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Influence of Short-Term topical naltrexone treatment on the lacrimal functional unit in diabetic rats

Abstract:

Dry eye syndrome (DES) often correlates with the prevalence of diabetes. One underlying factor is a dysfunctional lacrimal functional unit (LFU) consisting of lacrimal glands, conjunctiva, and corneal epithelium, that are responsible for tear production and tear homeostasis. Naltrexone (NTX) is an opioid receptor antagonist that blocks the Opioid Growth Factor receptor (OGFr), and when used topically to treat dry eye in Type 1 diabetic (T1D) rats, restores corneal epithelial sensitivity and tear production to normal levels within days of the initiation of therapy. The mechanism of this action is not known. One hypothesis is that elevated OGF levels in diabetes alter the morphology and function of the LFU, and that topical NTX blocks OGF-OGFr interaction thereby reversing LFU complications. Adult male and female rats were rendered hyperglycemic and considered T1D after 6 weeks. Ocular complications of dry eye and reduced sensitivity were recorded prior to treatment. Cohorts of each sex were randomized to receive topical NTX (5 x 10-5 M) twice daily for ten days. The next day, dry eye and corneal sensitivity in T1D+NTX rats were comparable to normal animals. OGFr levels remained elevated in plasma and ocular tissue of all T1D animals. LFU tissue was harvested for morphology and had decreases in number and size of lacrimal gland acini ($p<0.001$) and Meibomian glands ($p<0.001$) in T1D rats relative to normal animals. Ten days of NTX did not reverse these deficits suggesting that NTX-mediated reversal of dry eye may involve neuronal mechanisms.

Biography

David Diaz has completed his Master of Science degree in Anatomy in 2021 from Case Western Reserve University and is currently in the PhD program in Anatomy at Penn State College of Medicine. His research interests involve understanding mechanisms related to dysregulation of the OGF-OGFr regulatory axis and ocular complications in diabetes. David is also an active teacher of human gross anatomy to medical students, physician assistant students, and undergraduates.