

Relevance of 24S-Hydroxycholesterol as a Biomarker of Optic Neuropathies

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Abstract

Purpose: 24S-Hydroxycholesterol is formed by enzymatic oxidation of cholesterol via cholesterol-24S-hydroxylase (CYP46A1) activity in neurons, including retinal ganglion cells and neurons from the inner retina. We investigated whether neurodegeneration could be associated with the release of 24S-hydroxycholesterol in acute neuropathies, and therefore 24S-hydroxycholesterol could be considered as a biomarker of retinal cell degeneration in the course of optic neuropathies.

Methods: Retinal neurodegeneration was induced in rats by severe elevation of intra-ocular pressure. For that purpose, rats were submitted to 532nm-laser photocoagulation of the episcleral veins, limbus and trabecular meshwork. Intra-ocular pressure was monitored in a time course study at 1, 3, 7, 14, 21, 30 and 60 days post laser injury using Tonolab®. Rat retinal and plasma 24S-hydroxycholesterol levels were quantified by gas-chromatography mass spectrometry using deuterated internal standard at the same time points. Plasma levels of 24S-hydroxycholesterol were similarly monitored in patients suffering from anterior ischemic optic neuropathy.

Results: Intra-ocular pressure was significantly raised by a factor of five in the laser treated-eyes of the rats compared to fellow eyes, during the first two weeks after photocoagulation, and returned to baseline afterwards. The levels of 24S-hydroxycholesterol were lowered in the first three days in the retina injured by laser, compared to fellow eye. Meanwhile, plasma levels of 24S-hydroxycholesterol were raised by a factor of three. Patients suffering from anterior ischemic optic neuropathy showed increased plasma levels of 24S-hydroxycholesterol, compared to age-matched normal subjects (H=6.86, P=0.009 by Kruskal-Wallis test).

Conclusions: Increased plasma levels of 24S-hydroxycholesterol were associated with acute phases of optic neuropathies, suggesting its relevance as a biomarker of retinal neurodegeneration.

Keywords: retinal degenerations: cell biology • inner retina dysfunction: biochemistry and cell biology • ischemia