ORIGINAL ARTICLE

REHABILITATION OF PATIENTS WITH LONG-TERM AFTEREFFECTS OF MILD COMBAT TRAUMATIC BRAIN INJURY

DOI: 10.36740/WLek202201226

Korshnyak V.O.[1], Pulyk O.R.[2], Stoyanov O.M.[3]
[1]SI "INSTITUTE OF NEUROLOGY, PSYCHIATRY AND NARCOLOGY OF THE NATIONAL ACADEMY OF MEDICAL SCIENCES OF UKRAINE", KHARKIV, UKRAINE
[2]UZHHOROD NATIONAL UNIVERSITY, DEPARTMENT OF NEUROREHABILITATION, UZHHOROD, UKRAINE
[3]ODESA NATIONAL MEDICAL UNIVERSITY OF THE MINISTRY OF HEALTH OF UKRAINE, ODESA, UKRAINE

ABSTRACT

The aim: To analyze the effect of Korean red ginseng on status of the vegetative nervous system and well-being of patients with asthenic syndrome assotiated with mild combat traumatic brain injury.

Materials and methods: We have examined 42 patients. Duration of their injury was from 4 to 6 years. We have investigated the indices of the vegetative tonus, vegetative reactivity and vegetative provisioning, its neurally mediated component – adrenaline and noradrenaline and melatonin hormone in daily urine. Some neuropsychological data were investigated with the help of HAM method (Health, Activity and Mood scale).

Results: After the treatment with Korean red ginseng all indices of the vegetative nervous system improved significantly. Accordingly, the rates of adrenaline and noradrenaline and the hormone melatonin, which were reduced before treatment in most of the examined, increased. The HAM values also improved after the treatment.

Conclusions: The use of Korean red ginseng restores efficiency, sleep, activity, and improves the mood of patients with aftereffects of mild traumatic brain injury and does not cause any adverse reaction.

KEY WORDS: aftereffects of mild combat traumatic brain injury, Korean red ginseng, asthenic disorders, autonomic nervous system, catecholamines

Wiad Lek. 2022;75(1 p.2):300-303

INTRODUCTION

The beginning of the XXIst century in Ukraine was marked by active military operations. Among the victims are a large number of individuals with mild combat traumatic brain injury. The special nature of mild combat traumatic brain injury aftereffects is associated with the peculiarity of damaging mechanisms due to the nature of blast wave impact on the injured person. Brain damage caused by mine-explosive trauma is primarily associated with the direct action of the blast wave, a sharp fluctuation in atmospheric pressure, the influence of a sound wave, and acceleration effect while the victim is thrown back. At the same time, the strong and simultaneous irritation of extero - and interoreceptors on a significant area of the body surface as a result of the blast wave causes the formation of numerous stable foci of arousal in the central nervous system (CNS). Acoustic trauma (the result of exposure to a sound wave) in milliseconds makes a strong effect on the brain substance, the cortical organ, causing further dystrophic and atrophic changes in them [1].

One of the main complaints of patients in the long-term period of mild combat traumatic brain injury (TBI) is a complaint of rapid fatigue, a sharp decrease in performance, poor sleep, drowsiness during the day and muscle weakness, which does not go away after rest and is a component of the clinical picture of asthenic syndrome.

Asthenic condition of patients in the long-term period of mild combat TBI is a pathological process that develops gradually. Rest does not restore the patient's activity. This distinguishes asthenia from ordinary fatigue, which disappears after rest. The fundamental difference between asthenic syndrome and fatigue is that the latter occurs due to a decrease in energy reserves, while asthenia is the result of dysregulation, primarily at the level of brain centers.

Etiologically, asthenia can be divided into two groups: organic and functional. The causes of organic asthenia are post-traumatic, infectious, and gastroenterological diseases. Functional asthenia is characterized primarily by its reversibility since it occurs in the structure of time-limited pathological conditions. These include acute asthenia, which occurs in the postpartum period, as well as after infectious diseases and traumatic brain injury.

The main signs of asthenia as a result of traumatic damage to the central nervous system are considered to be a combination of asthenia with relative insufficiency of adrenal function, changes in muscle tone. This leads to the changes in the vegetative nervous system (VNS), that are more often paroxysmal in nature, are the cause of prolonged exacerbations, often progressive, undulating course, accompanied by senestopathy, with no effect from psychotherapy.

The pathogenetic basis of asthenia in the traumatic pro-

cess is a violation of the processes of energy formation in brain cells, which are caused by structural changes, changes in CSF circulation and hemodynamics, and neuroendocrine changes. Changes in neurodynamics are secondary – they are mediated by insufficient energy supply of organic processes or their consequences. This can explain the persistence and monotony of asthenia symptoms, sometimes the presence of psychoorganic disorders, as well as sluggish, unstable compensation for impaired functions [2].

In the genesis of asthenic state, various pathophysiological mechanisms are predicted, which include: a) violation of neurodynamics of cortical processes – weakening of internal inhibition, depletion of arousal, damage to the midbrain and weakness of the activating effect of ascending reticular formation; b) violation of the activity of limbic mechanisms of emotions, motivations and activated non-specific systems of the intermediate and midbrain, which leads to asthenization of the cerebral cortex and disorders of cortical-subcortical ratios.

The criteria for choosing a drug for treatment of asthenic syndrome are: the presence of a specific antihypoxic and antioxidant effect of the drug; possibility of correction of neurotransmitter imbalance; the presence of a specific antiasthenic effect; high grade of safety; impact on the cognitive and psychoemotional sphere and the presence of minimal potential for interaction between different drugs [2] .

Red Korean ginseng root extract has a number of healing properties that, when taken, allow the human body to adapt to climatic changes and other adverse environmental factors. It contains a large number of different types of saponins (saponins are called ginsenosides, which play a key role in the therapeutic effect on the human body), which have a calming effect on the human psyche, relieve stress, have an anti-inflammatory effect and slow down the aging process. None of the ginseng (Chinese, Russian, American), but only Red Korean ginseng contains 32 types of saponins. And what is most important and valuable is that the saponins of Red Korean ginseng are antioxidants.

The main components of Korean ginseng are carbohydrates – starch, polysaccharides, cellulose (up to 70%). Along with this, it contains various unique compounds that are found only in ginseng – these are ginsenosides, polyacetylites, Vit. Groups B and C, trace elements (potassium, phosphorus, zinc, iron and magnesium), amino acids, flavanoids, etc. Different types of ginseng (Korean, American, Chinese, Russian) differ from each other both quantitatively and in the composition of ginsenosides; the quantitative and qualitative composition of these compounds largely determines the level of pharmacological activity of plants and their therapeutic effect. 29 types of ginsenosides (Ro, Ra_1, Ra_2, RA_3, Rb3, Rb_2, Rg_1, etc.) were found in Korean ginseng (R. ginseng). In American ginseng (P.guinguefolium L.) - a total of 13 types (Rg, Rb, etc.)

Ginseng is also called the «root of life» and this is not for nothing: its two main components, saponins Rg1 and Rb, are responsible for vital signs.

Rg_1 is a concentrated vigor. It is thanks to this that ginseng fights fatigue so well and increases performance – both physical and mental. And Rb has the opposite effect. It allows the body to relax, relieves stress, mental and physical exertion.

In addition, ginseng root contains organic acids such as citric acid, malonic acid, succinic acid, ketoglutamic acid, pyroracemic acid, isopropyl formic acid, n-butyric acid, delphinic acid, propyl-acetic acid, n- capronic acid etc.

Ginseng contains up to 70% of various carbohydrates: rhamnose, fructose, glucose, sucrose, maltose, etc.). Ginseng polysaccharides are water-soluble compounds that contain less than 5% protein, as well as various sugar residues associated with uronic acid. These polysaccharides are acidic and have immunomodulatory and anti-proliferative properties. Recent studies have found an acid polysaccharide that exhibits immunostimulatory properties - called ginsan.

Ginseng also contains nitrogenous compounds (15%) - proteins, amino acids, alkaloids, etc. It is rich in the following amino acids: serine, alanine, cysteine, valine, methionine, leucine, tyrosine, arginine, proline, aspartic acid.

Thus, Korean red ginseng is a unique natural remedy that is successfully used in the treatment of many diseases and, most importantly, it has no side effects.

THE AIM

To analyze the effect of red Korean ginseng on the state of the autonomic nervous system and the well-being of patients with asthenic syndrome due to mild combat traumatic brain injury.

MATERIALS AND METHODS

We have examined 42 male patients, aged 28 to 43 years, with long-term effects of a mild combat traumatic brain injury. The duration of the disease ranged from 4 to 6 years. Combat trauma was confirmed by the source documents. A detailed clinical and neurological examination revealed neurological symptoms characteristic of combat TBI in the vast majority of patients – convergence insufficiency, small-swinging horizontal nystagmus, pain at the exit points of the occipital nerve, sensitivity disorders, anisoreflexia, decreased muscle strength in the extremities, impaired coordination and sleep, severe general weakness, drowsiness during the day and VNS deviations – cutis marmorata on the hands, acrocyanosis, distal hyperhidrosis, palpitations, fluctuations in blood pressure. The presence of general weakness dramatically reduced the quality of life of patients in the whole group.

The duration of asthenic manifestations in the examined patients ranged from 5 to 9 months and was caused at the first stages by stressful situations, both in everyday life and at work. Most of the patients were already taking psychotropic drugs, such as tranquilizers, sedatives, antidepressants, and sleeping pills before coming to the Institute's clinic. This class of drugs is known to have a calming effect that reduces mental tension and causes mental relaxation, relieves anxiety, fear, infectious insensitivity, as well as the

Table I. Dynamics of vegetative indexes in patients with aftereffects of mild combat TBI before and after treatment

Vegetative indices	Patients with aftereffects of mild combat TBI			
	before treatment		after treatment	
	Amount	%	Amount	%
Kerdo vegetative index				
Eytonia	4	9,5	22*	52,3
Sympathicotonia	6	14,3	9	21,4
Parasympathicotonia	32	76,2	11*	26,2
Vegetative provisioning				
Normal	5	11,9	21*	50,0
Insufficient	30	71,4	14*	33,3
Excessive	7	16,7	7	16,7
Vegetative reactivity				
Normal	4	9,5	23*	54,8
Insufficient	27	64,3	10*	23,8
Excessive	6	14,3	4	9,5
Distorted	5	11,9	5	11,9

Note:*p<0,05

Table II. Value of catecholamines in patients with aftereffects of mild combat TBI

Examination period	Adrenaline nmol/day	Noradrenaline nmol/day
Before treatment	18,6 ± 2,1	95,7 ± 7,2
After treatment	31,0 ± 2,4*	141,4 ± 10,2*

Note: * - p < 0,05.

ability to normalize the impaired vegetative functions. At the same time, the entire spectrum of action of the listed drugs in most cases does not allow using them as a therapy for individuals who require saving active attention and speed of reactions. In addition, the high cost of the drugs, their prolonged use, a large range of adverse reactions, and in some cases signs of dependence, lead to unnecessary results in the process of rehabilitation.

Taking into account all of the above, we have proposed Red Korean ginseng extract for the rehabilitation of patients, which was kindly provided by KGC – Korea Ginseng Corporation.

The concentrated extract of red Korean ginseng root is a thick mass of dark brown color in a glass jar, which should be dissolved in warm or cool water. Red Korean ginseng extract was prescribed in one measuring spoon per 80 ml of warm water 2-3 times a day for 1 month.

To objectify the well being of patients during treatment the studies were conducted according to the generally accepted scheme [3]: we studied changes in the state of autonomic nervous system (vegetative tonus, autonomic reactivity, and vegetative provisioning) before and after treatment, we also studied the neurotransmitter link of the sympathoadrenal system (epinephrine, norepinephrine, and the hormone melatonin) in daily urine [4], and a psychological study using the HAM scale (health, activity, mood) was conducted [5]. For mathematical processing we used the program «STATISTICA» [6].

RESULTS

Assessment of the VNS status was carried out both before and after rehabilitation measures using red Korean ginseng. As can be seen from the presented data (Table I) in the majority of patients before treatment, vegetative tonus was reduced, in 32 patients (76.2%) parasympathicotonia prevailed according to the Kerdo regulation index. The vegetative provisioning (VP) in the majority of patients - 30 individuals and autonomic reactivity (AR) in 27 individuals were insufficient. After treatment, the vegetative provisioning was normalized in 21 (50%) patients ($p<0.05$), and vegetative reactivity in 23 (54.8%) patients ($p<0.05$).

At the same time, adrenaline and noradrenaline production improved. In this group of patients before the start of treatment, there was a sharp decrease in the amount of catecholamines (CA) in the bloodstream (Table II). After treatment, the excretion of adrenaline almost doubled from 18.6 ± 2.1 nmol/day to 31.0 ± 2.4 n/mol/day (normal range 33.3 ± 2.7 nmol/day); noradrenaline - from 95.7 ± 7.2 nmol/day to 141.4 ± 10.2 nmol/day (normal range 157.5 ± 10.7 nmol/day), i.e. there is a tendency to normalization.

After the treatment the number of patients with normal melatonin levels increased: if before treatment the indicator below the norm (n = 62-84 nmol / l) was observed in 31 patients (73.8%), and within the norm - in 7 individuals (16.6%), then a month later the number of patients with normal melatonin levels increased to 29 patients (69%; $p<0.05$).

Data of psychological examination of patients by the method of diagnostics of operational evaluation of health, activity and mood (HAM) after treatment with red Korean ginseng had shown that the vast majority of patients showed regression of symptoms and marked subjective improvement in well-being. During the treatment, the average score of well-being self-esteem increased from 2.5 ± 0.7 points to 5.1 ± 0.4 points, activity - from 2.4 ± 0.5 points to 5.5 ± 0.3 points, mood - from 3.3 ± 0.3 points to 5.7 ± 0.4 points.

DISCUSSION

Study of the effect of red Korean ginseng in patients with asthenic syndrome on the background of long-term aftereffects of mild combat traumatic brain injury showed its positive effect on the studied indicators of VNS and its neurally mediated component (adrenaline, noradrenaline) and the hormone melatonin.

Melatonin positively influences the carbohydrate and fat metabolism, reduces the amount of cholesterol in the blood. Another mechanism of the regulatory effect of melatonin lies in the close link between the hypothalamic-hypophyseal-adrenocortical system, which plays a leading role in the endocrine response to stress. In a stressful

situation the epiphysis increases the secretion of melatonin, which restricts the secretion of corticosteroids [7,8].

Based on the results of a large number of experimental studies it was possible to explain the role of epiphysis as one of the brain apparatuses, which contributes to the protection of the body against external adversities, including stress. There are two groups of arguments in favor of this. Firstly, judging from morphological and biochemical data, the body changes its structural and functional characteristics in response to various stress influences. On the other hand, administration of epiphysial peptides and melatonin clearly interferes with the manifestations of stress reaction, including concomitant changes in the emotional sphere [9,10].

The analysis of the obtained data showed that melatonin excretory indices slightly increased in 33.0% of the patients and decreased in 77.0% of the patients. On the one hand, this is a manifestation of compensatory reaction (their increase), but on the other hand, it is a depletion of reserve capacities of epiphysis, which can lead to the disorders of cyclic neurally mediated processes of the body.

Normalization of melatonin excretion in turn enhances inhibitory processes in emotional structures of the brain by mobilizing specific melatonin receptors on their neurons, regulates the hypothalamic-pituitary-adrenal system, which plays a leading role in response to prolonged stress reaction [11,12].

CONCLUSIONS

1. In patients with mild traumatic brain injury who underwent rehabilitation treatment with red Korean ginseng, there was a probable improvement of autonomic nervous system functioning after the treatment.
2. After treatment with red Korean ginseng, most patients showed normalization of catecholamine excretion and normal melatonin levels.
3. In the vast majority of patients who used red Korean ginseng there was a regression of asthenic symptoms and marked subjective improvement in well-being.
4. No adverse reactions were found in patients undergoing rehabilitation treatment with red Korean ginseng.

REFERENCES

1. Korshnyak V.O. Gostra boyova kontuziyna cherepno-mozkova travma: patogenez, dlagnostika, likuvannya. in Korshnyaka V.O. Kharkiv. IE Liburkina L.M. Publ., 2018. 156p. (In Ukrainian).
2. Korshniak V.O. Naslidky lehkoi cherepno-mozkovoi travmy (patohenez, klinika, reabilitatsiia). in Kharkiv. IE Liburkina L.M. Publ., 2017. 225p. (In Ukrainian).
3. Veina A.M. Vehetatyvnye rasstroistva: klynyka, lechenye, dyahnostyka. in A.M. Veina. M.: MYA, 2000. 752p. (In Russian).
4. Nazarenko G.I., Kishkun A.A. Klinicheskaya otsenka rezultatov laboratornyih issledovaniy. Moscow. Meditsina Publ., 2000. 544p. (In Russian).
5. Luriya A.R. Osnovyi neyropsihologii. Moscow. «Akademiya» Publ., 2002. 145p. (In Russian).
6. Rebrova O.Yu. Statisticheskiy analiz meditsinskih dannyih. Primenenie paketa prikladnyih programm «STATISTICA». Moscow. Miedia Sfera Publ., 2002. 312p. (In Russian).
7. Korshnyak V.O. Rol melatoninu v neyroendokrinniy regulyatsiyi nervovoyi sistemi u hvorih iz naslidkami zakritih cherepno-mozkovih travm. Mizhnarodniy nevrologlchniy zhurnal. 2016; 4 (82):108 – 113. (In Ukrainian).
8. Bondarenko L.O. Znachennya vzaemodiyi faktoriv vnutrishnogo ta zovnishnogo seredovischa v regulyatsiyi funktsionalnoyi aktivnosti pinealnoyi zalozi. Avtoreferat disertatsiyi doktora biologichnih nauk. Kiyiv. 2003. 36p. (In Ukrainian).
9. Kovalzon V.M. Osnovyi somnologii. Moscow. «BINOM» Publ., Laboratoriya znaniy, 2012. 239p. (In Russian).
10. Arushanyan E.B. Epifizarnyiy gormon melatonin i narushenie poznavatelnoy deyatelnosti golovnogo mozga. Russkiy meditsinskiy zhurnal. 2006;9:673 – 678. (In Russian).
11. Anisimov V.N. Melatonin – rol v organizme, primenenie v klinike. Sankt-Peterburg. Sistema Publ. 2007. 40p. (In Russian).
12. Arushanyan E.B. Hronobiologicheskaya priroda narusheniya poznavatelnoy deyatelnosti mozga. Zhurnal nevrologii i psihiatrii. 2005;105:73 – 78. (In Russian).

ORCID and contributionship:

Korshnyak V.O.: A-F
Pulyk O.R.: E,F
Stoyanov O.M.: B,C,E

Conflict of interest:

The Authors declare no conflict of interest.

CORRESPONDING AUTHOR

Pulyk O.R.
Department of Neurorehabilitation,
Uzhhorod National University, Uzhhorod, Ukraine
e-mail: apulyk@gmail.com

Received: 11.07.2021
Accepted: 30.11.2021

A - Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis, **D** – Writing the article, **E** – Critical review, **F** – Final approval of the article