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Effect of antioxidants on ocular blood flow and endothelial function in an endotoxin-induced inflammatory model in humans

Berthold Pemp, Elżbieta Polska, Alexander Minichmayr, Katharina Karl, Michael Lasta, Gerhard Garhöfer, Michael Wolzt and Leopold Schmetterer*

Address: Department of Clinical Pharmacology, Medical University of Vienna, 1090 Vienna, Austria

Email: Leopold Schmetterer* - leopold.schmetterer@meduniwien.ac.at

* Corresponding author

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Background

Oxidative stress, which refers to cellular damage caused by reactive oxygen species (ROS), has been implicated in many disease processes. The Age-Related Eye Disease Study (AREDS) showed that daily intake of a combination of the antioxidants beta carotene, vitamins C and E, zinc and copper may retard the progression of age related macular degeneration by reducing ROS [1]. We investigated the effect of the AREDS combination of antioxidants on retinal and choroidal blood flow and on retinal vascular reactivity under normal conditions and in a standardized experimental inflammatory model in humans.

Methods

Twenty-one healthy male volunteers between 18 and 35 years were included in this randomized, double masked, placebo-controlled study. Retinal blood flow was assessed by measurement of retinal vessel diameters, laser-Doppler velocimetry and the blue field entoptic technique. Choroidal blood flow was assessed by laser-Doppler flow-metry. The reactivity of retinal vessels and retinal blood flow to systemic hyperoxia was investigated during breathing of pure oxygen. Infusion of 2 ng/kg *Escherichia coli* endotoxin (lipopolysaccharide, LPS) was used as a model of systemic inflammation. Measurements were performed before and 4 hours after administration of the LPS bolus. After the first study day the subjects had to take either the AREDS combination of antioxidants or placebo

for 14 days. Thereafter a second study day with the same measurements and procedures was performed.

Results

After administration of LPS we found a reduced vasoconstriction of retinal arteries during systemic hyperoxia. Likewise the oxygen-induced impairment of retinal blood flow was reduced after LPS. Both effects were significantly diminished after two weeks of AREDS antioxidants compared to placebo. Choroidal blood flow tended to be higher in the test group on the second study day.

Discussion

Our findings support previous data showing that the inflammatory response after administration of LPS induces impaired endothelial function. The normalization of the retinal perfusion reaction to hyperoxia after LPS infusion in the test group indicates that antioxidants may reduce endothelial dysfunction due to oxidative stress by eliminating ROS.

References

Age-Related Eye Disease Study research group: A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for agerelated macular degeneration and vision loss: AREDS report no. 8. Arch Ophthalmol 2001, 119:1417-1436.