

Is There Room for Modern Stem Cell-Based Therapy in Patients with Retinal Diseases?

Giovanna Soares Nutels, Samantha Sartore Duque Estrada Medeiros, André Luis Ayres da Fonseca, Marcelo Vicente de Andrade Sobrinho
Departamento de Oftalmologia do Hospital PUC-Campinas

INTRODUCTION

Globally, over 2 billion people suffer from vision impairment, a main cause of disability, loss of quality of life and a huge global financial burden.^{1,2} Retinal diseases, such as age-related macular degeneration (AMD) and diabetic retinopathy, are some of the leading global causes of blindness over the age 50³ and modern Stem Cell Based-Therapies are recently been investigated as promising strategies for currently untreatable retinal diseases.⁴⁻⁶ This presentation reviews clinical trials to explore the potential of modern therapeutic Stem Cell Transplantation in retinal diseases in addition to enhancing its visibility and repercussions to scientific research.

METHOD

We conducted a search of clinical trials at Pubmed up to February 17th of 2024 with the terms (Stem Cell Transplantation) OR (Stem Cell-Based Therapy) OR (Stem Cell) AND (Retinal Diseases OR Retina) adding a “Randomized Controlled Trial” (RCT) filter. From 9 articles, 4 did not relate stem cell therapy to retinal diseases and only 2 were randomized. Due to the scarce number of RCTs, we included an extra analysis of clinical trials in the last 5 years using the “Humans” species filter. Of 18 studies, 10 were consistent with our search field.

RESULTS

Both randomized clinical trials^{7,8} demonstrated statistically significant results in improving best corrected visual acuity (BCVA) and visual function on microperimetry in eyes affected by dry AMD, and in reducing the progression of diabetic retinopathy with no major adverse effects.

Study	Population	Retinal Disease	Study	Outcomes	Conclusion
Limoli, 2018	N=25 (mean age 71.5 y); BCVA \geq 1 (logMAR)	Dry age-related macular degeneration	Suprachoroidal autologous graft by LRRT (n=11) x No intervention (n=14)	BCVA and MY test increased significantly in the intervention group	A greater increase of VA in the grafted group after six months
Bonora, 2021	N=41 (mean age 57.4 y)	Diabetic retinopathy	Fenofibrate orally (n=21) x placebo (n=20)	Significantly increased levels of HSPCs; and reduced endothelial differentiation of CD34+ cells	Increased HSPCs levels may explain why fenofibrate reduces retinopathy progression

Abbreviations: BCVA: best-corrected visual acuity; logMAR: logarithm of the minimum angle of resolution; LRRT: Limoli Retinal Restoration Technique; MY: microperimetry; VA: visual acuity; HSPCs: haematopoietic stem/progenitor cells

Recent Clinical Trials Overview

OUTCOMES			STEM CELLS		DISEASES
Increasing of visual function 70			Human Embryonic Stem Cell-derived Retinal Pigment Epithelium Cells 60		STARGARDT DISEASE 40
					RETINITIS PIGMENTOSA 30
Safety and Tolerability 30			BM-MSC 10	HuCNS-SC 10	Geographic Atrophy secondary to Dry Age-related Macular Degeneration 30
			UCMSC 10	WJ-MSC 10	
Slowing of Disease Progression 10	Intra-operative exploratory measures 10	Positive structural + functional results 10			

Abbreviations:

- BM-MSC: Bone Marrow-derived Mesenchymal Stem Cells
- HuCNS-SC: Human Central Nervous System Stem Cells
- UCMSC: Human Umbilical Cord Mesenchymal Stem Cells
- WJ-MSC: Wharton's Jelly-derived Mesenchymal Stem Cells

An overview of recent trials⁹⁻¹⁸ illustrates equivalent focus on Stargardt disease, retinitis pigmentosa and geographic atrophy related to AMD. Most therapies were based on subretinal transplantation of stem cells-derived retinal pigment epithelial cells, having safety and increased visual function as the main outcomes. Positive structural and functional results were also investigated for geographic atrophy - assessed through ellipsoid zone widths, outer retinal thickness, visual acuity, and visual field sensitivity - as well as intraoperative exploratory measures to analyze reduction in the extension of atrophic areas and the best surgical technique.

DISCUSSION/CONCLUSION

Stem Cells Based-Therapy is a promising field for scientific research with known useful interventions in general clinic conditions and, more recently, has been studied for currently untreatable retinal diseases. Although still in their initial phases, in general, such studies demonstrate safety and tolerability, with no severe adverse effects, and promote improvements in visual acuity and in slowing diseases' progression. Surgical combined techniques appear to bypass eventual limitations of subretinal transplantation and to improve its structural and functional results. The need for larger randomized clinical trials is imperative to better evaluate the efficacy of such modern therapies and to assure methodological quality, allied to internal and external validity, which may provide the power of guiding clinical decisions in a hopefully near future.

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