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Evaluation of Early Chorioretinal Abnormalities in Hypercholesterolemic Rabbits Submitted to the PPAR-gamma Agonist Treatment (Rosiglitazone): Histological and Histomorphometric Study

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1.Purpose: To evaluate, in a rabbit model, the degenerative histological abnormalities in the choroids and sclera following the daily administration of high cholesterol dosages as well as the possible prevention of these degenerative abnormalities following systemic administration of oral rosiglitazone, an activator of agonist PPAR ocular gamma receptors.

2.Methods: 55 New Zealand rabbits were studied and they were divided in four groups based on the diet that animals were submitted (normal diet or diet containing high levels of cholesterol): Control Group (CG) (06 rabbits): normal diet for six weeks; Second group (G1) (13 rabbits): 1% cholesterol diet for two weeks and then a 0.5% cholesterol diet for 4 weeks. Third group (G2) (18 rabbits): 1% cholesterol diet for two weeks and then a 0.5% cholesterol diet for 4 weeks. Additionally, this group also received 3 mg of rosiglitazone daily after the third week since the beginning of the experiment. Fourth group (G3) (18 rabbits): 1% cholesterol diet for two weeks and then a 0.5% cholesterol diet for 4 weeks. Additionally, this group also received 3 mg rosiglitazone since the beginning of the experiments. Data was analysed by Shapiro-Wilks-Test and P values lower than 0.05 were considered statistically significant. **3.Results:** No abnormalities were observed in CG. However, G1 group showed a significant increase in sclerochoroidal thickness (301,48 +/-50,12) compared with CG (239,09 +/-24,33) (p=0,005). The G2 group showed a sclerochoroidal thickness thinner (282,08 micrometers/DP36,44) than G1 (301,48 +/-50,12); however, this value was not statistically significant (p=0,222). The G3 group showed a sclerochoroidal thickness thinner (266,11 +/-47,94) than G1 (301,48 +/-50,12); this value was statistically significant (p=0,02). A high number of histiocytes was observed in the scleral wall of rabbits submitted to a diet containing high levels of cholesterol (G1), followed by G2, G3 and CG, in a decreasing manner. **4.Conclusions:** This study revealed that hypercholesterolemia may lead to early degenerative abnormalities of the

choroids and sclera of rabbits and that the activation of agonist PPAR ocular gamma receptors, by means of oral administration of rosiglitazone, proved to be effective for the preservation of choroids and sclera anatomy. These findings may have clinical relevance as the rosiglitazones may offer a new treatment modality for dry and/or exudative AMD in human eyes.