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AMD and Atherosclerosis: Physiopathogenic Similarities and Possible Therapeutics

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Chronic inflammatory diseases induced by oxidized Low-Density Lipoprotein (LDL) used to be associated with atherosclerosis. The findings that the hypofunction of the Retinal Pigment Epithelium (RPE) induce accumulation of lipids in the Bruch's membrane have contributed to the understanding of the physiopathogenesis of the Age-Related Macular Disease (AMD) [1-3]. It has been possible to conclude that the interactions that occur in the formation of the atherosclerotic plaques may also occur in the sclera-choroid-retina complex, that is, the oxidized LDL induces the production of the monocyte chemotactic protein-1 (MCP-1) and increases the expression of the Intercellular Adhesion Molecule-1 (ICAM-1) andVascular Cell Adhesion Molecule-1 (VCAM-1) by the activated endothelial cells. These molecules attract the circulating monocytes and promote adhesion to the vascular wall. When the recruited monocytes enter the vascular wall intima, they ingest the oxidized LDL and differentiate into macrophages. These cells secrete inflammatory cytokines, enzymes and vascular growth factors and may induce the formation of the Choroidal Neovascularization (CNV).

This hypothesis has been consolidated by different experimental studies. The surgical removal of the CNV has confirmed the increase in the MCP-1 expression by the RPE cells [4], the role of the matrix metalloproteinase in the progressive growth of the CNV and the angiogenic potential role of the macrophages, stimulating the production of the Vascular Endothelial Growth Factor (VEGF) by the RPE [5,6]. In mice with targeted homozygous disruption of the CD18 and ICAM-1 genes, laser-induced neovascular membranes smaller than in normal mice were observed [7]. The same result was obtained in Plasminogen Activator Inhibitor-1 (PAI-1) gene-deficient mice [8]. Moreover, it has been demonstrated that generalized macrophage depression decreases the volume and angiographic leakage of the CNV [9,10].

These experimental evidences have enabled researchers to infer that the measures adopted to prevent the development of atherosclerosis may have the same level of efficiency to prevent the evolution of AMD. In this regard, epidemiological studies have demonstrated that smoking tobacco significantly increases the risk of age-related macular disease [11] and that physical activities [12], a healthy diet [13,14] and the control of serum cholesterol [15,16] are important factors for the prevention of AMD.

Regarding therapeutic procedures, it is possible to assert that the drugs that stimulate the reverse cholesterol transport can also yield similar positive effects on AMD. It is important to point out that macrophages and RPE cells express CD36 [17], Apolipoprotein E (ApoE) [18], scavenger receptor BI (SR-BI) [19], ATP-binding cassette subfamily members A1 (ABCA1) [20] and ApoA1, the major protein constituent of HDL [21]. These components have the potential to remove lipids from RPE and Bruch's membrane into the choriocapillaries to be metabolized by the liver [21,22]. As in atherosclerosis, the control of the macrophages as well as of their liberation products such as the inflammatory cytokines, enzymes and growth factors may appear to have the same beneficial effects on the control of AMD.

Hence, nowadays, when we discuss oxidized LDL-induced chronic inflammatory diseases, AMD must also be considered.

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