Oxidation stress in eye diseases

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Abstract

The short literature review is devoted to some recent findings in the field of the oxidative stress role in the pathogenesis of certain eye diseases. Age-related cataract, primary open-angle and age-related macular degeneration disease are diseases of elderly. Thus, oxidative stress in their emergence and development has a long, decades-lasting impact. Elements of oxidative damage and antioxidant protection are numerous and of specific features in each segment of the eye, and they are influenced by systemic factors, as well.

Introduction

Human is daily and aerobic organism. Oxidative and photooxidative stress are consequences of these evolutionary advantages, as sunlight and oxygen have the dual nature— they are necessary for life, but have damaging potential. This is obvious in some eye diseases.

Oxidative stress (OS) is caused by an imbalance between the production of reactive oxygen species (ROS) and ability of biological systems to readily detoxify the reactive intermediates or easily repair the resulting damage. Photooxidation is OS resulting from photochemical or photosensitization effect initiated by light photons. Antioxidants appear as evolutionary adaptation to OS. By their effects, they are quenchers or scavengers of ROS. By their biological nature they are enzymes or low-molecular substances—proteins, peptides, urates, aminoacids, hormones and vitamins.

Lens-oxidation and Antioxidant protection

Mitotic epithelial cells are the first to meet with solar electromagnetic radiation (UV spectral part). Their chromophores are absorbing DNA bases and tryptophan. During OS appear DNA photoproducts and changes of the quantity and type of mRNA. Cells have enzymes reparatory for damage caused. Incomplete repair leads to permanent damage of DNA, the synthesis of aberrant proteins, mutations and cell death.

There are evident posttranslation proteins modifications and lipid peroxidation, as well, in lens epithelial cells and fibers. The influence of sunlight is undoubted. Yet, exposure in childhood has not been adequately quantified and we can only estimate occupational and recreational exposure of adults. In some cataract types genesis proven are genetic factors, secondary senium factors. Lens local defense system is based on low O₂ pressure, slow and predominantly anaerobic metabolism, slow lens growth, high percent of Vitamin C, high glutathione content and abundance of lens crystallines and antioxidant enzymes some hormones and lens architecture. Antioxidant activity depends on the mechanism of oxidative damage, which is dependent on the medium polarity and type of damage caused.

Cortical cataract

This cataract type appears more frequently in people with high sunlight exposure and diabetes, female sex, people of African heritage and ones with smaller lens.

Cortical cataracts involve the disruption of fiber cell membranes and water influx, followed by disintegration of the cytoplasmic contents of the damaged fiber cells. Disruption of the plasma membrane would allow glutathione and other antioxidants to diffuse out of the fiber cells, resulting in the oxidation of the remaining cytoplasmic content.

It is difficult to decide whether cortical cataracts are caused by oxidation or whether oxidation follows the cellular disruption that precedes opacification or some of both. 'Mixed' nuclear and cortical cataracts are common, even though the risk factors for each type tend to be distinct. Nearly 200 genes and loci are
Risk factors are aging, female sex, white race, environmental factors, inflammation, cataract, life habits (smoking, nutrition, obesity), but some genetic factors, as well.5,7,20,17,8

Macular oxidation and neovascularisation promote, also, lipofuscin in postmitotic RPE cells, reduced capacity in RPE phagocytosis, synthesis of collagen IV (blue part of the spectrum), thickening and linear deposits in Bruch’s membrane, decreased exchange of hormones, vitamins and the elimination of waste products, damage to mitochondrial DNA (regulation of apoptosis), Pigment Epithelium Derived-Factor (PEDF) suppression at the level of gene regulation and Inflammatory factors.5,7,20,17,8

Antioxidant capacity of the macula consists mostly of numerous antioxidant enzymes, of which some are tissue specific, hormone melatonin, pigment melanin and carotenoids lutein and zeaxanthin.5,4

Primary Open-Angle Glaucoma (POAG)

Glaucoromatous subjects might have a genetic predisposition, rendering them more susceptible to reactive oxygen species-induced damage. It is likely that specific genetic factors contribute to both the elevation of IOP and susceptibility of the optic nerve/retinal ganglion cells to degeneration.10

Oxidative stress plays a fundamental role during the arising of glaucoma-associated lesions,10,11,13,9 first in the trabeculum and then, when the balance between nitric oxide and endothelins is broken, in neuronal cell. Vascular damage and hypoxia, often associated with glaucoma, lead to apoptosis of retinal ganglion cells. Elevated intraocular pressure in experimental conditions causes changes in the retinal redox system: SOD and catalase activities decrease, melatonin decreases, increases reactive lipid peroxidation and NO synthetase 2 level in optic nerve head.15,14 Evidence of mitochondrial abnormalities in POAG patients,1 demonstrates a general metabolic disorder in POAG with restricted capability to cope with oxidative stress. Reduced glutathione levels and elevated levels of malondialdehyde, a reactive catabolite formed in the course of lipid peroxidation, have been found in untreated glaucoma patients.16 There is, in addition, disturbance of the vitamin balance, including reduced vitamin Bl levels,2 as well as the presence of some other systemic risk factors.12

Posterior subcapsular cataract

Opacities in posterior subcapsular cataract show swollen cells with eosinophilic cytoplasm, suggesting fiber cells that failed to elongate. They are more frequent in myopia, diabetes and exposure to therapeutic doses of steroids and ionizing radiation, history of cancer (therapy?) and diabetes.5,3

It appears, usually, in younger patients and has faster progression.

Age-Related Macular Degeneration (AMD)

There are numerous factors which predispose macula to OS-cumulative solar radiation during life (blue spectrum), good retinal vascularization (high oxygen content), high content of unsaturated lipids, permanent phagocytosis in retinal pigment epithelium (RPE) and photosensitisizers in retina (lipofuscin, cytochrome c oxidase, rodopsin, hemoglobin).19,6

Nuclear cataract

Nuclear cataracts occur in bigger lens size. It depends on vitreous gel status also, as intact vitreous maintains low oxygen pressure (vitrectomy, except in ischemic diabetic retinopathy, is a risk factor).5,3 This cataract type is more often in cigarettes smokers, people exposed to cooking smoke, those with poorer diet habits, lower socio-economic and educational level, also in people who live in tropical regions and who were exposed to hyperbaric oxygen therapy. Low serum albumin concentration is another risk factor, as well as some systemic diseases.21

Aggregation and insolubilization of lens proteins and their increased association with membranes happen in nuclear cataract. Their nucleuses are pigmented nucleus, what promote further oxidation.5,3,18 Higher level of oxidative stress is evident in lenses with nuclear opacification.5,18 Mixed opacities with nuclear component and severe nuclear ones could be independent predictors of 2-year mortality.

Radovi izloženi na Simpozijumu
identified in cataractogenesis (they code structural and regulatory proteins). EphA2is associated with age-related cortical cataract in mice and humans.
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Acta Ophthalmologica 2010 36:15-18

Aqueous dynamic changes with the age and glaucoma-flow of antioxidant decreases, as well as drain of oxidants.\textsuperscript{10}

Conclusion

In mentioned eye diseases pathogenesis there are few factors which we can influence and a lot more we cannot. Certainly, we should try decreasing oxidation stress by changing life habits, preferably at an earlier age.*

\*Remark-Some published results of our team research in this area had, as a consequence and tribute not only this presentation (on Serbian-German Symposium in 109. DOG-Congress "Challenges in Ophthalmology", 29.9.-2.10.2011 Berlin), but also an earlier offer for a special issue of Frontiers in Bioscience magazine managing. It is realized and is dedicated to oxidative stress in ocular disease (Frontiers in Bioscience, the Special issue: "Eye and oxidation stress", Managing Editor: Lepsa Zoric, http://www.bioscience.org/current/special/zoric.htm), from which are some of the key references in this short review (5,6,10).

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\textbf{Literature}
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