Steroid-induced ocular hypertension/glaucoma: Focus on pharmacogenomics and implications for precision medicine

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Elevation of intraocular pressure (IOP) due to therapeutic use of glucocorticoids is called steroid-induced ocular hypertension (SIOH); this can lead to steroid-induced glaucoma (SIG). Glucocorticoids initiate signaling cascades ultimately affecting expression of hundreds of genes; this provides the potential for a highly personalized pharmacological response. Studies attempting to define genetic risk factors were undertaken early in the history of glucocorticoid use, however scientific tools available at that time were limited and progress stalled. In contrast, significant advances were made over the ensuing years in defining disease pathophysiology. As the genomics age emerged, it appeared the time was right to renew investigation into genetics. Pharmacogenomics is an unbiased discovery approach, not requiring an underlying hypothesis, and provides a way to pinpoint clinically significant genes and pathways that could not have been discovered any other way. Results of the first genome-wide association study to identify polymorphisms associated with SIOH, and follow-up on two novel genes linked to the disorder, GPR158 and HCG22, is discussed in the second half of the article. However, knowledge of genetic variants determining response to steroids in the eye also has value in its own right as a predictive and diagnostic tool. This article concludes with a discussion of how the Precision Medicine Initiative®, announced by U.S. President Obama in his 2015 State of the Union address, is beginning to touch the practice of ophthalmology. It is argued that SIOH/SIG may provide one of the next opportunities for effective application of precision medicine.