Mini Review

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Regenerative in endodontics: how, when and where

Abstract

Undeveloped teeth are defenseless against infections, trauma and abnormal anatomies. Apexification has been considered as the standard treatment of immature permanent immature teeth that have suffered from irreversible pulpitis. This course of action boosts the shaping of an apical blockade to intercept the connection between the root canal and, the periodontal surroundings. In spite of that, these techniques have been unsuccessful in achieving root development which may expose the teeth to major side effects such as fractures. Recently, the most favorable therapy for immature or mature teeth with pulp necrosis is the regenerative endodontic treatment. This paper defines the biotic foundation and clinical regenerative endodontic processes currently used in dental practice.

Keywords: stem cell, regeneration, technique

Volume 9 Issue 6 - 2018

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Received: December 12, 2018 | **Published:** December 18, 2018

Introduction

The induction of human stem cells paves the way for a new age in the field of dental research.[1] Technically, stem cells are interpreted as cells having the propensity for self-renewal, or for provoking cell differentiation.[1] Sustaining the vivacity of teeth impaired due to dental decays or traumatic exposures is one of the objectives of pulp tissue treatment[1]. Predominantly, in case of immature permanent teeth, preserving the pulp vitality is of important significance for continuous apical closure. Treating of immature teeth with pulp necrosis was typically worked out with the conventional utilization of calcium hydroxide apexification and apical barrier procedures with mineral trioxide aggregate (MTA).[1] However, the high risk of fracture and tooth loss would be inevitable due to the fact that the roots would still be underdeveloped.[1–3] Lately, regenerative endodontic techniques have extended in the past decade, being assimilated into an endodontic firm, and growing to be a replacement therapy for mature and immature teeth.□ When set side by side with MTA apexification, papers have claimed indistinguishable success and survival rates for regenerative endodontics. The latter has been clarified as biologically rooted mechanisms intended to take the place of the destroyed anatomy such as dentin and cells of the pulp-dentin complex. This review focuses on the current regenerating methods in regenerative endodontics.

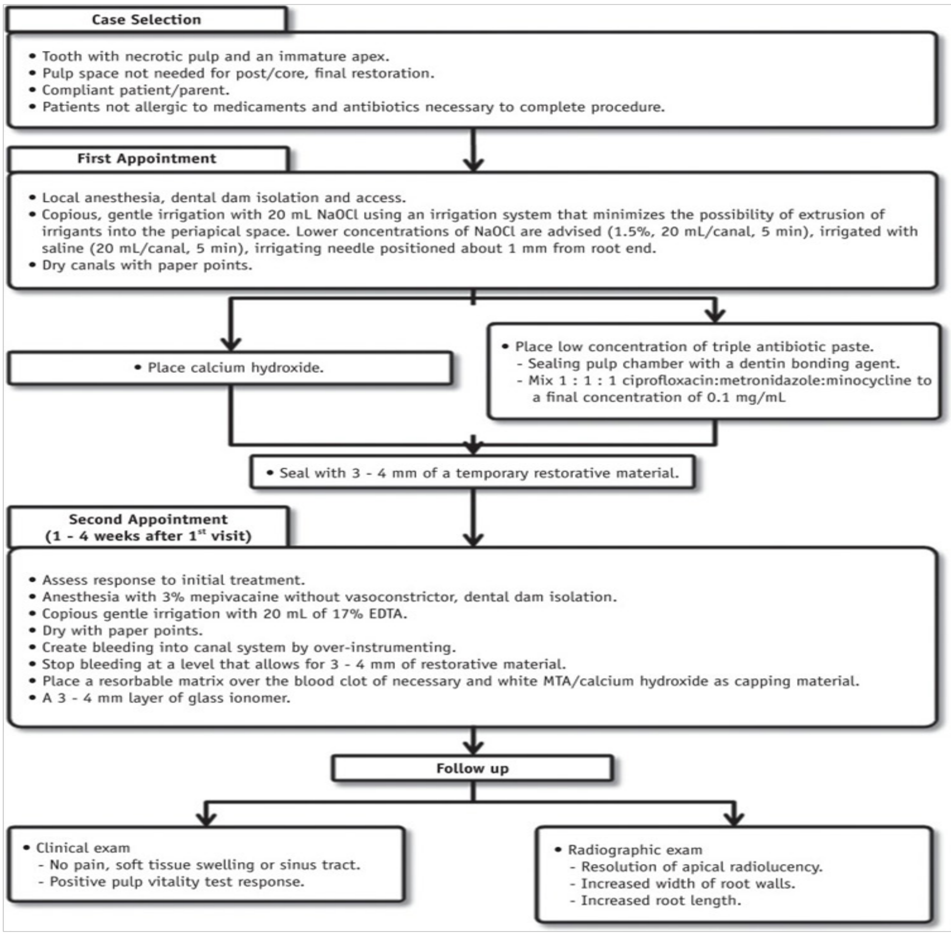
Origin of stem cells used for regenerative endodontic treatment

The mesenchymal stem cells, which are found in the apical papilla of immature teeth, can be easily used in infected immature permanent teeth.[3] These stem cells (SCAP) are competent to be transformed into odontoblast-like cells.[5] the dental pulp stem cells (DPSCs) represent another category of mesenchymal cells. Besides, DPSCs are capable too to convert into odontoblast-like cells and compose dentin/pulp-like system.[6] Nevertheless, some papers suggested the existence of many differences between SCAP and DPSCs.[1] It was discovered that SCAP exhibited a remarkably greater rate of cell proliferation, and tissue regeneration ability than DPSCs.[1] Given these points SCAP might be considered a finer cell origin for tissue regeneration.[1] On the other hand, a recent study, supported with evidences, showed that stem cells can be derived from a periapical lesion surrounding a mature tooth.[2]

Regenerative endodontic processes

In 1961, regenerative endodontic treatment was first reported by the pioneers Nygaard-Östby. They suggested the use of over-instrumentation beyond the apex to induce bleeding, for a possible root repair. Decades later, successive records have been revised to be more stem cell-friendly. Consequently, a term called revascularization' which was conducted by a number of researchers, scores a continuous root development and thickening of root canal walls with mineralized tissue on immature teeth with necrotic pulps.[2] Accordingly, many clinical considerations were taken for regenerative endodontics.[1] First, although the operations of regenerative endodontics are mainly used on mature teeth, most of the publicized cases are performed on juvenile patients with the immature infected teeth suffering from pulp necrosis, which induced the cessation of root. Success is interpreted by three means: symptom abolishment and signs of bony healing, as a primary and an essential target. Expansion in root wall thickness and/or root length, comes as a secondary target. As a tertiary target vitality testing should give a rise to a positive response. As the first aim is the ultimate target for all endodontic treatments; in the case of an immature tooth, increasing the root's wall thickness or/ and length is germane, (AAE). It is supposed that the incidence of root fracture can be decreased by the promotion of root maturation connected with the apical closure of the immature root apex. Concerning the third goal, it is surmised that the organized vital pulp tissue is associated with the return of neural capacity. Many cases revealed a positive response to pulp sensitivity testing, according to many reviews. Second, Regenerative endodontic treatment favors minimal filing of the canal or none at all. However, a failed regenerative treatment showed that the apical portion of the canal accommodated a large number of bacteria, where a biofilm was created on its walls and pierced its way into the dental tubules. From this milestone, it was conjectured by some that some level of mechanical removal of the damaged part may be needed to derange the biofilm and aggrandize the maturation of the root. Moreover, infections decrease the success of the regenerative treatments where it inhibits the activity of stem cells and the renovation of the root.[1] For this reason, it is of great importance to sanitize and disinfect the root canal system.[1] When choosing a disinfectant, its bactericidal properties should be taken into consideration, to make sure it does not harm or affect the survival and the multiplication capacity of the stem cells.[7]

For the sake of safety, the protocol expresses a two-visit proposition for the use of intra-canal medication. It proposes the spraying of 20ml sodium hypochlorite while avoiding any discharge into the periapical space (a closed-end needle can help).[1] The concentrations used should be guarded as well, not exceeding 1.5% for 5 minutes of exposure time, then it should be washed with saline or EDTA (17%) for 5 minutes as well, through the use of a 1mm needle. All of this procedure aims to lessen cytotoxicity to stem cells found in the apical tissues. Growth factors contained in the dentine matrix are released by endodontic irrigants. EDTA has the power to demineralize the dentin, and it also reveals its matrix triggering it to liberate growth factors. Exposure of the dentin matrix by EDTA also appeared to increase the adherence of newly formed mineralized tissue to the root walls; in addition to the role it plays in the differentiation of dental pulp stem cells towards dentin. Hence, the use of EDTA is indeed essential, especially before blood clot formation. Third, a double antibiotic paste of metronidazole and ciprofloxacin was used in the first report of revascularization in a contaminated immature tooth, in 2001. The report that followed, declared the use of a "3 mix" of antibiotics consisting of metronidazole, ciprofloxacin and minocycline. The basis of that use lies in the fact that a number of studies reveled that a concentration of 100μg/mL of each drug will be able to eradicate bacteria completely from the infected root canals whether *in vivo* or *in vitro*.[8] Concentrations that are no greater that 0.1 mg/ml will be able to successfully disinfect the area where they are applied without interfering with the regenerative properties of the stem cells. Another study advocates for the use of calcium hydroxide over the use of the "3 mix" antibiotic[11]. It revealed that the survival outcomes of stem cell of apical papilla treated with calcium hydroxide eclipsed those that were treated with the "3 mix" antibiotics. However, some studies reported the possible cytotoxicity of calcium hydroxide.[2] In contrast, the use of minocycline might induce teeth discoloration.[2] Ultimately, ergo, growth factors, survival chances and proliferation of stem cells should be always be put into thought.[2] Further, following the disinfection of the canal and resolution of symptoms, regenerative treatment usually involves a scoring in the periapical tissues to originate bleeding or the use of platelet-rich plasma or platelet-rich fibrin.[9] The rationale of such an action is the engendering of a notable amount of undifferentiated stem cells into the canal area.[10] The whole process depends on the interaction of stem cells with the environment created.[10] Later, A coronal barricade should be constructed after the initiation of a blood clot, in order to avert the exudation of microorganisms. Some recent endorses that when a blood clot is established, a piece of a kind of plug should be ready to get situated on top of that clot.[3] Thus, the placed piece would serve as an internal matrix for the disposition of approximately 3 mm of white MTA followed by a 3–4mm layer of glass ionomer layer. Atop of it, reinforced composite resin restoration would settle. MTA is applicable for its bioactive properties that resists bacterial accommodation.[11] All in all, no standard protocol of regenerative endodontic treatment has been set. As revealed above, regenerative endodontic processes for immature permanent teeth with noninfected and infected necrotic pulps in humans varies markedly in terms of concentrations of sodium hypochlorite irrigant and "3 mix" antibiotics in all published studies.[12] The processes are summarized in the figure below based on a regimen performed by the American Association of Endodontics (Figure 1).



Are we regenerating?

Regeneration is the operation of renovation and reconditioning that makes biological tissues flexible to natural alterations that generate disruption or damage.[1] Regeneration can create the same new tissue, or it can produce a tissue-like fibrosis where the process is called repair instead of regeneration.[3].The human body is distinctly known for its capacity to regenerate.[2] However, the dental pulp has a slight aptitude of regeneration. In regenerative endodontic processes, the pulp stem cells are differentiated into odontoblast-like cells by the growth factors delivered into the root canal system after EDTA treatment, and form reparative dentin.[13] Nonetheless, many animal and human studies reported the inability of the mesenchymal cells to metamorphose into odontoblast-like cells and bring forth the dentin-pulp system.[14] By the same token, after probing the regenerative endodontic processes in animal and human models suffering from immature teeth with necrotic pulps and periodontitis, it was revealed that the tissues founded in the canal area were full of minerals, paralleling the nature of the cementum, bone and fibrous connective tissues.[1] Consequently, fabricating a periodontal ligament. Histologically speaking, the mentioned processes are regarded as reparative rather than regenerative in the cases of human immature permanent teeth with necrotic pulps.[2] As to which it is concluded that a histological verification is critical for assessing whether a dentin-pulp complex is regenerated or not.[2] Rectifying teeth may be taken as an option if the ruling goal of the regenerative endodontic methods, was oriented towards the termination of clinical symptoms and signs and apical periodontitis; not recommended much.[15–35]

Conclusion

Despite this technology constraints, regenerative endodontic treatment has the capability to reshape endodontic treatment.[3] Vital teeth have been appeared to be less defenseless to decays than endodontically treated teeth, and with regenerative endodontic procedures, a viable neurovascular tissue embedded with defense mechanisms takes up the root canal system instead of fabric materials.[2] This treatment offers to teeth the opportunity to win back their vitality and reinstall their function.

Acknowledgments

None.

Conflicts of interest

The authors declare no conflict of interest.

References

1. Andreasen JO, Andreasen FM. Textbook and color atlas of traumatic injuries to the teeth. Copenhagen: Munsgaard; 1994.
2. Banchs F, Trope M. Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol? *J Endod*. 2004;30(4):196–200.
3. Becerra P, Ricucci D, Loghin S, et al. Histologic study of a human immature permanent premolar with chronic apical abscess after revascularization/revitalization. *J Endod*. 2014;40(1):133–139.
4. Chrepa V, Henry MA, Daniel BJ, et al. Delivery of apical mesenchymal stem cells into root canals of mature teeth. *J Dent Res*. 2015;94(12):1653−1659.
5. Liao J, Al Shahrani M, Al-Habib M, et al. Cells isolated from inflamed periapical tissue express mesenchymal stem cell markers and are highly osteogenic. *J Endod*. 2011;37(9):1217−1224.
6. Majno G, Joris I. Cells, tissues, and disease. 2nd ed. Oxford, London: Oxford University Press; 2004.
7. Shah N, Logani A, Bhaskar U, Aggarwal V. Efficacy of revascularization to induce apexification/apexogensis in infected, nonvital, immature teeth: a pilot clinical study. *J Endod*. 2008;34(8):919–925.
8. Shin SY, Albert JS, Mortman RE. One step pulp revascularization treatment of an immature permanent tooth with chronic apical abscess: a case report. *Int Endod J*. 2009;42(12):1118–1126.
9. Diogenes A, Ruparel NB, Shiloah Y, et al. Regenerative endodontics: a way forward. *J Am Dent Assoc*. 2016;147(5):372−380.
10. Jeeruphan T, Jantarat J, Yanpiset K, et al. Mahidol study 1: comparison of radiographic and survival outcomes of immature teeth treated with either regenerative endodontic or apexification methods: a retrospective study. *J Endod*. 2012;38(10):1330−1336.
11. Rafter M. Apexification: a review. *Dent Traumatol*. 2005;21(1):1–8.
12. Shi S, Bartold PM, Miura M, Seo BM, et al. The efficacy of mesenchymal stem cells to regenerate and repair dental structures. *Orthod Craniofac Res*. 2005;8(3):191–199.
13. Huang GJ. Apexification: the beginning of its end. *Int Endod J*. 2009;42(10):855–866.
14. Huang GT, Lin LM. Letter to the editor: Comments on the use of the term "revascularization" to describe root regeneration. *J Endod*. 2008;34(5):511.
15. Reynolds K, Johnson JD, Cohenca N. Pulp revascularization of necrotic bilateral bicuspids using a modified novel technique to eliminate potential coronal discolouration: a case report. *Int Endod J*. 2009;42:84–92.
16. D›Arcangelo C, D›Amario M. Use of MTA for orthograde obturation of nonvital teeth with open apices: report of two cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2007;104:e98–e101.
17. Dummett CO, Thikkurissy S. Anomalies of the developing dentition. In: Casamassimo PS, Fields HW, McTigue DJ, Nowak A, editors. *Pediatric dentistry. Infancy through adolescence*. 5th ed. Philadelphia: WB Saunders Co.;2013:54–80.
18. Forghani M, Parisay I, Maghsoudlou A. Apexogenesis and revascularization treatment procedures for two traumatized immature permanent maxillary incisors: a case report. *Restor Dent Endod*. 2013;38(3):178–181.
19. Galler KM, Buchalla W, Hiller KA, et al. Influence of root canal disinfectants on growth factor release from dentin. *J Endod*. 2015;41(3):363–368.
20. Goyal L. Clinical effectiveness of combining platelet rich fibrin with alloplastic bone substitute for the management of combined endodontic periodontal lesion. *Restor Dent Endod*. 2014;39:51–55.
21. Hoshino E, Kurihara-Ando N, Sato I, et al. *In-vitro* antibacterial susceptibility of bacteria taken from infected root dentine to a mixture of ciprofloxacin, metronidazole and minocycline. *Int Endod J*. 1996;29(2):125–130.
22. Hotwani K, Sharma K. Platelet rich fibrin - a novel acumen into regenerative endodontic therapy. *Restor Dent Endod*. 2014;39(1):1–6.
23. Huang GT, Sonoyama W, Liu Y, et al. The hidden treasure in apical papilla: the potential role in pulp/dentin regeneration and bioroot engineering. *J Endod*. 2008;34(6):645–651.

24. Huang GT. A paradigm shift in endodontic management of immature teeth: conservation of stem cells for regeneration. *J Dent*. 2008;36(6):379–386.

25. Iwaya SI, Ikawa M, Kubota M. Revascularization of an immature permanent tooth with apical periodontitis and sinus tract. *Dent Traumatol*. 2001;17(4):185–187.

26. Kumar V, Abbas AK, Fausto N, et al. Robbins and cotran pathologic basis of disease. 9th ed. Philadelphia (PA): Saunders; 2014.

27. Lenzi R, Trope M. Revitalization procedures in two traumatized incisors with different biological outcomes. *J Endod*. 2012;38(3):411–414.

28. Lovelace TW, Henry MA, Hargreaves KM, et al. Evaluation of the delivery of mesenchymal stem cells into the root canal space of necrotic immature teeth after clinical regenerative endodontic procedure. *J Endod*. 2011;37(2):133−138.

29. Martin G, Ricucci D, Gibbs JL, et al. Histological findings of revascularized/revitalized immature permanent molar with apical periodontitis using platelet-rich plasma. *J Endod*. 2013;39(1):138–144.

30. Nakashima M, Nagasawa H, Yamada Y, et al. Regulatory role of transforming growth factor-beta, bone morphogenetic protein-2, and protein-4 on gene expression of extracellular matrix proteins and differentiation of dental pulp cells. *Dev Biol*. 1994;162(1):18–28.

31. Osorio RM, Hefti A, Vertucci FJ, Shawley AL. Cytotoxicity of endodontic materials. *J Endod*. 1998;24(2):91–96.

32. Paryani K, Kim SG. Regenerative endodontic treatment of permanent teeth after completion of root development: a report of 2 cases. *J Endod*. 2013;39:929−934.

33. Saoud TM, Sigurdsson A, Rosenberg PA, et al. Treatment of a large cystlike inflammatory periapical lesion associated with mature necrotic teeth using regenerative endodontic therapy. *J Endod*. 2014;40(12):2081−2086.

34. Thomson A, Kahler B. Regenerative endodontics-biologically-based treatment for immature permanent teeth: a case report and review of the literature. *Aust Dent J*. 2010;55(4):446–452.

35. Wang X, Thibodeau B, Trope M, et al. Histologic characterization of regenerated tissues in canal space after the revitalization/revascularization procedure of immature dog teeth with apical periodontitis. *J Endod*. 2010;36(1):56–63.

Citation: Rima ALA, Sanaa B, Sarah S, et al. Regenerative in endodontics: how, when and where. *J Dent Health Oral Disord Ther.* 2018;9(6):531–534.
DOI: 10.15406/jdhodt.2018.09.00444