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Biodontics: A Review

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Abstract:- Regeneration can be done by stem cells derived from exfoliated deciduous teeth. Teeth that are formed from stem cells are denoted to as "tissue-engineered" teeth. In dentistry, mesenchymal stem cell-like populations were identified from both dental and non-dental tissues has offered sensational opportunities for the application of tissue engineering as well as gene based therapies. These methods have the possibility to lead towards the growth of new approaches for regenerative periodontal therapy. Biodontics is the practice of dentistry that leads to the promotion of repair, restoration, and replacement of dental, oral, and craniofacial structures with natural biological materials of cellular source and it will substitute xenodontics, the practice of dentistry that uses external materials(eg, metals and plastics) for this purpose.

I. INTRODUCTION

The tooth is considered a complex biotic structure that includes various tissues like enamel, dentin, cementum, and pulp. Loosening of teeth due to a wide range of etiologies is usually an ordinarily and regularly occurring complication in elderly people. These deficiencies are presently preserved with fixed or removable prosthesis (FPD/RPD), auto-transplantation, and dental implants or implant supported prosthesis. The investigation of recently developed approaches for tooth restoration has become a talking point. Tooth redevelopment is a forthcoming pragmatic possibility with fundamentals of experimental biology, developmental and molecular biology, and the postulates of bio-mimetics. Various ways had been projected for the attainment of biological tooth substitution. They are tooth regeneration based on scaffold, cell pellet engineering, chimeric tooth engineering, activation of a third dentition, and gene-manipulated tooth regeneration. It is an appealing concept that a third dentition might be locally induced to replace missing teeth.1

Loss of teeth due to trauma, hypoplasia or any periodontal disease are detrimental. Various grafting measures have been endeavoured, but restricted sources and unstable prognosis have limited their use2. The restoration of missing or damaged teeth by fixed or removable prosthesis or dental implants, may lessen ideality of life due to their incomplete physical use or immunological dismissal. Hence, the development of a tooth with natural materials is a viewpoint with the development of tissue engineering. Biodontics is a noteworthy support to endorse biotechnology to dentistry. An emerging dental department, Biodontics, has been theorized, established and cultured by Dr. Edward Rossomando, a professor of Biostructure and Function, in the U Conn School of Dental Medicine with a determination to transport biotechnology more proficiently from scientists and inventors to dental experts. Biodontics relates molecular biology and biotechnology to dentistry. Dental students, dental residents and dental school faculty will be trained with the use of biotechnology to improve the oral health of the public. The concept to educational realism is being made with all the efforts.

II. BIODONTICS

Biodontics is the developing branch of dentistry that repairs, restores, and replaces dental, oral, and craniofacial structures with natural biological materials of cellular origin and it will replace xenodontics, the practice of dentistry that uses foreign materials (e.g, metals and plastics) for this purpose2.

Materials with cellular origin used in tissue engineering are the adult stem cells and not the contentious embryonic stem cells These cells have distinctive properties of:

- Self-renewal: Stem cells can proliferate themselves almost indefinitely.
- Differentiation: Stem cells can metamorphose into cells with specialized characteristics and function. Teeth produced from stem cells are known as "tissue-engineered teeth."

The three major factors that play a role in tissue engineering are:

- Morphogenic signals: Growth factors and differentiation factors play an important role in multiplication and differentiation of stem cells. BMPs (bone morphogenic proteins),which are the multifunctional growth factors, belong to the transforming growth factor beta superfamily and cytokines of the immune system play a vital part in organogenesis, e.g. in differentiation of dental pulp stem cells into odontoblasts which is the main requirement of teeth tissue engineering.
- Responding stem cells: They are initially attained from the patient and preserved under good conditions to uphold their distinctive capability to differentiate into a wide-ranging cells, are later coaxed in the lab to transform it into a tooth bud.

- Scaffold: It provides a mechanical support to the cells required for regeneration of any tissue and it has to be biodegradable and speed of degradation has to coincide with the speed of tissue development. The scaffold has to be permeable which aids in cell nutrition, proliferation and migration for tissue vascularization as well as formation of new tissues. Mechanical stability of the implant is improved by the porous surface by the mechanical interlocking between the scaffolds and surrounding tissues 3.

Titanium scaffolds are bio-compatible and suitable for hard-tissue applications, such as the growth and differentiation of rat dental pulp progenitor cells into odontoblast-like cells. To improve their efficacy, metal scaffolds can be covered with biological compounds, like titanium fibres pre-coated with extracellular matrix (ECM) components that support the osteogenic differentiation of rat bone marrow mesenchymal stem cells (BMSCs). A second class of scaffold is naturally occurring organic material that provides a bio-mimetic environment for stem cells.

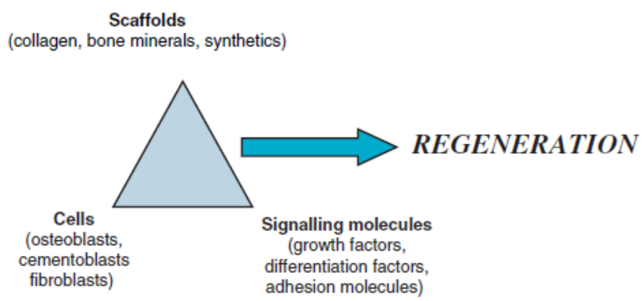

Fig 1:- Tissue engineering concept

Natural scaffolds provide mechanical strength. Additionally, they can contain biological agents that influence stem cell fate.

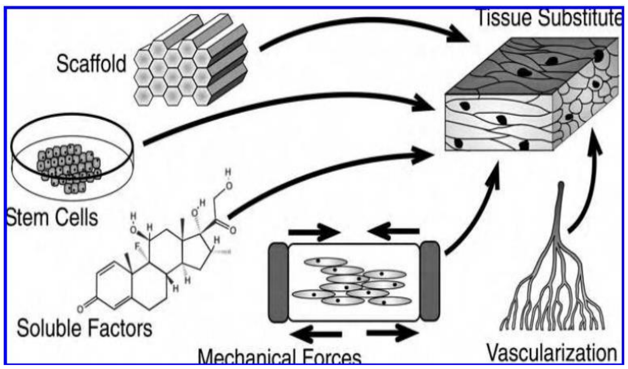

Fig 2:- Constituents of engineered tissue prepared with adult stem cells:

Scaffold having a biocompatible configuration and a porous structure, adult stem cells and their differentiated progeny, signalling molecules to regulate stem cell fate comprising covalently bound ligands and controlled release agents incorporated into scaffold design, physical forces for the stimulation of spatial organization and differentiation, and microvasculature comprising endothelial progenitor cells to ameliorate tissue survival.

➢ *Mechanical Forces*

After embedding stem cells in a 3D scaffold, physical forces lead to spatial organization and differentiation, simulating signs the cells receive in vivo.5 Human BMSCs in hyaluronan-gelatin scaffolds, in the presence of chondrogenic medium show more cartilaginous matrix formation when the scaffolds are exposed to cyclic physical compression than do uncompressed samples. Various methods can be followed in building a bio tooth. They are:

- By the reconstruction of a mature tooth as is evident in the oral cavity.
- By the replication of embryonic evolution in the oral cavity.
- By the induction of third dentition.
- A scaffold in the shape of tooth is created, few cells are placed in the scaffold and are allowed to grow.

➢ *Recreate the Mature Tooth as is Evident in the Oral Cavity*

The components of a tooth, i.e, crown, dental pulp, enamel and root are distinctly created from the materials and right embryonic cells. The disadvantage of this method is that the process has a high level of procedural difficulty. Contrarily, the advantage is a high level of control on the process and the possible automation and scale-up6.

➢ *Inducing a Third Dentition*

It works with the addition of molecules of either of the earlier two dentitions in the growth of initiating the de novo of the tooth after tooth loss or the de novo restraint or stimulation of candidate genes such as RUNX2 or USAG-1 could stimulate the third dentition so that new tooth formation is induced7.

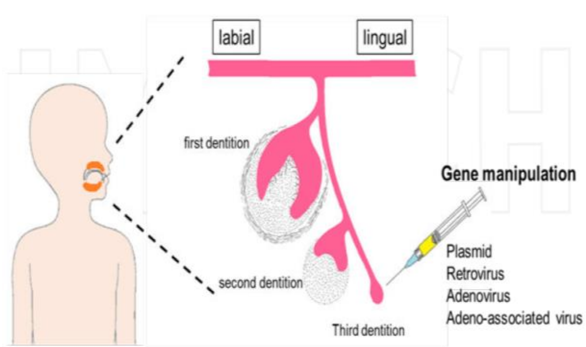

Fig 3:- In vivo gene delivery method for the tooth redevelopment by third dentition stimulus

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- ➢ *Build a Tooth Shaped Scaffold, Place few Cells in them, and let the Cells Grow*

This method is highly productive, and practices tissue engineering procedure. It includes seeding of biodegradable scaffolding with cells, and generation of these tissues will mold on to the form of the scaffolding. These scaffolds can be used in several ways, and they may even be capable of regenerating teeth and other organs, but this concept is yet under research.

- ➢ *Formation of a Biotooth*

- Biomembrane scaffolds are seeded with stem cells implanted in the jaw at socket or prepared site. (BMSC and DPSC) scaffold may be collagen hydrogel, chitosan, poly-LLactic acid, poly-L-Glycolic acid, HA+TCP8.
- Scaffold implantation done (Orthotopic or ectopic) by soak system, low pressure system, pipette system or syringe system. Osteogenic differentiation takes around 2 weeks.
- Osteogenic differentation-SDF1 and BMP 7 plays role in angiogenesis
- Positional information and tooth morphogenesis (barx1, 3-D bioprinting, EDA, TRAF6) play role.
- Bone regeneration and alveolodental ligament regeneration

- ➢ *Stem (somatic) Cells Storage. Stem cells can be stored as*

1. Cryopreservation
2. Magnetic freezing

- ➢ *Tooth Stem Cell Banking*

The earliest commercial tooth bank (dental stem cell storage) was set in 2004 at National Hiroshima University, Japan 9. The institute was entitled “Three Brackets” (Suri Buraketto). Establishments like Store-A- Tooth (Provia Laboratories, Littleton, Massachusetts, USA) and StemSave (Stemsave Inc, New York, USA), BioEden (Austin, Texas, USA) are now expanding their horizon globally in favor of tooth stem cells banking10. Stemade Biotech familiarized the idea of dental stem cells banking in India lately by beginning its operations in Mumbai and Delhi11.

- ➢ *Uses in Dentistry*

In the knowledge domain of dental research, stem cell study targeted towards the accomplishment of following; redevelopment of impaired coronal dentine, pulp, resorbed roots, cervical or apical dentine and alveolodental ligament; besides plugging of perforations, repair of craniofacial defects and whole tooth regeneration. Dental pulp stem cells (DPSCs) characterize a kind of adult cell colony which have the strong capability of self–renewal and multiline differentiation. These somatic cells appear to be the basis of odontoblasts that donate to the formation of dentin pulp complex. Few research works have evidenced that DPSCs have the capability of producing dental tissues in vivo including dentin, pulp and crown like structures, where as further research suggested that these stem cells can bring about formation of bonelike structures. Hypothetically, a bio-tooth produced from autogenous PSCs should be the best option for experimental tooth restoration. It was established by Granthos et al, that in both in vitro and in vivo, dental pulp stem cells (DPSCs) of animals were capable of forming ectopic dentin and associated pulp tissue. An in vivo stem cell transplantation system by Batouli et al was used to study differential regulatory mechanisms of bone marrow stromal stem cells (BMSCs) and DPSCs. It was found out that DPSCs were capable of generating a reparative dentine like tissue on the superficial part of human dentin in vivo9.

- ➢ *Redeveloping Alveolodental Ligament*

Periodontal tissue regeneration has always remained a task as it involves both hard and soft tissue regeneration. A combination of autologous bone marrow (MSC) and allo-collagen were used by Kawaguchi et al (2004) to regenerate alveolodental ligament in experimental grade III defects in dogs. There was redevelopment of cementum, periodontal ligament, and alveolar bone, a month after implantation was done. Hasegawa et al 5 demonstrated that autologous alveolodental ligament cells cultured in vitro were re-implanted into periodontal defects in order to promote periodontal regeneration in dogs and the results were successful. A subsequent study confirmed this evidence in humans10.

- *Cell Injection Therapy*

The injection of inherently intelligent cells into the defect, particularly stem cells, have been shown to regenerate tissues since the tissue formation resulted from cellular actions. Immunological rejections and the ability of the injected cells to maintain their phenotype are however other challenges.

- *Cell Induction Therapy*

The limitations of cell injection therapy led to the clear and discrete shift towards the recruitment of circulating body cells to redevelop the tissues.

- *Cells Seeded Scaffolds*

This approach is dependent on the segregation of suitable cell population take from a biopsy of the patient or a donor. These are presently being acknowledged as a crucial cell type that retains significant immunomodulatory characteristics able to treat a broad range of immune-related disorders.

➢ *Regeneration of The Dentine-Pulp Complex*

- *Conception Of Root Canal Revascularization By Blood Coagulation*

Revascularization of the necrotized root canal structures by antisepticising, followed by instituting bleeding into the canal system by over instrumentation has shown successful results for revascularization of root canals12,13.

- *Postnatal Stem Cell Therapy*

Postnatal stem cell derivatives of the skin, buccal mucosa, fat, and bone are being introduced into germ-free root canal systems once the apex is allowed access.

- *Pulp Implantation*

The pulp cells can be grownup on biodegradable membrane filters to convert two-dimensional into three-dimensional cell cultures.

- *Three-Dimensional Cell Printing*

The three-dimensional cell printing technique can be used to accurately station cells so that they have the probability to create tissue constructs that simulate the normal tooth pulp tissue structure.

- *Gene Therapy*

In mice, Huang et al discovered that stem cells from apical papilla can replace pulp-like tissue anew in an empty root canal space and dental pulp that produce odontoblast-like cells, regenerating dentin-like tissue on the prevailing dentinal walls through the stem/progenitor cell-based methods and tissue engineering methodologies.

III. CONCLUSION

The prospect of these treatments comprising further biotic methodologies and the practical usage of dental tissue stem cells is favourable and progressing. There could also be an important concern of their application and broader probability to cure illnesses past the craniofacial region.

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