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REVIEW

Therapeutic use of stem cells obtained from the cord umbilical in patients with diabetes mellitus type I

Uso terapéutico de células madres obtenidas del cordón umbilical en pacientes con diabetes mellitus tipo I

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ABSTRACT

Current medicine with a boom in stem cell therapies has great enthusiasm and hope to advance in the cure of some diseases that for many years have affected a large part of the world's population and that as the years go by, the incidence, relapses increase. of the disease, crisis, hospitalizations, comorbidities, complications that can not only affect the patient's health more, but also increase costs for hospitals and the state, in the midst of saving the lives of these patients; For years, the pharmaceutical industry has also produced different medications in search of a less invasive and more specific treatment for each patient, also increasing the cost of maintaining this disease; said disease diabetes mellitus (DM). Diabetes mellitus is a metabolic disease characterized by hyperglycemia and ß-cell dysfunction. In this research we have the objective of focusing the therapeutics and efficacy on stem cells derived from the umbilical cord. that specifically provide several advantages and unique characteristics for said disease.

Keywords: Cells; Disease; Diabetes; Therapy; Umbilical Cord.

RESUMEN

La medicina actual con auge en terapias con células madre tiene una gran ilusión y esperanza para avanzar en la cura de algunas enfermedades que por muchos años ha afectado a gran parte de la población mundial y que a medida que pasan los años aumentan la incidencia, recaída de la enfermedad, crisis, internaciones, comorbilidades, complicaciones que no solo le puede afectar más la salud del paciente, sino que también aumenta costos para hospitales y el estado, en medio de salvar la vida a estos pacientes; la industria farmacéutica también durante años ha producido diferentes medicamentos en busca de un tratamiento menos invasivo y más específico para cada paciente, incrementando así mismo el costo de manutención de esta enfermedad; dicha enfermedad diabetes mellitus (DM). La diabetes mellitus es una enfermedad metabólica caracterizada por hiperglucemia y disfunción de las células ß. En esta investigación tenemos el objetivo de enfocar la terapéutica y eficacia en células madre derivadas del cordón umbilical que proporcionan específicamente varias ventajas y características únicas para dicha enfermedad.

Palabras clave: Células; Enfermedad; Diabetes; Terapéutica; Cordón Umbilical.

INTRODUCTION

Diabetes mellitus is a disease whose incidence is increasing. It currently affects around 463 million people worldwide, expected to grow to 700 million by 2045.(1) It is estimated that 1 in 10 Argentines aged 18 or older

has diabetes, which has led us to seek alternative sources of treatment. Regenerative medicine focuses on and encourages us to research various types of stem cells for their therapeutic potential in diabetes mellitus in preclinical and clinical settings.[2] Among the different sources of stem cells, the umbilical cord has proven to be a unique source, providing several advantages over others. Most importantly, stem cells derived from the umbilical cord are readily available and can be obtained non-invasively during the process. This intervention is currently in phase I/II clinical trials to evaluate its efficacy and condition and its safety for improving insulin resistance and treating diabetes mellitus.

General Objective

To analyze diabetic patients undergoing treatment with umbilical cord-derived stem cells that improve glycemic control compared to diabetic patients undergoing exogenous insulin treatment.

To evaluate the current medical therapies and treatments for the benefit of metabolic control in type I diabetic patients.

METHOD

This thesis is based on a comprehensive review of the scientific literature on the therapeutic use of hematopoietic mesenchymal stem cells obtained from umbilical cord or gelatin in patients with type I diabetes mellitus. To this end, a systematic approach was followed to search and analyze relevant articles addressing this topic.

Literature Search

The computer-based literature was reviewed extensively in databases such as Scopus, Web of Science, MEDLINE/PubMed, the Cochrane Library for clinical trials, the public database of clinical trials (ClinicalTrials.gov), and the Argentine government's glossary website. This search was conducted in databases up to June 2024. In general, searches were conducted in the database using the following keywords: (umbilical cord OR Wharton's jelly mesenchymal stem cells OR umbilical cord blood) AND (diabetes mellitus OR hyperglycemia). The term "stem cell transplantation" was also used when searching the Cochrane Library and the Scopus database, and the MeSH term "umbilical cord blood stem cell transplantation" was also used when searching MEDLINE/PubMed.

In more detail, for MEDLINE/PubMed, the following query was performed: ((Wharton's jelly mesenchymal stem cells) OR (umbilical cord blood stem cell transplantation [MeSH Terms])) OR (umbilical cord [MeSH Terms]), and then the following query: (diabetes mellitus [MeSH Terms]) OR (hyperglycemia [MeSH Terms]), then search for reports standard to both search queries as follows: ((diabetes mellitus [MeSH Terms]) OR (hyperglycemia [MeSH Terms])) AND ((Wharton's jelly mesenchymal stem cells) OR (umbilical cord blood stem cell transplantation [MeSH Terms])) OR (umbilical cord [MeSH Terms])). The reports found in all databases were downloaded to the citation manager, who identified and attempted to exclude duplicates and review irrelevant articles and reports. Finally, in the search in the public clinical trial database, "diabetes mellitus" (DM1) was used as the disease, and "umbilical cord" was used as an additional search term. During the search, no restrictions were specified regarding the type of article, and all relevant published analyses and their reference lists and bibliographies were also checked.

This process allowed us to identify relevant studies, clinical trials, systematic reviews, and meta-analyses that contribute to understanding the therapeutic potential of umbilical cord-derived stem cells in type I diabetes.

Article Selection

Inclusion and exclusion criteria were established to select the articles to be reviewed. The articles included in this review were those that:

- Were published in the last 10 years to ensure current information.
- Presented results on the efficacy and safety of umbilical cord stem cell treatment in type I diabetic patients.
- Were clinical studies, systematic reviews, or relevant case reports.

On the other hand, studies that did not specifically address the use of stem cells in treating type I diabetes were excluded, as were those that did not provide precise data on methodology or results.

Data Analysis

Once the selected articles were compiled, each one was critically analyzed. Data on the methods used, the population studied, the results obtained, and the authors' conclusions were extracted. This process included evaluating the methodological quality of the studies, which allowed for the identification of studies from

reliable and trustworthy sources based on the evidence presented.

Synthesis of Results

Finally, the most relevant findings were synthesized, organizing the information into thematic categories that address different aspects of the therapeutic use of umbilical cord stem cells in patients with type I diabetes mellitus. This synthesis was structured according to the reported benefits, the proposed mechanisms of action, and the side effects associated with the treatment.

RESULTS

Umbilical cord stem cell therapy was applied in five patients either through intravenous infusion in the four studies of type 1 diabetes mellitus included or intrapancreatic infusion in the only study of type 2 diabetes mellitus excluded from the patients to be treated.[1,2,3,4] As with umbilical cord-derived stem cells obtained from Wharton's jelly mesenchymal cells, to evaluate the therapeutic efficacy of umbilical cord cells, an analysis should be performed for the specified outcomes HbA1c% and C-peptide levels before and after the stem cell intervention and also compare these outcome measures between patients who received the intervention and those who did not receive it and are on exogenous insulin therapy.

The literature review on the therapeutic use of hematopoietic and mesenchymal stem cells obtained from the umbilical cord in patients with type I diabetes mellitus has revealed promising results about glycemic control and β-cell function, as measured by hemoglobin A1c (HbA1c) and C-peptide.

Glycemic Control

Several reviewed studies indicate that the infusion of hematopoietic or mesenchymal umbilical cord stem cells can significantly improve glycemic control.[2,5,6] In a clinical trial involving patients with type I diabetes, HbA1c levels were reduced from an initial average of 8,5 % to 6,5 % six months after treatment with hematopoietic or mesenchymal umbilical cord blood stem cells. This decrease is significant compared to control groups that only received exogenous insulin, where HbA1c remained virtually unchanged.

Beta Cell Function

Beta cell function also showed improvements in the studies reviewed. C-peptide levels, an indicator of beta cell function, increased in patients treated with hematopoietic or mesenchymal umbilical cord blood stem cells. In specific studies, C-peptide levels increased from 0,5 ng/mL before treatment to 1,2 ng/mL at six months.[7,8] This increase is relevant, as it suggests possible regeneration or improvement in β-cell function, in contrast to patients who received insulin treatment alone, whose C-peptide levels showed no significant changes.

Insulin Dose

The review also notes that the use of hematopoietic or mesenchymal umbilical cord stem cells may reduce insulin requirements in patients with type I diabetes. Some studies reported that patients who received infusions of hematopoietic or mesenchymal umbilical cord stem cells reduced their daily insulin dose by 30 % at six months, while patients on conventional exogenous insulin therapy showed no change in their doses.[1,2,9]

Side Effects and Safety

Regarding safety, most studies reported that treatment with hematopoietic or mesenchymal umbilical cord stem cells was well tolerated. The adverse effects reported were mild and transient, such as fever or general malaise, which resolved without medical intervention.[4] No serious adverse effects associated with stem cell therapy were documented.

Quality of Life

Finally, the review also included data on patients' quality of life. Studies suggest that those treated with hematopoietic or mesenchymal umbilical cord blood stem cells reported significant improvements in their quality of life, reflected in high scores on standardized questionnaires.[2,5,6] This improvement may be related to better glycemic control and decreased insulin requirements.

DISCUSSION

The literature review on the therapeutic use of hematopoietic or mesenchymal umbilical cord blood stem cells in patients with type I diabetes mellitus reveals promising findings regarding improved glycemic control and β-cell function, as measured by hemoglobin A1c (HbA1c) and C-peptide.

Improved Glycemic Control

The analyzed studies indicate that the infusion of hematopoietic or mesenchymal umbilical cord blood stem

cells may significantly reduce HbA1c in patients with type I diabetes.[1,3,4] These improvements suggest that stem cells could be fundamental in modulating glycemic metabolism. The ability of hematopoietic or mesenchymal umbilical cord stem cells to influence the immune microenvironment and stimulate β-cell regeneration is postulated as a key mechanism.[2] However, there is a critical need for further research into how these cells interact with the immune system and metabolic pathways to optimize their clinical application.

β Cell Function and C-Peptide Levels

Increased C-peptide levels in patients treated with hematopoietic or mesenchymal umbilical cord stem cells highlight the potential restoration of β cell function.[5] This observation is relevant, as preserving insulin function is crucial for the long-term management of type I diabetes. The literature suggests that hematopoietic or mesenchymal umbilical cord blood stem cells may release growth factors that protect and promote the health of these cells.[6] This raises an intriguing possibility: if treatment protocols that maximize these effects are identified and developed, it may be possible to improve glycemic control and reverse aspects of the disease.

Comparison with Exogenous Insulin Treatment

Results comparing patients treated with hematopoietic or mesenchymal umbilical cord stem cells with those on standard exogenous insulin therapy reveal significant differences.[7] Patients receiving stem cells not only experience better glycemic control but also show a decrease in insulin requirements. This finding suggests that stem cell therapies could complement or even replace traditional approaches, opening new avenues for research.[8] Further exploration is needed to determine how these therapies can be integrated into existing treatment regimens and the duration of their effects.

Safety and Tolerance of Therapy

The review also highlights that most studies report a favorable safety profile for using hematopoietic or mesenchymal umbilical cord stem cells.[8,9] Side effects are generally mild and transient, suggesting that these therapies could be viable for patients. However, to consolidate this perception, it is essential to conduct larger, long-term studies that evaluate safety in diverse patient populations, including those with comorbidities.

Implications for Clinical Practice and Future Research

Identifying the needs for future research is crucial. A multidisciplinary approach that considers cell biology, patient psychology, health economics, and the ethical aspects of stem cell therapy is required. In addition, clinical trials need to be designed to include a variety of conditions and treatment protocols to determine how best to apply these therapies in clinical practice.

Speculating on the broader implications of these findings, one can imagine a future where stem cells contribute to improved glycemic control and prevent complications associated with type I diabetes. The possibility of regenerating β cells and restoring insulin function suggests that we are on the threshold of a new era in diabetes treatment, where cell therapies could offer long-term solutions and perhaps even a cure.

In conclusion, stem cells obtained from the umbilical cord show great potential in treating type I diabetes mellitus, with significant benefits in glycemic control and β cell function. However, continued commitment to research is needed to fully explore its capabilities and define its place in the therapeutic arsenal for this chronic disease.

CONCLUSIONS

To conclude this thesis, it is essential to summarize the findings on the use of umbilical cord stem cells in treating diabetes. Throughout this study and the literature reviewed, these cells' regenerative and differentiating capacity has been analyzed, as well as their potential to reverse or improve damage to pancreatic cells, a key aspect for managing this chronic disease. Based on the results obtained and the exhaustive analysis of the scientific literature, the contributions this type of cell therapy offers to diabetic patients were found, and the main limitations and opportunities for future research were identified. The main conclusions are detailed here.

Regenerative Potential of Stem Cells: Stem cells derived from the umbilical cord have shown significant regenerative potential in various studies. Their ability to differentiate into pancreatic beta cells may offer a promising solution for restoring insulin production in patients with type 1 diabetes mellitus. This approach could change the current treatment paradigm, which focuses primarily on managing symptoms rather than addressing the underlying cause of the disease.

Safety and Efficacy in Therapy: To date, clinical trials have indicated that umbilical cord stem cells are safe, with minimal adverse effects reported. Although some initial studies suggest improvements in pancreatic function and glycemic control, further research is crucial to validate these findings and establish standardized treatment protocols that maximize therapeutic efficacy.

Immunomodulatory Properties: Umbilical cord stem cells are notable for their ability to exert

immunomodulatory effects. This is especially relevant in the context of type 1 diabetes, where the immune system mistakenly attacks the beta cells of the pancreas. By potentially reducing the autoimmune response, these cells could contribute to prolonging disease remission and improving patients' quality of life.

Ethical Considerations and Accessibility: Collecting umbilical cord stem cells presents fewer ethical dilemmas than embryonic stem cells. In addition, they are relatively easy and accessible to obtain, making them an attractive option for cell therapy. This accessibility could facilitate the implementation of large-scale treatments in the future.

Need for Continued Research: Despite promising advances, research on the use of umbilical cord stem cells in type 1 diabetes is still in its early stages. More controlled, long-term clinical trials that evaluate not only the efficacy of the treatment but also its long-term side effects and the best way to integrate this therapy into standard clinical care are essential.

Future Prospects and Technological Development: Advances in umbilical cord stem cell collection, processing, and administration technologies could significantly impact therapeutic outcomes. Innovations in these areas may facilitate the clinical application of this therapy, allowing for a more personalized and practical approach to treating type 1 diabetes mellitus.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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