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Stem cell therapy in Retinitis Pigmentosa: a systematic-review and meta-analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

Support - The project has been funded by Indian Council of Medical Science with Ref. ICMR-Call for Application: Eol-2023-000271, (Title of the project: "Evidence Based Guidelines on the Use of Stem Cell Therapy").

Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202450119

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 May 2024 and was last updated on 25 May 2024.

INTRODUCTION

Review question / Objective In patients with retinitis Pigmentosa, what is the efficacy and safety of stem cell therapy as compared to usual care?

Rationale This systematic review and meta-analysis will be the first one to evaluate safety and efficacy of stem cell therapy in retinitis pigmentosa with predefined objectives and methodology with extensive literature search in which evidence will be solely derived from the published randomized control trial.

Condition being studied Retinitis Pigmentosa of all age group.

METHODS

Search strategy (“retinitis pigmentosa” OR "night blindness" OR “hereditary retinal degeneration”) AND ("stem cell" OR "stem cell therapy" OR "precursor cell").

Participant or population Patient with retinitis Pigmentosa of all age group. Retinitis Pigmentosa is defined based on typical ophthalmological findings with or without support by genetic testing.

Intervention Any Stem cell and product derived from stem cells.

Comparator Usual Care/ Conventional Care/no treatment/Placebo therapy.

Study designs to be included Randomized control trials in human in the population of retinitis pigmentosa in which one arm evaluate safety and efficacy of Stem cell therapy.

Eligibility criteria Inclusion criteria:
1. Randomized controlled trials, in human including patients of retinitis pigmentosa
2. All age group, both sex
Exclusion criteria:
1. Animal study
2. Non randomized controlled trials, observational studies, case series and case reports.
3. In-silico, in-vitro and preclinical in-vivo studies will be excluded.

Information sources Data search: A comprehensive literature search will be done by two authors AB and HK using appropriate key words without language restriction in 4 literature databases (PubMed, Embase, Web of Science and Cochrane Library). In case a study is published in a language other than English, the article will be translated to English language using google translate and data will be extracted. Incase the translated article is non comprehensible, the article will be excluded. First the title and abstract will be screened and full text will be screened for the relevant article.
Data extraction: After searching databases, and removal of duplicates, two authors (AB and PS) will independently screen the titles/abstracts using the inclusion/exclusion criteria. For relevant articles, full text will be obtained and evaluated as per inclusion/exclusion criteria. In case of any discrepancy, PS and RK will be consulted, and data extraction will be done independently by three authors (BM, AB and HK) using pre-tested data extraction form following the template provided by the Cochrane data extraction form. After independent verification by PS and RK, the data will be entered into Metaphor R package will be used for the meta-analysis by PS.
Strategy for data synthesis: RevMan, Comprehensive meta-analysis software, open meta-analyst and Metaphor R package will be used for the data analysis. For continuous data, mean difference (MD) and 95% confidence interval (CI) will be calculated. On the other hand, risk ratio will be calculated for dichotomous data. Heterogeneity among the included studies will be estimated using χ^2 and I^2 test. I^2 more than 50% indicated significant heterogeneity and in that case random effect will be used otherwise fixed effect model will be used for analysis. $P<0.05$ will be considered being statistically significant while calculating overall effect in each parameters.

Main outcome(s) Improvement in visual acuity Safety: Severe adverse event.

Additional outcome(s) Important: Quality of Life, quality of vision, Other adverse events.

Data management For continuous data, mean difference (MD) and 95% confidence interval (CI) will be calculated. On the other hand, risk ratio will be calculated for dichotomous data. Heterogeneity among the included studies will estimated using ?^{2} and I^2 test. I^2 more than 50% indicated significant heterogeneity and in that case random effect will be used otherwise fixed effect model will be used for analysis. P?0.05 will be considered being statistically significant while calculating overall effect in each parameters. Continuous data: mean difference with 95% C.I will be calculated. For dichotomous data: Risk ratio will be calculated (95% C. I.).

Quality assessment / Risk of bias analysis We will use ROB2 tool for risk of bias evaluation. We will use GRADE prolifier software to create summary of findings (SOF) table for critical and important outcomes of the study.

Strategy of data synthesis RevMan, Comprehensive meta-analysis software and Metaphor R package will be used for the data analysis. For continuous data, mean difference (MD) and 95% confidence interval (CI) will be calculated. On the other hand, risk ratio will be calculated for dichotomous data. Heterogeneity among the included studies will be estimated using I^2 test. I^2 more than 50% indicated significant heterogeneity and in that case random effect will be used otherwise fixed effect model will be used for analysis. P0.05 will be considered being statistically significant while calculating overall effect in each parameters.

Subgroup analysis Subgroup analysis will be done based on type of stem cell used, route of administration, concentration of stem cell used, and follow up months.

Sensitivity analysis Will be done if high heterogeneity is found in any outcome for studies contributing high heterogeneity.

Language restriction No language restriction.

Country(ies) involved India.

Other relevant information The project has been funded by Indian Council of Medical Science with Ref. ICMR-Call for Application: EoI-2023-000271,

(Title of the project: "Evidence Based Guidelines on the Use of Stem Cell Therapy", Grant no: Grant number EOI/ syst.review/RMRU/2023/11/BMS).

Keywords Stem cell; retinitis pigmentosa; night blindness.

Dissemination plans Article will be published in an indexed journal once it is complete.

Contributions of each author

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