increased in dependence of the severity of the disease: 14.34±1.25, 18.90±1.79 and 32.10±3.18 pg/mL of serum in G1, G2 and G3 groups, respectively. That was significantly ($p=0.001$) higher in comparison with control level (3.40pg/mL of serum). The analysis has shown that CNTF concentrations differ significantly between investigated groups: 1.32-fold between the G2 and G1 groups, 1.7-fold between the G3 and G2 groups and 2.24-fold between the G3 and G1groups ($p<0.05$).

After citicoline treatment CNTF concentration significantly decreased by 1.7, (8.31±1.62), 1.5 (12.59±1.52) and 1.3 (24.45±2.90) times in G1, G2 and G3 groups, respectively ($p< 0.05$), in comparison with the level before treatment. These changes in CNTF concentration were followed by the improvement of clinical status of patients.

Discussion

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. As it was said above CNTF plays an important role in neuroprotection and may influence cognitive processes [8]. However, CNTF does not exhibit neuroprotective action. It was shown that mental disorders are followed by increased permeability of blood-brain barrier [9]. We hypothesize that CNTF generated in response to a pathological process immediately leaks into the blood through a damaged blood–brain barrier. Therefore, in such a situation the CNTF concentration in brain tissue cannot reach the level required for neuroprotection [9,10]. Earlier we have found that melancholic depression is also followed by significant increase of CNTF concentration in blood serum [11].

Inclusion of citicoline in the antiepileptic treatment process resulted in decrease of CNTF concentration in blood serum that was coincided with the improvement of patient's clinical status. Decrease of CNTF concentration in blood serum after citicoline treatment points out on the tendency to restoration of blood–brain barrier function and to normalization of metabolic processes.

Conclusion

We can state that in some clinical conditions ciliary neurotrophic factor cannot reveal its neuroprotective functions because of damaged blood-brain barrier, Decrease of CNTF concentration in blood serum after inclusion of citicoline in treatment process points out on the tendency to restoration of blood–brain barrier function and to normalization of metabolic processes.

One of the main aims of therapeutic pharmacological intervention should be the restoration of the normal function of the blood–brain barrier.

References

1. Kalinin VV, Zemlyanaya AA, Zheleznova EV, Sokolova LV. Neurobiological and clinical predictors of remission and antiepileptic treatment efficacy in partial epilepsies. J. Epileptology. 2013; 21: 23–33; 1–3.
2. Jankowsky JL, Patterson PH. The role of cytokines and growth factors in seizures and their cequelae. Progress in Neurobiology. 2001; 63: 125-149.
3. Verkhratsky A, Butt AM, editors. Glial Physiology and Pathophysiology. Wiley-Blackwell. 2013.
4. Sariola H, Sainio K, Arumäe U, Saarma M. Neurotrophins and ciliary neurotrophic factor: their biology and pathology. Ann Med. 1994; 26: 355-363.
5. Bechstein M, Haussler U, Neef M, Hofmann HD, Kirsch, et al. CNTF-mediated preactivation of astrocytes attenuates neuronal damage and epileptiform activity in experimental epilepsy. Exp Neurol. 2012; 236: 141-150.
6. Saver Zh. Citicoline: a new data about a promising drug with neuroprotective and neuroreparative effects. International neurologic zhurnal (Mezhdunarodniy nevrologicheskiy zhurnal). 2010; 1: 108-117.
7. Musina LO, Zinkovski KA, Zubareva GM, Butavin NYu. Peculiarities of changes of infrared spectrum of blood serum in women with epilepsy. Herald of Tver State University. Series: Biology and ecology. 2011; 32: 157.
8. Peruga I, Hartwig S, Merkler D, Thöne J, Hovemann B, Juckel G, et al. Endogenous ciliary neurotrophic factor modulates anxiety and depressive-like behavior. Behav Brain Res. 2012; 229: 325-332.
9. Najjar S, Pearlman D, Devinsky O, Najjar A, Zagzag D. Neurovascular unit dysfunction with blood-brain barrier hyperpermeability contributes to major depressive disorder: a review of clinical and experimental evidence. Journal of Neuroinflammation. 2013; 10: 142-158.
10. Brondino N, Rocchetti M, Fusar-Poli L, Damiani S, Goggi A, Chiodelli G, et al. Increased CNTF levels in adults with autism spectrum disorders. World J Biol Psychiatry. 2018; 19: 1-5.
11. Uzbekov M, Shikhov S. Ciliary neurotrophic factor disturbances in patients with melancholic depression. Biomed J Sci & Tech Res. 2019; 13: 1-2.