



THE CONTENT OF ENDOTHELIN AND HOMOCYSTEINE IN BLOOD AND LACRIMAL FLUID IN PATIENTS WITH HYPERTENSIVE RETINOPATHY

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Abstract

Currently, endothelin-1 (ET-1) is considered as a marker and predictor of the severity and outcome of many diseases associated with vascular pathology. Thus, the determination of ET-1 content in blood plasma is recommended to be used as a laboratory test in patients with arterial hypertension (AH) to determine the severity of vascular complications

Keywords: arterial hypertension, retina, endothelin, homocysteine

Introduction

Currently, endothelin-1 (ET-1) is considered as a marker and predictor of the severity and outcome of many diseases associated with vascular pathology. Thus, the determination of the content of ET-1 in blood plasma is recommended to be used as a laboratory test in patients with arterial hypertension (AH) to determine the severity of vascular complications. ET-1 is one of the most powerful vasoconstrictors. It is an oligopeptide that consists of 21 amino acids and is formed from proendothelin-1 under the influence of an endothelin -converting enzyme. ET-1 secretion is influenced by numerous physical (hypoxia) and humoral factors, such as cytokines. The concentration of ET-1 in blood plasma is usually insignificant (0.26-0.5 fmol / ml). At the same time, the role of ET-1 as a circulating hormone that affects hemodynamic parameters has been proven. Homocysteine is a natural sulfur-containing amino acid that is not found in proteins. There is information about the relationship between the exchange of endothelins and homocysteine. Elevated levels of ET-1 and homocysteine contribute to the death of ganglion cells in the retina, i.e. the development of hypertensive neuropathy and retinopathy Thus, in the pathogenesis of violations of regional microcirculation in the retina and the development of hypertensive retinopathy and neuroretinopathy, endothelins and homocysteine components play a large role. The question of their relationship in ophthalmic pathologies remains open.





The aim of the work is to study the content of endothelin and homocysteine in the blood and lacrimal fluid in patients with arterial hypertension.

Material and Methods

We examined 18 patients with HC (stages 1–2), mean age 45 ± 4.3 years. The control group included 15 people who did not have a history of arterial hypertension. material for laboratory research were: serum blood (SC) and lacrimal fluid (CL). In all patients, tears were collected with a microcannula . from lower conjunctival vault eyes in dry sealed test tube. Blood took away on an empty stomach in morning clock from ulnar veins in dry centrifuge test tube . Determination of the content of ET-1 was carried out using the enzyme immunoassay method (Biomedica , Austria). Determination of the level of homocysteine in the blood serum was carried out by enzyme immunoassay using a set of the firm " Human ". All measurements were carried out on a plate analyzer (LM 01A, Immunotech , Czech Republic). Statistical processing of the obtained results was carried out using the program Statistica . Significance of differences was determined using Student's t-test.

Results and Discussion

As a result of the study in patients with HC , an increase in the content of ET-1 and homocysteine in the lacrimal fluid and blood was revealed. A significant increase ($p < 0.005$) by 3 times in the content of ET-1 and homocysteine in the lacrimal fluid with HC (4.9 ± 0.48 fmol /ml) compared with the control group (0.87 ± 0.4 fmol /ml) was shown.) .In the blood serum, there was a tendency to increase the level of ET-1 (1.9 ± 1.0 fmol /ml, the norm is 2.3 ± 0.6 fmol /ml). Patients also showed a significant increase in the content of homocysteine in the tear (49.1 ± 3.0 mmol / ml, the norm is 30.6 ± 2.8 mmol / ml; $p < 0.07$) and a tendency to increase the level of homocysteine in the blood serum (142.7 ± 39.9 mmol / ml, the norm is 113.3 ± 3.8 mmol / ml). However, no significant correlation was found between the levels of ET-1 and plasminogen in blood and tears in the examined patients. Based on the above, the data obtained indicate a significant (4.5-5.0 times) increase in the content of ET-1 and homocysteine in tears in patients with HC. At the same time, there was a tendency to increase the level of ET-1 and homocysteine in the general bloodstream. When studying the literature, we did not find information on the content of ET-1 in the lacrimal fluid in HC . Apparently, a local increase in the content of ET-1 and homocysteine is promoted by local hypoxia and ischemia, characteristic of HC , which enhance the transition of proendothelin to ET-1. In addition to its vasoconstrictive action, ET-1 triggers hyperplasia reactions, which can lead to the progression of



retinopathy . An increased content of ET-1 in the tissues and liquid media of the eye is one of the factors in the development of hypertensive neuroretinopathy in AH, as it leads to ischemia and hypoxia of the optic nerve due to a deterioration in its blood supply, which is the cause of ganglion cell death . At the same time, ET-1 enhances the formation of nitric oxide (NO), which also promotes apoptosis of retinal ganglion cells. A local increase in the level of homocysteine in HC may indicate its insufficient splitting, which leads to inhibition of the local fibrinolytic potential. A local increase in the content of ET-1 and homocysteine and a simultaneous decrease in the activity of fibrinolysis are among the most important causes of impaired microcirculation and microthrombosis of blood vessels in the retina in HC .

Conclusion

Thus, endothelin-1 (ET-1) and homocysteine (HC) - this powerful vasoconstrictors that are capable of intensify products cytokines chemoattractant molecules, potentiate synthesis And secretion of various growth factors such as fibroblast growth factor, epiregulin . A significant increase in the level of ET-1 and HC in the systemic circulation with cardiovascular diseases noted many researchers , but there are only single messages on marker research endothelial dysfunction in patients with retinal lesions on the early stages arterial hypertension . In this regard, we have shown that in eye diseases, in the pathogenesis of which local and systemic microcirculation disorders play an important role, there is a significant increase in the content of ET-1 and HC in the lacrimal fluid and blood . Measurement of the content of ET-1 and HC in tears and blood can be an additional informative and non-invasive method for predicting, assessing the severity and monitoring the treatment of local and systemic microcirculatory disorders in the eye.

Literature

1. Barsukov A.V., Shcherbakova K.A., Maltsev D.S., Burnasheva M.A., Kulikov A.N. The relationship of indicators of the state of the retina with other organ changes in uncomplicated hypertension // Arterial hypertension. 2020. V. 26. No. 4. S. 410-420.
2. Bely Yu.A., Tereshchenko A.V., Teschin V.V., Bashuk V.V. Ultrasonic criteria for the course of thrombosis of the central retinal vein // Kuban Scientific Medical Bulletin. 2011. No. 1 (124). pp. 48-51.
3. Borisova A.V., Shchuko A.G., Akulenko M.V., Bukina V.V. Evaluation of structural and functional changes in the retina in the treatment of diabetic retinopathy using





- various laser technologies// XI All-Russian scientific conference of young scientists "Actual problems of ophthalmology".-2016.-p.27-31
4. Gavrilova N.A., Ioileva E.E., Gadzhieva N.S., Tishchenko O.E., Kutrovskaya N.Yu., Kuzmina A.V., Zinovieva A.V. Diagnostic capabilities of optical coherence tomography of the retina during compression in the chiasmal-sellar region // *Ophthalmology*. 2020. V. 17. No. 1. S. 5-12.
 5. Danilenko O.A., Markova E.V. The study of the antiaggregatory activity of the vascular wall in patients with arterial hypertension who have undergone occlusive lesions of the vessels of the retina and optic nerve // *Medical Bulletin of Bashkortostan*. 2017. Vol. 12. No. 2 (68). pp. 61-63.
 6. Direev A.O., Munts I.V., Kuleshova O.N., Maszrova E.V., Ryabikov A.N., Malyutina S.K. Pathological changes in the retina in cardiovascular diseases and diabetes // *Atherosclerosis*. 2020. V. 16. No. 2. - S. 49-62.
 7. Zadionchenko V.S., Adasheva T.V., Shamshinova A.M., Arakelyan M.A. The eye is a mirror of cardiovascular disease . in the relationship between the functional state of the retina and the severity of arterial hypertension // *Rational pharmacotherapy in cardiology*. 2011. V. 7. No. 2. S. 185-192.
 8. Carl E. Glaucoma and arterial hypertension // *Russian Journal of Ophthalmology*. -2016. T. 9. No. 1. - S. 105-111.
 9. Kubarko A.I., Bur E.A., Kubarko Yu.A., Avdey L.L. The state of retinal vessels, light sensitivity of the visual system and their relationship with structural changes in the brain in patients with arterial hypertension.// *Urgent Cardiology and Cardiovascular Risks*, 2017, Vol.
 10. Makhkamova D.K. Etiopathogenesis of the development of ocular ischemic syndrome // *Bulletin of ophthalmology*. 2017. V. 133. No. 2. S. 120-124.
 11. Midlenko T.A., Vozhennikov A.Yu. Hypertensive remodeling of the central retinal artery in patients with arterial hypertension of 1-2 degrees // *Modern problems of science and education*. 2014. No. 6. S. 1168.
 12. Moshetova L.K., Vorobieva I.V., Dgebuadze A. Impaired ocular blood flow in arterial hypertension . with systemic and local changes // *Tauride Medical and Biological Bulletin*. 2018. V. 21. No. 3. S. 186-193.
 13. Munts I.V., Malyutina S.K., Gusarevich O.G., Shapkina M.Yu., Ryabikov A.N. Fundus changes and cardiovascular diseases // *Atherosclerosis*. 2017. V. 13. No. 1. S. 29-34.
 14. Ponomareva M.N., Klyashev S.M., Klyasheva Yu.M. and other Thrombosis of the central retinal vein associated with the pathology of the cardiovascular and hematopoietic systems // *Ural Medical Journal*. 2019. No. 9 (177). pp. 67-72.





15. Khokhlova D. Yu., Drozdova E. A. Analysis of systemic risk factors in patients with retinal vein occlusion // Medical Bulletin of Bashkortostan. 2014. No. 2. –S.18-21
16. Shelkovnikova T.V., Takhchidi Kh.P., Vavin G.V., Barkova N.Yu., Shishlyannikova N.Yu. Complex treatment of macular edema in patients with retinal vein occlusion and disorders in the hemostasis system. Clinical ophthalmology. 2018. No. 4. pp.203-208
17. Shcherbakova, K.A. Hypertensive angiopathy of the retina as a target organ and marker of cardiovascular risk / K.A. Shcherbakova, M.V. Yasenovets , A.V. Barsukov // Doctor. - 2018. - No. 10. - P.18-21.
18. Arriozola- Rodriguez KJ, Serna-Ojeda JC, Martinez- hernandez VA, Rodriguez-Loaiza JL Hypertensive Retinopathy as the First Manifestation of Advanced Renal Disease in a Young Patient: Report of a Case Case Reports in Ophthalmology. 2015 ;6 (3):415–419.
19. Bertelli PM, Pedrini E., Guduric- Fuchs J., Peixoto E., Pathak V., Stitt AW, Medina RJ Vascular regeneration for ischemic retinopathies: Hope from cell therapies. // Curr . Eye Res. 2020; 45(3): 372–384.
20. Callizo J., Feltgen N., Pantenburg S., Wolf A., Neubauer AS, Jurklies B., Wachter R., Schmoor C., Schumacher M., Junker B., Pielen A. Cardiovascular risk factors in central retinal artery occlusion : results of a prospective and standardized medical examination. //Ophthalmology. 2015; 122(9): 1881–1888.
21. Călugăru D, Călugăru M, Țălu Ș. Bevacizumab in the treatment of acute central/hemicentral retinal vein occlusions. //Rom J Ophthalmol . 2016 Jul-Sep;60(3):145-152
22. Chandra A., Seidemann SB, Claggett BL, Klein BE, Klein R., Shah AM, Solomon SD The association of retinal vessel calibers with heart failure and longterm alterations in cardiac structure and function: the Atherosclerosis Risk in Communities (ARIC) Study. //Eur. J. Heart failure. 2019; 21(10): 1207–1215.
23. Cousins CC, Pan BX, Chou JC, Shen LQ, Gordon MO, Kass MA, Ritch R, Pasquale LR. Densitometric Profiles of Optic Disc Hemorrhages in the Ocular Hypertension Treatment Study.//Am J Ophthalmol . -2020-Sep;217:10-19
24. Donati S; Maresca AM; Cattaneo J; Grossy A; Mazzola M Optical coherence tomography angiography and arterial hypertension: A role in identifying subclinical microvascular damage?// European journal of ophthalmology .- 2021 Jan; Vol. 31(1), pp. 158-165;
25. Harjasouliha A, Raiji V, Garcia Gonzalez JM. Review of hypertensive retinopathy. // Dismon. 2017 ;63: 63–9.



26. Hosari S, Hohberger B, Theelke L, Sari H, Lucio M, Mardin CY. OCT Angiography: Measurement of Retinal Macular Microvasculature with Spectralis II OCT Angiography - Reliability and Reproducibility.// *Ophthalmologica* . 2020 ;243 (1):75-84.
27. Križanović A, Bjeloš M, Bušić M, Elabjer BK, Rak B, Vukojević N. Macular perfusion analyzed by optical coherence tomography angiography after uncomplicated phacoemulsification: benefits beyond restoring vision. // *BMC Ophthalmol* . 2021 Feb 5 ;21 (1):71.
28. Lee WH, Park JH, Won Y, Lee MW, Shin YI, Jo YJ, Kim JY. Retinal Microvascular Change in Hypertension as measured by Optical Coherence Tomography Angiography. // *Sci Rep*. 2019 Jan 17;9(1):156
29. Meyer M.L.; Klein B.E.; Klein R; Palta P Central arterial stiffness and retinal vessel calibers: the Atherosclerosis Risk in Communities Study-Neurocognitive Study. // *Journal of hypertension* .- 2020 Feb; Vol. 38(2), pp. 266-273
30. Milioti G, Langenbacher A, Seitz B, Löw U. Der Einfluss von morphologischen und funktionellen Parametern auf die okulare Pulsamplitude : eine Analyse bei verschiedenen Glaukomformen und okulärer Hypertension [Effect of Morphological and Functional Parameters on Ocular Pulse Amplitudes: An Analysis in Ocular Hypertension and Different Types of Glaucoma]. // *Klin monbl Augenheilkd* . Feb 2017 ;234 (2):223-230.
31. Pascual-Prieto J; Burgos- Blasco B; Utility of optical coherence tomography angiography in detecting vascular retinal damage caused by arterial hypertension.// *European journal of ophthalmology* . - 2020 May; Vol. 30(3), pp. 579-585;
32. Pesin N, Mandelcorn ED, Felfeli T, Ogilvie RI, Brent MH. The role of occult hypertension in retinal vein occlusions and diabetic retinopathy.// *Can J Ophthalmol* . 2017 Apr;52(2):225-228
33. Pilotto E, Leonardi F, Stefanon G, Longhin E, Torresin T, Deganello D, et al. Early retinal and choroidal OCT and OCT angiography signs of inflammation after uncomplicated cataract surgery. // *BrJ Ophthalmol* . 2019 ;103: 1001–7.
34. Santana- Garrido Á, Reyes-Goya C, Pérez-Camino MC, André H, Mate A, Vázquez CM. Retinoprotective Effect of Wild Olive (Acebuche) Oil-Enriched Diet against Ocular Oxidative Stress Induced by Arterial Hypertension.// *Antioxidants (Basel)*. 2020 Sep 18;9(9):885
35. Wagner SK, Fu DJ, Faes L., Liu X., Huemer J., Khalid H., Ferraz D., Korot E., Kelly C., Balaskas K., Denniston AK, Keane PA Insights into systemic disease through retinal imaging -based oculomics . // *translate . vision sci. & Technol*. 2020; 9(2):6–6.

