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Identification of new candidate genes for retinopathy in type 2 diabetics

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Introduction: The cases of diabetes mellitus (DM) are constantly increasing worldwide. Therefore, early detection programs and the development of validated biomarkers are necessary to transfer molecular and genetic studies to the clinic, to prevent the presentation of DM and the complications derived from the chronicity of the process, including diabetic retinopathy. Although in the etiopathogenesis of DM2 various mechanisms are involved, such as inflammation, angiogenesis, and apoptosis, the genetic factor is essential to complete the knowledge of the molecular base of this disease.

Objectives: To identify genes involved in the pathogenic mechanisms of non-proliferating diabetic retinopathy (DR), such as oxidative stress, alteration of the extracellular matrix and / or apoptosis, to assess the risk of developing it in a population of type 2 diabetics (DM2).

Material and Methods: This study was carried in 81 participants, both genders and ages 25-85 y, classified in: 1) group DM2 (n = 49), with DR (+ DR ; n = 14) and without DR (-DR; n = 35), and 2) control group (GC; n = 32). A personal interview, ophthalmological examination and blood extraction were performed and processed to analyze the DNA and determine the gene expression of: TP53, MMP9 and SLC23A2 in all the participants. It was used SPSS v22.0 to perform statistical analyses.

Results: The TP53 and MMP9 genes increased their expression in the DM2 group compared to the GC, although only significantly in the MMP9 gene (TP53: 10.40 ± 1.20 vs. 8.23 ± 1.36, p = 0.084; MMP9: 1.45 ± 0.16 vs. 0.95 ± 0.16, p = 0.036) and the SLC23A2 gene significantly decreased its levels in DM2 vs. GC (5.58 ± 0.64 vs. 11.66 ± 1.90, p = 0.026). When subdividing the DM2 group according to the presence of DR, the expression of the TP53, MMP9 and SLC23A2 genes showed significant differences between the DM2-DR, DM2 + DR and GC groups (TP53: 9.95 ± 1.47 vs. 11.52 ± 2.05 vs. 8.23 ± 1.36, p = 0.038, MMP9: 1.47 ± 0.20 vs. 1.41 ± 0.27 vs. 0.95 ± 0.16, p = 0.021; SLC23A2: 5.61 ± 0.77 vs. 5.51 ± 1.21 vs. 11.66 ± 1.90, p = 0.018).

Conclusions: The regulatory genes of apoptosis (TP53) and extracellular matrix integrity (MMP9) could be involved in the susceptibility for the development / progression of DR, as well as the SLC232A2 gene (transporter of ascorbic acid) can behave as a risk protector for this pathology.

Keywords: Diabetic Retinopathy; Genes; Molecular Diagnosis