Journal of Advanced Medical and Dental Sciences Research

@Society of Scientific Research and Studies ***NLM ID:*** *101716117*

Journal home page: www.jamdsr.com doi: 10.21276/jamdsr Index Copernicus value = 85.10

(e) ISSN Online: 2321-9599; (p) ISSN Print: 2348-6805

Review Article

The Role of Stem Cells in Orthodontics - Current Trends

Dr. Sutharsan shanmugam sundaram[1], Dr.Chandhni Suresh kumar[2], Dr.Manicka Mani J[3], Dr.Selvakumar ramar[4]

[1]Consultant Orthodontist, Mayiladuthurai;
[2]Consultant Orthodontist, Chennai;
[3]Consultant Orthodontist. Sivakasi;
[4]Consultant Orthodontist, Chennai

ABSTRACT:
The craniofacial structures are mesenchymal cell derivatives. Mesenchymal stem cells are the progeny of mesenchymal cells following asymmetrical division and it reside in the various craniofacial structures in the adult. Cells with similar characteristics of adult stem cells have been isolated from the dental pulp, the deciduous dentition and the periodontium. Stem cell therapy has gained its attention from worldwide researchers. Craniofacial deformities like cleft lip and palate, ear microtia, craniofacial microsomia and head and neck cancers are not only major problem and it is considered as major burden in day today life. This article is an insight into the review of the current knowledge on stem cells and its extensive use in the orthodontics and dentofacial orthopaedics.
Keywords: stem cells, craniofacial anomaly, orthodontics.

Received: 23/07/2020 **Modified:** 18/08/2020 **Accepted:** 20/08/2020

Corresponding Author: Dr. Sutharsan shanmugam sundaram, Consultant Orthodontist, Mayiladuthurai

This article may be cited as: Sundaram SS, Kumar CS, J Mani M, Ramar S. The Role of Stem Cells in Orthodontics - Current Trends. J Adv Med Dent Scie Res 2020;8(10):68-72.

INTRODUCTION

Recent advance in the branch of orthodontics and dentofacial orthopedics are self-ligating bracket system, nanotechnology , rapid canine retraction, corticotomy , low friction are some of the approaches which helps in reduce the treatment duration . Enhancement of facial aesthetics is one of the major elective objectives of patients seeking orthodontic treatment. The craniofacial anomalies and dentofacial deformities need multidisciplinary approach in order to re-establish facial structures. Recent management of craniofacial deformities can reduce the severity of these deformities but their final aesthetic outcomes are still not attractive. Stem cells procedure in orthodontics plays major role to enhance facial esthetics, reduces treatment timing etc. This article reviews the clinical use of stem cells in craniofacial deformities, with reference to the field of orthodontics and dentofacialorthopedics.

STEM CELL

E.D. Wilson first coined the term ‘stem cell’ in 1896 . Stem cells are ‘undifferentiated cells that can proliferate and have the capacity for self-renewal and the ability to produce one or more highly differentiated progenitors’ .[1,2] Stem cells are also named as self-renewal cells which can differentiate toward innumerable cells under suitable circumstances.[3]Around the same time , Dr. James Thomson of the United States and Dr. Yamanaka of Japan discovered that adult human cells could be reprogrammed to an embryonic state by over expressing the strong stem cell genes in 2007.Such different type of stem cells are known as induced pluripotent stem cells (IPPS).[4]

SOURCE OF STEM CELL

Possible s ources for collecting stem cells such as muscle, dermis, bone marrow, adipose tissue, periosteum, blood, umbilical cord, synovial membrane and teeth.(5,6)The differentiation and proliferation of mesenchymal stem cells are acquired

from human pulp, periodontal ligament(PDL), or exfoliated deciduous teeth[7-10].

TYPES OF STEM CELLS :

The stem cells are broadly classified into three types

Human embryonic stem cells :
Embryonic stem cells are derived from inner cell layers of blastocyst, created by *in vitro* fertilisation. They are pluripotent in nature which have ability to differentiate into all type of body cells except placenta and umbilical cord.[11,12]

Adult stem cell : It is also called as tissue specific stem cells or somatic stem cells. They are more specialised stem cells which have the ability to differentiate in particular tissue or organ where they live. Tissue specific stem cells can be difficult to isolate in human body unlike embryonic stem cells do. [13,14]

Mesenchymal stem cells: Mesenchymal stem cells are the cells isolated from stromal connective tissue that surrounds tissues and organs. They are also called as stromal cells. It is first discovered from bone marrow and were shown to be capable of producing bone, cartilage and fat cells.

Induced pluripotent stem cells : They are engineered in the lab by converting tissue specific cells such as skin cells into the cells that behave like embryonic stem cells.[15]

PROPERTIES OF STEM CELLS
The specific properties of stem cells are [16]

- Stem cells are unspecialized cells .
- The stem cells can divide and renew themselves for a longer period of time.
- Stem cells can divide and become specialized cells in the body
- They can replace dying cells, damaged or old cells.

APPLICATION OF STEM CELLS IN ORTHODONTICS AND DENTOFACIAL ORTHOPAEDICS

1. EXTERNAL ROOT RESORPTION:-
ERR is the most common and unfavorablesequelae after orthodontic tooth movement . Undesirable forces during orthodontic tooth movement may induce inflammatory root resorption that results in loss of cementum in initial stages and advanced stages,it affects dentin which leads to loss of tooth structure. Battistutta et al [17,18]described that Root resorption occurs as a part of elimination of hyalinised zone and there is an imbalance between resorption and deposition by cementoclasts/osteoclast cells.[19]

As ERR is an irreversible phenomenon, currently there is no definite treatment protocol has been introduced so far. However recent discovery of tissue engineering and application of stem cell therapy have paved a way for better advancement. Several studies shows odontoblasts can be derived from mesenchymal stem cells (MSC), dental pulp stem cells (DPSC), stem cells extracted from an exfoliated deciduous tooth (SHED), while cementoblasts can be derived from mesenchymal stem cells (MSC) and dental follicular stem cells (DFSC). Thus, these two kinds of stem cells may be used before orthodontic treatment, in order to prevent root resorption or post treatment for repairing the damage.[20]Oshima et al in their Animal study transplanted the whole tooth structure through tissue engineering, and introduced into rodent and beagle dogs, results showed that there is a possible regeneration of cementum and dentinal layers of damaged tooth structure and the study further to achieve a functional human tooth structure through tissue engineering [21,22]

2. RAPID MAXILLARY EXPANSION
In 1860, Emerson C. Angell introduced Rapid Maxillary Expansion. Transverse maxillary deficiency is the most common problem in orthodontic patients which affects smile aesthetics, occlusal abnormalities, facial development associated with functional problems like altered pharyngeal airway , increased nasal resistance, abnormal tongue posture and mouth breathing habit. [23] RME is indicated in younger patients in mixed dentition stage, to improve the skeletal and dental disharmony by producing expansion at the mid palatal suture. It is contraindicated in patients who have completed the growth spurts. RME is an effective orthopaedic appliance used to treat unilateral or bilateral crossbites, cleft lip and palate cases, to gain arch length in patients with moderate maxillary crowding and patients with nasal respiratory problems. Maxillary constriction can be corrected by slow maxillary expansion, rapid maxillary expansion, and surgically assisted rapid palatal expansion (SARPE), and by orthognathic surgery. The most common side effect of RME is increased rate of relapse, unless definite retentive protocol system is followed.[24]

The role of stem cells in maxillary expansion have been studied by many authors, due to its ability to differentiate into osteogenic cells and bone formation occurs. Ekizer et al in their animal study investigated whether mesenchymal stem cells (MSC's) have the ability to induce new bone formation in midpalatal suture region, the results showed that single local injection of mesenchymal stem cells (MSC's) into the mid palatal suture resulted in new blood vessel formation with accerlated bone formation. The author further states that this approach might further reduce the duration of treatment and increased retention[25,26].

3.DISTRACTION OSTEOGENESIS

Distraction osteogenesis (DO) is surgical procedure for triggering bone formation after corticotomy or an osteotomy and slow and steady distraction. The method is based on the tension-stress principle occurs by deliberate parting of the bone fragments by traction which was proposed by Ilizarov in 1989. The gradual bone distraction creates mechanical stimulation which brings biological responses and subsequently regeneration of bone . This is accomplished by a cascade of biological events like differentiation of pluripotent cells, angiogenesis, osteogenesis and bone mineralization [27,28]

The source of the stem cells used in this method are exfoliated deciduous teeth (SHED)of human being, bone marrow and adipose tissue. Other modified source of stem cells are demineralized bone matrix parts, scaffolds and Platelet-rich Plasma(PRP) have been seen in various studies[29-31]. Ischemia is one of the major disadvantage during distraction osteogenesis. It has been suggested that stem cells significance in distraction osteogenesis showed that it accelerate bone regeneration in the distraction gap and enhance consolidation[32].

Lai QG et al performed animal experiments in new Zealand with white rabbits which underwent left mandibular osteodistraction and were randomly divided into group A, B, and C .Autologous bone marrow mesenchymal stem cells and physiological saline were injected into the distraction gap of groups A, group B, and group C, respectively. Finally , BMMSCs exchanged with osterix (OSX). It was observed that there was tremendous bone callus formation in groups A and B. The group C animals showed fragile bone formation in the distracted callus, when compared to group A and group B[33]

4. PERIODONTAL REGENERATION USING STEM CELLS

The periodontal ligament is a group of specialized connective tissue fibres that basically attach a tooth to the alveolar bone . It inserts into cementum of the root on one side and onto alveolar bone on the another side. PDL cells are derivative of the dental follicle and this occurs after crown formation is completed .PDL formation will start at the cementoenamel junction (CEJ) and ended in an apical direction. Successful orthodontic treatment depends on the health of the periodontium[34]. The most common periodontal complication related to field of orthodontics includes gingivitis, periodontitis, dehiscence, fenestrations, interdental bone loss, gingival recession and hyperplastic gingiva .The stem cells plays most important role in the regeneration of periodontium through the process of mitosis.

According to the study conducted by Duan X et al in 2011, they implanted pluripotent stem cells with a silk fibroin scaffold with enamel matrix derivative gel into a mouse periodontal fenestration defect site . The outcome of the study shows that there is advanced rate of cementum and alveolar bone development arisen [35].

5. ENVELOPE OF DISCREPANCY EXTENDED

The envelope of discrepancy shows the amount of movement that could be obtained by orthodontic tooth movement(OTM) alone, orthodontic tooth movement(OTM) combined with growth modification and orthognathic surgery. The three dimensional movements like anteroposterior, vertical, and transverse movement of treatment modalities are possible in orthodontics and they are conveyed as an "envelope of discrepancy" . In this sites in which the buccal or lingual cortex bone are fragile and gingival tissue are extremely thin. Hence, lower incisors of the patients presents with a prominent chin like class III tendency and compensated lingual tipping of the teeth which possess bony defects like fenestrations and dehiscence.

Stem cells with bone regeneration procedures helps to overcome the limitation of envelope of discrepancy. The bone marrow stem cells (BMSCs) have ability to generate dissimilar hard tissues like bone. Hence, stem cell treatment is a favourable method for regeneration of alveolar bone. [36-38]The effect of regeneration showed a propensity to improve formation of new bone.

6. ACCELERATED ORTHODONTIC TOOTH MOVEMENT

The rapid movement of tooth is accomplished by remodelling of periodontal ligament and alveolar bone in response to the application of mechanical force.In 2016,Feng et al observed that improved periodontal ligament progenitor cells with suppressed expression of type 1 collagen (Col-I) occurred during application of orthodontic force and Col-I expression arose after removal of orthodontic force. During application of orthodontic force ,where periodontal ligament stem cells can able to respond with suppressed collagen expression.[39]

The common use of stem cells is to accelerate orthodontic tooth movement in response to application of orthodontic forces. Once orthodontic force is applied, there is delayed orthodontic tooth movement until necrosis tissue is removed. In clinical practice, stem cells transplantation in the pressure sites may trigger the process, which promotes accelerated orthodontic tooth movement(OTM).

7. ALVEOLAR BONE AUGMENTATION:

The cleft anomaly is one of the most prevalent congenital malformation, where most of the patients possess osseous defects of the pre maxilla alveolar bone .The treatments modalities of alveolar cleft defects involve autologous bone grafting at the deficient site. These cleft patients frequently need a secondary bone graft ,to permit the eruption of the anterior teeth segment and assisting orthodontic management. Stem cell therapy act as potential

treatment option for correcting deficient alveolar bone region. This was experimented with the help of bone marrow stem cells in the rat alveolar defect segment and fibrin glue composition was promising method to treat alveolar defect[40].

Waite PD et al at 1996, osteoplasty for clefted region was done for nine-year-old female patient where mesenchymal stem cells were used instead of bone grafts. After six months the cleft bridged with 79.1% of the grafted region where eruption of lateral incisor and canine in the deficient part after six months in the remodelled alveolar ridge[41]

8. REGENERATION OF TMJ DEFECT:

Cells from different sources like fibroblasts, articular cartilage cells, mesenchymal stem cells and human umbilical cord matrix cells were used to reconstruct the TMJ defect.[42,43] The tissue-engineered mandibular condyle is most advanced technique in regeneration of TMJ which was created from bone marrow mesenchymal stem cells embedded in the stratified layers of cartilage and bone . This is later formed into the form of mandibular condyle of human.[44-47].

CONCLUSION

Stem cell therapy is considered as most preferred areas of investigation in craniofacial tissue engineering. The usage of stem cells therapy in the field of orthodontics is limited because, it is incredibly costly. Stem cell treatment is a multidisciplinary method, which need lot of lot of experience to manage such techniques.

REFERENCES

1. Daruwala N, Mahadevia S, Paneriya PR. Stem cells: The future of dentistry. JADCH 2010;1:12–17.
2. Polak JM, Bishop AE. Stem cells and tissue engineering: Past, present and future. Ann N Y Acad Sci 2006;1068:352–66.
3. Khojasteh A, Motamedian SR. Mesenchymal Stem Cell Therapy for Treatment of Craniofacial Bone Defects: 10 Years of Experience. Reg Reconst Restor 2016;1:1-7.
4. Takahashi K, Yamanaka S. Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell 2006;126:663–76.
5. Mafi R, Hindocha S, Mafi P, Griffin M, Khan WS. Sources of adult mesenchymal stem cells applicable for musculoskeletal applications - a systematic review of the literature. Open Orthop J 2011;5: 242-8
6. Hass R, Kasper C, Böhm S, Jacobs R. Different populations and sources of human mesenchymal stem cells (MSC): A comparison of adult and neonatal tissue-derived MSC. Cell Commun Signal 2011;9:12.
7. Motamedian SR, Tabatabaei FS, Akhlaghi F, Torshabi M, Gholamin P, Khojasteh A. Response of Dental Pulp Stem Cells to Synthetic, Allograft, and Xenograft Bone Scaffolds. Int J Periodontics Restorative Dent 2017;37:49-59.
8. Gay IC, Chen S, MacDougall M. Isolation and characterization of multipotent human periodontal ligament stem cells. Orthod Craniofac Res 2007;10:149-60.
9. Khojasteh A, Motamedian SR, Rad MR, Shahriari MH, Nadjmi N. Polymeric vs hydroxyapatite-based scaffolds on dental pulp stem cell proliferation and differentiation. World J Stem Cells 2015;7:1215-21.
10. Miura M, Gronthos S, Zhao M, Lu B, Fisher LW, Robey PG, et al. SHED: stem cells from human exfoliated deciduous teeth. Proc Natl Acad Sci USA 2003;100:5807-12
11. Gay IC, Chen S, MacDougall M. Isolation and characterization of multipotent human periodontal ligament stem cells. Orthod Craniofac Res 2007;10:149-60
12. Strem BM, Hicok KC, Zhu M, Wulur I, Alfonso Z, Schreiber RE, et al. Multipotential differentiation of adipose tissue-derived stem cells. Keio J Med 2005;54:132–41.
13. Odorico JS, Kaufman DS, Thomson JA. Multilineage differentiation from human embryonic stem cell lines.Stem Cells 2001;19:193–204.
14. Wu DC, Boyd AS, Wood KJ. Embryonic stem cell transplantation: Potential applicability in cell replacement therapy and regenerative medicine. Front Biosci 2007;12:4525–35.
15. Conrad C, Huss R. Adult stem cell lines in regenerative medicine and reconstructive surgery. J Surg Res 2005;124:201–8
16. Kabir R, Gupta M, Aggarwal A, Sharma D, Sarin A, Kola M. Imperative role of dental pulp stem cells in regenerative therapies: A systematic review. Niger J Surg 2014;20:1-8.
17. Pizzo G, Licata ME, Guiglia R, Giuliana G. Root resorption and orthodontic treatment. Review of the literature. Minerva Stomatol 2007;56:31–44.
18. McNab S, Battistutta D, Taverne A, Symons AL. External apical root resorption following orthodontic treatment. Angle Orthod. 2000;70:227–32.
19. Sameshima GT, Sinclair PM. Predicting and preventing root resorption: Part II. Treatment factors. Am J Orthod Dentofacial Orthop 2001;119:511–5
20. Bluteau G, Luder HU, De Bari C, Mitsiadis TA. Stem cells for tissue engineering. Eur Cells Mater 2008;16:1–9.
21. Ikeda E, Morita R, Nakao K, Ishida K, Nakamura T, TakanoYamamoto T, et al. Fully functional bioengineered tooth replacement as an organ replacement therapy. Proc Natl Acad Sci USA 2009;106:13475-80.
22. Ono M, Oshima M, Ogawa M, Sonoyama W, Hara ES, Oida Y, et al. Practical whole tooth restoration utilizing autologous bioengineered tooth germ transplantation in a postnatal canine model. Sci Rep 2017;7:44522.
23. Vidya V, Sumathi F. Rapid maxillary expansion as a standard treatment for obstructive sleep apnea syndrome: a systematic review. J Dental Med Sci 2015;14:51–5.
24. Aloufi F, Preston CB, Zawawi KH. Changes in the upper and lower pharyngeal airway spaces associated with rapid maxillary expansion. ISRN Dent 2012;2012:290964.
25. De Rossi M, De Rossi A, Hallak JE, Vitti M, Regalo SC. Electromyographic evaluation in children having rapid maxillary expansion. Am J Orthod Dentofacial Orthop 2009;136:355–60.
26. Ekizer A, Yalvac ME, Uysal T, Sonmez MF, Sahin F. Bone marrow mesenchymal stem cells enhance bone formation in orthodontically expanded maxillae in rats. Angle Orthod 2015;85:901.

27. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues. Part I.The influence of stability of fixation and soft-tissue preservation. Clin Orthop Relat Res 1989;238:249–81.
28. Ilizarov GA. The tension-stress effect on the genesis and growth of tissues: Part II. The influence of the rateand frequency of distraction Clin Orthop Relat Res1989;239:263–85.
29. Lee DH, Ryu KJ, Kim JW, Kang KC, Choi YR. Bone marrow aspirate concentrate and platelet-rich plasma enhanced bone healing in distraction osteogenesis of the tibia. Clin Orthop Relat Res 2014;472:3789-97.
30. Hatzokos I, Stavridis SI, Iosifidou E, Karataglis D, Christodoulou A. Autologous bone marrow grafting combined with demineralized bone matrix improves consolidation of docking site after distraction osteogenesis. J Bone Joint Surg Am 2011;93:671–8.
31. Sun Z, Tee BC, Kennedy KS, Kennedy PM, Kim DG, Mallery SR, Fields HW. Scaffold-based delivery of autologous mesenchymal stem cells for mandibular distraction osteogenesis: preliminary studies in a porcine model. PLoS One 2013;8:e74672.
32. Qi M, Hu J, Zou S, Zhou H, Han L. Mandibular distraction osteogenesis enhanced by bone marrow mesenchymal stem cells in rats. J Craniomaxillofac Surg 2006;34:283–9
33. Lai QG, Yaun KF, Xu X, Li DR, Li GJ, Wei FL, et al. Transcription factor osterix modified bone marrow mesenchymal stem cells enhance callus formation during distraction osteogenesis. Oral Surg Med Oral Pathol Oral Radiol Endod 2011;111:412–9.
34. Vizitiu T, Ionescu E. Microbiological Changes in Orthodontically Treated Patients. Ther Pharmacol Clin Toxicol 2010;14:283-6.
35. Duan X, Tu Q, Zhang J, Ye J, Sommer C, Mostoslavsky G, et al. Application of induced pluripotent stem (iPS) cells in periodontal tissue regeneration. J Cell Physiol 2011;226:150–7.
36. Rickert D, Sauerbier S, Nagursky H, Menne D, Vissink A, Raghoebar GM. Maxillary sinus floor elevation with bovine bone mineral combined with either autogenous bone or autogenous stem cells: a prospective randomized clinical trial. Clin Oral Implants Res 2011;22:251–8.
37. Payer M, Lohberger B, Strunk D, Reich KM, Acham S, Jakse N. Effects of directly autotransplanted tibial bone marrow aspirates on bone regeneration and osseointegration of dental implants. Clin Oral Implants Res 2014;25:468–74.
38. Yamada Y, Nakamura S, Ueda M, Ito K. Osteotome technique with injectable tissue-engineered bone and simultaneous implant placement by cell therapy. Clin Oral Implants Res 2013;24:468–74
39. Feng L, Yang R, Liu D, Wang X, Song Y, Cao H, et al. PDL Progenitor-Mediated PDL Recovery Contributes to Orthodontic Relapse. J Dent Res 2016;95:1049–56.
40. Zhang L, Wang P, Mei S, Li C, Cai C, Ding Y. In vivo alveolar bone regeneration by bone marrow stem cells/fibrin glue composition. Arch Oral Biol 2012;57:238–44.
41. Waite PD, Waite DE. Bone grafting for the alveolar cleft defect.Semin Orthod 1996;2:192–6.
42. Bailey MM, Wang L, Bode CJ, Mitchell KE, Detamore MS. A comparison of human umbilical cord matrix stem cells and temporomandibular joint condylar chondrocytes for tissue engineering temporomandibular joint condylar cartilage.Tissue Eng 2007;13:2003–10.
43. Schek RM, Taboas JM, Hollister SJ, Krebsbach PH. Tissue engineering osteochondral implants for temporomandibular joint repair. Orthod Craniofac Res 2005;8:313–9.
44. Alhadlaq A, Mao JJ. Tissue-engineered neogenesis of human-shaped mandibular condyle from rat mesenchymal stem cells.J Dent Res 2003;82:951–6.
45. Alhadlaq A, Mao JJ. Tissue-engineered osteochondral constructs in the shape of an articular condyle. J Bone Joint Surg Am 2005;87:936–44.
46. Alhadlaq A, Elisseeff JH, Hong L, Williams CG, Caplan AI, Sharma B, et al. Adult stem cell driven genesis of human-shaped articular condyle. Ann Biomed Eng 2004;32:911–23.
47. Mao JJ. Calvarial development: Cells and mechanics. Curr Opin Orthop 2005;16:331–7.