Neuroprotection in Glaucoma: Towards Clinical Trials and Precision Medicine

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PURPOSE: The eye is currently at the forefront of translational medicine and therapeutics. However, despite advances in technology, primary open-angle glaucoma remains the leading cause of irreversible blindness worldwide. Traditional intraocular pressure (IOP) -lowering therapies are often not sufficient to prevent progression to blindness, even in patients with access to high-quality healthcare. Neuroprotection strategies, which aim to boost the ability of target cells to withstand a pathological insult, have shown significant promise in animal models but none have shown clinically relevant efficacy in human clinical trials to date. We sought to evaluate the current status of neuroprotection clinical trials for glaucoma and identify limitations which have prevented translation of new glaucoma therapies to date.

METHODS: Literature searches identified English language references. Sources included MEDLINE, EMBASE, the Cochrane Library and Web of Science databases; reference lists of retrieved studies; and internet pages of relevant organisations, meetings and conference proceedings, and clinical trial registries.

RESULTS: We discuss six key neuroprotective strategies for glaucoma that have reached the clinical trial stage. Delivery of neurotrophic factors through gene therapy is also progressing towards glaucoma clinical trials. Refinements in trial design and the use of new modalities to define structural and functional endpoints may improve our assessment of disease activity and treatment efficacy. Advances in our understanding of compartmentalised glaucomatous degeneration and continued progress in the molecular profiling of glaucoma patients will enable us to predict individual risk and tailor treatment.

CONCLUSION: New approaches to future glaucoma neuroprotection trials could improve the prospects for new glaucoma therapies. Glaucoma treatment tailored according to an individual's unique risk profile may become increasingly common in the future.

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