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Brief summary of the study

Title: Metabolomic and pharmacogenomic evaluation of glaucoma therapy

Glaucoma is a second leading cause of blindness worldwide. Due to the multi-factorial nature of glaucomatous etiology, precision medicine will become the prerequisite for forthcoming glaucoma therapeutics. This study aimed was to identify the localized and systemic alterations in metabolomic, lipidomic, and proteomic profiles in POAG and PACG patients and was compared to non-glaucomatous controls. Quantitative analysis of targeted metabolites using NMR revealed significantly elevated levels of glutamate, ascorbate, and TCA metabolites in the glaucomatous group as compared to cataract control. Studies using HRMS revealed the alteration in omics studies and their metabolic pathway analysis indicated the occurrence of altered galactose, amino-sugar, and nucleotide-sugar metabolism associated with PACG. Altered TCA cycle, sphingolipids, glutamate-glutamine metabolism are associated with POAG. Analyzing biologically relevant amines indicated the 5-fold elevation of histamine and 2.5-fold elevation of adrenaline levels in the aqueoushumor of POAG and PACG respectively. Elevated trace amines in the aqueous humor of POAG group were subsequently demonstrated in the animal model about its propensity to cause mydriasis. Proteomic analysis revealed the pattern of neurodegeneration, necroptosis, elevated O-glycosylated protein (mucin like protein 1), lipoprotein alteration, Wnt signalling dysregulation were involved in the pathophysiology of POAG. Proteins involved in the abnomal fibrotic events and dopaminergic synapse dysfunction were the major factors contributed for PACG. Although this study demonstrated an altered lipidome in aqueous humor and plasma in glaucomatous conditions, the functional role of individual lipid species and their involvement in offering trabecular meshwork outflow resistance and mechano-signaling is yet to be understood. Genetic polymorphism studies conducted using selective SNPs revealed the possibility of variation in the adrenergic β2-receptors in POAG patients. The multi-Omics approaches adopted in this study indicated many significant findings having immense importance in understanding the pathophysiology of glaucoma and other possibilities to develop newer pharmacological interventions.

(Signature of nominator)

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