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Editorial

Biomarkers of oxidative stress and inflammation in dry eye disease

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Dry eye disease (DED) is a chronic inflammatory condition involving tear film and ocular surface such as the cornea, conjunctiva, meibomian glands and lacrimal glands. Disease is multi-factorial and is characterized by tear film instability and tear hyperosmolarity. It affects a large part of population worldwide with reported prevalence range in Asia is from 3.8 to 64%[1] and it constitutes a large spectrum of symptoms such as burning sensation, grittiness, ocular discomfort, redness, visual disturbance, etc.[2]

The core mechanism of dry eye disease is found to be hyperosmolarity of tear film which activates oxidative stress singling pathways and pro-inflammatory effect on ocular surface epithelium resulting in epithelial damage and inducing cell death by apoptosis, loss of goblet cells with lack of mucin expression and exacerbation of tear film instability.[3] The integrity of tear fluid and ocular tissue plays a key role in expression of antioxidants and protective enzymes which help in maintaining the homeostasis of ocular surface.[4] In most cases of dry eye diseases extrinsic factors (like environmental pollution, ozone, UV radiation, smoke etc.) or intrinsic factors (e.g. aging, autoimmunity and medications etc.) may initiate inflammatory cycle and oxidative stress. Surgical stress (cataract surgery or refractive surgeries) can also induce inflammation and free radical generation.It has been observed that the increasing burden of free radical stress (reactive oxygen species) in ocular surface leads to oxidative and anti-oxidative imbalance which plays a key role in pathophysiology of dry eye disease.[5] Biomarkers of ocular surface inflammation and oxidative stress are specific molecular structure like protein / enzymes, gene, lipid or metabolites which can aid diagnosis, predict prognosis and help in monitoring therapeutic response to guide treatments.

Various biomarkers of oxidative stress which were studied in tear film included lactoferrin, lipid peroxidase, malondialdehyde, myeloperoxidase, xanthine oxidase, 4-hydroxynonenal and antioxidant enzymes like super-oxide dismutase (SOD), catalase and glutathione peroxidase. Several studies had been conducted in which comparisons were made between oxidative stress markers and antioxidants among patients having DED and healthy individuals.[6] It was found that there was significant increase of oxidative stress markers in tear content and conjunctival sample in patients with dry eye disease compared to healthy individuals.[7] Among antioxidants catalase was found to be decreased in DED patients and glutathione dependent enzymes showed no significant correlation. Most of the glaucoma patients using multi-dose eye drops on daily basis which contain benzalkonium chloride as preservative solution which induce cell toxicity and mitochondrial alteration and lead to decrease in levels of antioxidants.[8,9] It is also seen that high levels of lactoferrin in tear film is a protective factor against UV light radiation and oxidative stress.

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Hyperosmolar stress in DED stimulate secretion of pro-inflammatory cytokines, chemokines (that attract inflammatory cells) and matrix-metalloproteinase such as MMP-3 & MMP-9. Cytokines which have been reported to be highly over-expressed in DED are TNFα, IL-1β, IL-6.[10] Other cytokines which have been reported to be dysregulated in DED include IL-2, IL-4, IL-9, IL-10 and INF-γ. These cytokines controls tissue growth, migration and differentiation.[11] IL-8 is a pro-inflammatory chemokine secreted by epithelial cells and macrophages, results in fibrosis, neovascularization and endothelial dysfunction.

Using preservative free eye drops, topical cyclosporine which especially reduces T- cell mediated lacrimal tissue inflammation leading to rise in goblet cells and reversal of squamous metaplasia of conjunctiva. Further research in this area can be helpful in understanding and treating this disease better.

Conflict of Interest

None.

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