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REVIEW ARTICLE

Use of stem cells in endodontic treatments

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ABSTRACT

Introduction: bioengineering has boosted pulp regeneration with stem cells from various sources, improving recovery and avoiding invasive treatments, which represents a significant advance for dentistry and patient health.
Objective: describe stem cells and regeneration factors applied in endodontics.
Methods: a systematic search was conducted in databases such as Scielo, Elsevier, Google Scholar, and PubMed, including studies in English and Spanish published in recent years on stem cells in dentistry. Relevant articles on endodontic treatments and pulp regeneration were selected, excluding those unrelated to this field.
Development: currently, bioengineering has advanced as much as other sciences, carrying out the process of pulp regeneration with stem cells obtained from different parts of the human body. The studies analyzed highlight the application of stem cells in dentistry, especially in endodontic and periodontal regeneration. It was found that stromal cells combined with bone preserve bone structure better than stem cells alone. Furthermore, their cell migration and differentiation capacity allow for the treatment of lesions in the oral cavity, although their function may be affected in diabetic patients. Regenerative medicine shows advances in less invasive treatments, although technical challenges persist.
Conclusions: stem cells have great potential in dentistry, promoting endodontic regeneration and tissue restoration. Their application faces ethical challenges, but research continues to optimize biological treatments and effectively expand their clinical uses.

Keywords: Stem Cells; Stromal Cells; Regenerative Endodontics.

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INTRODUCTION

Endodontics is the ideal therapy for preserving natural teeth, protecting the pulp and periapical tissues. However, loss of pulp vitality can be due to trauma, infection, or deep caries, which is treated with pulp extraction and biocompatible materials such as composites and gutta-percha. Although effective, endodontics can weaken teeth, making them prone to fractures and reinfection due to leaks. Furthermore, factors such as excessive heat, inadequate irrigation, or disproportionate instrumentation can cause inflammation, affecting treatment success.[1,2]

In the early 2000s, while scientists were studying tooth regeneration, they were able to identify stem cells from dental pulp by observing how they created new, unique colonies in cultures, with in vitro multi-differentiation. Three years later, stem cells from deciduous teeth were identified, and a year later, stem cells from the periodontal ligament were isolated. In 2005, stem cells from the dental follicle of wisdom teeth were identified, and in 2006, stem cells from the apical papilla of immature teeth were recognized.[3]

Therefore, it can be detailed how, in the last 20 years, dental regenerative medicine has provided us with an immeasurable effectiveness and advancement in the conservation and application of stem cells in the dental field. These cells, fundamental in the development of the 200 cell types of the human body, have great potential in endodontic treatments thanks to their capacity for self-renewal and differentiation into specialized cells. This process allows their proliferation and adaptation without losing their properties, facilitating tissue repair after injury. Their application in dentistry represents a promising advance in pulpodentinal regeneration and other restorative procedures.[3]

Stem cells are classified according to their origin as embryonic, capable of differentiating into any cell type, and adult, whose differentiation is limited to their embryonic germ layer of origin. They are also categorized by their potential: totipotent cells generate a complete individual; pluripotent cells can differentiate into any cell except an embryo; multipotent cells specialize within their germ layer of origin and are found in bone marrow, adipose tissue, muscle, and dental tissue; oligopotent cells generate a smaller group of cells; and unipotent cells differentiate into only one cell type.[2]

The purpose of this research study is to describe stem cells and regeneration factors applied in endodontics, through the analysis and review of scientific studies conducted in the last 5 years. This will allow us to see the advances and applications that have been developed for possible functional and adequate pulp regeneration in the field of endodontics.

METHODS

An initial systemic electronic search was conducted in databases such as Scielo, Elsevier, Google Scholar, and PubMed. Systematic reviews, case reports, theses, pilot studies, and scientific articles written in English and Spanish and published within the last five years were included. The following terms were used as search criteria: "stem cells in primary teeth," "stem cells as a regenerative treatment in dentistry," "stem cells in dental practice," and "stem cells of dental origin." The following selection criteria were used to select articles:

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- Articles related to stem cells in endodontic practice.
- Studies on the impact of stem cells on dental pathologies.
- Case reports of apical and chamber revascularization.
- Research on dental pulp stem cell culture protocols.
- Articles on obtaining stem cells from teeth.
- Articles that have been published in the last five years
- Research conducted in English and Spanish.
- Research papers available in full text.

Studies detailing the effect on other parts of the body were discarded, as well as those that did not link stem cells to the dental field.

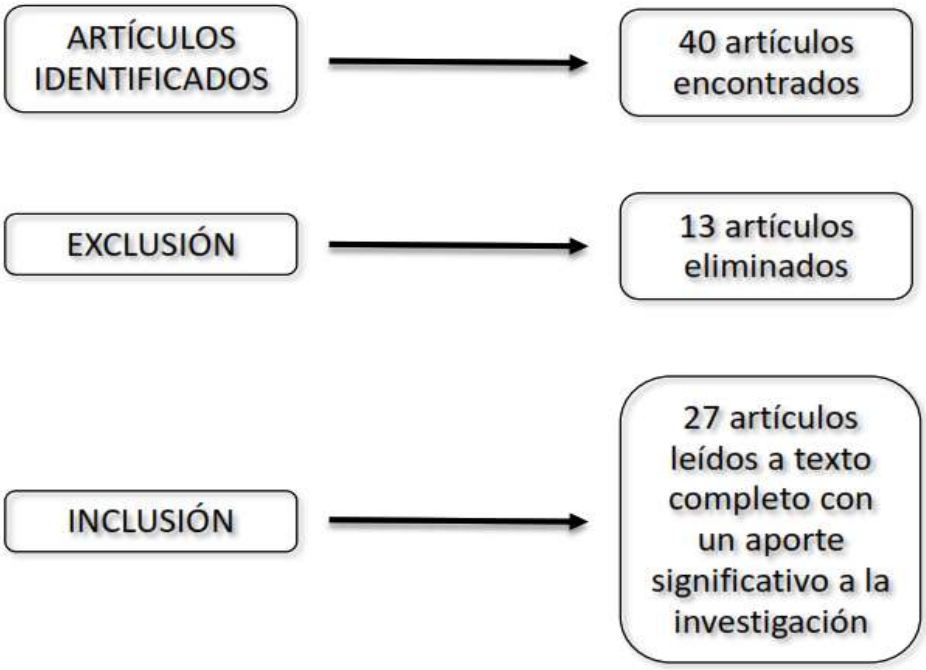

Fig. 1 Flowchart.

The flowchart presented in Figure 1 shows the selection process for scientific articles related to the use of stem cells in endodontic treatments. Initially, 40 studies were collected, and after applying inclusion and exclusion criteria, 27 articles with significant contributions to research were selected. Thirteen studies that did not meet the specific criteria for the dental field were excluded. This refinement allowed the analysis to focus on relevant sources, providing a clear view of recent advances in the application of stem cells in dentistry.

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DEVELOPMENT

The first article highlights that better results were obtained with the use of bone marrow stromal cells in combination with bovine bone than with stem cells, since the tissue structure of the bone is preserved in the area where the improvement is estimated. It also mentions that studies on human stem cells combined with bovine bone have not confirmed the excellent results obtained in animal studies. However, it is evident that stem cells with bone marrow aspirate for implant treatment did not achieve significant results. The authors demonstrate that stem cells in dental practice do not show significant differences compared to a conventional procedure performed by the professional.[4]

In this article, the authors Cifuentes and cols,[5] mentioned in their study that stromal cells have a high power of cellular migration, which allows them to go to the site of the generated lesion, considering that in the oral cavity they can be isolated in areas such as alveolar bone, periodontal ligament, dental pulp, dental follicle, apical papilla, exfoliated deciduous teeth, oral mucosa and gum. In addition, diabetic patients are highlighted as a risk factor, and among the manifestations of this disease at the oral level are dry mouth, caries, periodontal disease, fissured tongue, lichen planus and others. However, due to the close connection between diabetes and oral conditions, extensive research has begun in recent years on the properties of stem cells.
It has been highlighted that high blood glucose levels in diabetic patients affect the differentiation and proliferation capacity of stem cells in the periodontal ligament, making it clear that diabetes directly affects the oral cavity and its cells, thereby losing the capacity for self-renewal and cell migration.

It is shown that, thanks to the evolution of regenerative medicine, the use of restorative and rehabilitative materials can be reduced in order to achieve both aesthetic and functional harmony in the oral cavity, restoring anatomy to affected areas by using the patient's own stem cells. In addition, they mention that in the endodontic field, when there are dental organs with incomplete apices due to trauma, they become fragile, and in this instance it is appropriate to induce apical closure and endodontic treatment, but thanks to bioengineering, new pulp tissue could be created to allow root development. Also, due to its great therapeutic potential, it is possible today to prevent endodontic treatment in adults by obtaining stem cells from teeth other than third molars.[6]

Guerra and García,[7] in their study mention that pulp stem cells are located in the pulp itself and in the cell-rich zone. And other authors in past years report that they were found in the cell-poor zone or Weil's basal layer. To create dental pulp through regenerative medicine, stem cells from adult pulp or deciduous teeth are used. They also emphasize that the implantation of stromal cells for the treatment of temporomandibular joint disorders is possible and there are pioneers in the world who have successfully performed it.

This article analyzes stem cells according to their origin (embryonic or adult), tissue type (bone marrow, skin, adipose tissue, among others), and their differentiation capacity (totipotent, pluripotent, multipotent, oligopotent, and unipotent). In dentistry, their application in the regeneration of the dentin-pulp complex stands out, with potential in apicogenesis and apicoformation treatments. Although complete pulp regeneration has not yet been achieved, studies show improvements in tertiary dentin, the periodontal ligament, and interaction with biomaterials. The ethical dilemmas of the use of stem cells are emphasized, given the debate over the status of the embryo and the creation of human eggs.[8]

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Aquino,[9] mentions that tooth absence today is caused by periodontitis, an irreversible disease not treated in time in the adult population, and regenerative medicine has managed to regenerate affected periodontal tissues thanks to stem cells, and has shown excellent results in surgical periodontal damage in pigs. However, there are concerns that plague researchers such as the possible rejection of a transplant by the host.

Francia et al.,[10] investigated the culture of stem cells from human dental pulp using samples from patients who had undergone extraction of healthy third molars for orthodontic treatment. To avoid contamination, the pieces were placed in an acrylic cabin and the periodontal ligament was removed with a curette. The pulp was obtained in a sanitized flow chamber and fragmented for culture using the explant method, ensuring fragments smaller than 1 mm. The protocol was successful, preserving cell viability and morphology thanks to strict compliance with biosafety measures.

Jucht et al.,[11] alluded in their research that in the endodontic field, ex vivo therapy is optimal, in which stromal cells are isolated from the pulp, in their process of odontoblastic differentiation and the transplant to be performed. And they mentioned an experiment performed on mice over a period of 14 to 28 days, in which endothelial cells were implanted in the subcutaneous tissue and the researchers were able to observe the presence of pulp tissue, mentioning that when there are incomplete apices due to trauma, it is ideal to give rise to new pulp tissue with bioengineering and prevent premature loss of dental organs, avoiding endodontic treatment thanks to the capacity of stem cells. This study carried out on animals proves that stem cells can be applied in dental specialties such as endodontics. But the possibility of continuing to experiment with stromal cells in the future to complete the study is not ruled out.

Rocha al.,[12] made a case report of a seven-year-old patient, in which his stem cells were collected because an extraction was performed for having softened teeth, for which he accepted the informed consent and the obtaining of stromal cells from the pulp of primary teeth, applying all the extraction protocols to avoid possible contamination, for which a prophylaxis was performed prior to the procedure, the teeth were transferred to test tubes with saline solution and then they were stored in a thermal container to preserve pulp vitality. For the culture, the teeth were washed, and the apical papilla was removed, and then the pulp was removed using a Kerr file #15. The tissues were fragmented with the measure <1 mm and placed in Petri dishes, which were monitored daily. The cells were fixed to the plate and cell growth was observed. For this purpose, it was described that if cells are properly stored following all biosafety protocols, they can be stored, preserving their vitality, in an optimal culture medium for later use.

The authors emphasize that the ideal stem cell for culture is one that is abundant, can be obtained with minimal morbidity, differentiates reliably, and can be safely transplanted. Umbilical cord stromal cells were isolated and cultured, giving the Dental Research Center the opportunity to expand into the molecular field for the use of stem cells in regenerative therapy.[13]

Centeno,[14] in his study noted that the preservation and regeneration of a vital and functional pulp is essential for the treatment of diseases that affect these tissues, within this it can be noted that there are "molecular signals" which are the grouping of chemical messengers that induce the differentiation of cells that lead to the dental pulp and the regeneration that is sought to be found in this type of tissue, with this and the advances that currently exist with the use of Stem cells in pulp regeneration, a favorable prognosis is expected when using them in our endodontic treatments.

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Guadarrama and Robles,[15] mentioned that most in vivo studies indicate that scaffolds with hydroxyapatite gave optimal results in dentin regeneration, it was also observed that through the use of umbilical cord stem cells (HUVECs), they presented greater endothelial regeneration, favoring the treatment for our filling process and regeneration of the dentin-pulp complex.

It was shown in the study by Cea-Sanhueza and Sanchez,[16] how in the oral cavity, adult stromal cells can be classified into two types, according to their ability to generate dentin-pulp complex or not; dental (those that do have the ability to regenerate) and non-dental (those that are not capable of generating dentin-pulp complex). It was possible to verify which cells can serve us for regeneration and give a good result in the treatment.

Bernini et al., [17] clarified that the concept of stem cells are those that can and are capable of self-regeneration and differentiation, presenting a multifactorial potential, such as: the high proliferation rate for tissue regeneration. In addition, a case report was made of a 23-year-old patient and through a dental extraction 107 cells were obtained that were transferred to the 15 ml Falcon tube, centrifugation was performed at 1500 rpm for 10 minutes. These cells were transplanted into immunocompromised mice to study the evolution of the immune system, bones, and teeth, which were becoming healthier, with this they determined that stem cells from third molars serve for the regeneration of dental and pulp pathologies.

Nanoparticles with potential for pulp regeneration applications must be cytocompatible and stimulate cell differentiation. By using stem cells and lithium nanoparticles, both pulp and osteogenic regeneration could be obtained. The studies carried out by Durán,[18] are a great contribution when carrying out treatments with stem cells, demonstrating that they have favorable regeneration capacities in different affected tissues.

Villa et al.,[19] mentioned that currently the largest source of stem cells comes from the bone marrow and adipose tissue of the human body. However, for dental treatments they are obtained from teeth, specifically from the pulp chamber, and since teeth extracted from patients are considered biological waste, it is very easy to find stem cell donors, it is important to emphasize that these pieces must be healthy, that is, free of pathologies, cavities, pitting and bacterial contamination. In addition, it was announced that they could be used in autologous stem cell therapy from the dental pulp in patients who have suffered strokes.

Thanks to the scientific contribution of Llivisaca,[20] it was noted that Stem cells are used for temporomandibular treatments. The application of Stem cells was performed in a sterile syringe and 2 ml were injected into the upper joint space; then the patient was followed up after seven days, then every one, six and 12 months. It was also shown that it is possible to obtain favorable results for the use of Stem cells inside the pulp cavity, helping the regeneration of tissue affected by microorganisms.

Haro, [21] indicated that through the use and intervention of calcium hydroxide Ca (OH) 2, on the affected surface of the dental pulp, a superficial necrosis could be generated by the alkaline Ph that it has, the same that together with the basal membrane of the odontoblasts and the ions of the substance transformed into granules of calcium carbonate, are dispersed at the level of the surrounding tissues to begin a process of dentinogenesis and through stem cells of the adipose tissue of the patient the process could be completed, being a favorable result after an evolution of the patient at three months, radiographically it could be observed that the pulp and dentin are in an optimal state of health, thus being a successful treatment.

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Santiago DE, et al.,[22] indicated thatThe regenerative process of the dental pulp complex is controlled by complex interactions between undifferentiated cells, growth factors, and dental-derived biomaterials, and the microenvironment in which regeneration is intended. A detailed understanding of the signaling mechanisms and interactions is essential, given that dental tissue is the basis for regeneration. The environmental conditions in which this process takes place influence regeneration and play an important role in regulating tissue differentiation.

According to Herrera,[23] dental stem cells have attracted widespread interest from the scientific community in recent years due to their high proliferation potential, multipotency, self-renewal, and ability to differentiate into several cell types. Literature analyses have shown that the most commonly used type of dental pulp stem cells in in vitro and in vivo studies are dental pulp stem cells.

For Gualli,[24] the basis of dental pulp regeneration technology is the formation of a biological scaffold that creates a three-dimensional area that allows tissue growth and provides several growth factors that promote differentiation, growth, development and maturation of stem cells. This innovative alternative is important in the field of modern dentistry since it allows the preservation of intraoral dental segments and opens a new paradigm in the field of endodontics.

CONCLUSIONS

This study highlights the impact of stem cells in dentistry, driven by advances in bioengineering. Stromal cells, with their capacity for self-renewal and regeneration, show great therapeutic potential, especially in pulp regeneration treatments. Calcium hydroxide has been used prior to their application to ensure a healthy, infection-free environment. Although their use is in its initial phase in some Latin American countries due to ethical conflicts, biological therapeutic approaches offer promising alternatives for endodontic regeneration, replacing damaged tissue and restoring tooth function. Research should continue with controlled clinical trials to optimize conservative procedures and expand future applications.

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