An Examination of the Relationship Between Ocular Surface Tear Osmolarity Compartments and Epitheliopathy

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ABSTRACT A 2014 PubMed search for *tear hyperosmolarity* and *corneal stain* yielded 2960 results. Selections from those providing evidence of variations in osmolarity were used to refine the compartmentalization model of tear osmolarity over the ocular surface. This new model includes the low point of freshly produced isotonic tears in the upper conjunctival sac, with osmolarity increasing successively in the upper meniscus, the upper area of exposed ocular surface, the lower area of over-exposed ocular surface, the lower meniscus, and the lower conjunctival sac. Compartmentalization is used to explain epitheliopathy over the ocular surface as resulting from variable degrees of exposure to hyperosmolarity-induced insult and/or friction-related mechanical damage. Also recognized is the role of localized increases in osmolarity, which appear likely to occur in the black lines and tear breakup areas of the exposed ocular surface. Variables such as the influence of ambient conditions of air humidity, temperature and movement have been considered, as well as rates of complete and incomplete blinks and associated potential for over-exposure of the inferior area of the normally exposed ocular surface. The exacerbating contribution from contact lens wear has been included. Friction-related damage may be the primary basis for lid wiper epitheliopathy, but tear hyperosmolarity could have an important contributory role. Subcompartmental consideration of variation in osmolarity may improve understanding of different presentations of epitheliopathy.

KEY WORDS blinking, compartment, dry eye, epitheliopathy, evaporation, exposure, ocular surface, osmolarity

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I. INTRODUCTION

Tears are necessary for the health of the ocular surface, maintaining the non-keratinized surface essential for corneal transparency as well as the lubrication required for movement of lid on globe.[1] The mucosae of the ocular surface (the visible bulbar conjunctiva and the cornea) are exposed directly to the ambient air and are therefore at risk of desiccation through water loss[2] and associated increased tear osmolarity.

Any quantitative or qualitative inadequacy of the tear lipid layer increases water loss.[3] People with reduced blink frequency or incomplete blinks have longer interblink intervals and greater tear evaporation due to increased exposure of the ocular surface.[4] Exposure to adverse ambient conditions, such as low humidity and/or increased air temperature and/or air movement, also increases evaporation.[5] The performance of tasks that reduce the overall blink rate and/or produce incomplete blinks are likely to greatly increase evaporation.[4] Studies of evaporation rates that use goggles do not address the influence of ambient conditions.[5,6] Moreover, the goggles may interfere with blinking frequency and completeness, altering interblink intervals and evaporation rates. Evaporation rates from ocular surfaces under ambient conditions may be four to five times faster than the average of the values found when goggles are worn.[7]

Prior to evaporation, the lacrimal secretion is generally considered to be isotonic with blood.[8] The osmolarity of human serum is 290 mOsm/l, equivalent to a 0.9% NaCl aqueous solution.[9] A meta-analysis of published data taken from 16 studies indicated a mean value for "normal eye"

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lower meniscus tear osmolarity of 302+/−8 mOsm/I.[10] The mean value for 11 studies of tear osmolarity in keratoconjunctivitis sicca was 326+/−22 mOsm/I.[10] The TearLab osmometer (San Diego, CA, USA) method of assessing osmolarity, which assesses lower meniscus samples, using a cutoff of 312 mOsms/l, achieved 73% sensitivity and 92% specificity.[11] As with other measures of dry eye disease (**DED**), there may be overlapping of the distributions for hyperosmolarity findings between normals and DED subjects. However, tear film osmolarity was found to be the single best marker of disease severity across normals and mild/moderate and severe categories of DED.[12]

In the open eye, the tears are distributed in three compartments: the conjunctival sac, the preocular tear film, and the tear menisci.[3] It has been suggested that in the open eye, tear osmolarity is not uniformly distributed between the tear compartments, but differs between the conjunctival sac (the preocular tear film and the fornical compartment behind the lids and in the fornix), the preocular tear film; and the tear menisci.[2] Consequently, measurement or specification of tear osmolarity would require identification of the tear compartment in which measurements are taken. Osmolarity has been found to vary only diurnally in normals, but not during normal assessment hours.[13,14] However, it can vary significantly during normal assessment hours in eyes with DED, and this may contribute to variations in findings among DED subjects.[14]

Exposure to different conditions (e.g., during sustained reading and/or major variations in air movement or humidity) before or during assessment might also contribute to variations in osmolarity. The location of tear sampling in the lower meniscus may be important.[15] For example, the increased staining of Marx's line nasally (further discussed below)[15] suggests that there might be a corresponding increase in osmolarity in the nasal portions of the menisci.

This review examines the evidence for compartmental variations in osmolarity and associated potential for ocular surface and lid wiper epitheliopathy. (Lid wiper refers to a localized portion of the marginal conjunctiva of the upper eyelid that has a rubbing effect on the ocular surface during blinking.) In particular, the significance of considering the upper and lower menisci, the upper and lower areas of exposed ocular surface, and the upper and lower conjunctival sacs as separate compartments is discussed.

II. MECHANISMS FOR TEAR VOLUME REDUCTION

Apart from evaporation, tears can be lost by tangential flow and drainage into the lacrimal sacs and by movement into the epithelium of the cornea or conjunctiva.[7] However, under conditions of hyperosmotic tears, transfer of water from the epithelium into tears appears more likely.[5] It is possible for tears to be transferred into a hydrophilic contact lens, but the primary routes of exit are by evaporation and tangential flow.[5]

A blink mechanism is necessary for effective tear drainage, although the puncta close during blinking.[16] Tear exit occurs even when the lids do not meet during a blink.[16] The puncta actually come into full contact after one-third to one-half of the full downward excursion of the upper lid.[17] Lid closure during blinks has both vertical and lateral-to-medial components.[18] The tears are not only swept vertically down the cornea during a blink, but also pushed medially toward the sites of drainage at the medial canthi.[18] A driver of fluid from the meniscus into the nasolacrimal drainage system was proposed under the name of the "lacrimal pump."[17,19] This mechanism assumes that contraction of the orbicularis muscle during the blink compresses the lacrimal sac.[19] The negative pressure produced by the subsequent expansion of the lacrimal sac is transmitted to the tear menisci at the start of the interblink interval (and relaxation of the orbicularis muscle), resulting in drainage.[17]

The central parts of the lid margins, described as the *occlusal surfaces*,[20] do not touch in spontaneous blinks due to their misalignment, with the top lid overhanging the bottom lid.[21] The keratinized portions of the upper and lower lid margins do not make complete contact during deliberate blinking.[22] Even with forced blinks, when greater contact occurs between the lids, an over-blink can still be observed.[21] Depending on how easily the lid stretches, lid tightness and compressive loading on the ocular surface may increase during the initial down-phase of a blink, as the lid must stretch over increasing corneal sag height. Tightness and compressive loading likely reaches a peak as the lid moves over the maximum sag height at the corneal apex. As the blink moves down beyond this position, the corneal sag height or vault is reduced, and lid tightness as well as its compressive loading of the ocular surface may diminish accordingly. Perhaps the lids have not fully recovered from their stretching over the corneal apex when they complete their downward excursion. Residual upper lid stretch or looseness may contribute to the degree to which they over-blink or overhang the lower lid at the completion of the down phase of a complete blink. When passive closure is sustained, giving the upper lid time to regain normal length (compared to a blink), the overhang of the top lid lessens or even disappears, allowing the two menisci to fuse. However, lid overhang does not seem to help menisci fusion during a spontaneous blink.

Differences in lid anatomy among racial groups may affect blink functions. For example, compared to Caucasians, Asian (Korean) lids have more subcutaneous and suborbicularis fat, with a pretarsal fat component being present.[23] The upper lid crease is also a feature of