SECTION 3. MEDICAL AND BIOLOGICAL SCIENCES: INNOVATIONS OF THE FUTURE

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THERAPY WITH THE ANGIOTENSIN-CONVERTING ENZYME INHIBITOR ZOFENOPRIL AS A NEW DIRECTION IN THE TREATMENT OF PRIMARY GLAUCOMA

ТЕРАПІЯ ІНГІБІТОРОМ АНГІОТЕНЗИН-ПЕРЕТВОРЮЮЧОГО ФЕРМЕНТУ ЗОФЕНОПРІЛОМ ЯК НОВІТНІЙ НАПРЯМОК ЛІКУВАННЯ ПЕРВИННОЇ ГЛАУКОМИ

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Primary Open-Angle Glaucoma (POAG) remains one of the leading causes of visual impairment and blindness among the working-age population, making it a significant medical and social issue in the modern world. Despite treatment withexisting treatments, the problem of effective therapy and prevention of glaucoma complications remains relevant today [13, p. 2087]. Currently, glaucoma is considered a chronic multifactorial optic neuropathy characterized by degenerative and dystrophic changes ranging from the retina to the cortical part of the visual analyzer, with metabolic and functional disorders at its core [1, p. 172; 2, p. 1; 12, pp. 10, 17].

Scientific studies indicate that oxidative stress [7, p. 1] and endothelial dysfunction, involving an imbalance of vasoconstrictive and vasodilatory compounds, play a significant role in the development of glaucoma. Disruptions in the levels of vascular tone regulators (such as endothelin-1 and nitric oxide) correlate with intraocular pressure (IOP) [8, p. 5; 10, pp. 1, 8]. Recently, the role of gaseous transmitters such as endogenous nitric oxide (NO) and hydrogen sulfide (H_2S) in the pathogenesis of various diseases, including glaucoma, has been actively studied [6, p. 4; 7, p. 3]. H_2S is of particular interest because, in addition to its cytoprotective and antioxidant properties, it has a regulatory effect on metabolism [7, pp. 3, 6].

Modern scientific literature places considerable emphasis on studying the physiological effects of the angiotensin-converting enzyme (ACE) inhibitor zofenopril. Zofenopril has been shown to improve vascular function in animal models of spontaneous hypertension, an effect associated with H_2S release [4, pp. 1, 141]. The specific properties of zofenopril, including its cardioprotective action and antioxidant effect due to its thiol groups, significantly expand its potential applications [3, p. 1; 5, p. 7].

Zofenopril increases endothelial NO synthase activity, leading to the production of physiological levels of NO [5, p. 5]. In addition to H_2S, this drug induces endothelial NO production, which accounts for its vasodilatory effects [5, pp. 5, 6, 11]. It is known that ACE inhibitors can influence IOP by reducing angiotensin II levels in the aqueous humor, affecting uveoscleral outflow, and slowing fluid formation by reducing blood flow in the ciliary body [9, pp. 125, 126].

Some studies suggest that drugs blocking the renin-angiotensin system, such as ACE inhibitors, could serve as potential anti-glaucoma agents in the future. The IOP-lowering effect of enalapril and ramipril has been demonstrated in models of acute and chronic ocular hypertension [11, p. 1]. Given zofenopril's potential as an H_2S donor [4, p. 143] and the lack of publications on its possible use in treating POAG, studying its effects on the key pathogenic mechanisms of this disease appears promising.

Thus, our objective was to investigate NO metabolism disorders (NO metabolites—nitrate anions (NO^{-3}), nitrite anions (NO^{-2}), and total

constitutive NO synthase (cNO synthase) activity), the potential regulation of endogenous H_2S content in the trabecular meshwork, retina, and optic nerve tissues of rabbits with adrenaline-induced glaucoma (AIG) using the ACE inhibitor zofenopril, as well as to study IOP changes under these experimental conditions.

AIG was modeled in rabbits using adrenaline tartrate solution (1.80 mg/mL), with 0.1 mL administered intravenously every other day for three months (40 injections in total). During AIG modeling, some animals received zofenopril orally as a 1 mL aqueous suspension (1 mg/kg body weight) for three months (40 doses in total).

Our studies showed that in AIG rabbits, there was a significant increase in IOP along with a decrease in endogenous H_2S levels, stable NO metabolites (NO^{-2} and NO^{-3}), and total cNO synthase activity in the trabecular meshwork, retina, and optic nerve tissues.

Treatment with zofenopril led to a significant reduction in IOP by 29.6% on day 90, accompanied by increased H_2S levels in the trabecular meshwork tissues (by 36.8%), retina (by 31.5%), and optic nerve (by 28.0%) compared to untreated AIG rabbits.

Zofenopril administration during AIG modeling resulted in a significant increase in NO^{-3} levels in the examined tissues compared to untreated AIG rabbits. Moreover, zofenopril significantly activated cNO synthases in the trabecular meshwork (by 38.7%), retina (by 35.8%), and optic nerve (by 30.6%) relative to untreated AIG animals.

Thus, this new experimental therapy suggests that the ACE inhibitor zofenopril can be used to normalize IOP by regulating cNO synthase activity and endogenous NO^{-3}, NO^{-2}, and H_2S levels in the trabecular meshwork, retina, and optic nerve tissues. This represents a novel approach in treating this ophthalmic disease. The experimentally developed treatment method paves the way for improving conservative therapy for primary glaucoma by assessing its clinical effectiveness.

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