SECTION 4. MEDICAL AND BIOLOGICAL SCIENCES: INNOVATIONS OF THE FUTURE

DOI https://doi.org/10.30525/978-9934-26-655-3-24

THE EFFECT OF ADRENALINE-MEDIATED STRESS ON NITROSATIVE STATUS AND THE DYNAMICS OF INTRAOCULAR FLUID IN EXPERIMENTAL ANIMALS

ВПЛИВ АДРЕНАЛІН-ОПОСЕРЕДКОВАНОГО СТРЕСУ НА НІТРОЗАТИВНИЙ СТАТУС І ДИНАМІКУ ВНУТРІШНЬООЧНОЇ РІДИНИ У ЕКСПЕРИМЕНТАЛЬНИХ ТВАРИН

Mikheytseva I. M.
Doctor of Biological Sciences, Professor, Head of the Biochemistry Department State Institution «The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine» Odesa, Ukraine

Михейцева І. М.
доктор біологічних наук, професор, завідувачка лабораторії біохімії Державна установа «Інститут очних хвороб і тканинної терапії імені В. П. Філатова Національної академії медичних наук України» м. Одеса, Україна

Storozhuk N. V.
Junior Researcher at the Biochemistry Department State Institution «The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine» Odesa, Ukraine

Сторожук Н. В.
молодший науковий співробітник лабораторії біохімії Державна установа «Інститут очних хвороб і тканинної терапії імені В. П. Філатова Національної академії медичних наук України» м. Одеса, Україна

Alobaisi Mayar
Junior Researcher at the Biochemistry Department State Institution «The Filatov Institute of Eye Diseases and Tissue Therapy of the National Academy of Medical Sciences of Ukraine» Odesa, Ukraine

Алобісі Маяр
молодший науковий співробітник лабораторії біохімії Державна установа «Інститут очних хвороб і тканинної терапії імені В. П. Філатова Національної академії медичних наук України» м. Одеса, Україна

The involvement of gaseous transmitters, in particular nitric oxide (NO), in many pathological conditions is being actively studied. This important intercellular messenger is formed intracellularly, but its gaseous nature allows it to diffuse through cell membranes. Nitric oxide plays a role in smooth muscle vasodilation, neurotransmission, and cytotoxicity.

The study of the effect of nitric oxide on the dynamics of intraocular fluid (IOF) is a promising area of experimental and clinical ophthalmology, taking into account the significance of these mechanisms in the pathogenesis of severe ocular diseases such as various types of glaucoma. This applies both to endogenous NO and to NO introduced exogenously in the form of medicinal preparations for therapeutic purposes.

Adrenaline-mediated stress affects IOF through activation of α- and β-adrenoreceptors in the structures of the anterior segment of the eye. Stimulation of β_2-adrenoreceptors of the ciliary epithelium leads to an increase in IOF secretion, which contributes to an increase in intraocular pressure (IOP). At the same time, activation of α-adrenoreceptors may enhance uveoscleral outflow, creating a compensatory mechanism. Under conditions of acute stress, these effects are transient; however, with chronic adrenaline-mediated activation, the balance between IOF production and outflow may shift toward a hypertensive response, which is considered one of the pathophysiological risk factors for glaucomatous damage [1, p. 453–505]. At the same time, adrenaline can modulate ocular hydrodynamics not only through a direct effect on adrenoreceptors of the ciliary body and trabecular meshwork, but also indirectly through the nitric monoxide system [2, p. 1614–1620].

Materials and methods. The experiment was conducted on adult chinchilla rabbits, which were randomly divided into two groups. Adrenaline-induced stress (AIS) was induced by intravenous administration of an adrenaline solution into the ear vein for 3 months according to a scheme developed by us [3]. The control group consisted of intact animals. Parameters of intraocular fluid dynamics were studied using electronic tonography. After completion of the modeling, after 90 days, the animals were withdrawn from the experiment, and indicators of nitric oxide metabolism, namely the content of nitrate and nitrite anions and the total activity of constitutive NO synthase (endothelial and neuronal), were determined in the tissues of the ocular drainage zone.

Results. It was established that in rabbits with AIS, the level of the stable metabolite of nitric oxide, the nitrate anion, was significantly reduced in the tissues of the drainage zone by 36.5% compared with the control group of animals. The level of nitrite anions after AIS modeling in these tissues was reduced by 44.9% relative to control.

The results of the study also indicate a significant decrease in the activity of the total fraction of endothelial and neuronal nitric oxide synthase – cNO synthase – in the tissues of the drainage zone by 45.8% in animals with AIS on day 90 of the study compared with control.

In vivo study of intraocular fluid dynamics in experimental animals under conditions of chronic adrenaline stress modeling showed the following results. On day 90 of the experiment, ocular hydrodynamics were significantly impaired. The rate of IOF outflow from the anterior chamber of the eye under AIS was reduced by 36.8%. At the same time, the IOP level in rabbits under stress conditions was increased by 46.7%. Correlations were established between indicators of nitric oxide metabolism and ocular hydrodynamics. Correlation analysis showed an inverse correlation between IOP indicators and NO synthase activity.

Our data are consistent with the opinion of the authors [4], who also believe that the effect of adrenaline on ocular hydrodynamics is dual in nature and is determined by the relationship between NO-mediated enhancement of outflow and adrenaline-induced changes in intraocular fluid secretion.

Thus, adrenaline can modulate ocular hydrodynamics not only through a direct effect on adrenoreceptors of the ciliary body and trabecular meshwork, but also indirectly through the nitric monoxide (NO) system. A decrease in eNOS activity leads to a reduction in nitric oxide production, which was confirmed by our finding of decreased levels of nitric oxide metabolites – nitrite and nitrate anions – in the tissues of the ocular drainage zone of experimental animals. Such metabolic changes lead to contracture of smooth muscle and contractile cells of the trabecular meshwork and Schlemm's canal, increased resistance to IOF outflow, and elevated IOP.

Bibliography:

1. Ruan Y., Buonfiglio F., Gericke A. Adrenoceptors in the eye: physiological and pathophysiological relevance. *Handbook of Experimental Pharmacology*. 2024. Vol. 285. P. 453–505. DOI: 10.1007/164_2023_702.

2. Garhöfer G., Schmetterer L. Nitric oxide: a drug target for glaucoma revisited. *Drug Discovery Today*. 2019. Vol. 24. P. 1614–1620. DOI: 10.1016/j.drudis.2019.05.033.

3. Патент України № 61478. Спосіб моделювання адреналін-індукованого стресу. Опубл. 20.07.2011.

4. Han B., Song M., Li L., Sun X., Lei Y. The application of nitric oxide for ocular hypertension treatment. *Molecules.* 2021. Vol. 26, № 23. Article 7306. DOI: 10.3390/molecules26237306.