AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 02, Issue 02, 2024 ISSN (E): 2993-2149

LYMPHOTROPIC DECONEDEMA THERAPY IN COMPREHENSIVE TREATMENT OF PATIENTS WITH TRANO BRAIN INJURY

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Annotation. The effectiveness of lymphotropic decongestant therapy in patients with traumatic brain injury was studied. Based on the obtained clinical and laboratory data, comparatively the main and control groups, the effectiveness of lymphotropic decongestant therapy was revealed, which prevents the progression of edema during traumatic brain injury.
Keywords: cerebral edema, traumatic brain injury, lymphotropic therapy.

Relevance. Considering the achievements and capabilities of neuroresuscitation care, treatment of cerebral edema (CED) remains exclusively reactive and is included only after problems with intracranial pressure arise. Recent reviews have focused on the molecular factors causing brain swelling after injury and on the development of therapeutic approaches to combat this problem [12].

It has been experimentally confirmed that the tracer, injected into the ventricles of the brain, where the cerebrospinal fluid is located, is found in the system of lymphatic vessels at the base of the skull, and then in the unchanged lymph nodes. This indicates the existence of a connection between the glymphatic , meningeal and lymphatic systems [19].

The discovery of meningeal lymphatic vessels is a necessary breakthrough in the development of new methods of neuroresuscitation based on the control of lymphatic drainage processes to remove toxins and unnecessary molecules from the central nervous system. This could be an innovative step in the development of new ways to deliver drugs to the brain, bypassing the blood-brain barrier [8,20,21].

The available scientific literature contains works that continue to expand our knowledge of the functioning of the lymphatic system of the brain and may have important practical applications in the field of neurology and neurosurgery [2,18,25,26].

Recent studies have also confirmed the circulation of fluid from the meningeal lymphatic system of the brain with macromolecules and immune cells from the central nervous system in the deep cervical lymph nodes. Labeled particles and macromolecules injected into the brain and/or cerebrospinal fluid mainly drain into the cervical lymph nodes [4,6,15].

At the same time, none of the available methods for correcting ICH (decompressive craniectomy and osmotherapy) do not stop the underlying molecular cascade leading to cerebral edema. Research into the molecular principles of cerebral edema is identifying new targets for treatment, such as exposure factors, vascular permeability, and fluid-electrolyte balance. This opens up

opportunities for the development of new drugs and therapeutic approaches that can more effectively target the molecular pathways that cause cerebral edema [10].

First discovered less than a decade ago, the glymphatic system

(GS) provides a pathway for the influx of cerebrospinal fluid into the brain (via the periarterial space) and the removal of interstitial fluid from the brain (perivenous spaces) with a key role for aquaporin-4 (AQP4) channels at the vascular ends of astrocytes . Although this system has been widely studied in the context of neurodegenerative diseases (amyloid-b and tau clearance) and sleep pathways, recent efforts have also implicated it in the development of AMS after ischemic stroke[11,18].

Subsequent studies of subarachnoid hemorrhage (SAH) and traumatic brain injury (TBI) also identified GS disruption as a contributing factor to cerebral edema, secondary injury, and BBB dysfunction [13,14].

The discovery of the lymphatic drainage system, which maintains brain homeostasis and is involved in immune surveillance, represents a new therapeutic target for the treatment of neurological dysfunctions. This not only changed the understanding of fluid circulation in the brain, but also contributed to the understanding of the pathology of the central nervous system and the mechanisms of neuroinflammatory diseases [3,16,17].

More and more studies highlight the importance of lymphatic function in various neurological diseases. As a widespread clearance system in the brain, GS may influence many neurological disorders, providing a new direction for future research into disease mechanisms and treatments [22,23,24,27,28].

Drainage from the CNS to the cervical lymph nodes has been documented in numerous studies using tracers or injection of antigen into the cerebrospinal fluid. Lymphoid-like structures in the meninges have been described in the adult mouse brain, and this pathway may transport extracellular solutes to the cervical ganglia [5,6].

The discovery of HS opens a new direction in the understanding of brain diseases, which shifts the focus from changes in specific brain structure to the general circulation of fluid in the brain. An example is the crucial role of GS in understanding the occurrence of cerebral edema. However, recent studies of HS have shown that CSF is the main source of initial cerebral edema rather than blood leakage [7,29].

Improving drainage of the brain lymphatic system may have potential clinical implications in neurovascular and neuroinflammatory diseases. Developing strategies to improve the impaired function of the lymphatic drainage system is a priority in the treatment of neurological diseases [1,10,21].

Taking into account the anatomical and functional relationship of the central nervous system and the lymphatic system, the circulation of cerebrospinal fluid and lymph, it seems justified and pathogenetically justified to use the method of indirect lymphostimulation in the treatment of patients with cerebral edema due to TBI.

The purpose of the study is to evaluate the effectiveness of lymphotropic decongestant therapy for cerebral edema in patients with severe head injury.

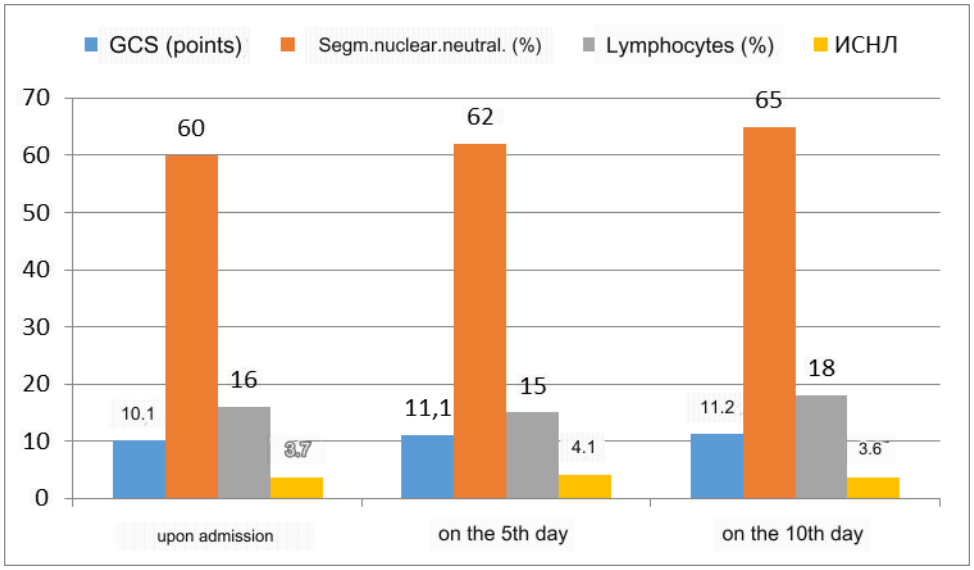
Materials and methods of research : The study was carried out in the neuroreanimation department of the Bukhara branch of the Russian Research Center for Emergency Medicine. Materials from 38 patients with TBI were studied. Age _ patients ranged from 37 to 68 years (mean age was 58.2±2 years) . All patients underwent standard diagnostic methods (assessment of

neurological status during a joint examination by a neurologist and neurosurgeon, multislice computed tomography (MSCT), as well as laboratory tests - leukemia formula, neutrophil-to-lymphocyte ratio index (INLR). Neurostatus was assessed using the Glasgow Coma Scale (GCS) , in which the average score upon admission to the hospital was 9.3 ± 2.1. MSCT of patients with TBI revealed subdural 24 (63.1%), parenchymal 10 (26.3%), and brainstem hemorrhages 4 (10 .5%) and areas of brain contusion that did not require surgical intervention .

All patients with TBI were divided into two groups. The first is a control group (20 patients) who received standard therapy. The second is the main group (18 patients), whose patients received lymphotropic decongestant therapy. For the purpose of anti-edematous therapy in the mastoid area on the left or right submastoidal injected the solution lidocaine a 2% -1 ml, dexamethasone a 4 mg, 10% glucose solution 3 ml. in one syringe (the method was approved at a meeting of the Ethics Committee of the Ministry of Health of the Republic of Uzbekistan , protocol No. 7 of November 9, 2023). Submastoid lymphotropic injections were performed in within 5 days, along with conservative treatment, including: antibacterial, decongestant, membrane stabilizing, hemorheological, cerebroprotective and symptomatic therapy.

A comparison of clinical and laboratory parameters was carried out in three stages: the first stage - upon admission, the second stage: day 5, the third stage - 10 days of intensive therapy.

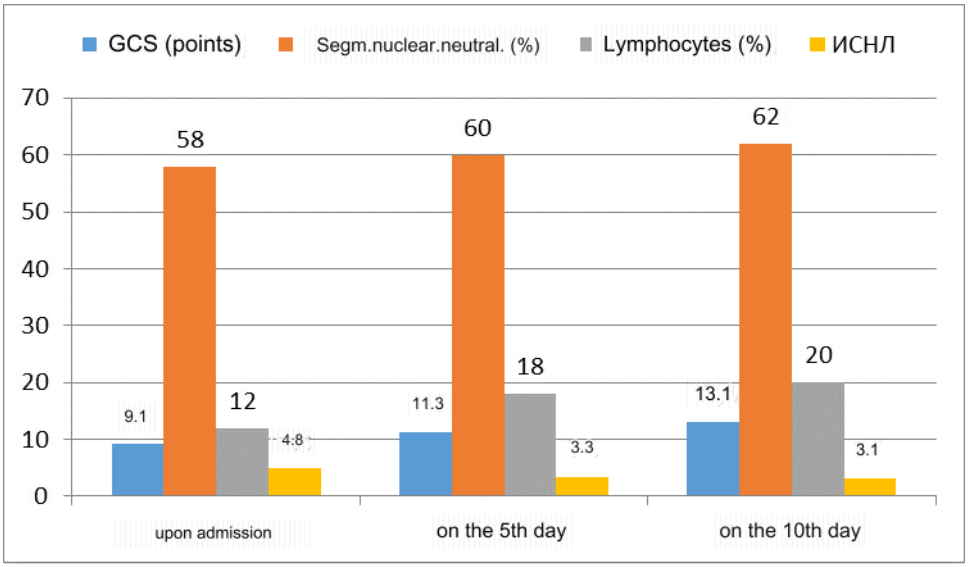
Results and discussion : Analysis of the results of the control group of patients with TBI (n=20), who received standard treatment methods, showed that the level of impairment of consciousness at the time of admission to the hospital (the first stage of the study) averaged 10.1 points on the GCS. At this stage, in the blood test, segmented neutrophils amounted to 60%, and the number of lymphocytes - 16%, while the ratio index of segmented neutrophils to lymphocytes was 3.7. On the 5th day of treatment (the second stage of the study), the level of consciousness impairment was 11.1 points on the GCS.



Graph 1 . Dynamics of indicators in the control group of patients with TBI.

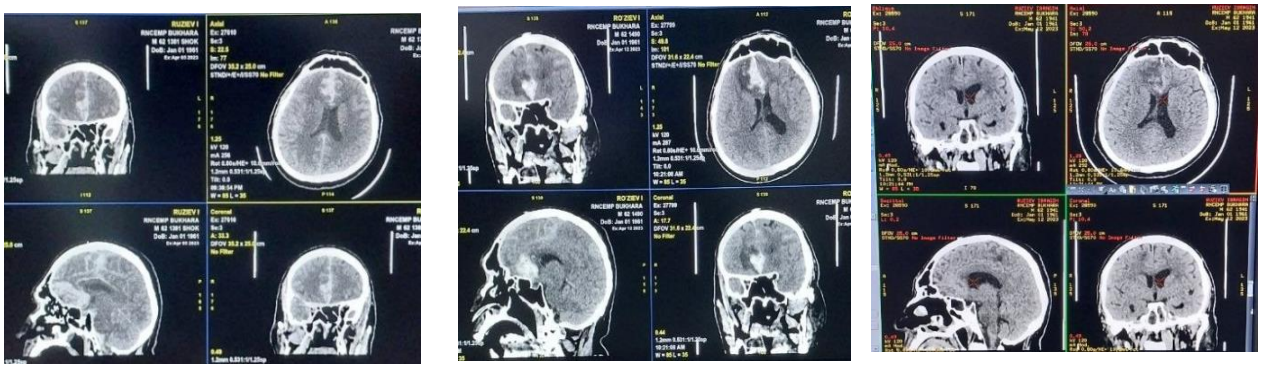
The number of segmented neutrophils was 62%, lymphocytes 15%, respectively, the ISNL indicator was 4.1. On the 10th day of the study, the neurological status remained the same, amounting to 11.2 points on the GCS. At the same time, the number of segmented neutrophils was 65%, lymphocytes 18%, and the ISNL was 3.6 (graph 1).

When analyzing the results of patients in the main group of patients with TBI who underwent lymphotropic decongestant therapy (n=18), the following data were revealed - at the first stage of the study, the level of impairment of consciousness averaged 9.1 points on the Glasgow scale. In laboratory blood tests, the number of segmented neutrophils was 58%, and lymphocytes - 12%, while the ISNL indicator was 4.8. At the second stage of the study, the assessment of the level of consciousness was 11.3 points on the GCS. Segmented neutrophils in the blood accounted for 60%, and lymphocytes 18%, respectively, the ISNL indicator was 3.3. At the third stage of the study, a noticeable increase in all these indicators was observed. There was clearing of consciousness to stupor, the average score of which was 13.1 points. And the indicators of the general blood test were: segmented neutrophils 62%, lymphocytes 20%, and ISNL 3.1 (graph 2).



Graph 2 . Dynamics of indicators of the main group of patients with TBI who underwent lymphotropic decongestant therapy.

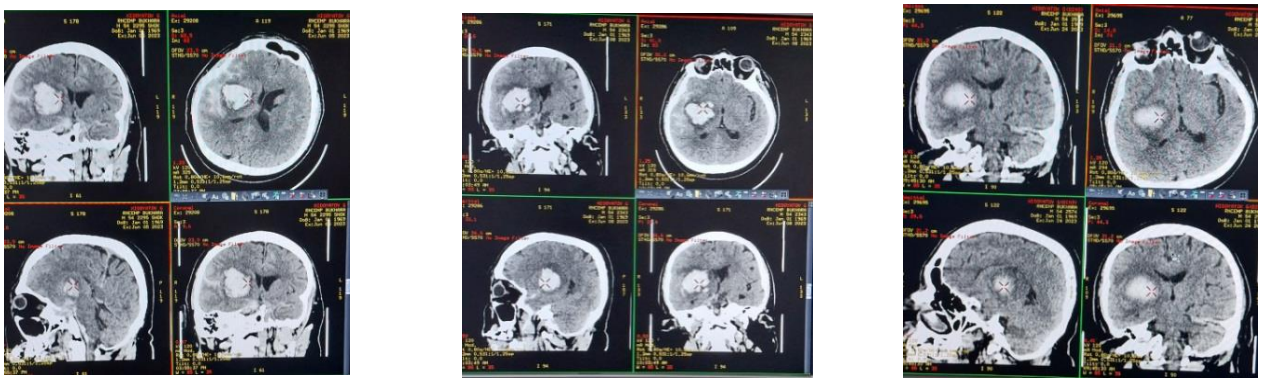
The characteristics of the clinical data of patients with TBI of the main group who received lymphotropic decongestant therapy corresponded to dynamic changes on MSCT, which was expressed by a decrease in the size of the hematoma, contusion area and perifocal area of edema (Fig.1), compared to data from patients in the control group (Fig.2).



A) B) C)

Figure 1. MSCT of a patient with a traumatic brain injury of the main group

(A – upon admission, B – on the 5th day, C – on the 10th day).



A) B) C)

Figure 2. MSCT of a patient with traumatic brain injury in the control group
(A – upon admission, B – on the 5th day, C – on the 10th day).

Dynamic changes in the neurological status and computed tomography in both groups corresponded to changes in laboratory parameters that reflected changes in the leukocyte formula (graph 1, 2). Rapid positive dynamics were observed in the main group of patients who received lymphotropic decongestant therapy as part of intensive care.

Conclusion. Lymphotropic decongestant therapy increases the effectiveness of intensive basic treatment in combination prevents progression of cerebral edema in patients with TBI . Dynamic neuromonitoring using MSCT in comparison with clinical and laboratory data allows for objective monitoring of cerebral edema.

Literature

1.Kuldashev K.A., Kuldasheva Y.M., Khakimova Z.K. and others. Diagnosis and surgical treatment of ICH of traumatic origin and intracranial infectious and inflammatory complications in combined traumatic brain injury. Journal of Dentistry and Craniofacial Research. 2021. No. 3, pp. 36-39.

2. Semyachkina-Glushkovskaya O.V. et al . Lymphatic drainage system of the brain: a new player in neuroscience. Journal of evolutionary biochemistry and physiology, 2023, volume 59, no. 1, p. 3–19.

3. Yankova G.S., Bogomyakova O.B. Lymphatic drainage system of the brain: imaging capabilities and the current state of the problem. Complex problems of cardiovascular diseases. 2020; 9 (3): 81-89. DOI: 10.17802/2306-1278-2020-9-3-81-89.

4. Yarilin A.A. Immunology. - M.: GEOTAR-Media, 2010. P. 381

10.Ahn JH et al. Meningeal lymphatic vessels of the skull base drain cerebrospinal fluid. Nature. 2019; 572:62–66. doi : 10.1038/s41586-019-1419-5

5.Ahn JH et al. Meningeal lymphatic vessels of the skull base drain cerebrospinal fluid. Nature. 2019; 572:62–66. doi :10.1038/s41586-019-1419-5.

6.Aspelund A, Antila S, Proulx ST, Karlsen TV, Karaman S, Detmar M, Wiig H, Alitalo K (2015) A dural lymphatic vascular system that drains brain interstitial fluid and macromolecules. J Exp Med 212(7):991–999. https://doi.org/10.1084/jem.20142290 _

7. Ding Z, Fan X, Zhang Y, Yao M, Wang G, Dong Y, Liu J and Sun W (2023) The glymphatic system: a new perspective on brain diseases. Front. Aging neuroscientists. 15:1179988. doi: 10.3389/fnagi.2023.1179988
8.Gao Y, Liu K, Zhu J. Glymphatic system: an emerging therapeutic approach for neurological disorders. Front Mol Neurosci. 2023 Jul 6;16:1138769. doi: 10.3389/fnmol.2023.1138769. PMID: 37485040; PMCID: PMC10359151.
9.Graham MS, Mellinghoff IK (2021) Meningeal lymphatics prime tumor immunity in glioblastoma. Cancer Cell 39(3):304–306. https://doi.org/10.1016/j. ccell.2021.02.012
10.Jha RM , Kochanek PM, Simard JM. Pathophysiology and treatment of cerebral edema in traumatic brain injury. Neuropharmacology. 2019 Feb ;145 (Pt B):230-246. doi: 10.1016/j.neuropharm.2018.08.004. Epub 2018 Aug 4. PMID: 30086289; PMCID: PMC6309515.
11.Ji S, Yu X, Xu W, et al. The role of the lymphatic system in the formation of cerebral edema after ischemic stroke. Exp Neurol. 2021. March;113685 .
12. Cuff , Nicholas et al. Post-traumatic cerebral edema: pathophysiology, key players, and current management. Archives of Medical Research, [Sl], vol. 10, no. Oct 10 2022. ISSN 2375-1924. Available at: <https://esmed.org/MRA/mra/article/view/3297 > . doi.org/10.18103/mra.v10i10.3297.
13.Christensen J. , Wright DK, Yamakawa GR et al. Repeated mild traumatic brain injury alters the rate of glymphatic clearance in the limbic structures of female adolescent rats. scientific representative. 2020 Apr ;10:6254 .
14.Fan Y, Shi X, Ren R, et al. Pituitary adenylate cyclase-activating polypeptide attenuates cerebral edema by protecting the blood-brain barrier and glyphatic system after subarachnoid hemorrhage in rats. Neurotherapy . September 2020; 17: 1954–1972.
15.Foldi M. et al. Uber Wirkungen der Unterbindung der Lymphgefasse und Bohr T, Hjorth PG, Holst SC, Hrabětová S, Kiviniemi V, Lilius T, Lundgaard I, Mardal KA, Martens EA, Mori Y, Nägerl UV, Nicholson C, Tannenbaum A, Thomas JH, Tithof J , Benveniste H, Iliff JJ, Kelley DH, Nedergaard M. The glymphatic system: Current understanding and modeling. iScience. 2022 Aug 20 ;25 (9):104987. doi: 10.1016/j.isci.2022.104987. PMID: 36093063; PMCID: PMC9460186.
16. Liu, Q., Zhu, J., Chang, Y., Lin, Z., Shi, Z., Li, H., et al. (2021). Reducing cerebral edema helps restore the function of the lymphatic system after status epilepticus. JCI Insight 6: e151835. DOI: 10.1172/jci.insight.151835
17. Lohela TJ, Lilius TO, Nedergaard M. The glymphatic system: implications for drugs for central nervous system diseases. Nat Rev Drug Discov . 2022 Aug 10. doi : 10.1038/s41573-022-00500-9. Epub ahead of print. PMID: 35948785.
18.Mestre H., Du T., Sweeney AM, Liu G., Samson AJ, Peng W., Christian NM, Frederick FS, Steger FF, Bork PAR etc. The influx of cerebrospinal fluid causes acute ischemic tissue edema. The science. 2020; 367: eaax7171–eaax7224.
19.Proulx ST. Cerebrospinal fluid outflow: a review of the historical and contemporary evidence for arachnoid villi, perineural routes, and dural lymphatics. Cell Mol Life Sci. 2021 Mar ;78 (6):2429-2457. doi: 10.1007/s00018-020-03706-5. Epub 2021 Jan 11. PMID: 33427948; PMCID: PMC8004496.
20. Semyachkina-Glushkovskaya O, Fedosov I, Shirokov A, Vodovozov E, Alekseev A, Khorovodov A, Blokhina I, Terskov A, Mamedova A , Klimova M , Dubrovsky A , Ageev V,

Agranovich I, Vinnik V, Tsven A, Sokolovski S, Rafailov E, Penzel T, Jürgen Kurths J (2021) Photomodulation of lymphatic delivery of liposomes to the brain bypassing the blood-brain barrier: new perspectives for glioma therapy. Nanophotonics 10(12):3215–3227. https://doi.org/10.1515/nanoph-2021-0212.

21.Semyachkina-Glushkovskaya O, Postnov D, Lavrova A, Fedosov I, Borisova E, Nikolenko V, Penzel T, Kurths J, Tuchin V (2021) Biophotonic Strategies of Measurement and Stimulation of the Cranial and the Extracranial Lymphatic Drainage Function. IEEE J Selected Topics in Quantum Electron 27(4):1–13. https://doi.org/10.1109/JSTQE.2020.3045834

22. Xuan X, Zhou G, Chen C, Shao A, Zhou Y, Li X, Zhou J. Glymphatic System: Emerging Therapeutic Target for Neurological Diseases. Oxid Med Cell Longev . 2022 Jun 11; 2022:6189170. doi: 10.1155/2022/6189170. PMID: 35726332; PMCID: PMC9206554.

23. Yankova G, Bogomyakova O, Tulupov A. The glymphatic system and meningeal lymphatics of the brain: new understanding of brain clearance. Rev Neurosci . 2021 Feb 23; 32(7):693-705. doi: 10.1515/revneuro-2020-0106. PMID: 33618444.

24.Eshonov O. Sh ., Yarashev AR A New Scale for Assessing the Severity of the Condition and Prediction of Neuroreanimational Patients. European journal of life safety and stability (ejlss).Volume 28, April -2023 ||Page 91-99.

25. Eshonov O.Sh. Lymphotropic therapy for the prevention of intracranial infectious and inflammatory complications in traumatic brain injury. Journal of Universal Science Research 30.03.2023.pp.56-60.

26 . Eshonov O. Sh., Boltayev EB Lymphotropic Therapy in Patients with Acute Brain Injury in the. International Journal of Health Systems and Medical Science Volume 1 | #6 | Dec-2022.p.368-373.

2 7.Eshonov O.Sh., Yarashev AR Diagnostics of microcirculation disturbances in critical conditions in patients with acute ceremonial circulation disorder and severe cranio-brain international injury journal of medical sciences and clinical research.Volume 03 Issue 01-2023.p.21-28.

28. Yarashev AR, Eshonov O.Sh. Monitoring of hematological indicators in predicting outcomes in critical conditions in neurocritical patients. Vestnik TMA No. 1, 2023. pp. 180-187.

29. Yarashev A.R Eshonov O.Sh. Neuroimaging monitoring for evaluating the effectiveness of lymphotropic therapy in stroke. SCHOLAR. ISSN: 2181-4147 volume 1 | issue 28 | 2023. pp. 359-366. https://t.me/openscholar Multidisciplinary Scientific Journal October, 2023.