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Title.

Stem cell therapy for patients with diabetes: a systematic review and meta-analysis of metabolomics-based risks and benefits.

Introduction.

Diabetes mellitus (DM) is a major health problem and the leading cause of death in the world; it is particularly responsible for 4 million deaths per year (1). The prevalence and incidence of DM in many societies, especially in developing countries, have been increasing more rapidly (2). In 1985, pieces of evidences revealed that 30 million people worldwide had DM; moreover, up to 230 million individuals were affected by 2008; and by the year 2025, the number of individuals with DM is expected to reach 300 million (3).

The traditional therapeutic methods such as administration of exogenous insulin through daily injections is the most prominent treatment for DM, but its administration is frequently associated with failure in glucose metabolism control, which ultimately leads to hyperglycemia episodes. Stem cell therapy holds a promising strategy to avoid the issues related to insulin daily injections. It is expected that this therapeutic method should produce, store, and supply insulin to maintain glucose homeostasis. Cell-based therapies are aimed at producing functional insulin-secreting β-cells to completely cure diabetes (4-6).

Over the years, researchers have been searching for ways to replace the destroyed beta cells in the pancreas (insulin-producing cells) with healthy ones by the immune system of a person with DM. Nowadays, the latest method of transplantation and replacement of pancreatic cells, in which clusters of insulin-producing cells, called islet, are transplanted from a donor pancreas to another liver, have provided excellent results for the treatment of type 1 diabetes patients (7). Changing the amount of insulin is often accompanied by a drop in blood glucose level or hypoglycemia, which can lead to medical emergencies such as coma. On the contrary, in the islet transplantation technique if the transplant works properly, the results will be very promising; thus, glycemic control is done by the body itself, and the amount of insulin needed is given to the body with respect to the amount of body glucose in the body; and homeostasis is done normally. Stem cell therapy for DM, which is in fact an attempt to eliminate insulin injections, leads to complications such as infectious diseases and cancer (8-10). Side-effects can occur at any time during, immediately, or several days or months after stem cell transplantation. Short-term side-effects (acute) usually occur within the first 100 days post-transplantation, while long-term side-effects (chronic) usually occur after 100 days or more after transplantation. Infectious diseases are among the most common primary side effects of stem cell transplantation which occurs due to very low white blood cell count and weak immune system. Though bacterial infections are the most common, viral or fungal infections may also occur.

To ensure that the emerging field of stem cell therapy fulfills its promise to patients with diabetes, we must first understand its risks and benefits; thus, if there will be greater health benefits and fewer risks, it may lead to developing a novel therapeutic approach based on sound science. A systematic review and meta-analysis was performed using all available clinical trials to determine the benefits and risks associated with stem cell therapy in patients with diabetes (both T1DM and T2DM).

Methodology.

This systematic review and meta-analysis was conducted according to the guidelines of the Centre for Reviews and Dissemination for undertaking systematic reviews (11), as well as the Meta-analysis of Observational Studies in Epidemiology (MOOSE) (12), and PRISMA guidelines (13). This research was approved by Ethics Committee of Tehran University of Medical Sciences (TUMS).

Types of studies

All relevant clinical trials examining the effectiveness of stem cells for the treatment of patients with diabetes were included without restrictions on publication status.

Types of participants

There was no limitation on age and sex for the inclusion in the study. Participants were excluded if they had further pathologies or changed endocrine status other than diabetes.

Types of interventions

Stem cell therapy is a method of using various types of stem cell in the treatment of T1DM and T2DM. The interventions and comparison include: (I) stem cell therapy compared to the control group; (II) stem cell therapy compared to placebo; (III) stem cell therapy compared to traditional treatment.

Types of outcome measures

Outcome measures included the type of stem cells [e.g., bone marrow mesenchymal stem cells (BM-MSCs), BM hematopoietic stem cells (BM-HSCs), umbilical cord MSCs (UC-MSCs), adipose stem cells (ASCs), mesenchymal precursor cells (MPCs), fetal stem cells (FSCs)], number of injected cells, method of stem cell delivery (intravenous or intrapancreatic administration), and follow-up time after cell therapy.

Search strategy

All studies on stem cells therapy in the treatment of diabetes were entered with no time limitation (all studies conducted by the end of July, 2017). A literature search strategy was developed using medical subject headings (MeSH) and keywords.

Electronic bibliographic databases

The following electronic bibliographic databases were searched: PubMed, Scopus, Web of Science, EMBASE and the Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL). The search strategy included stem cells, progenitor cells, BM, BM-HSCs, BM-MSCs, UC-MSCs, ASCs, MPCs, FSCs, DM, T1DM, T2DM, and hyperglycemia. Limitation was placed on the search using English language and human subject filters. The search strategy for PubMed is shown in Figure S1.

Figure S1

Figure S1

PubMed search strategy.

Searching other resources

To ensure literature saturation, reference lists of selected studies or relevant reviews were scanned.

Inclusion criteria

Articles fulfilling the following criteria, including clinical trial studies on various stem cell therapies for both T1DM and T2DM, were considered. Besides, no language limitation was applied.

Exclusion criteria

Other article types such as reviews (narrative or systematic), observational studies, commentaries, letters to the editor, case series or case reports, and pooled analyses of original data were excluded.

Data collection

Selection of studies After an electronic search, the records were uploaded using EndNote software. Titles and abstracts of studies were retrieved using the search strategy and those from additional resources were reviewed individually by two authors (F Rahim and K Shirbandi) to detect studies that possibly meet the inclusion criteria. The full text of these possibly qualified articles was retrieved and evaluated individually by the same authors.

Any disagreements between the two authors were resolved through discussion. The whole process of study selection is summarized in the PRISMA flow diagram.

Data extraction and management A standardized data collection form was used for assessing the quality of selected studies, as well as for evidence synthesis. The extracted information includes:

General information (author, title, publication year, journal, location).

Participant demographics and baseline characteristics [sample size, mean (range) age].

Details of the intervention (cell type, number of cells injected, method of cell) delivery (intravenous or intra-pancreatic administration).

Control conditions (no treatment, placebo therapy).

Outcome measures (reported outcomes, adverse events, follow-up time and mechanism).

Assessment of risk of bias in included studies The risk of bias was assessed independently by the two authors using the CONSORT checklist for reporting details of intervention for the treatment of diabetes (14).

The following domains were assessed for the risk of bias:

Selection bias in terms of random sequence generation and allocation concealment.

Performance bias in terms of blinding of participants, investigators and outcome assessors.

Detection bias in terms of blinding of outcome assessment.

Attrition bias in terms of incomplete outcome data.

Reporting bias in terms of selective outcome reporting.

Other bias in terms of for example, conflicts of interest, follow-up, non-intention-to-treat or per-protocol analysis. Disagreements between the authors in certain articles were resolved by discussion.

Measures of treatment effect

Review Manager 5.3 was used for data analysis and quantitative data synthesis. The treatment effect was measured using standardized mean difference (SMD) with 95% confidence intervals (CIs) in the case of continuous variables. Besides, a risk ratio (RR) with 95% CIs for analysis was used for categorical variables.

Unit of analysis issues

In the included trials, subjects were randomized into two intervention groups; and a measurement for each outcome was collected and analyzed. Data from the parallel group-designed and cross-over designed trials were included.

Dealing with missing data

Attempt was made to contact the corresponding authors of the studies that had missing or insufficient data. If it is not possible to get the missing data, then only the available data were analyzed and a sensitivity analysis was performed to determine whether the results are inconsistent.

Assessment of heterogeneity

Heterogeneity between the studies in terms of the measures of effect was assessed using both the Chi-square based Q test and I2 statistics. The result of the Q test was considered statistically significant at

P<0.1. If the I2<50%, the study would be considered as not having heterogeneity. However, I2≥50% indicated significant statistic heterogeneity which would be reported accordingly, and meta-regression or a subgroup analysis was performed to explore the possible causes.

Assessment of reporting biases

Publication bias was assessed using the Egger test. Also, Funnel plots were used to detect possible reporting biases.

Data synthesis

Meta-analysis was performed using Review Manager 5.3. The results of Q test were presented using either a fixed effect or random effect models. In case of significant statistical heterogeneity, a random effect model was used; otherwise, a fixed effect model was used. Also, subgroup analyses or meta-regression were conducted if heterogeneity was present.

Subgroup analysis

If significant heterogeneity was observed, subgroup analyses were performed using both following assumptions:

Comparison between stem cell therapy and no treatment.

Comparison between stem cell therapy and placebo.

Sensitivity analysis

A sensitivity analysis was conducted considering the quality of selected studies (risk of bias) in order to investigate potential sources of heterogeneity. The methodological quality was assessed based on sample size and the effect of missing data. The meta-analysis was repeated and low-quality studies were excluded. The results were compared and discussed according to the extracted results from other studies.

Ethics and dissemination

In this study, ethical approval was not required because the data were extracted from peer-reviewed publications.

Ethical approval

This research was approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran.

Results.

Search results and description of studies

Overall, a total of 4,629 relevant studies were initially found. After removing 990 duplicates studies and the title-abstract screening also excluded 3,639 studies, a total of 27 studies were finally used for the systematic review and meta-analysis. Figure 1 outlines the search method and the number of studies identified and selected during each phase of the search.

Table 1 provides a detailed overview of the 27 studies. Out of the 27 trials, the mean patient age with diabetes was 31.71±21.47 years. The total of the patients were 705 subjects among whom 245 were females (34.75%) and the remaining were male. Stem cell therapy had been practiced in patients with both T1DM (16 studies, 342 patients) and T2DM (11 studies, 363 patients).

General characteristics of the included studies

Given the source of cells, six trials used HSCs (149 patients), six studies used BM-mononuclear cells (BM-MNCs) (195 patients), five studies used UCB (74 patients), two trials used UC-MSCs (51 patients), 3 studies used a combination of various stem cells (73 patients), one study used BM-MSCs (20 patients), and one study used placenta-derived MSCs (PD-MSCs, 10 patients). Two studies used MPCs (91 patients) and one study used FSCs (42 patients). These studies locations were India (n=4), Brazil (n=1), USA (n=4), Poland (n=1), China (n=12), Germany (n=1), Sweden (n=1), Australia (n=1), Ukraine (n=1), and Lebanon (n=1).

The outcome of stem cell therapy for T1DM

The mean age of patients with T1DM was 17.31±11.08 years. Stem cell therapy was performed in 16 trials [342 patients with T1DM, 132 females (38.59%)] (Table 1). Stem cell therapy improved the c-peptide levels as well as glycosylated hemoglobin (HbA1C), and had a positive effect on these variables, but induced a negative impact on insulin daily requirement and failed to resolve this problem (Table 2, Figures 2 and 33).

The effect of stem cell therapy on the insulin daily requirement levels, HbA1C and peptide in different types of diabetes

Forest plots showing the individual results of administrating different types of stem cells in diabetes mellitus: (A) HbA1C (%); (B) C-peptide (ng/mL); (C) daily insulin requirement (U/kg per day). HbA1C, glycosylated hemoglobin.

Funnel plot of comparing the individual results of administrating different types of stem cells in diabetes mellitus: (A) HbA1C (%); (B) C-peptide (ng/mL); (C) daily insulin requirement (U/kg per day). HbA1C, glycosylated hemoglobin.

The outcome of stem cell therapy for T2DM

The mean patient age with T2DM was 56.20±7.49 years. Stem cell therapy was performed in 11 studies [363 patients with T2DM, 113 females (31.12%)] (Table 1). Stem cell therapy improved the insulin daily requirement levels, as well as HbA1C, and had a positive effect on these variables, but had a negative impact on c-peptide (Table 2, Figures 2 and 33).

Our review concluded that 20 various adverse events were reported for patients treated with stem cells among which fever was the highest reported symptom with an incidence rate of 0.14%. Also, muscle strain, contusion, viral gastroenteritis, hematuria, and folliculitis complications were the lowest reported adverse effects, with an incidence rate of 0.02%

Conclusions.

Stem cells have the ability to be self-renewed and differentiate into a variety of cells, including blood, heart, nervous and cartilage cells. Paradoxically, it has been stated that these cells also have the potential to form cancer cells. These possible risks necessitate that both medical specialists and patients should proceed the treatment with caution; thus, it is critically crucial to conduct further research on stem cell therapy considering their risk and benefits in the first place.

References.

1. Tabish SA. Is Diabetes Becoming the Biggest Epidemic of the Twenty-first Century? Int J Health Sci (Qassim) 2007;1:V-VIII. [PMC free article] [PubMed] [Google Scholar]

2. Ramachandran A, Snehalatha C, Shetty AS, et al. Trends in prevalence of diabetes in Asian countries. World J Diabetes 2012;3:110. 10.4239/wjd.v3.i6.110 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

3. Scully T. Diabetes in numbers. Nature 2012;485:S2-3. 10.1038/485S2a [PubMed] [CrossRef] [Google Scholar]

4. Farooq T, Rehman K, Hameed A, et al. Stem Cell Therapy and Type 1 Diabetes Mellitus: Treatment Strategies and Future Perspectives. Adv Exp Med Biol 2018. [Epub ahead of print]. 10.1007/5584_2018_195 [PubMed] [CrossRef] [Google Scholar]

5. Rattananinsruang P, Dechsukhum C, Leeanansaksiri W. Establishment of Insulin-Producing Cells From Human Embryonic Stem Cells Underhypoxic Condition for Cell Based Therapy. Front Cell Dev Biol 2018;6:49. 10.3389/fcell.2018.00049 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

Note.

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Effort by

Dr. Muhammad Iqbal arain.