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A review of Stem Cells: Classification and Clinical Applications

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Abstract: Stem cells are undifferentiated cells, capable of renewing themselves. Via differentiation, they have the potential to develop into many different cell lineages. There are different kinds of stem cells, depending on the type of cells they can create and the location in the body. In recent years, studies have shown that oral tissues are a source of stem cells. Structuring of tissue in dentistry has revealed promising results in the regeneration of oral tissue or organs. There are multiple factors that can produce alveolar bone resorption due to tooth extraction or loss because of severe cavities, trauma, or root fracture or even because of periodontal diseases. In edentulous patients, bone resorption continues throughout life particularly in the mandible, which makes it difficult to substitute the missing teeth with dental implants.

Key words: Stem Cell, Mesenchymal, Totipotent, Pluripotential cell

Introduction: Stem cells are pluripotential cells that can divide and multiply for an extended period of time, differentiating into a diverse range of specialized cell types and tissues. Adult mesenchymal stem cells, of which dental stem cells are a subset, are highly proliferative and have the ability to differentiate into many cell lines. The most familiar application of adult stem cell therapy is bone marrow transplantation to treat hematopoietic cancers, metabolic disorders, and congenital immunodeficiency syndromes. Stem cell therapy is undergoing clinical testing for other conditions such as Parkinson's disease, diabetes, and brain trauma/spinal cord injuries. Suggested applications related to oral health care have included wound healing and regeneration of dental and periodontal tissues as well as craniofacial structures (e.g., repair of cleft lip/palate). Parents may elect to preserve umbilical cord blood of their child for future harvesting of stem cells if autologous regenerative therapies are indicated. Pulpal tissue of exfoliating primary teeth, oral mucosa fibroblasts, surgically removed third molars, periodontal ligament, and gingival fibroblasts may serve as a source of mesenchymal stem cells.

Stem cells are defined as clonogenic cells capable of both self-renewal and multilineage differentiation. They are also termed as progenitor cells. It has found various applications in the

field of dentistry in the recent years after the discovery of dental stem cells. There are primarily two types of stem cells, namely, embryonic stem cells (ESCs) and adult stem cells (ASCs) or somatic stem cells. Dental stem cell, a type of ASC, exhibits multipotent differentiation capacity and is drawing worldwide attention because of its various applications. The advances in applications of dental stem cells seem to be unsurpassed in the near future, for which specialized skills and knowledge in this arena are of prime significance. Hence, there is a need to acquire more knowledge about dental stem cells to obtain maximum benefits from it in the coming years. Dental stem cells in India are still at the budding stage, and there seems to be limited awareness regarding dental stem cells. Therefore, this study aimed to assess the awareness of stem cells among the dental professionals.

Review of literature

(Paz, Maghaireh, & Mangano, 2018) studied "Stem cells in dentistry: Types of intra- and extraoral tissue-derived stem cells and clinical applications" and found that Stem cells are undifferentiated cells, capable of renewing themselves, with the capacity to produce different cell types to regenerate missing tissues and treat diseases. Oral facial tissues have been identified as a source and therapeutic target for stem cells with clinical interest in dentistry.

(Khazaei, Bozorgi, Khazaei, & Khademi, 2016) studied "Stem cells in dentistry, sources, and applications" and found that Stem cells (SCs), known as cells with characteristics such as self-renewal and multilineage differentiation, are generally obtained from two sources: Embryonic stem cells (ESCs) and adult stem cells (ASCs). SC research is expected to play a pivotal role in future medicine.

(Caruso, Sgolastra, & Gatto, 2014) studied "Dental pulp regeneration in paediatric dentistry: The role of stem cells" and found that AIM In the last decade, tissue engineering has undergone enormous expansion in the fields of regenerative medicine and dentistry. In response to mechanical and chemical injuries, the dentine-pulp complex possesses a regenerative ability due to a spetic population of mesenchymal stem cells, which have been widely described in literature.

(Report, 2017) studied "Stem Cells in Dentistry: A Study Regarding Awareness of Stem Cells among Dental Professionals" and found that Dental stem cell, a type of adult stem cell, exhibits

multipotent differentiation capacity and is drawing worldwide attention because of its numerous applications. The advances in applications of dental stem cells seem to be unsurpassed in the near future, for which specialized skills and knowledge in this arena is of prime significance. Hence, there is a need to acquire more knowledge about dental stem cells to obtain maximum benefits from it in the coming years.

(Telles, Machado, Sakai, & Nör, 2011) studied "Pulp tissue from primary teeth: New source of stem cells" and found that Shed (stem cells from human exfoliated deciduous teeth) represent a population of postnatal stem cells capable of extensive proliferation and multipotential differentiation. Primary teeth may be an ideal source of postnatal stem cells to regenerate tooth structures and bone, and possibly to treat neural tissue injury or degenerative diseases.

Classification

According to source obtained, dental stem cells can be classified into the following Fig. (**1**):

- DPSC: Dental Pulp Stem Cells
- Pulp obtained from teeth extracted for orthodontic reasons and extracted third molars.
- PDLSCs: Periodontal Ligament derived Stem Cells
- GMSCs: Gingiva derived Mesenchymal Stem Cells
- SHED: Stem cells from Human Exfoliated Deciduous teeth
- IDPSCs: Immature Dental Pulp Stem Cells from deciduous teeth
- DFSCs: Dental Follicle Stem Cells
- TGPCs: Tooth Germ Progenitor Cells
- SCAP: Stem Cells from the Apical Papilla

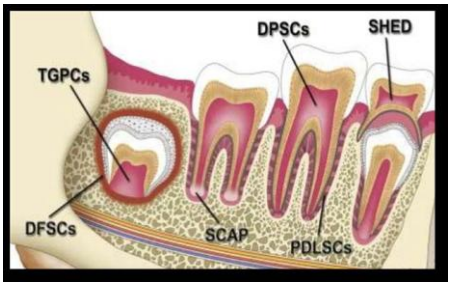

Figure 1. Stem cells from dental tissues

Effectiveness of the stem cells:

A stem cells *Potency* its capacity or efficiency specifies to differentiate into different cell types and accordingly the cells can be divided into several categories of efficiency.

- ***Totipotent stem cells:*** These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent. Totipotent stem cells can differentiate into embryonic and extraembryonic cell types. Such cells can construct a complete, viable, organism.
- ***Pluripotent stem cells*** are the descendants of totipotent cells and can differentiate into nearly all cells, i.e. cells derived from any of the three germ layers.
- ***Multipotent stem cells*** can differentiate into a number of cells, but only those of a closely related family of cells.
- ***Oligopotent stem cells*** can differentiate into only a few cells, such as lymphoid or myeloid stem cells.
- ***Unipotent cells*** can produce only one cell type, their own, but have the property of self-renewal which distinguishes them from non-stem cells (e.g. muscle stem cells).

Clinical applications

- **Evolution in Regenerative Therapy in Dentistry:** Stem cell action contributes as a main factor to the capacity of selfrenewal and differentiation of every organ and tissue. The regeneration of lost oral tissue is the target of stem cell research. Owing to the fact that bone imperfections that ensue after tooth loss can result in further bone loss which limits the success of dental implants and prosthodontic therapies, the rehabilitation of alveolar ridge height is prosthodontists' principal interest.
- **Tissue Regeneration Based on Scaffolds:** The periodontal regenerative therapy concept is based on the principal that, firstly, the source of infection must be removed and, secondly, a space for the cells to grow must be provided. Guided tissue regeneration (GTR) is the most documented material used in periodontal regeneration Growth Factor Delivery-Based Tissue Regeneration. Approaches which combine with scaffold-based tissue regeneration options have been increased by the growth factor delivery.

- **Stem Cells' Regenerative Therapy Requirements Augmentation of Alveolar Bone:** Taking into consideration that regular bone grafting materials have no osteoinductive properties, it is difficult to accomplish through material/growth factor-based procedures such as bone augmentation of the acutely atrophic alveolar ridge, especially vertical bone augmentation during guided bone regeneration or sinus-lifting.

- **Treatments Based on Stem Cells:** The clinical application of stem cells has been analyzed in cases of alveolar ridge augmentation in dental implant rehabilitation. The clinical applications of stem cell-based bone augmentation are split into two groups: the chair-side cellular grafting and the tissue engineering approach. Approach of Tissue Engineering. The regenerative strategies using stem cells have utilized cell culture techniques to achieve bone tissue engineering.
- **Approach of Chair-Side Cellular Grafting:** Cellular graft derived from patients and prepared clinically or an allograft bone matrix that contains native MSCs is another alternative of bone regeneration based on stem cells.
- **Tissue Regeneration Based on Cell Sheet:** Cell sheet based tissue regeneration has been applied successfully in tissue regeneration. Enzymatic cell digestion and cell-to-cell contact are not needed since they remain intact, which is an advantage for regeneration of tissue. In addition, ECM proteins can be applied without requiring an additional scaffold.
- **Regenerative Therapy Based on Stem Cells:** Influencing Factors. The therapy based on stem cells is a new technology that has shown promising results for orofacial bone regeneration; nevertheless, these procedures are still poorly understood.
- **Transplanted Cells' Survival:** Osteogenic cells which have the ability to retain the cellular activity to allow the cells that are transplanted to be able to produce ECMs for tissue regeneration are required for tissue engineering to be successful through cell transplantation.
- **Donor Cells:** The Preculture Condition. The preculture condition of cells that are transplanted was widely analyzed on bone formation. It has been suggested that human BMSCs lose their in vivo osteogenic capacity in in vitro expansion, when cultured not regarding the osteogenic induction length.

- **Cellular Grafting:** Local Immune Responses. Ectopic bone formation applying stem cells that are transplanted in animal models does not have clinically predictable results for orthotopic bone formation in individuals.

- **Complex Oral Tissue/Organ Regeneration:** Preclinical Studies. Due to their developmental and structural complexity, it was not possible to do a clinical trial about regeneration technologies for complex oral organs and tissues on the head and neck.
- **Root/Tooth Regeneration:** The aim of tooth regeneration is to obtain a functional tooth which can replace the lost one. Root regeneration is now a more clinical applicable approach. Studies reported that using the root/ periodontal complex constructed using periodontal and apical papilla stem cells would be able to support an artificial crown to provide normal tooth function in a model of a swine.
- **Regeneration of Salivary Glands:** Salivary gland regeneration is an interesting topic especially for head and neck oncology experts. Two regenerative approaches to restore the function of salivary glands have been applied.

- **Regeneration of Mandible Condyle:** Tissue regeneration can be a solution to temporomandibular joint disc condyle defects or trauma. El-Bialy et al. reported in their study that BMSCs could increasingly regenerate a rabbit condyle that was enhanced by using pulsed ultrasound.
- **Tongue Regeneration:** Tongue regeneration has already been reported in animal studies with the objective of reconstructing tongue defects and reestablishing speech, swallowing function, and air protection. Immunotherapy with MSCs. MSCs have been expanded for the therapy of immune diseases.
- **Application BMSCs in Immune-Mediated Diseases:** BMSCs constitute an important HSC niche component in the bone marrow. They act in the repair process, thanks to cytokine and growth factors' secretion and endogenous progenitor cells' proliferation and differentiation.

- **Immunotherapy with MSCs in Dentistry:** Possible Applications. Reports demonstrated that transplanted allogeneic PDLSC sheets show decreased immunogenicity and marked immunosuppressive ability.
- **Banking of Stem Cells in Dentistry:** Specialized studies have demonstrated that dental tissues are a rich source of MSCs, which can be applied in medical fields, particularly in immune and regenerative therapies.

CONCLUSION

Given the wide therapeutic applications and currently available technology to preserve stem cells, dental stem cells will have a greatest future impact towards the health of the human race. Although there are many areas left to be further investigated, the research done till date has undoubtedly and lucidly proven SHED to be a better and beneficial resource. With the ease and convenience of extracting stem cells from the tooth, it would be appreciable if higher number of pedodontists, clinicians and dental clinics residing in the middle income and high-income countries become a part of banking services. The scenario for low-income countries has to be still improved, however, there is no harm in providing awareness on the tremendous use of dental stem cells. In this context, the academics can make an effort to include dental stem cells as part of the curriculum.

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