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Review Article

Dental stem cells and their applications in pediatric dentistry

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ABSTRACT

Regenerative medicine has garnered significant attention due to its transformative impact on disease management and the restoration of optimal bodily functions. Stem cells, a cornerstone of regenerative medicine, are particularly renowned for their remarkable capacity to facilitate tissue regeneration and repair, revolutionizing modern healthcare by offering diverse treatment avenues for multiple conditions. Dental pulp stem cells (DPSCs), a subset of postnatal stem cells, are especially noteworthy for their extensive proliferation and ability to differentiate into various specialized cell types. In the realm of pediatric dentistry, there exists a pressing need for advancements in regenerative medicine. Thorough research in this domain has the potential to propel evidence-based pediatric dentistry, ensuring that children receive tailored, high-quality care. Stem cells hold immense promise in pediatric dentistry by offering less invasive and regenerative solutions for a range of childhood dental issues and congenital anomalies. This research, initiated on 04 October 2023, was instigated following an exhaustive review of existing literature utilizing databases like PubMed, Web of Science, and Cochrane. The literature search encompassed a wide array of medical terminologies. Dental stem cells are categorized into four major types: DPSCs, stem cells from human exfoliated deciduous teeth (SHED), stem cells of the apical papilla (SCAP), and periodontal ligament stem cells (PDLSCs). Pediatric dentistry, encompassing endodontics, orthodontics, periodontics, and the treatment of craniofacial defects, stands to benefit significantly from the potential of dental stem cells. The preservation of dental pulp stem cells extracted from deciduous and permanent teeth through tooth banking offers a source for future regenerative therapies. The preservation process involves multiple comprehensive steps. In summary, dental stem cells present a promising avenue within pediatric dentistry, offering multifaceted applications ranging from pulpal regeneration and dentin repair to orthodontic support and the treatment of craniofacial anomalies.

Keywords: Dental stem cells, Regenerative medicine, Pediatric dentistry, Stem cell regeneration

INTRODUCTION

Regenerative medicine has recently gained much attention due to not only its profound impact on disease management but also the regeneration and restoration of the ideal functionality of the human body.[1] In this regard, stem cells play a very significant role, and serve as a cornerstone of regenerative medicine. They are particularly popular for their remarkable role, and profound potential in tissue regeneration and repair, and have revolutionized the modern medicine by providing a wide range of treatment options for diseases such as cancers, brain and spinal cord injuries, and heart failure.[2] One of the pressing challenges faced by medical and dental practitioners today is addressing organ failure or tissue loss. While various prosthetic devices and mechanical replacements have been employed to substitute for damaged or lost tissues, they often fall short of fully restoring the original form and function.[3] Consequently, the integrity of the host tissue remains compromised, leading to potential complications. Moreover, these prostheses can trigger inflammatory reactions within the host tissue and may experience wear and tear with extended use. The advent of stem cell research and its practical applications has been a game-changer in addressing these challenges. Stem cells offer a promising solution by not only repairing damaged tissues but also restoring them to their natural form and function.[2] This revolutionary approach has the potential to transform the way we treat and manage a myriad of medical conditions, ultimately improving the quality of life for countless individuals.

Stem cells are generally of three types, hematopoietic stem cells, postnatal stem cells, and bone marrow stromal cells. Dental pulp stem cells fall into the category of postnatal stem cells, and they are known to possess the ability to extensively proliferate, and differentiate into various specialized cell types.[4] These cells, originally derived from dental pulp, can differentiate into odontoblasts, chondrocytes, adipocytes, osteoblasts, neural progenitors, endotheliocytes, and smooth muscle cells.[5] This wide range of differentiation capabilities makes dental pulp stem cells highly attractive for regenerative medicine and tissue engineering. They hold promises for addressing a variety of medical and dental conditions by facilitating the regeneration of diverse tissue types. Moreover, their postnatal origin simplifies the ethical and practical considerations associated with their use in therapeutic applications. As research in this field continues to expand, dental pulp stem cells may play a pivotal role in advancing regenerative medicine, offering innovative solutions for tissue repair and regeneration across a broad spectrum of medical disciplines.

Pedodontics, also commonly known as pediatric dentistry, has several critical needs in regenerative medicine. Comprehensive research can potentially contribute to the advancement of evidence-based pediatric dentistry, ensuring that children receive the highest quality of care tailored to their unique needs. Stem cells have the potential to bring about significant advancements in the field of pediatric dentistry by offering less invasive and regenerative solutions for a variety of childhood dental conditions and congenital anomalies.[6] Their versatility in terms of cell differentiation makes them exceptionally well-suited for addressing issues commonly encountered in pediatric dentistry, such as dental caries, tooth trauma, and developmental anomalies. The integration of stem cell-based approaches in pedodontics seeks to not only enhance the outcomes of dental treatments but also reduce the necessity for more invasive procedures. What distinguishes dental stem cells as particularly appealing is their ubiquity in both baby teeth (deciduous) and permanent teeth.[6] This accessibility ensures a relatively non-invasive means of harnessing these cells, which can subsequently be coaxed to differentiate into an impressive array of dental and craniofacial tissues.[6] This approach seeks to do more than merely treat dental conditions; it aspires to restore and rejuvenate, enhancing the long-term oral health and overall quality of life for children.

The study rationale for exploring dental stem cells and their applications in pediatric dentistry is grounded in the potential of dental stem cells to revolutionize the field of pediatric oral healthcare. In the context of pediatric dentistry, where patients often require minimally invasive and highly effective treatments, dental stem cells offer an innovative approach. They can be harnessed to regenerate damaged or lost dental tissues, including dentin, pulp, and periodontal structures, which are commonly affected in pediatric dental conditions such as dental caries, trauma, and congenital anomalies. This research aims to explore the spectrum of possibilities that dental stem cells offer in pediatric dentistry, ultimately advancing the field and improving the quality of care for young dental patients. However, rigorous scientific investigation, safety assessment, and clinical validation are imperative to unlock the full potential of dental stem cell-based therapies in pediatric dentistry while ensuring the highest standards of patient well-being and ethical practice.

METHODS

This research, which commenced on 04 October 2023, was initiated following an extensive review of existing literature, utilizing databases such as PubMed, Web of Science, and Cochrane. The literature search involved the use of a wide array of medical terminology combinations. Additionally, manual searches of relevant research terms were conducted using Google Scholar. The primary objective of this literature review encompassed several key areas, including the assessment of the prevalence of pediatric dental diseases, investigations into regenerative medicine and its applications in dental cell therapy, considerations in orthodontics, and examinations of craniofacial disorders. It's worth noting that the articles selected for inclusion in this study were chosen based on multiple criteria, ensuring a comprehensive and robust review process.

DISCUSSION

Types of dental stem cells

Dental stem cells represent a remarkable category of stem cells residing within various dental tissues, including the pulp of both deciduous (baby) and permanent teeth. There are four major types of dental stem cells.

Dental pulp stem cells

These cells are commonly obtained from the pulp of permanent teeth that have been extracted due to orthodontics or other reasons.[7] Dental pulp stem cells (DPSCs) are particularly versatile and hold great promise for regenerative procedures, offering the potential to generate a wide array of dental and craniofacial tissues. The proliferation and differentiation of these cells were actively observed after an infection or injury of the dental pulp due to a bacterial infection. Moreover, studies also suggest that DPSCs play a vital role in reducing and inhibiting dental inflammation.[8,9]

Stem cells from human exfoliated deciduous teeth

Derived from the pulp tissue of deciduous teeth, stem cells from human exfoliated deciduous teeth (SHED) represents a valuable source of dental stem cells [7]. As deciduous teeth naturally exfoliate, they provide a non-invasive means of obtaining these cells, making SHED an ethical and practical choice for regenerative therapies. Due to their ability to differentiate into a vast range of cells, SHED represents a specific population of stem cells that are immature yet more multipotent than DPSC.[8]

Stem cells from apical papilla

Stem cells from apical papilla (SCAP) is localized in the apical papilla of developing teeth and can be easily isolated from third molars in their developing phase.[10] This unique niche of dental stem cells contributes to tooth development and repair, making them significant players in regenerating dental structures.[8]

Periodontal ligament stem cells

Periodontal ligament stem cells (PDLSCs) are commonly found within the periodontal ligament anchoring teeth to the jawbone and are known to play a vital role in maintaining tooth stability.[7] They have shown promise in periodontal regeneration and repairing damaged periodontal tissues.

These types and their significant role in dentistry have been summarized in Figure 1.

Applications of dental stem cells in pediatric dentistry

Pediatric dentistry involves the care and treatment of children's oral health, and dental stem cells can play a role in various aspects of this field. Saving and banking deciduous teeth containing dental pulp stem cells can provide a source of stem cells for future regenerative therapies.

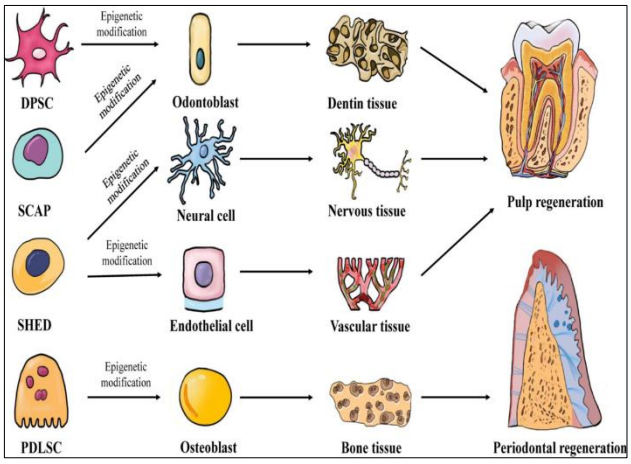

Figure 1: Types of dental stem cells and their applications.[22]

Since SHED are obtained from deciduous teeth, pediatric dentistry has a crucial role in the extraction of these multipotent cells.[7] DPSC and SHED both are proven to contain the potential to regenerate damaged dental tissue, such as vital and vascularized dental pulp, dentin, and periodontal tissues.[7] Pericytes found in DPSC can also differentiate into both osteoblasts and odontoblasts, promoting dental tissue regeneration.[10,11] DPSCs can be utilized in cases where pulp exposure occurs due to dental caries or trauma in pediatric patients. Instead of traditional pulpectomy (removal of the pulp), DPSCs can facilitate pulpal regeneration, allowing the preservation of the tooth's vitality and function. Regeneration of the root of an immature tooth, commonly known as apexogenesis, was also observed in animal studies done on mice and canines through the induction of SCAP and SHED.[11] SCAP was found to be vitally promoting the revascularization of dental tissue, which will potentially also aid in the apexification of damaged or infected roots.[12] PDLSC can also similarly differentiate into osteoblasts, adipocytes, and chondrocytes and can be utilized for periodontal ligament regeneration procedures, which can reduce tooth mobility, especially in dental trauma cases.[13] For children who experience dental trauma resulting in pulp exposure, DPSCs can be employed to promote the repair and regeneration of damaged pulp tissue, increasing the chances of saving the affected tooth. DPSCs can also differentiate into odontoblasts, which are responsible for dentin formation. This property makes them valuable for regenerating dentin in cases of dental caries or developmental defects such as dentinogenesis imperfecta and preserving tooth structure. In addition to that, regeneration of resorbed roots, and repair of cleft lip/palate are also noted advantages of stem cells, particularly in pediatric dentistry.[4] DPSC and SHED-based therapies are generally less invasive than traditional dental treatments,

making them well-suited for pediatric patients who may have dental anxiety or a fear of invasive procedures. Moreover, those stem cells that have been derived from the patient's tissue (autologous DPSCs) minimize the risk of immune rejection or adverse reactions. The population of DPSCs only consists of 1-3% of the total dental pulp cells, which is further reduced due to ageing, the extraction of these cells from the teeth of younger patients is significant.[6] After differentiation, SHED produces induced pluripotent cells (IDPSCs), which are additionally proven to be useful for the management of pediatric disorders.[14] DPSCs can also stay viable after prolonged freezing, or cryopreservation, enabling the use of previously frozen as functional and active stem cells.[15] Orthodontics is another branch of dentistry that primarily involves patients in the younger age group due to the maximum potential of tooth movement during their pubertal growth spurt. Dental stem cells, such as PDLSC, may be used in orthodontics to accelerate tooth movement and enhance the regeneration of periodontal tissues and intra-bony alveolar defects during orthodontic treatment.[16] Moreover, SHED, DPSC, and SCAP can aid in root resorption, a consequence of orthodontic tooth movement.[17] Regeneration of cranial tissues that are compromised due to injury or birth defects is also a possibility through the use of dental stem cells.[18] Periodontal diseases, ear microtia, and craniofacial microsomia are some disorders that can be managed through aesthetic help and regeneration from dental stem cells.[19]

Tooth banking

Tooth banking, also known as dental stem cell banking, is a process that involves the collection, preservation, and storage of dental tissues containing stem cells for potential future medical and dental treatments.[20] Tooth banking typically involves the extraction and preservation of dental pulp or dental tissues from naturally exfoliated deciduous teeth (baby teeth) or extracted permanent teeth. Since a major part of this extraction is done on immature or primary teeth, the role of tooth banking in pedodontics is crucial, and hence pedodontists/pediatric dentists have an essential role to play in this process. These dental tissues in their raw form are initially retrieved and processed in a laboratory to extract and isolate the dental stem cells. These stem cells are then cryogenically preserved, usually through a process of freezing at extremely low temperatures to maintain their viability.[21] The preserved dental stem cells are then stored in specialized facilities, often referred to as dental stem cell banks or tooth banks. These facilities are equipped with advanced cryopreservation technology to ensure the long-term viability of the stored stem cells.[21] The process of tooth banking has been summarized in Figure 2. Tooth banking is considered an ethical and non-invasive method of stem cell collection, especially in the case of deciduous teeth, as they naturally exfoliate. This eliminates the need for invasive procedures and ensures a painless and straightforward process for children. Additionally, tooth banks generally offer the option of family banking, allowing multiple family members to store their dental stem cells together. This can be valuable for genetic conditions or when a genetic match is required for a particular treatment.

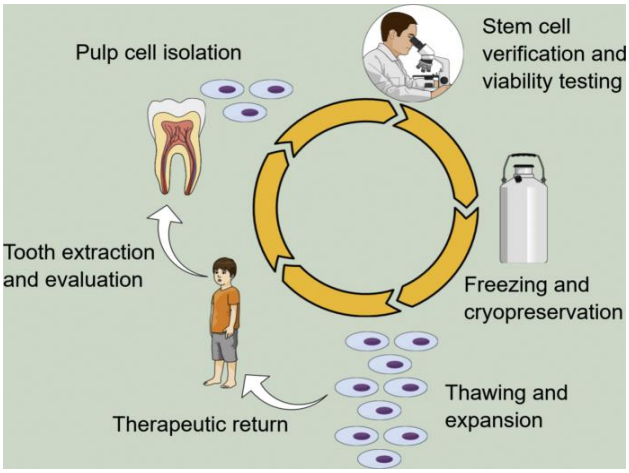

Figure 2: Procedure of tooth banking.[23]

Further research and ethical considerations

Research in dental stem cell therapy is ongoing, and there have been clinical trials exploring their potential applications. However, it's important to note that while dental stem cells show promise, they are not yet widely used in routine pediatric dentistry, and further research is needed to establish their safety and efficacy in various applications. Ethical and legal issues surrounding the collection, storage, and use of dental stem cells should be carefully considered, especially when banking deciduous teeth from children who may not fully understand the implications. Consent from the parents and, in some cases, assent from the children themselves should be obtained for such procedures that involve the preservation of the organic tissues of an individual.

CONCLUSION

Dental stem cells, including dental pulp stem cells, stem cells from human exfoliated deciduous teeth, stem cells from the apical papilla, and periodontal ligament stem cells, represent a remarkable avenue in pediatric dentistry with immense potential. These stem cells offer versatile applications ranging from pulpal regeneration, dentin repair, and orthodontic support to addressing craniofacial anomalies and periodontal regeneration. They hold promise for minimally invasive treatments, reducing the need for traditional, more invasive procedures that may cause anxiety in young patients. Additionally, the ethical collection of dental stem cells through tooth banking, especially from naturally exfoliated deciduous teeth, provides a valuable resource for potential future regenerative therapies, emphasizing the importance of pedodontists' involvement in this process. Nevertheless, rigorous research, clinical validation, and ethical considerations are imperative as dental stem cell therapies

continue to advance, ensuring the highest standards of patient care and safety in the realm of pediatric dentistry.

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