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Dry Eye Etiology: Focus on Friction

Ätiologie des trockenen Auges: Reibung im Fokus

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The “dry eye” continues to gain importance in everyday clinical practice. Not only is it often a challenge from a medical point of view of differential diagnosis, but also therapeutically, the way to success is neither short nor well predictable. The time required for these patients should not be underestimated as well as the often-enormous suffering that is sometimes in no relation to the anatomical or physiological findings. Therefore, the models for dry eye and its pathogenesis are so important, as they often offer the most important guidance in the search for appropriate diagnosis and therapy for the ophthalmologist, especially if there is a lack of measurable findings. Trust in these models carries an obligation. Being a field of great dynamics, subject to newer and deeper insights into the dynamics of events, a constant reassessment and transformation of each model is therefore a compulsory necessity. In comparison to the previous, more static models, we are currently on the threshold of new thinking, appreciating more the dynamics and the physiological variability of the ocular surface and its lubrication dynamics. Most recently, the Tear Film and Ocular Surface Society (TFOS) published in its Dry Eye Work Shop II (DEWS II) report of the current expert consensus on the definition and classification of dry eye as a disease characterized by a loss of homeostasis of the tear film [1]. The definition of tear film homeostasis remained vague, acknowledging the possibility of many different changes that can occur in the tear film and ocular surface. The current classification of dry eye distinguishes two underlying but often overlapping etiologies: aqueous deficient and evaporative tear film. The report concludes that Meibomian Gland Disease is considered the leading cause of dry eye in clinic and population-based studies. The TFOS DEWS II tear film report states that it is purported that the tear film lipid layer is responsible for the resistance of healthy tears against evaporation [2]. On the other hand, King-Smith and colleagues suggested a lack of correspondence between dry eye and both the lipid layer thickness and thinning rate [3]. The thinning rate of the tear film was not affected by apparent thickening of the lipid layer with lipid emulsion-based eye drops, suggesting that lipid was a poor barrier to evaporation [4]. Therefore, the DEWS II report concluded that the thickness of the lipid layer may not affect the evaporation rate unless it is very thin or completely absent. The TFOS pathophysiology report points to the enormous water-binding capacity of gel-forming mucins, like MUC5AC, secreted by the goblet cells of the conjunctiva as well as their moistening effect and lubricative function at the ocular surface [5 – 7].

The concentration of mucin MUC5AC in tears of patients with dry eye may be significantly decreased [8, 9]. Moreover, the observed difference in tear and cellular conjunctival MUC5AC mobility suggests the possibility of cleavage of the molecule to smaller components [10]. Mucin deficiency causes functional and structural changes of the ocular surface [11, 12]. The viscosity of the fluid-forming film is a major factor in the maintenance of a stable and coherent tear film. Polymeric mucous glycoproteins of high molecular weight are the main constituent molecules of all mucous secretions, and are responsible for the principle biochemical and physiological properties of these secretions [13]. From dilute high molecular weight hyaluronan solutions, it is known that the reduction of the concentration from 0.2 to 0.1 percent is associated with a decrease in viscosity at rest (zero shear viscosity) by a factor of 10 [14]. The same effect is associated with the decrease of average molecular weight of hyaluronan molecules in aqueous solution [15]. The decrease in concentration, glycosylation, or molecular weight of MUC5AC is associated with a very significant loss in lubricating efficacy of the tear film and an increase of friction between the cellular structures of the ocular surface.

Membrane-bound mucins at the apical surface of corneal and conjunctival epithelial cells, in particular, MUC1, MUC4 and MUC16, contribute to the antiadhesive character of the ocular surface [16, 17]. Danjo and colleagues reported a significant alteration in the mucin on conjunctival epithelia in dry eyes [18]. This is likely to be one of the reasons for decreased wettability of the ocular surface in dry eye patients. Dogru and colleagues reported that in patients with atopic keratoconjunctivitis, the level of secreted MUC5AC is significantly below that of controls, whereas, the level of membrane-bound mucines is above that of controls [19, 20]. They conclude that persistence of inflammation and a decline of the expression of the major ocular surface mucin, MUC5AC, may stimulate the upregulation of other epithelial mucins to protect the ocular surface.

The decrease in either molecular weight, glycosylation, or concentration of MUC5AC in the tear film is, moreover, associated with a significant loss of the water binding capacity of glycosaminoglycanes, which constitute the side chains of mucins [21]. This might well be one of the main causes for evaporative dry eyes.

The elevated friction, reduced hydration, and increased evaporation rate of mucous-deficient tear film in combination with alterations in the membrane-bound mucins of the ocular surface are likely to be the main causes for lid wiper epitheliopathy, LIPCOF, and sandbank epitheliopathy [22 – 24].

Other clinical situations resulting in increased friction between lids and the ocular globe are anatomical irregularities of the ocular surface [25]. These may be caused by tissue-related changes, like in keratoconus, as a consequence of infection or burns, or, frequently, as a consequence of ocular surgery [26]. Unless controlled, increased friction may be a major cause of tissue scarring.

None of these clinical situations has an aqueous deficient or evaporative tear film as the underlying etiology, but the elevated friction may be caused by a mucous deficient tear film, insufficient antiadhesive properties, or irregularities of the ocular surface. It is therefore proposed to recognize friction as an additional independent etiology for dry eye disease.

Conflict of Interest

The authors declare that they have no conflict of interest.

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