



## The Role of Inflammatory Cytokines in Dry Eye Diseases

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### ABOUT THE STUDY

Many visual problems, including keratoconjunctivitis, retinopathy, Dry Eye Disease (DED), cataract, nerve palsies, glaucoma, and macular edema, can be brought on by Diabetes Mellitus (DM). Among recent years, the significant prevalence of dry eye disease in diabetics has drawn attention in addition to the wide spread attention that diabetic retinopathy has gotten for its role in causing blindness. Studies have indicated that diabetics are more prone to DED. The development of DED in diabetics is characterized by unstable tear production and tear volume, squamous metaplasia of the conjunctiva, a decrease in goblet cell density, a decrease in the hydrophilicity and stability of tear film, and the accumulation of inflammatory cytokines, in which the ocular surface is continuously harmed. Although the pathophysiology of DED in diabetics has not been well studied, it is widely acknowledged that inflammation plays a significant part in this process. In this study, we examined the concentrations of Nuclear Factor- $\kappa$ B (NF- $\kappa$ B), Transforming Growth Factor-1 (TGF-1), Interleukin-1 (IL-1), Tumour Necrosis Factor (TNF), and chemokines in the tears and conjunctiva of diabetics with DED and contrasted the findings of this group with those of the normal controls. We demonstrated that the expression of the inflammatory cytokines indicated above was significantly higher in the diabetic group when compared to the healthy control group.

DED induced by diabetes has received a lot of attention in recent years due to the rise of diabetics. Although the pathophysiology of DED in diabetics has not been well studied, it is widely recognized that the inflammatory response plays a significant part in this process. The goal of this study was to investigate the mechanism of inflammatory cytokines on ocular surface damage from dry eye in diabetics in order to effectively identify and treat DED in diabetics as well as to determine clinical significance. There has recently been a rise in the idea among academics that type 2 diabetes and its long-term effects are mostly immune-mediated, including aberrant cellular immunity and humoral immunity. Studies have demonstrated that immunological dysfunction in diabetics can result in

oxidative stress, a personal hyperglycemia situation, and a significant number of oxidative stress products that can activate the NF- $\kappa$ B signaling pathway to up-regulate or down-regulate the expression of inflammatory cytokines. When the NF- $\kappa$ B signaling pathway was activated in the pathogenesis of diabetic dry eye, a large number of NF- $\kappa$ B and TGF-1 were produced. NF- $\kappa$ B dimers are found in the cytoplasm of non-stimulated cells. The level of IL-6 was found to be significantly correlated with the BUT, SIt, and density of conjunctival goblet cells. These findings suggested that IL-6 levels are related to disease severity and correlate with various tear film and ocular surface parameters. IL-1, IL-6, and TNF- may contribute to ocular surface inflammation by activating the NF- $\kappa$ B signaling pathway. Many studies have found that when the NF- $\kappa$ B signaling pathway is activated, a large number of inflammatory cytokines are released. Chemokines are cytokines that can be found on the surface of endothelial cells and play a role in chemotaxis and inflammatory cell activation. Chemokines induce chemotaxis to inflammatory cells that express corresponding chemokine receptors and recruit a large number of inflammatory factors to participate in the inflammatory response after binding with their receptors. In this study, CCR5+, CD4+ and CCR6+, CD4+ were found to be significantly overexpressed in the conjunctiva when compared to normal eyes. This suggests that chemokines may be involved in the inflammatory response in diabetics with dry eyes. Inflammatory mediators Activate Immature Antigen-Presenting Cells (APCs) and prime naive T cells in the lymphoid compartment, resulting in the expansion of auto reactive CD4 helper T cell Th17 cell subsets. According to research, CCR6 induces chemotaxis and migration of Th-17 cells to participate in the inflammatory response. In this study, the DM group had higher levels of CCR6+, CD4+ and IL-17+, CD4+T cells in the conjunctiva than the control group. These findings suggest that the chemokines CCR6 and Th17 cells were significantly higher in the conjunctiva of those with dry eye and diabetes compared to the control group, and that they may play an important role in the inflammatory response.

DED is significantly more common in diabetics than in healthy people. The inflammatory cytokines in the conjunctiva and tears

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differ significantly between diabetics with dry eyes and healthy people. The immune inflammatory response and the NF- $\kappa$ B signaling pathway may be important in the pathogenesis of dry eye in type 2 diabetic patients. Furthermore, our findings suggest that IL-6 levels are related to disease severity and are

correlated with ocular surface parameters. We can provide new ideas for the diagnosis and treatment of this disease by studying the pathogenesis of dry eye in diabetics. This experiment is only a preliminary investigation of the pathogenesis more research in diabetics with DED is required.