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Association between Neural Stem Cells and Biomaterials in Spinal Cord Injury Therapies: A Systematic Review and Bayesian Network Meta-Analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202450060

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 May 2024 and was last updated on 13 May 2024.

INTRODUCTION

Review question / Objective Is the NSC (Neural Stem Cell)s and combination therapies using biomaterials effective in animal SCI models? The aim of this study was to elucidate the true therapeutic effects of NSPC (neural stem/progenitor cells)s and combination therapies in animal models of SCI by conducting NMA (network meta-analysis), thereby providing a basis for future clinical translation of NSPCs for SCI treatment.

Rationale Spinal cord injury (SCI) is associated with a significant healthcare burden, and it often results in permanent sensory and motor impairments as well as a spectrum of chronic complications. Advanced regenerative therapies have been proposed on the basis of preclinical research findings, but the transition of these therapies to clinical application is still pending. Therefore, we conduct a comprehensive network meta-analysis to evaluate the efficacy of neural stem cell (NSC) transplantation in animal models of spinal cord injury.

Condition being studied Spinal cord injury (SCI) is a serious neurological disease caused by traumatic and non-traumatic injuries, resulting in varying degrees of sensory motor injury and sphincter dysfunction. The incidence of SCI is high and increases annually. Recently, stem cells have been widely used for basic experimental and clinical studies for SCI. The purpose of these stem cells is to deliver growth factors, support nutrition, improve the microenvironment, control the inflammatory response, and rehydrate. They can all live in the host spinal cord for a certain period of time, and differentiate into neurons and glioblastics to promote function recovery. However, the efficacy of clinical trials is inconsistent.

METHODS

Search strategy We search PubMed, Cochrane databases, Scopus, and EMBASE databased from

inception until the end of May 2024 using the keywords ['neural stem cells' OR 'neural precursor cells' OR 'neural progenitor cells' OR 'glial progenitor cells' OR 'neurons' OR 'glial cells' OR 'astrocytes'] AND ['spinal cord injury' OR 'spinal cord contusion' OR 'spinal cord hemisection' OR 'spinal cord transection'].

Participant or population Various types of spinal cord injury of mice or rats.

Intervention Inclusion criteria: rodent models of spinal cord injury involving NSC transplantation with or without the combination of biomaterials. Exclusion criteria: rodent models of spinal cord injury which received stem cells subjected to genetic modification, transdifferentiation, direct conversion from somatic cells, or induction into neural stem cells, as these processes may alter the inherent characteristics of the original NSCs.

Comparator Rodent models of spinal cord injury which received sham treatments using distilled water or phosphate buffered solution.

Study designs to be included Clinical trials or randomized controlled trials.

Eligibility criteria 1) studies involving rodent models of SCI; 2) studies involving NSC transplantation with or without the combination of biomaterials; 3) studies in which comparisons of SCI experimental models with controls(receiving sham treatments using distilled water or phosphate buffered solution) are specified; and 4) studies in which outcomes were mean differences in motor function, electrophysiological function, bladder function, and histological and molecular changes.

Information sources Electronic databases (PubMed, Cochrane databases, Scopus, and EMBASE).

Main outcome(s) Our analysis categorized outcome measures into six domains, assessing a wide spectrum of functions and changes relevant to SCI: motor function, sensory function, bladder function, and electrophysiological function.

Additional outcome(s) Histological changes and molecular changes.

Quality assessment / Risk of bias analysis We performed risk of bias assessments using the RoB2 tool, which was developed by a team of methodologists and statisticians within the Cochrane Collaboration.

Strategy of data synthesis For Bayesian NMA, specific graphical analysis is completed using the “gemtc” package in R software v.4.2.1 (R Foundation for Statistical Computing). To compare the interventional groups (including the control group), the prior distribution and likelihood were fed into a Markov chain Monte Carlo (MCMC) simulation, and the distribution with the best convergence of the posterior distribution was chose.

Subgroup analysis Subgroup analyses (before treatment; cell types; cell numbers; transplantation methods).

Sensitivity analysis There is no sensitivity analysis.

Language restriction This search was conducted regardless of language or study type.

Country(ies) involved Republic of Korea.

Keywords spinal cord injury; network meta-analysis; neural stem cells; scaffold; hydrogel.

Contributions of each author

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