The role of Omega-3 Fatty Acids in Aging Retina

Abstract

Purpose: To evaluate the therapeutic effects of omega-3 (ω3) fatty acids in aged wild type C57BL/6 mice, in CCL2$^{-/-}$ animal model of retinal degeneration and in patients with dry age-related macular degeneration (AMD); when the blood levels of arachidonic acid (AA)/eicosapentaenoic acid (EPA) ratio is <2.

Methods: Pre-clinical assessment of ω3 efficacy was performed in two year-old wild type C57BL/6 and in 9 month-old CCL2$^{-/-}$ mice. ω3 treatment lasted 3 months and comprised daily gavage administration of EPA and docosahexaenoic acid (DHA). Blood and retinal fatty acid analysis was performed using gas chromatography. Eyecups were histologically examined using transmission electron microscopy and/or confocal microscopy to evaluate lipofuscin granules and the photoreceptor layer. Mass spectrometry-based proteomics was performed using eyecups from different groups. Inflammatory markers were examined using qRT-PCR and Western blotting.

A clinical observational study was performed in 74 patients with dry AMD (including 119 eyes and with mean initial visual acuity 6/18). ω3 supplementation (3-4 g EPA/day and some DHA) lasted for 6 months, whereas the AA/EPA was examined at different time points.

Results: EPA levels increased and AA levels decreased in the blood and retinas of the treatment group in both animal models. Significantly fewer lipofuscin granules were observed in the aged C57BL/6 treatment group. The thickness of the outer nuclear layer was significantly greater in the treatment

group than in the untreated, in both models. Proteomic analysis indicated significant increase in myelin regulatory factor-like protein, myelin basic protein and myelin proteolipid protein in the aged C57BL/6 treatment group. Three different pathways were significantly affected from ω3 treatment, namely fatty acid elongation, biosynthesis of unsaturated fatty acids and metabolic pathways. In the CCL2$^{-/-}$ treated model, there was decreased gene expression of TLR3 and NF-κB and reduced IL-18 protein compared to the untreated control.

Clinical observational studies demonstrated that following a 6-month supplementation with ω3 in patients with dry AMD there was an average of 14 letters gained. Mean AA/EPA ratio was maintained below 2 throughout the study.

Conclusions: ω3 supplementation (when AA/EPA < 2) protects the photoreceptors through different mechanisms, i.e. reduction of lipofuscin granules, decrease in inflammatory markers and increase in myelin-related proteins. The protective effect of ω3 was evident in aged and CCL2$^{-/-}$ mice of retinal degeneration. In addition, there is evidence to support that this effect was also confirmed in patients with dry AMD. Therefore, ω3 supplementation may have the potential as a therapeutic regime for patients who suffer from retinal-related pathologies when the blood AA/EPA is <2.