INPLASY

Stem Cell-Derived Insulin-Producing and Pancreatic Endocrine Cells in Type 1 Diabetes: Pioneering Approaches to a Functional Cure

INPLASY2024110116
doi: 10.37766/inplasy2024.11.0116
Received: 27 November 2024
Published: 27 November 2024

Hirani, K; Saavedra, D; Doshi, J; Lemos, J; Hirani, K; Mittal, R.

Corresponding author:
Rahul Mittal

r.mittal11@med.miami.edu

Author Affiliation:
University of Miami Miller School of Medicine.

ADMINISTRATIVE INFORMATION

Support - Not Applicable.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2024110116

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 27 November 2024 and was last updated on 27 November 2024.

INTRODUCTION

Review question / Objective What is the efficacy and safety of stem cell-derived insulin-producing and pancreatic endocrine cell transplantation in achieving functional glycemic control and reducing insulin dependence in human patients with Type 1 Diabetes (T1D)?

Rationale Type 1 Diabetes (T1D) is characterized by the autoimmune destruction of insulin-producing pancreatic beta cells, leading to chronic hyperglycemia and the need for lifelong insulin therapy. Recent advancements in stem cell biology have opened new avenues for developing functional cures through the generation of stem cell-derived insulin-producing and pancreatic endocrine cells. This systematic review aims to critically evaluate the outcomes of stem cell-derived cell therapies in T1D, with an emphasis.

Condition being studied Type 1 Diabetes.

METHODS

Participant or population This systematic review focuses on human patients diagnosed with Type 1 Diabetes (T1D), including children, adolescents, and adults, who have undergone transplantation of stem cell-derived insulin-producing cells (SC-IPC) or pancreatic endocrine cells (PEC). The population includes individuals at various stages of the disease, from newly diagnosed to those with long-standing T1D, aiming to evaluate the clinical application of these therapies. Studies will be included if they report on outcomes related to glycemic control, insulin independence, safety, and overall functional improvement following transplantation.

Intervention The primary intervention under review involves the transplantation of stem cell-derived insulin-producing cells (SC-IPCs) or other stem cell-derived pancreatic endocrine cells into human patients with Type 1 Diabetes (T1D).

Comparator The comparator group for this systematic review will include studies that assess outcomes before and after the transplantation of stem cell-derived insulin-producing and pancreatic endocrine cells in human patients with Type 1 Diabetes (T1D).

Study designs to be included The studies included in the systematic review will encompass clinical trials and observational studies assessing the safety, efficacy, and functional outcomes of stem cell-derived insulin-producing and pancreatic endocrine cell transplantation in Type 1 diabetes patients, utilizing pre- and post-treatment comparisons and, where available, placebo-controlled designs.

Eligibility criteria Studies must involve human participants receiving stem cell-derived insulin-producing or pancreatic endocrine cell transplantation.Must report outcomes related to Type 1 Diabetes treatment or management.Must include a comparator group (e.g., before and after treatment, placebo, or alternative interventions).Published in peer-reviewed journals.Written in English.Must provide quantitative or qualitative data on clinical outcomes (e.g., glycemic control, insulin independence, adverse effects).Studies must be full-text articles (conference abstracts, case reports, and editorials are excluded).

Information sources The electronic databases to be searched for the systematic review include PubMed/MEDLINE, EMBASE, Cochrane Library, Web of Science, Scopus, ClinicalTrials.gov, and Google Scholar.

Main outcome(s) Improved glycemic control observed post-transplantation, with reduced insulin requirements in treated patients.
Sustained production of C-peptide indicating functional insulin secretion.
Enhanced HbA1c levels in patients receiving stem cell-derived cell therapies compared to baseline or control groups.
Reduction in the incidence and severity of hypoglycemic episodes.
Minimal immune rejection observed with immunosuppressive protocols or encapsulation techniques.
Evidence of engraftment and survival of transplanted cells in vivo based on follow-up imaging and biomarker analysis.
Patient-reported quality of life improvements, including fewer diabetes-related complications.
No significant adverse events reported related to the cell therapy in most studies.
Longevity of therapeutic effects documented over extended follow-up periods in a subset of studies.
Variability in outcomes attributed to differences in cell sources, preparation protocols, and patient-specific factors.

Data management All relevant studies will be systematically identified through comprehensive searches of peer-reviewed databases such as PubMed, Embase, and Web of Science. Search results, including titles, abstracts, and full texts, will be screened. Study selection will follow predefined inclusion and exclusion criteria, with decisions recorded in a PRISMA flow diagram. Extracted data will be stored in a standardized, secure format, including key variables such as study design, patient population, intervention details, outcomes, and comparators. Quality assessment of included studies will be documented using validated tools. All data will be reviewed independently by multiple authors to minimize bias and ensure consistency, with discrepancies resolved through discussion or consultation with a third reviewer.

Quality assessment / Risk of bias analysis The quality assessment and risk of bias analysis for this systematic review will be conducted using the Joanna Briggs Institute (JBI) critical appraisal tools. The JBI tool will be employed to evaluate methodological rigor across various study designs, including randomized controlled trials (RCTs), cohort studies, and case series. Each study will be assessed for key domains such as patient selection, allocation concealment, blinding, attrition, outcome measurement, and statistical analysis. Particular attention will be given to the reporting of baseline characteristics, the use of appropriate control groups (e.g., placebo or standard of care), and the clarity in defining outcomes, including glycemic control, insulin independence, and adverse events. Risk of bias will be identified in studies with incomplete follow-up data, inadequate blinding, or insufficient control for confounding factors.

Strategy of data synthesis The data synthesis will focus exclusively on human studies assessing the safety, efficacy, and functional outcomes of stem cell-derived insulin-producing and pancreatic endocrine cell therapies for Type 1 Diabetes (T1D). Key outcomes include glycemic control (HbA1c, C-peptide, insulin requirement reduction), safety (adverse events, immune reactions), immunological markers (autoantibodies, T-cell activation), and quality-of-life improvements. Findings will be summarized descriptively, highlighting variations in stem cell sources, delivery methods, and follow-up

durations. Qualitative outcomes, including patient-reported experiences and safety profiles, will be thematically analyzed to identify trends and challenges. Risk of bias will be assessed using standardized tools, and results will be presented in structured tables and narrative summaries to provide a clear understanding of the current state of research, highlighting gaps and opportunities for future investigation. Limitations, such as small sample sizes and short follow-up periods, will be acknowledged for balanced interpretation.

Subgroup analysis Not Applicable.

Sensitivity analysis Not Applicable.

Country(ies) involved USA.

Keywords Stem Cell-Derived Insulin-Producing Cells; Pancreatic Endocrine Cells; Type 1 Diabetes.

Contributions of each author
Author 1 - Krish Hirani.
Author 2 - Danay Saavedra.
Author 3 - Jhanvi Doshi.
Author 4 - Joana Lemos.
Author 5 - Khemraj Hirani.