Orexin Blockers' Role in Glucose Homeostasis and Diabetic Retinopathy

Braden Baker[1], Rupinder Kaur Sodhi[2], Neha Mahajan[2], Ashay Dilip Bhatwadekar[1,2]

[1]Department of Ophthalmology, Indiana University School of Medicine, Terre Haute, Indiana University, Indiana

[2]Department of Ophthalmology, Eugene and Marilyn Glick Eye Institute, Indiana University Indianapolis, Indiana

Background:

Diabetic retinopathy (DR) is the most common complication of diabetes and can lead to blindness if untreated. Orexin is a neuroprotein produced by the hypothalamus that regulates the sleep/wake cycle. Orexin-blockers are prescribed for insomnia which recent studies have shown decrease blood glucose levels, suggesting a potential therapeutic for DR. The purpose of this study is to explore orexin-blockers' role in glucose homeostasis and diabetic retinopathy through in-vitro, in-vivo, and chart-review methods.

Methods:

1. In-vitro – Glucose uptake by human retinal endothelial cells (HRECs) was determined with exposure to varying levels of Suvorexant, a commonly prescribed orexin-blocker, and orexin. Additionally, Orexin expression under varying glucose concentrations was examined using fluorescent staining.
2. In-vivo – Diabetic (db/db) and non-diabetic (db/m) mice were injected with Suvorexant or DMSO daily. Mice weights and blood glucose were taken regularly to compare.
3. Chart-review – A review that examines individuals retrospectively to determine if orexin-blockers decrease percentages of developing vision-threatening DR or macular edema compared to patients NOT taking orexin-blockers.

Results:

1. In-vitro – HRECs exposed to Suvorexant had increased glucose uptake while those exposed to orexin had a decreased glucose uptake. There were no significant results in orexin expression in HRECs exposed to varying glucose concentrations.
2. In-vivo – Mice treated with Suvorexant showed a downward trend in body weight, food intake, and better glucose tolerance than DMSO-injected diabetic mice.
3. Chart-review – 41 patients were identified as having non-vision threatening DR and taking orexin-blockers in 2014. MRN's for these patients are currently being retrieved by Regenstreif Institute.

Conclusion:

The results of both the in-vitro, pre-clinical, and clinical chart review studies indicate Suvorexant has blood glucose-lowering properties. Data will continue to be collected for the clinical chart review to further determine the effects of orexin blockers on diabetic retinopathy and HbA1c.