Thematic Section: Biochemical Research. **Full Paper**
Subsection: Medicinal Chemistry. *The Reference Object Identifier* – ROI: jbc-01/20-63-7-119
The Digital Object Identifier – DOI: 10.37952/ROI-jbc-01/20-63-7-119
Submitted on July 21, 2020.

Assessment of the severity of endogenous intoxication in Alzheimer's disease

© **Maria G. Engalycheva**,*+ **Maria A. Fomina**, **Dmitry S. Petrov**,
Daria I. Miroshnikova, and **Natalia V. Korotkova**
Ryazan State Medical University. Vysokovoltnaya St., 9. Ryazan, 390026. Russia.
Phone: +7 (4912) 97-18-98. E-mail: biochem_rzn@mail.ru

*Supervising author; +Corresponding author

Keywords: endogenous intoxication, Alzheimer's disease, neurodegeneration, leukocytes, low and medium molecular weight substances

Abstract

The development of neurodegenerative pathologies, among which the leading positions worldwide belong to Alzheimer's disease, is accompanied by the activation of free radical processes in the tissues of the brain and in the patient's body as a whole, which leads to the accumulation of products of oxidative modification of proteins, lipids, nucleic acids, and the formation of a syndrome of endogenous intoxication. An integral indicator reflecting the severity of this syndrome is the level of substances of low and medium molecular weight in various biological media. It is known that changes at the molecular level in Alzheimer's disease occur 5-10 years before the clinical manifestation of pathology. The development of polymodal panels for biochemical screening, diagnostics, monitoring of the course of pathology is underway. The aim of this study was to determine the severity of endogenous intoxication in patients with Alzheimer's disease and vascular dementia. The object of the study was the blood plasma of patients, as well as fractionated leukocytes - mononuclear and polymorphonuclear. The choice of biological material for the study is dictated by the need to search for a prognostic marker of the disease available for diagnosis, as well as by the accumulated theoretical material on various metabolic changes in peripheral blood cells in neurodegenerative diseases. According to the results of the study, it was found that in patients with Alzheimer's disease in mononuclear leukocytes of peripheral blood, the level of substances of low and medium molecular weight is higher than in patients with vascular dementia and patients without signs of neurodegeneration. In addition, in this fraction of leukocytes, the concentration of hypoxanthine, inosine, xanthosine and their derivatives is high, which may be a consequence of the oxidative modification of nucleic acids in the cells under study.

References

[1] S. Shadfar, C.J. Hwang, M.S. Lim, D.Y. Choi, J.T. Hong. Involvement of inflammation in Alzheimer's disease pathogenesis and therapeutic potential of anti-inflammatory agents. *Arch Pharm Res*. **2015**. Vol.38. No.12. P.2106-2119. doi:10.1007/s12272-015-0648-x

[2] P. Agostinho, R.A. Cunha, C. Oliveira. Neuroinflammation, oxidative stress and the pathogenesis of Alzheimer's disease. *Cur Pharm Des.* **2010**. Vol.16. No.25. P.2766-2778. DOI: 10.2174/138161210793176572

[3] K. Blennow, H. Zetterberg. Fluid biomarker-based molecular phenotyping of Alzheimer's disease patients in research and clinical settings. *Prog Mol Biol Trans Sci*. **2019**. No.168. P.3-23.

[4] P. Lewczuk, P. Riederer, S.E. O'Bryant, M.M. Verbeek, B. Dubois, P.J. Visser, K.A. Jellinger, S. Engelborghs, A. Ramirez. Cerebrospinal fluid and blood biomarkers for neurodegenerative dementias: An update of the Consensus of the Task Force on Biological Markers in Psychiatry of the World Federation of Societies of Biological Psychiatry. *W J Biol Psy*. **2018.** Vol.19. No.4. P.244-328.

[5] J.L. Molinuevo, S. Ayton, R. Batrla, M.M.Bednar, T. Bittner, J. Cummings, A.M. Fagan, H. Hampel, M.M. Mielke, A. Mikulskis, S. O'Bryant, P. Scheltens, J. Sevigny, L.M. Shaw, H.D. Soares, G. Tong, J.Q. Trojanowski, H. Zetterberg, K. Blennow. Current state of Alzheimer's fluid biomarkers. *Acta Neuropathologyca.* **2018**. Vol.136. No.6. P.821-853.

[6] Z. Chen, C. Zhong. Oxidative stress in Alzheimer's disease. *Neurosci Bull*. **2014**. Vol.30. No.2. P.271-281. doi: 10.1007/s12264-013-1423-y.

[7] E. Tönnies, E. Trushina. Oxidative stress, synaptic dysfunction, and Alzheimer's disease. *J Alzh Dis*. **2017**. Vol.57. No.4. P.1105-1121. doi: 10.3233/JAD-161088.

[8] M.G. Uzbekov, I.Ya. Gurovich, S.A. Ivanova. Potential biomarkers of mental illness in a systems approach. *Soc Clin Psy*. **2016**. No.26. P.77-93. (russian)

[9] N.M. Krotenko, A.S. Boyko, E.M. Epanchintseva, S.A. Ivanova. Indicators of oxidative stress and endogenous intoxication in peripheral blood in patients with exogenous organic disorders in the dynamics of pharmacotherapy. *Bul. Sib. Med*. **2012**. No.1. P.179-185. (russian)
[10] S.N. Shikhov. Serological markers of endogenous intoxication in a comprehensive assessment of the rehabilitation potential of patients with ischemic stroke. *Soc Clin Psy*. **2011**. Vol.3. No.21. P.54-57. (russian)
[11] V.A. Nikolskaya, Yu.D. Danilchenko, Z.N. Memetova. The biochemical aspect of considering the role of average mass molecules in the body. *Scientific Notes of V.I. Vernadsky Crimean Federal University. Biology. Chemistry.* **2013**. Vol.26. No.65. P.139-145. (russian)
[12] V.V. Alekseev. Medical laboratory technology: a guide to clinical laboratory diagnostics under. ed. A.I. Karpishchenko. 3rd ed., Rev. and add. T.2. *Moscow: GEOTAR-Media*. **2013**. P.755-762. (russian)
[13] V.V. Alferova, M.G. Uzbekov, E.Yu. Misionzhnik, E.V. Lukyanyuk, A.B. Gekht, V.M. Shklovsky, M.R. Guseva. Endogenous intoxication and compensation reactions in the recovery period of ischemic stroke. *S.S. Korsakov Journal of Neurology and Psychiatry.* **2010**. Vol.110. No.4. P.36-41. (russian)
[14] B. Galunska, D. Paskalev, T. Yankova, P. Chankova. Two-faced Janus of biochemistry: is uric acid an oxidant or an antioxidant? *Nephrology.* **2004**. Vol.8. No.4. P.25-31. (russian)
[15] T. Mikami, Y. Yoshino, A. Ito. Does the relationship exist between the urate pool in the body and lipid peroxidation during exercise? *Free Rad Res.* **2000**. Vol.32. No.1. P.31-39.
[16] N. Esteras, C. Alquézar, de la Encarnación A., Á. Martín-Requero. Lymphocytes in Alzheimer's disease pathology: Altered signaling pathways. *Cur Alzh Res*. **2016**. Vol.13. No.4. P.439-49. DOI: 10.2174/1567205013666151116124912
[17] M.T. Heneka, M.J. Carson, J. El Khoury, G.E. Landreth, F. Brosseron, D.L. Feinstein, A.H. Jacobs, T. Wyss-Coray, J. Vitorica, R.M. Ransohoff. Neuroinflammation in Alzheimer's disease. *Lancet Neurol*. **2015**. No.14. P.388-405.
[18] P.A. Ivanov, A.A. Shmakova, N.M. Mikhailova. Neutrophil's functional state in Alzheimer's disease. *VII International symposium «Interaction of the nervous and immune systems in health and disease», St. Petersburg.* **2019**.
[19] J. Popp, A. Oikonomidi, D. Tautvydaitė, L. Dayon, M. Bacher, E. Migliavacca, H. Henry, R. Kirkland, I. Severin, J. Wojcik, G.L. Bowman. Markers of neuroinflammation associated with Alzheimer's disease pathology in older adults. *Brain Behav Immunol*. **2017**. No.62. P.203-211. doi: 10.1016/j.bbi.2017.01.020.
[20] C. Achilli, A. Ciana, G. Minetti. Brain, immune system and selenium: a starting point for a new diagnostic marker for Alzheimer's disease? *Perspect Public Health*. **2018**. Vol.138. No.4. P.223-226. doi: 10.1177/1757913918778707.
[21] A. Mietelska-Porowska, U.T. Woida. Lympocytes and Inflammatory Mediators in the Interplay between Brain and Blood in Alzheimer's Disease: Potential Pools of New Biomarkers. *J Immunol Res.* **2017**. 4626540 doi: 10.1155/2017/4626540
[22] A.V. Shcherina, K.E. Kroshchikhina. Free radical activity in the pathogenesis of brain tumors. *Eruditio Juvenium.* **2018**. No.1. P.6-12. (russian)
[23] M.A. Bradley-Whitman, M.D. Timmons, T.L. Beckett, M.P. Murphy, B.C. Lynn, M.A. Lovella. Nucleic acid oxidation: an early feature of Alzheimer's disease. *J. Neurochem*. **2014**. Vol.128. No.2. P.294-304.