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Proteomic profiling of inflammatory signaling molecules in the tears of patients on chronic glaucoma medication

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To uncover characteristic tear proteins associated with the chronic use of glaucoma medication using proteomic analysis, and to compare these proteins to those previously identified from primary dry eye disease. Eighteen patients treated with topical anti-glaucoma medications (range: 2-149 months) and 10 normal age-matched subjects with no prior topical treatment were recruited for the study. Tears were collected using a standard clinical procedure (Schirmer's type I) and analyzed using chemical tagging (iTRAQ) for the tear proteins using mass spectrometry. Conjunctival samples were also collected and protein expression determined by Western blot analysis from subjects that underwent glaucoma filtration surgery during the study period. Of the 124 identified tear proteins (99% confidence, ProtScore ≥ 2.0), we found that the tear levels of S100A8, A9, Mammaglobin B and 14-3-3 ζ/δ were significantly increased in the medicated group compared to non-medicated group, ($P<0.05$). Eyes on topical medication for more than one year showed a decrease of proline-rich 4 protein tear level ($p = 0.0049$) compared to non-medicated group. Use of topical medication for less than 1 year did not reach statistical significance compared to the control, non-medicated group. The tear proteins detected in the medicated group differed from the primary dry eye group.

Glaucoma patients on longstanding topical medication demonstrate distinct changes in inflammatory proteins. Duration of topical anti-glaucoma medications longer than one year may start to induce ocular surface inflammation as indicated by the general increase of inflammation associated proteins in tears. The inflammatory tear protein profile present in chronically medicated glaucoma eyes appears to be different to that found in primary dry eye. Identification of tear proteins specific to medicated glaucoma eyes will help to specifically develop targeted screening modalities and therapeutic agents different to current conventional dry eye management.

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