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STUDY OF MACRO- AND MICROELEMENTS COMPOSITION IN THE BIOLOGICAL MEDIA, CLINICAL AND NEUROLOGICAL CHANGES IN PATIENTS WITH CONSEQUENCES OF TRAUMATIC BRAIN INJURY

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ABSTRACT

The aim of this research was to investigate the macro- and microelements composition in the cerebrospinal fluid and in the blood serum of patients, with different consequences of TBI before and after complex treatment, with the use of endolumbal and intracystal introduction of ozone and pyracetam in dynamics.

Macro- and microelements composition was investigated in the cerebrospinal fluid and serum of 83 patients. State of neurological disorders in patients evaluated by the Glasgow Outcome Scale was extended. Thus, positive changes may be noted in the metabolism of macro- and microelements in the blood serum and cerebrospinal fluid of patients who were treated according to our suggested methods – endolumbal introductions of nootropic ozone mixture and endocystal introductions of ozone.

UDC CODE & KEYWORDS

■ UDC: 577.17.049:616.8.001 ■ Macroelements ■ Microelements ■ GOSE ■ Consequences ■ TBI ■ Cerebrospinal

INTRODUCTION

Traumatic brain injury (TBI) has been one of the most actual and complex problems of modern neurosurgery for a long time that many domestic and foreign authors noted in their publications (Konovalov, Likhterman, & Potapov, 1998; Konovalov et al., 2012; Mamadaliev, 2009, 2012; Akshulakov, 1995). This is stipulated not only by a high frequency of occurrence, the complexity of the pathogenesis, clinical manifestations and high mortality, but also by an enormous economic damage. One of the most important circumstances stipulating the actuality of the problem is the frequent victims' disability, which arises due to the development of various pathological conditions, persistent symptom complex, united under the name of the consequences of TBI. Just their formation, in the most cases stipulated economic damage caused by cranial injuries (Konovalov, Likhterman, & Potapov, 2002; Konovalov et al., 2012; Mamadaliev, 2012).

The Ozonated saline solution has been successfully used by intravenous introduction in patients with severe TBI in the acute period (Mamadaliev, 1993, 2013; Agzamov, 1995; Bakiev, 2002; Dubrovina, 2007). One of the first endolumbal introductions of ozone-oxygen mixture has been carried out in 1967, by A. B. Bolgaev in patients with post-traumatic epilepsy. Madiyarov (1990) has been used once endolumbal introduction of ozone-oxygen mixture as the prevention of cerebral arachnoiditis in patients with severe TBI in the volume of 15 cm^3. In 1994, M. K. Agzamov carried out scientific researches on the application of nootropic-ozone mixture in the complex treatment of severe TBI (Mamadaliev, 1993, 2013; Agzamov, 1995). In 2007, 25 patients with meningitis of different etiologies have been successfully treated by V. M. Belopukhov and his colleagues using endolumbal introduction of ozone-oxygen mixture in the complex treatment (Dubrovina, 2007).

The beginning of the 21st century marked not only the accumulation of fundamental knowledge in the field of neuroimmunology and neuroelementology but also the beginning of the application of this knowledge in practice, according to the concept of metabolic protection of the brain (Mazurina, 2005; Boldyrev, Eshchenko, Ilyukha, & Kaivarainen, 2010; Druzhinin, Novikov, & Lysikov, 2010).

In recent years, the problem of determining the role and significance of separate chemical elements presented in tissues and biological fluids of the human organism is important both in normal condition and in a variety of diseases, in particular of the nervous system. Variations in the content of macro- and microelements and imbalance of metalloligands' homeostasis are caused by both food and ecological factors, as well as somatic diseases, which change the status of the nervous system and form an unfavorable background not only for the beginning and development of injuries and diseases of the nervous system but also for the restoration process. The above changes have a significant influence on the understanding of neurorehabilitation measures (Boldyrev, Eshchenko, Ilyukha, & Kaivarainen, 2010; Druzhinin, Novikov, & Lysikov, 2010; Stepanchenko, 2005; Ullubiev, 2008; Shakirova, 2006; Bradbury, 1999; Connor, 1992).

The study of domestic and foreign literatures have shown the absence of researchers devoted to the content of macro- and microelements in the cerebrospinal fluid in the consequences of TBI.

The aim of the study

The aim of this research was to investigate the composition of macro- and microelements in the cerebrospinal fluid and in the blood serum of patients with different consequences of TBI before and after complex treatment with the use of endolumbal and intracystal introduction of ozone and pyracetam in dynamics.

Materials and methods

The data from 83 patients with various consequences of TBI from the age of 1 year to 60 years (63 men and 20 women) have been included in the investigation carried out on those who were hospitalized in neurosurgical clinic of Samarkand

Medical Institute from 2009 to 2013. All patients equally with clinical and neurological X-ray investigations (MRI, CT) underwent laboratory investigations to determine the macro- and microelements (K, Na, Cl, P, Mg, Fe) in the blood serum and in cerebrospinal fluid with the use of "Roche-Hitachi" analyzer before and after 4-6 months of treatment. Among the examined patients, 31 patients (37,3%) were diagnosed with post-traumatic cerebral arachnoiditis (PTCA); 21 patients (25,3%) were being diagnosed with post-traumatic chronic subdural hematoma (PCSH); 15 patients (18,1%) were diagnosed with post-traumatic epilepsy (PE); 13 patients (15,7%) were diagnosed with post-traumatic arachnoid cyst (PTAC); and, 3 patients (3,6%) were diagnosed with chronic vegetative status (CVS) (Figures 1, 2).

For the treatment of patients with the consequences of TBI, we offered the new methods of endocystal ozone introduction and endolumbal introduction ozone with nootropics (certificates of priority № IAP 2011 0419 and 2011 0148 № IAP).

The treatment method for arachnoid liquor cysts entails that after the imposition of milling holes, dissection and excision of the cyst walls are made; the connection is established with subarachnoid and subdural spaces, and then vinyl chloride or silicone catheter is introduced into the cystic cavity and through this catheter with the use of a medical syringe in which ozone has been injected in the amount of 10-30 cm^3 depending on the cyst size. The catheter is left for 3-5 days in the re-introduction of ozone.

The next method is the endolumbal ozone and pyracetam insufflation in patients with different consequences of TBI, as mentioned above. These patients are put under sterile conditions after premedication and local anesthesia with the use of Novocain solution 0,5% – 10,0 ml, then a lumbar puncture was performed between the 3^{rd} and 4^{th} lumbar vertebrae and liquor is evacuated (20-40 ml depending on the liquor pressure); endolumbal ozone is injected first (10-30 cm^3), and then pyracetam 2,5% – 3% from 200 mg to 1000 mg depending on the age of the patient.

Patients were given the following methods of treatment: in patients with PCSH, mini-invasive removal of hematomas and endolumbal insufflation of ozone and pyracetam were performed 7-8 days after surgery; in patients with PTAC, mini-invasive cysts emptying and endocystal introduction of ozone were performed on the day of the surgery and 3-4 days after surgery. In PCA, PTE, and in patients with CVS after severe TBI, endolumbal insufflation of ozone and 2-3% solution of pyracetam (doubly per treatment course) was performed.

In order to assess the general condition and neurological changes in patients, Glasgow Outcome Scale Extended – GOSE has been used (Wilson, Pettigrew, & Teasdale, 1998, 2001; Levin et al., 2001; Teasdale, Pettigrew, Wilson, Murray, & Jennett, 1998).

Figure 1: Forms of TBI consequences (MRI and CT examples). a). Post-traumatic cystic cerebral arachnoidit. CT of patient K showed a small arachnoid cysts in the left frontal region and cystic-adhesive changes of convexital areas of the brain. b). Post-traumatic epilepsy. MRI of patient R showed the seat of epilepsy - posttraumatic cystic-glial degeneration in the right frontal region of the brain. c). Post-traumatic arachnoidal cyst. MRI of patient B showed an arachnoid cysts in the right temporal-basal region of the brain. d). Post-traumatic chronic subdural hematoma. MRI (axial, coronar scans) of patient A showed a chronic subdural hematoma in the left hemisphere of the brain. e). Chronic vegetative status. MRI of patient J showed a bilateral subdural hydroma fronto-temporal-parietal lobes and post-traumatic atrophic processes of the brain.

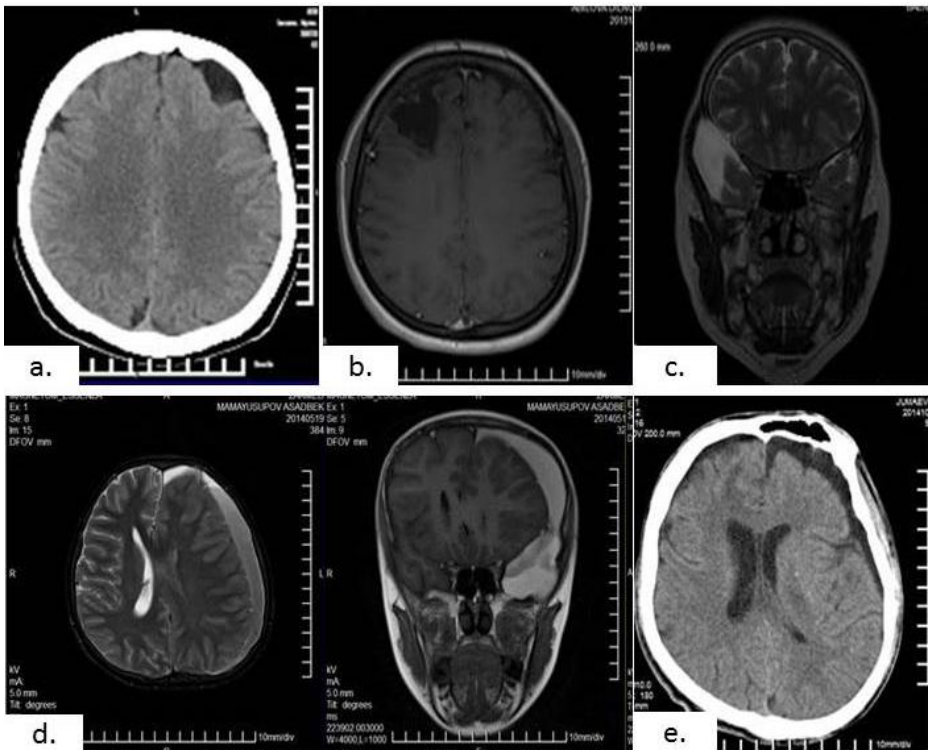

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Figure 2: Distribution of patients according to the forms of TBI consequences

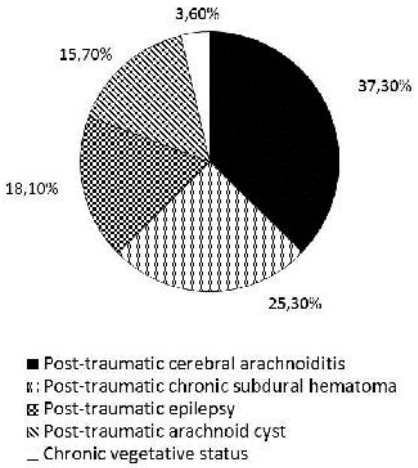

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Table 1: Glasgow Outcome Scale Extended (GOSE)

1 point Death (D)	Death (D) in the first 24 hours
2 point Death (D)	The death (D) of more than 24 hours
3 point Vegetative State (VS)	Condition of unawareness with only reflex responses but with periods of spontaneous eye opening.
4 point Low Severe Disability (LSD)	Patient who is dependent for daily support for mental or physical disability, usually a combination of both.
5 point Upper Severe Disability (USD)	
6 point Low Moderate Disability (LMD)	Patients have some disability such as aphasia, hemiparesis or epilepsy and/or deficits of memory or personality, but are able to look after themselves. They are independent at home but dependent outside. If they are able to return to work even with special arrangement, it is upper level of MD, if not then it is low level of MD.
7 point Upper Moderate Disability (UMD)	
8 point Low Good Recovery (LGR)	Resumption of normal life with the capacity to work even if pre-injury status has not been achieved. Some patients have minor neurological or psychological deficits. If these deficits are not disabling then it is upper level of GR, if disabling then it is lower level of GR.
9 point Upper Good Recovery (UGR)	

Source: Wilson et al., 1998

Results and Discussion

In order to determine the value of pathogenetic changes of macro- and microelements in the brain tissues during the consequences of CCT after using endocystal and endolumbal introduction of ozone and pyracetam, laboratory tests were performed, including determination of chemical elements phosphorus (P), calcium (Ca), iron (Fe), magnesium (Mg), sodium (Na), potassium (K) and chlorine (Cl) in the blood serum and in liquor, which play an important role in the activities.

Prior to treatment in the blood serum of patients, the following changes of macro- and microelements were identified, i.e. reduction of Ca – at 86,7% of patients, K at 21,7% of patients and Cl at 45,8% of patients. It has been revealed an increase average of P at 48,2% of patients, Fe at 71,1% of patients, Mg at 77,1% of patients and Na at 71,1% of patients (Table 2.).

Table 2: Quantitative indexes of macro- and microelements in the blood serum in patients with consequences of TBI (before treatment)

Elements	Average indexes (mmol/l)		Minimal indexes (mmol/l)		Maximal indexes (mmol/l)	
	In normal condition	Result	In normal condition	Result	In normal condition	Result
P	1,16	1,49	0,87	0,76	1,45	3,69
Ca	2,32	1,85	2,09	0,94	2,55	2,31
Fe	17	22,7	5,4	9,36	28,6	38,6
Mg	0,83	1,07	0,6	0,6	1,06	1,87
Na	135	147	124	127	146	186,3
K	4,3	3,46	3,5	2,22	5,1	4,64
Cl	102,5	97,5	95	61,1	110	117,7

Source: Author

As shown in Table 3, in the liquor tests of these patients, some distinctive changes were observed compared with those in the blood serum, i.e. amounts Ca decreased in 89,2% of patients and amounts of elements such as K and Cl were low in all (100%) patients. Minimal and maximal amounts of P, Fe and Na in the liquor were normal, but the average amounts of P and Na were high (41% and 86,7% accordingly). An increased amount of Mg in the liquor was noted in 38,6% (32) of patients in comparison with maximal indexes (Table 3).

Thus, the quantitative changes of all macro- and microelements in the blood serum and in the cerebro-spinal fluid in a range of research were noted. The occurrence of this condition has been proven as a result of deep metabolic-biochemical deficiency in the human organism during different consequences of TBI. This provided the basis to introduce new pathogenetically proved and effective treatment methods in the intermediate and distant periods of traumatic brain disease.

Table 3: Quantitative indexes of macro- and microelements in the liquor in patients with consequences of TBI (before treatment)

Elements	Average indexes (mmol/l)		Minimal indexes (mmol/l)		Maximal indexes (mmol/l)	
	In normal condition	Result	In normal condition	Result	In normal condition	Result
P	0,5	0,83	0,39	0,24	0,68	1,43
Ca	1,4	0,99	1,12	0,69	1,75	1,18
Fe	17	14	5,4	2,1	28,6	25,9
Mg	1,3	1,51	1,23	1,22	1,4	2,06
Na	132,5	140,2	120	121,1	145	151,9
K	3,7	2,3	3,07	2,01	4,35	2,68
Cl	204,5	149,3	197	119,5	212	192

Source: Author

Study and evaluation of the general condition and neurological status of patients with the use of the extended Glasgow Outcome Scale at admission to the clinic showed that in a vegetative state (VS) were 4,8% of patients, rough disability (LSD) was detected in 2,4% of patients, relatively severe disability (USD) was detected in 12,1% of patients, moderate disability (LMD) was detected in 15,7% of patients, relatively average disability (UMD) was detected in 35% of patients and relatively satisfactory restoration (LGR) was detected in 30,1% of patients (Table 4).

Taking into consideration the above conditions, it has been used the new method of treatment – endolumbal and endocystal insufflation of ozone and pyracetam in the intermediate and distant periods of traumatic disease of the brain and the following results were obtained. On the expiry of 3-6 months after treatment the amount of macro- and microelements in the blood serum and cerebrospinal fluid were tested and the overall condition and neurological status of patients according to GOSE in dynamics were assessed.

Table 4: Distribution of the investigated patients according to the GOSE criterion

Points	Contingent	Number of observations					
		PVS	PCSH	PTAC	PE	PTCA	In total
1 point	Death (D) in the first 24 hours	0	0	0	0	0	0
2 point	The death (D) of more than 24 hours	0	0	0	0	0	0
3 point	Vegetative State (VS)	3 (3,6%)	1 -1,2%	0	0	0	4 -4,8%
4 point	Low Severe Disability (LSD)	0	2 -2,4%	0	0	0	2 -2,4%
5 point	Upper Severe Disability (USD)	0	10 (12,1%)	0	0	0	10 (12,1%)
6 point	Low Moderate Disability (LMD)	0	8 -9,6%	3 (3,6%)	2 -2,4%	0	13 (15,7%)
7 point	Upper Moderate Disability (UMD)	0	0	8 (9,6%)	12 (14,5%)	9 (10,9%)	29 -35%
8 point	Low Good Recovery (LGR)	0	0	2 (2,4%)	1 -1,2%	22 (26,5%)	25 (30,1%)
9 point	Upper Good Recovery (UGR)	0	0	0	0	0	0
	In total	3	21	13	15	31	83

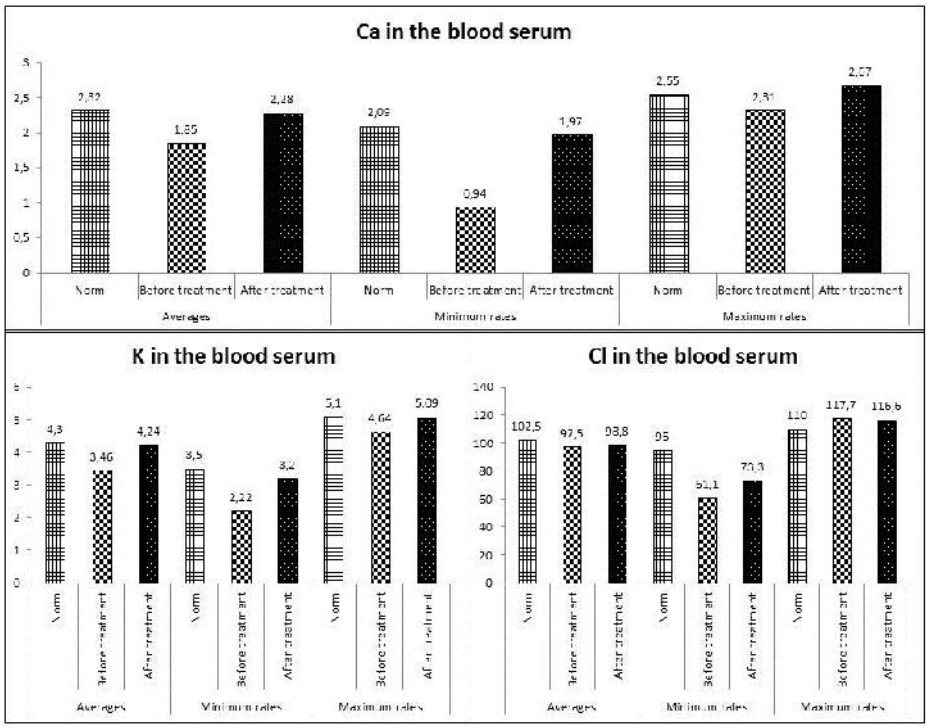
Source: Author

Quantitative indexes of macro- and microelements in the blood serum in the investigated patients were significantly improved. For example, the amount of Ca in comparison with the average index before treatment (1,85 mmol/l) has been increased in 1,3 times (until 2,28 mmol/l) and approximate to the normal index (2,32 mmol/l).

Quantitative changes of K and Cl microelements in the blood serum also have a tendency to increase after treatment and accordingly the amount of K before treatment was 4,24 mmol/l and after treatment it has been increased in 1,2 times, and the amount of Cl has been increased in 1,1 time from 97,5 mmol/l to 98,8 mmol/l (Figure 3).

Changes in the series of macro- and microelements in which the average indexes were up to the normal values before treatment have been determined by the following indication: reduction of the average amount of P from 1,49 mmol/l to 1,4

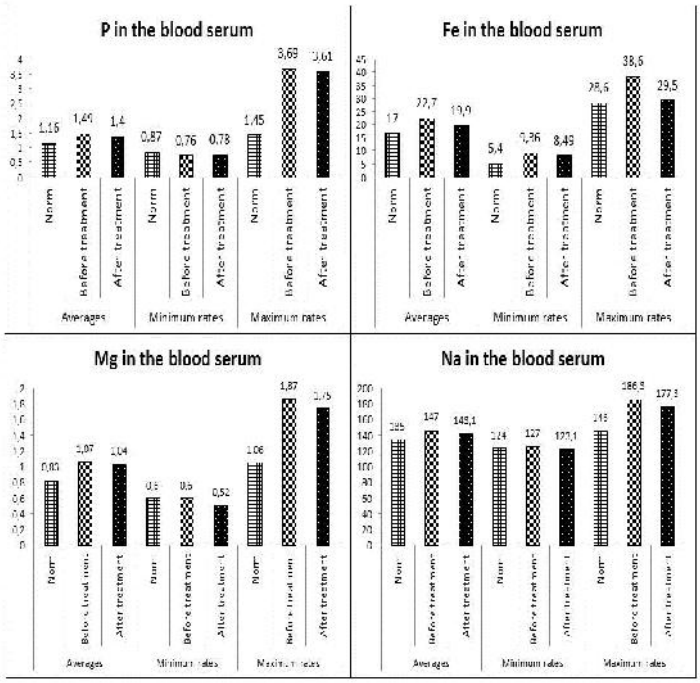
Figure 3: Changes in the structure of macro- and microelements in the blood serum in patients with the consequences of the TBI



Source: Author

mmol/l, the average amount of Fe from 22,7 mmol/l to 19,9 mmol/l (in 1,2 times), the average amount of Mg from 1,07 mmol/l to 1,04 mmol/l (in 1 time), and the average amount of Na from 147 mmol/l to 143,1 mmol/l. The changes are shown relatively approaching near the normal indexes (Figure 4).

Figure 4: Changes in the structure of macro- and microelements in the blood serum in patients with the consequences of the TBI



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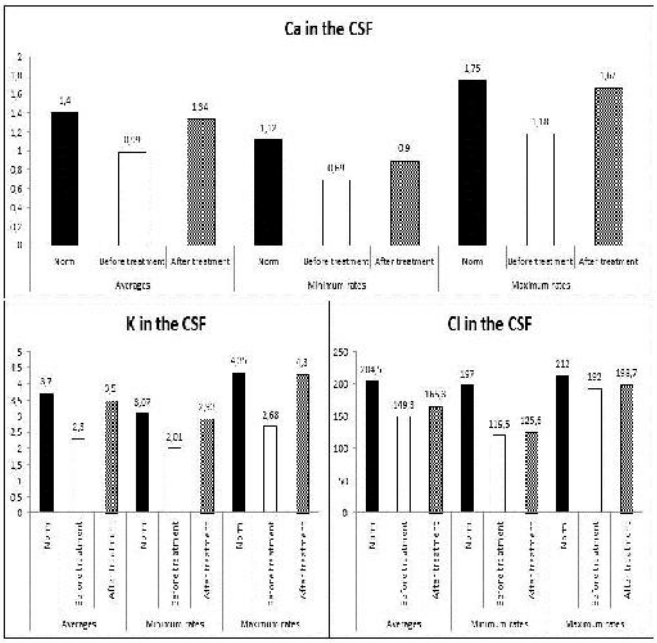
Dynamic changes of the structure of macro- and microelements in cerebrospinal fluid after treatment occurred in the following ways: the elevated amount of Ca from 0,99 mmol/l before treatment to 1,34 (in 1,4 times) mmol/l; the average index of K elevated from 2,3 mmol/l to 3,5 mmol/l (in 1,5 time); and, the average index of Cl elevated from 149,3 mmol/l to 165,3 mmol/l (in 1,1 time) (Figure 5).

Figure 5: Changes in the structure of macro- and microelements in the cerebrospinal fluid in patients with the consequences of the TBI



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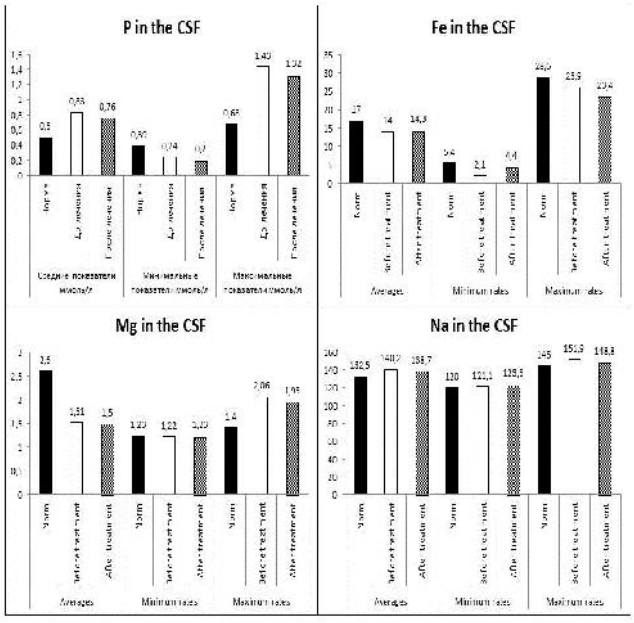
The reduction was noted in the average indexes of macro- and microelements, which went up to the normal values according to the quantitative indexes: the amount of P reduced from 0,56 mmol/l to 0,53 mmol/l; the amount of Na reduced from 140,2 mmol/l to 138,7 mmol/l; and the amount of Mg reduced from 1,51 mmol/l to 1,5 mmol/l (Figure 6).

The study of the general condition and neurological status of patients according to the GOSE showed that in all 4 patients who were in “vegetative state” (VS) (3 points) before treatment saw positive dynamic after treatment. In 1 patient from this group of patients, neurological status has been restored to “rough disabilities” (4 points), i.e. this patient had the ability to

Figure 6: Changes in the structure of macro- and microelements in the cerebrospinal fluid in patients with the consequences of the TBI



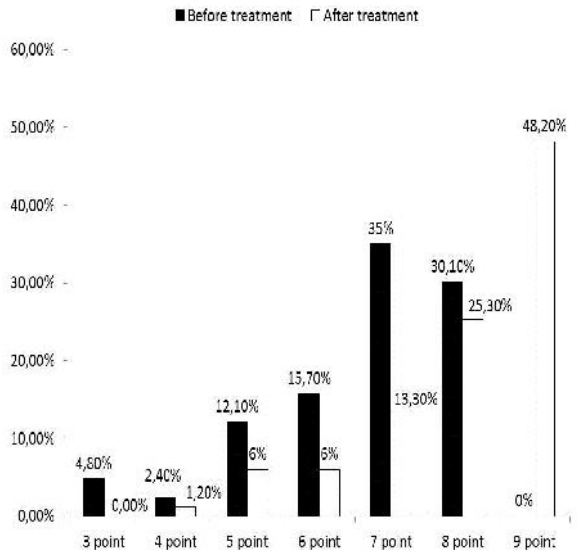
Source: Author

answer questions; in 1 patient with VS, neurological status has been improved to the condition of "relatively severe disability" (5 points); in 2 patients, this condition has been improved to "relatively moderate disability" (7 points).

During the evaluation of the patients' condition, due to GOSE after endolumbal introduction of ozone and pyracetam and endocystal introduction of ozone in the remaining patients, positive results were observed. It should be noted that an improvement was shown in a number of patients with "rough disabilities" (4 points) in 2 times after treatment, in contingent of patients with "relatively severe disability" (5 points) in 2 times, in patients with "moderate disability" (6 points) in 2,6 times, in patients with "relatively moderate disability" (7 points) in 2,6 times and in patients with "relatively satisfactory restoration" (8 points) in 1,2 times, i.e. by improving of metabolic processes and neurological status has been noted as "full restoration" of patients' condition (9 points), whose specific gravity has been reached to 48,2% (Figure 7).

Conclusion

Figure 7: Dynamic changes of the neurological deficits determined according to GOSE in patients with consequences of the TBI before and after treatment



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Quantitative changes of macro- and microelements in the blood and cerebrospinal fluid in patients with the consequences of the traumatic brain injury could contribute to metabolic disorders in the patients' organism and could be the index of the clinical-neurological pathological changes.

The investigation of the indices of macro- and microelements in dynamics in patients with the consequences of the traumatic brain injury could give us the possibility to determine the effectiveness of the pathogenetical treatment of patients.

Endocystal introduction of ozone and endolumbal insufflation of ozone and introduction of nootropics led to the normalization of macro- and microelements in the blood and in cerebrospinal fluid because of the metabolic improvement in the organism, and it could allow us to reach the early restoration of clinical-neurological disorders in patients with the consequences of the traumatic brain injury.

Thus, positive changes may be noted in the metabolism of macro- and microelements in the blood serum and cerebrospinal fluid of patients who were treated according to our suggested methods – endolumbal introductions and nootropic ozone and endocystal introductions of ozone.

REFERENCES

1. Agzamov, M. K. (1994). Comprehensive assessment of the efficacy of nootropic-ozone therapy in severe traumatic brain injury (The dissertation of candidate of medical sciences), Samarkand State Medical Institute, Uzbekistan.

2. Akshulakov, S. K. (1995). Clinico-epidemiological study of acute traumatic brain injury and its consequences in the Republic of Kazakhstan (The dissertation of doctor of medical sciences), Burdenko Neurosurgery Institute, Russian Federation.

3. Aliev, M. A., & Mamadaliev, A. M. (2013). Macronutrient composition of biological media in patients with post-traumatic cerebral arachnoiditis. In Dolgov V.V., Shevchenko O.P. (Eds.)., Proceedings of VIII All-Russian Scientific-Practical Conference "Analytical reliability and diagnostic value of laboratory medicine," Journal of Laboratory, №1/2013 (pp. 23.). Moscow, Russian Federation.

4. Aliev, M. A., & Mamadaliev, A. M. (2013). Study of Efficacy of Endocystal Ozonetherapy in the Operative Treatment of Posttraumatic Arachnoidal Cysts. In Hee-Won Jung, Black P. (Eds)., Proceedings of XV WFNS Congress, (FA0754)., Seoul, Korea.

5. Bakiev, S. S. (2002). The use of ozone in the treatment of patients with fractures of the maxillofacial bones (The dissertation of candidate of medical sciences), Samarkand State Medical Institute, Uzbekistan, in Russian.

6. Bolg'ayev, A. B., & Madiyarov, S. D. (1977). Treatment of chronic arachnoiditis via introduction of ozone in the subarachnoid space. Journal of Neurology and Psychiatry, 2, 227-231.

7. Boldyrev, A. A., Eshchenko, N. D., Ilyukha, V. A., & Kaivarainen, E. I. (2010). Neurochemistry. Proc. manual for schools. Moscow.

8. Bradbury, M. B. (1999). Transport of Iron in the Blood-Brain-Cerebrospinal Fluid System. Journal of Neurochemistry, 69(2).

9. Connor, J. R., & Benkovic S. A. (1992). Iron regulation in the brain: histochemical, biochemical, and molecular considerations. Annals of Neurology, 32, S51-61.

10. Druzhinin, P. V., Novikov L. F., & Lysikov, Y. A. (2010). Basics of Nutrition. Clinical management, Moscow.

11. Dubrovina, Y. A. (2007). Endolyumbal introduction of ozone-oxygen mixture in the treatment of traumatic brain injury and its complications: Clinical and neurophysiological evaluation (The dissertation of candidate of medical sciences), Kazan, Russian Federation.

12. Konovalov, A. N., Likhterman, L. B., & Potapov, A. A. (1998, 2002). Clinical guidelines for traumatic brain injury, 1 & 3. Moscow, “Antidor.”

13. Konovalov, A. N., Potapov, A. A., Likhterman, L. B., Kornienko, V. N., Kravchuk, A. D., Okhlopkov, V. A., Zakharova, N. Y., & Yakovlev, S. B. (2012). Reconstructive and minimally invasive surgery of outcomes of craniocerebral injury. Moscow.

14. Levin, H. S., Boake, C., Song, J., McCauley, S., Contant, C., Diaz-Marchan, P., Brundage, S., Goodman, H., & Kotrla, K. J. (2001). Validity and sensitivity to change of the extended Glasgow Outcome Scale in mild to moderate traumatic brain injury. Journal of Neurotrauma, 18, 575-584.

15. Mazurina, Y. M. (2005). Violation of calcium metabolism in children during the first three years of life with neurological disorders (The dissertation of candidate of medical sciences), Moscow, Russian Federation.

16. Mamadaliev, A. M. (1988). Predicting outcomes of traumatic brain injury in the acute period (The dissertation of doctor of medical sciences), Burdenko Neurosurgery Institute, Russian Federation.

17. Mamadaliev, A. M., & Agzamov, M. K. (1993). A method for treating severe traumatic brain injury in the acute period (The patent for the invention of the Russian Federation № 5042297/14/023170 on 07/21/93).

18. Mamadaliev, A. M., & Aliev, M. A. (2009). The Importance of the Duration Disorders of Consciousness to Prognosis of the Outcome of Cranio-Cerebral Trauma. In Black P. (Eds)., Proceedings of XIV WFNS Congress, Boston, USA.

19. Mamadaliev, A. M., Shodiev, A. S., Aliev, M. A., & Nabiev, A. A. (2011). By studying the composition of macronutrients are in biological media in post-traumatic cerebral arachnoiditis. In Bersnev V.P. (Eds.)., Abstracts of 10th Russian Scientific-Practical Conference of "Polenov reading's", St. Petersburg, Russian Federation.

20. Shakirova, E. G. (2006). Changes of plasma micronutrients in Parkinson's disease and Parkinson's syndrome (The dissertation of candidate of medical sciences), Moscow, Russian Federation.

21. Stepanchenko, O. A. (2005). Peculiarities of stroke when changing glucose in the blood and cerebrospinal fluid (The dissertation of candidate of medical sciences), Moscow, Russian Federation.

22. Teasdale, G. M., Pettigrew, L. E., Wilson, J. T., Murray, G., & Jennett, B. (1998). Analyzing outcome of treatment of severe head injury: A review and update on advancing the use of the Glasgow Outcome Scale. Journal of Neurotrauma, 15, 587-597.

23. Ullubiev, M. A. (2008). Changes of plasma micronutrients in ischemic hemispheric stroke (The dissertation of candidate of medical sciences), Moscow, Russian Federation.

24. Wilson, J. T., Pettigrew, L. E., & Teasdale, G. M. (1998). Structured interviews for the Glasgow Outcome Scale and the Extended Glasgow Outcome Scale: Guidelines for their use. Journal of Neurotrauma, 15, 573-585.

25. Wilson, J. T., Pettigrew, L. E., & Teasdale, G. M. (2001). Emotional and cognitive consequences of head injury in relation to the Glasgow Outcome Scale. Journal of Neurology, Neurosurgery, and Psychiatry, 70, 267-268.