11. ROLE OF MINERALOCORTICOID RECEPTOR PATHWAY IN THE PATHOGENESIS OF DIABETIC RETINOPATHY

Author: Toncoglaz Alexandra

Scientific advisor: Vudu Stela, Assistant Professor, Department of Endocrinology, *Nicolae Testemitanu* State University of Medicine and Pharmacy, Chisinau, Republic of Moldova; Lilia Tacu,MD, PhD, University Assistant, Department of Pathophysiology and Clinical Pathophysiology, *Nicolae Testemitanu* University;

Introduction. Diabetic retinopathy (DR) represents a major cause of irreversible blindness among the working-age population. Aldosterone has an important role in the pathogenesis of DR, through vascular regulation, oxidative stress, inflammation and angiogenesis (neovascularization). Thus, activation of the mineralocorticoid receptor pathway plays multiple roles in the pathogenesis of diabetic retinopathy and understanding these mechanisms offers possibilities for the treatment of DR.

Aim of study. The aim of study is to review recent articles (published during 2017-2023) that addressed the role of mineralocorticoid receptor pathway in the pathogenesis of DR.

Methods and materials. Articles from PubMed, Google scholar database were selected and analyzed using keywords: "mineralocorticoid receptor pathway in diabetic retinopathy", "aldosterone in diabetic retinopathy", "angiogenesis".

Results. It has been estimated that the activation of mineralocorticoid receptor pathway (MRP) induces blood pressure changes that is mediated by activation of renin-angiotensin-aldosterone system (RAAS) and has an important pathogenetic part in DR. Activation of RAAS can change the blood flow in the ciliary body, iris and retina, can also modify intraocular pressure by modulating the production and excretion of aqueous humor, it participates in the development of macular edema. Aldosterone promotes inflammatory response by inducing the production of pro-inflammatory factors such as interleukin (IL)-1β, IL-6, CCL5, TNF-α and neovascularization in DR, Müller cells express high levels of mineralocorticoid receptors and induce production of VEGF. It also enhances the expression of the epithelial Na+ channel ENaC α, the K+ channel Kir4.1 and the water channel AQP4 and promotes delocalization of Kir4.1 and AQP4 towards the outer limiting membrane, contributing to the accumulation of fluid in retina. However, spironolactone (an MR and aldosterone inhibitor) were shown to effectively reduce retinal angiopathy and inflammation, as well as prevent retinal neovascularization by reducing VEGF levels and inflammatory factors. In another study intraocular delivery of spironolactone has decreased the early and late pathogenic features of retinopathy in diabetic rats, such as retinal inflammation, vascular leakage, and retinal edema, through the upregulation of genes encoding proteins known to intervene in vascular permeability such as Hey1, Vldlr, Pten, Slc7a1, Tjp1, Dlg1, and Sesn2, but hasn't decreased VEGF. Spironolactone also has normalized the distribution of ion and water channels in macroglial cells.

Conclusion. MRP has an important pathogenetic role in DR by: 1. Activation of RAAS, modification of blood pressure, systemic and local effects in retina 2. Inducing the production of pro-inflammatory factors 3. Retinal neovascularization and modification in ion channels.Thus, an increased understanding of the role of these mechanisms in the pathogenesis of DR, will give us possibilities for treatment with MR inhibitors, which show positive effect in preclinical studies.