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Stem Cell Theraphy in Dentistry- Review

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Abstract:
Background: *Stem cells are unspecialized cells in the human body that are capable of becoming specialized cells, each with new specialized cell functions. The best example of a stem cell is the bone marrow stem cell that is unspecialized and able to specialize into blood cells, such as white blood cells and red blood cells, and these new cell types have special functions, such as being able to produce antibodies, act as scavengers to combat infection and transport gases. Thus one cell type stems from the other and hence them term "stem cell". Basically, a stem cell remains uncommitted until it receives a signal to develop into a specialized cell. Stem cells have the remarkable properties of developing into a variety of cell types in the human body. They serve as a repair system by being able to divide without limit to replenish other cells. When stem cells divide, each new cells has the potential to either remain as a stem cell or become another cell type with new special functions, such as blood cells, brain cells, etc.*
Most tissue repair events in mammals are dedifferentiation – independent events brought about by the activation of pre-existing stem cells or progenitor cells. By definition, a progenitor cells likes in between a stem cell and a terminally differentiated cell. However, some vertebrates such as salamanders regenerate lost body parts through the dedifferentiation of specialized cells into precursor cells. The dedifferentiated cells then proliferate and later form new specialized cells of the regenerated organ. In fact, some invertebrates such as the Planarian flatworm and the hydra regenerate tissues very quickly and with precision. The word "stem" actually originated from old botanical monographs from the same terminology as the stems of plants, where stem cells were demonstrated in the apical root and shoot meristems that were responsible for the regenerative competence of plants. Hence also the use of the word "stem" in "meristem". Today, stem cells have been isolated from preimplantation embryos, fetuses, adults and the umbilical cord and under certain conditions, these undifferentiated stem cells can be pluripotent (ability to give rise to cells from all three germ layers, viz. ectoderm, mesoderm and endoderm) or multipotent (ability to give rise to a limited number of other specialized cell types).[10]
Keywords: *stem cell, fetal,adult stem cell,,multipontent,pluripotent*
Material and methods: *over 96 article where selected for review following a comprehensive search of the literature from pubmed central.*
Results: *Clearly, advances in adult stem cell biology have provided a great deal of impetus for the biomedical community to translate their findings into clinical application. Given the fact that we have in hand populations of stem cells that reproducibly reform bone and its marrow, cementum, dentin and perhaps even periodontal ligament, it is possible envision complete restoration of the hard tissues in the oral cavity using the patient's own cells, thereby avoiding issues of histocompatability. Furthermore, advances in techniques to genetically modify the gene activity of stem cells during their ex vivo expansion offers the unique possibility to make a patient a own stem cells even better. For example, the activity of gems that regulate the aging process can be modified, thereby "rejuvenating" the stem cells and giving them a new lease on life. Another example relates to the molecular engineering of stem cells derived from patients with genetic diseases. In these cases, there is the possibility of replacing a gene activity that is missing or silencing a gene activity that is defective. However, replacing dental tissues with either cell or gene-based therapy may be complicated in areas of unresolved inflammation, thus highlighting the need for more research to understand potential complicating factors. While the technical hurdles to achieve these goals should not be underestimated, the recent recognition of stem cells and their role in tissue regeneration provide a strong basis upon which we can begin to actually impact on the clinical management of craniofacial defects.*

Research on stem cells allows us to learn about how an organism develops from a single cell and how healthy cells replaced damaged cells in adult organisms. This area of regenerative or reparative medicine is leading scientists to investigate the possibility of cell-based therapies to treat disease. Scientists primarily work with two kinds of stem cells from animals and humans: embryonic stem cells and adult stem cells. It is a

characteristic of stem cells that they may replicate many times, by means of a process called proliferation. Given their unique regenerative abilities, stem cells offer new potentials for treating diseases such as diabetes and heart disease. However, much more remains to be done in the laboratory and the clinic to understand how to use these cells for cell-based therapies to treat disease, which is also referred to as regenerative or reparative medicine.

Conclusion: *Moral issues surrounding the sources of stem cells[11]*

At present, there are three possible sources of stem cells;

- *Adult stem cells derived from pediatric or adult donors;*
- *Embryo germ cell stem cells (EG cells) derived from aborted fetuses; and*
- *Embryonic stem cells (ES cells) derived from disaggregated pre-implantation embryos.*

The first of these sources poses no special ethical problems for the majority of people. Adults and children can donate tissue so long as the appropriate conditions of consent are respected. Individuals who do not object to induced abortion will be less concerned about the use of EG cells than those opposed to abortion. The least ethically problematic case would be to harvest stem cells from spontaneously aborted fetuses. There are several obstacles to obtaining useful EG cells from spontaneously aborted tissue.[24]

Foremost is the problem of the harvesting healthy cells from fetuses. For the foreseeable future, extracting and culturing stem cells will be more of an art than an established technology. The amount of material that can be derived this way is limited even under the best circumstances. Results from several studies indicate that about 60% of all spontaneous abortions arise as a result of specific fetal anomalies; specific chromosomal abnormalities were identified in about 20% of those. While stem cells with damaged genetic complements may be useful for a limited number of experiments, they are unlikely to be the basis of experiments leading to useful "normal" tissue.[24]

Finally, there is the matter of timing. EG cells can only be obtained during a narrow developmental phase, within the first eight weeks after conception. Most spontaneous abortions that occur during this period do not take place in a hospital or clinic where the tissue can be readily obtained.[72]

One of the guide lines suggested was that there should be a full informed consent by the and/or patients.[7,11]

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I. Introduction:

Our body consists of mainly two kinds of cells; the ones which when damaged or lost cannot undergo the process of repair or regeneration. Any damage to these cells, either due to aging or injury may pose a threat to the whole system and thus has long been a concern to the mankind. On the contrary, it has also been observed that several tissues in the body (such as blood, skin and gastrointestinal tract) undergo rapid renewal, and have regenerative ability. This observation lead the scientists to hypothesize that the tissues with the regenerative potential may contain cells that initiate their replacement. These cells are termed as "stem cells". Stem cells are thus, the pioneer of regenerative medicine.[4,74,83]

II. Material And Method:

over 96 article where selected for review following a comprehensive search of the literature from pubmed central.

III. Discussion:

The term "stem cells" first appeared in the literature during the 19th century. Mesenchymal stem cells (MSCs) were first isolated in the 1970s and named fibroblast colony-forming units. The bone marrow is known to be a rich source for heterogeneous cell populations including hematopoietic stem cells and MSCs.

Ever since this realization, researchers as well as doctors have been working in this direction, hoping to make use of the concept of regeneration in the field of medicine and health.

A number of researchers have reported the isolation of stem cells from the pulp of human exfoliated deciduous teeth Miura et al (2003)[56] and / or from the periodontal ligament (PDL). According to Gronthos et al (2002)[27], dental pulpl cells were shown to form dentin-pulp-like complex when transplated in vivo.

The purpose of this dissertation is to give the dental surgeon a insight of the unprecedented opportunities of oral and tooth tissue regeneration, which though, have not reached the clinical set up today, but may become a norm in future, in the practice of every dental surgeon.

In a study on the oseogenesis in transplants of bone marrow cells conducted by Friedenstein AJ, Piatetzky-Shapirol II, Petrakoval KV (1966)21 it was observed that in bone marrow fragments and bone marrow

cell suspensions isotransplated to mice in diffusion chambers, reticular tissue developed and sometimes osteogenesis also occurred.

Owen M, Friedensten AJ (1988)[65] discussed that there were stromal stem cells present in the soft connective tissues associated with marrow and bone surfaces that are able to give rise to a number of different cell lines including the osteogenic line.

James A. Thomson et al (1998)[36] reported about Embryo0nic Stem Cell Lines Derived from Human Blastocysts. Human blastocyst-derived, pluripotent cell lines are described that have normal karyotypes, express high levels of telomerase activity, and express cell surface markers that characterize primate embryonic stem cells but do not characterize other early lineages.

In a report published by Audrey R Chapman (1999)[11], it was discussed that human stem cell research holds enormous potential for contributing to our understanding of fundamental human biology. Although it is not possible to predict the outcome from basic research, but further studies will offer the real possibility for treatments and ultimately for cures for many diseases for which adequate therapies do not exist.

Krebsbachl PH, Kuznetsov SA, Bianco P et al (1999)[45] reported that the bone marrow stroma consisted of a heterogeneous population of cells that provides – the structural and physiological support for hematopoietic cells.

Gronthos S, Mankani M, Brahim J, Gehron Robery P and Shi S, (2000)[26] found that Dentinal repair in the postnatal organism occurs through the activity of specialized cells, odontoblasts, that are thought to be maintained by an as yet undefined precursor population associated with pulp tissue.

Helen Gavaghan (2001)[28] reported about promise to stem cells. The most basic definition about stem cell is that a cell that can divide to give both another stem cell and a more specialized cell. It can be totipotent (able to form an entire organism), pluripotent (able to develop into most tissues of an organism) or multipotent (specialized for specific tissues, such as blood, skin, etc.).

In another study conducted by Gronthos S, Brahim J, Li W, Fisher L W et al (2002)[27] the self renewal capability, multi-linage differentiation capacity, and clonogenic efficiency of human dental pulp stem cells (DPSCs) were characterized.

Krebsbach PH, Pamela Gehron Robey (2002)[46] summarized and highlighted the differences between embryonic and adult stem cells and discussed the potential use of these cells for cellular therapeutics for craniofacial regeneration.

Dissociation of porcine third molar tooth buds into single-cell suspensions and seeding them onto biodegradable polymers was performed by Young CS, Terada S, Vacanti JP et al (2002)[95].

Batouli S, Miura M, Brahim J, (2003)[12] compared Stem-cell-mediated Osteogenesis and Bentinogenesis. They used an in vivo stem cell transplantation system to investigate differential regulation mechanisms of bone marrow stromal stem cells (BMSSCs) and dental pulp stem cells (DPSCs).

Maisam Mitalipova et al (2003)[53] studied about human pluripotent embryonic stem (ES) cells which have important potential in regenerative medicine and as models for human preimplantation development; however, debate continues over whether embryos should be destroyed to product human ES cells.

Masako Miura, Stan Gronthos, Mingrui Zhao et al, (2003)[56] studied about (SHED) stem cells from human exfoliated deciduous teeth. They collected normal exfoliated human deciduous incisors from 7-8 yrs old children.

Iohara K, Nakashima M, Ito M et al (2004)[35] reported that Dentin Regeneration by Dental Pulp Stem Cell Therapy with Recombinant Human Bone Morphogenetic Protein 2 The progenitor/stem cells are responsible for this regeneration. Culture of porcine pulp cells, as a three dimensional pellet, promoted odontoblast differentiation compared with monolayers.

In a case reported by Lendeckel S, Dicke AJ, Christophis P et al (2004)[47], autologous adipose derived stem cells were processed simultaneously and applied to the calvarial defect which had resulted from trauma.

Liu H, Li W, Gao C, Kumagai Y, Blacher RW and DenBesten PK, (2004)[50] investigated the role of Dentonin in dental pulp stem cell (DPSC) proliferation and differentiation. Matrix extracellular phosphogylcoprotein (MEPE) is a SIBLING protein, found in bone and dental tissues.

In a study, Seo BM, Miura M, Gronthos S et al (2004)[80], isolated human periodontal stem cells for the first time, cultured them in laboratory and when these were transplanted after loading into a hydroxyapatite carrier, these produced dense mixture of cementum and periodontal ligament.

Kanjimiyamoto, Kazuhikehayashi, Shinji Ichihara et al (2004)[44] evaluated the growth of primate ES cells (cynomolgus monkey ES cells; CMK6) on human amniotic epithelial (HAE) feeder cells and human chorionic plate (HCP) feeder cells derived from human placentas.

Shi S, Bartold PM, Miura M et al (2005)[82] conducted a study on stem cells in adult human dental pulp (dental pulp stem cells, DPSC), human primary teeth (stem cells from human exfoliated deciduous teeth, SHED), and periodontal ligament (periodontal ligament stem cells, PDLSC) by their capacity to generate clongenic cell clusters in culture.

The perspective of using stem cells in dental practice for conservative pulp therapies has been studied by Casagrande L, Mattuella LG, Araujo FB et al (2006)[15].

Lopez-Cazaux S, Blutean G, Magne D et al (2006)[51] in their study demonstrated that cell culture medium modulates human pulp cell behavior. They investigated the effect of two media; MEM (1.8mM Ca and 1mM Pi) and RPMI 1640 (0.8mM Ca and 5mM Pi) on the behavior of human dental pulp cells.

Mao JJ, Giannobile WV, Helms JA et al, (2006)[54] in a review discussed that adult stem cells have been isolated from the dental pulp, the deciduous tooth, the dental pulp of the wisdom tooth, supernumerary tooth, impacted tooth, and the periodontium.

Nagatomo K, Komaki M, Sekiya I et al (2006)[60] characterized human PDL cells to clarify their stem cell properties, including self-renewal multipotency and stem cell marker expression.

Robey PG and Bianco P (2006)[74] studied the use of adult stem cells in rebuilding the human face. They stated that science clearly indicates that the use of stem cells for regeneration, reconstruction or repair of bone is feasible in principle. Substantial advances have been made in our ability to handle skeletal stem cells in the laboratory and to exploit their inherent potential for building bone.

Suardita K (2006)87 in his article on the potential application of stem cells in dentistry emphasized that stem cells were found in dental pulp, periodontal ligament and alveolar bone marrow and because of their potential in medical therapy to treat diseases like Parkinson's Alzheimer, spinal cord injury, stroke, burns, heart diseases, diabetes, osteoarthritis and rheumatoid arthritis, stem cells were used to regenerated lost or damaged teeth and periodontal structures.

Wataru Sonoyanta, Yi Liu, Dhanji Fang et al (2006)[91], They conducted a study on mesenchymal stem cell – mediated functional tooth regeneration in swine. They collected 18 normal human impacted third molar and gently separated root apical papilla from the surface of the root of extracted tooth. They found that SCAP population demonstrated an elevated tissue regeneration capacity, higher telomerase activity than that of DPSCs from the same tooth and an improved migration capacity in the scratch assay, when compared to DPSCs from the same tooth.

In a study conducted by Weinand C, Pomerantseva I, Neville CM et al (2006)[93], used a tissue engineering approach to create bone replacements in vitro, combining bone-marrow-derived differential mesenchymal stem cells (MSCs) suspended in hydrogels and 3-dimensionally printed (3DP) porous scaffolds made of beta-tricalcium-phosphate (beta-TCP).

Junying Yu and James A. Thomson (2006)[43], discussed that Human embryonic stem (ES) cells are immortal and have an almost unlimited developmental potential.

Honda MJ, Tsuchiya S, Sumita Y et al (2007)[29], aimed to facilitate tooth regeneration using a novel technique to sequentially seed epithelial cells and mesenchymal cells so that they formed appropriate interactions in the scaffold.

Revazova ES, Turovets NA, Kochetkova OD et al (2007)[71], reported that the successful derivation of six pluripotent human embryonic stem cell (hESC) lines from blastocysts of parthenogenetic origin.

Sloan AJ, Smith AJ (2007)[79], reviewed about stem cells and the dental pulp and their potential roles in dentine regeneration and repair.

Odontogenic capacity of DPSCs (dental pulp stem cells) and BMSSCs (bone marrow stromal stem cells compared by YU J, Wang Y, Deng Z et al (2007)96, under the same inductive micro-environment produced by ABCs (aplical bud cells) from 2-day-old rat incisors.

Abbas A, Diakonov I, Sharple P (2008)[1], investigated the possible neural crest origin of dental pulp stem cells from exfoliated deciduous teeth (SHED). Neural crest cells are multi-protein cells that are capable of self-renewal and multi-lineage differentiation and play a major role in tooth development as they give rise to mesenchymal components of teeth including odontoblasts, pulp, apical vasculature and periodontal ligament.

A novel approach of harvesting stem cells from a supernumerarty tooth (a mesiodens) was done by Anderson Hsien – Cheng Huang, Yuk-Kwan Chen and Lin-Min et al (2008)[9].

Blutean G, Luder HU, De Bari C et al (2008)[13], reviewed stem cells for tooth engineering. Tooth development results from sequential and reciprocal interaction between the oral epitherlium and the underlying neural crest-derived mesenchyme.

Christian Morsczeck, Gottfried Schmatz, Torsten Eugen Reichert et al (2008)[16] reviewed on recent knowledge about somatic stem cells for their prospective use in regenerative dentistry.

Duilibi SE, Duailibi MT, Zhang W et al (2008)[19], they studied Bioengineered dental tissues crown in the rat jaw. There objective was to develop methods to form, in the jaw bioengineered replacement teeth that exhibit physical properties and functions similar to those of natural teeth which is useful for human tooth replacement therapies.

Hyun Ki Kang, Sangho Roh, Gabsang Lee et al (2008)[32], assessed the osteogenic potential of ESCs using in vitro culture conditions and in vivo differentiation in tooth sockets. Pluripotent ESCs can serve as an alterative source for the reconstruction of craniofacial structures.

Mabel M Cordeiro, Zhihong Dong, Tomoatsu Kaneko (2008)[52], they studied to evaluate morphologic characteristics of the tissue formed when SHED seeded in biodegradable scaffolds prepared with in human tooth slices are transplanted into immunodeficient mice.

Peneva M, VAnyo Mitev, Nikolai Ishketiev (2008)[68] studied to prove the presence of the primary structure of mensenchymal stem cells from the pulp of (temporary teeth) deciduous teeth and to establish the impact growth factors.

Peneva M, Vanyo Mitev, Nikolai Ishketiev (2008)[69] studied about isolation of mesenchymal stem cells from the pulpl of deciduous teeth.

Rania M. El-Backly, Ahmed G. Massoud, azza M. El-Badry et al (2008)[70] studied regeneration of dentine/pulp-like tissue using a dental pulp stem cell/poly (lactic-co-glycolic) acid scaffold construct in white rabbits.

Scheller EL, Chang J and Wang CY (2008)[77], isolated from post-natal human dental pulp (adult third molars). Canonical Wnt signaling plays a critical role in tooth development and stem cell self-renewal through β–certain.

Seo BM, Sonoyama W, Yamaza T et al, (2008)[81] studied that to examine whether SHED mediated bone regeneration can be utilized for therapeutic purposes and repaired critical-size calvarial defects in immune compromised mice.

Takeda T, Tezuka Y, Horiuchi M et al, (2008)[89], they studied characterization of dental pulp stem cells in human tooth germs (i.e.) hDPSCs isolated from an earlier developmental stage to evaluate the potential usage of these cells for tissue regenerative therapy.

Wataru Sonoyama, Yi Liu, Takayoshi Yamaza (2008)[92], studied about characterization of the Apical Papilla and its residing stem cells from human immature permanent teeth.

Alison MR, Islam S and Lim S (2009)[6], reviewed about how the liver regenerates itself after both acute and more chronic iterative damage. Under normal circumstances the differentiated peranchymal cells (hepatocytes) are the functional stem cells, but in more extreme circumstances a 'potential' stem cell compartment can be recruited into action, providing HPCs (hepatic progenitor cells) from the intrahepatic biliary system that can differentiate into hepatocytes.

Alison MR and Islam s (2009)[5], studied about attributes of adult stem cells and found that stem cells in different tissues have common attributes that enable their self-renewal, survival and maintenance of genomic integrity. In all tissues, stem cells are located in a specialized vascular microenvironment, the niche; intrinsic and extrinsic signals from the niche regulate-self-renewal and cell fate.

Carolyn Coppe, Yan Zhang and Pamela K. Den Besten (2009)[14], characterized dental pulp cells from human primary teeth and determined the potential of primary tooth pulp to signal (induce) epithelial cell differentiation, as occurs in tooth development.

Christian Morsczeck, Bernhard Frerich, Oliver Driemel (2009)17 reviewed Dental Stem Cell patents and found different categories of stem cells for regenerative dentistry in these patents: (a) Embryonic stem cells, (b) Somatic dental stem cells and (c) Somatic non-dental stem cells. The use of human embryonic stem cells is ethically controversial.

Friedlander LT, Cullinan MP and Love RM (2009)[22] reviewed about Dental stem cells and their potential role on apexogenesis and apexification. It appears that dental stem cells have the potential for continued cell division and regeneration to replace dental tissues lost through trauma or disease.

Jeremy J Mao (2009)[40] stated that Stem cells are typically quiescent cells that reside in virtually every tissue and organ in the body.

Li Peng, Ling Ye, Xue-dong Zhou (2009)[48] reviewed outlines the recent progress in the mesenchymal stem cells used in tooth regeneration. Tooth loss compromises human oral health.

Yalvac ME, Ramazanoglu M, Rizvanov AA, et al (2009)[94] have reported that human tooth germs contain multipotent cells that give rise to dental and periodontal structures.

Fred Michmershuizen (2010)[23] reported that recent has shown that normally shedding baby teeth and extracted wisdom teeth can be a source of stem cells that are the equivalent of umbilical cord blood stem cells.

IV. Conclusion

Research on stem cells allows us to learn about how an organism develops from a single cell and how healthy cells replaced damaged cells in adult organisms. This area of regenerative or reparative medicine is leading scientists to investigate the possibility of cell-based therapies to treat disease. Scientists primarily work with two kinds of stem cells from animals and humans: embryonic stem cells and adult stem cells. It is a characteristic of stem cells that they may replicate many times, by means of a process called proliferation. Given their unique regenerative abilities, stem cells offer new potentials for treating diseases such as diabetes and heart disease. However, much more remains to be done in the laboratory and the clinic to understand how

to use these cells for cell-based therapies to treat disease, which is also referred to as regenerative or reparative medicine.

We are at an exciting point of new era of restorative dentistry harnessing the biological activity of the dental tissues to facilitate wound healing and tissue regeneration. There is still much to learn of the nature, potentiality and behavior of dental stem/progenitor cells, but the opportunities for their exploitation in dental tissue regeneration are immense and will lead to significant benefits for the management of the effects of dental disease.

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