Reduced mitochondrial DNA copy number in peripheral blood lymphocytes of POAG patients

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Glaucoma is a group of complex optic neuropathies, which cause vision loss in more than 70 million people worldwide due to degeneration of the optic nerve. Its pathophysiology is not fully understood, various risk factors are known to be implied [1, 2]. Since retinal ganglion cells (RGCs), of which axons form the optic nerve, have a high energy demand, suboptimal mitochondrial function may put the survival of these neurons at risk [2]. In the present study, we explored if peripheral blood lymphocytes (PBL) mitochondrial DNA (mtDNA) quantity or quality could indicate a role of mitochondrial impairment in development of primary open angle glaucoma (POAG), the most common form of the disease. We have selected four age- and sex-matched groups, namely POAG patients with high intraocular pressure at diagnosis (high tension glaucoma: HTG; n=97), normal tension glaucoma patients (NTG, n=37), ocular hypertensive controls (OH; n=9), and cataract controls (C; n=32), all without remarkable comorbidities. PBL-DNA was isolated and mtDNA copy number was assessed by qPCR quantification of mitochondrial D-loop and nuclear B2M gene. In addition, the presence of the common 4,977 base pair mtDNA deletion was assayed by a sensitive PCR, which amplified the region containing the specific breakpoints in the mitochondrial genome. Analysis of the mtDNA copy number revealed a significant reduction in HTG patients (median mtDNA copies per cell (M): 60.84, interquartile range (IQR): 48.09-80.55) compared with C (M: 85.90, IQR: 71.82-105.1, p-value < 0.001), NTG patients (M: 76.77, IQR: 62.30-99.54, p-value < 0.01) and OH (M: 77.22, IQR: 67.98-109.8, p-value < 0.05). Furthermore, a significant linear age-related reduction is observed in NTG patients (p-value < 0.05). The common 4,977 base pair mtDNA deletion was not detected in any of the participants. In conclusion, the mtDNA copy number was reduced in PBL-DNA of HTG patients. Most likely, this reflects a suboptimal mitochondrial function, which together with ageing and/or high intraocular pressure, may lead to mitochondrial dysfunction during life in RGCs and may contribute to glaucoma pathology in some HTG patients. These patients may be amenable for a neuroprotective mitochondria-targeted drug treatment.

Keywords: Glaucoma, Mitochondria, Neuroprotection.

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