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Review

Pulp Revascularization and Regeneration: Differences, Utilization, and Outcome

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Abstract

Microbial, mechanical, physical, and chemical factors are strong enough to endanger tooth pulp, resulting in alterations and inflammation of its vasculature, and causing intolerable pain. Clinical and technical management of diseases of these tissues is oftentimes very difficult due to the vastly varied anatomical nature of the pulpal space. Root canal treatment has been used to scavenge the diseased pulp and allow healing of the supporting tissues. In a small proportion of teeth, the creation of the apical root structure Hertwig's Epithelial Root Sheath may not be completed (causing an open apex) because of trauma or breach of the pulp by caries. In these scenarios, alternative techniques have been found, which regenerate a functional pulp tissue optimally. Regenerative endodontic procedures are biologically based techniques devised for predictable replacement of injured, infected, or missing structures with live viable tissues that restore the normal physiologic functions of the pulp-dentine complex. Pulp revascularization is generally described as re-introduction of vascularity in the root canal system. Pulp regeneration, on the contrary, has not been accurately defined. Even though blood vessels are necessary components of dental pulp, pulpal regeneration is regarded incomplete without an odontoblastic layer bordering the dentin-pulp interface. Although the interactions with human pulp derived stem cells are still vague, it is suspected that conventional pulpal cells that resist infection can grow rapidly under the impact of Hertwig's epithelial root sheath even during the inflammation stage; generating odontoblasts which has the ability to give rise to atubular dentin, triggering apexogenesis. It is understood that similar and consistent outcomes in the endodontics are not always achieved. The pace of apex maturogenesis differs due to distinctive conditions of each case. A possibility of chronic necrosis my strip the pulpal tissue of remnants of viable cells and may lead to reduced capabilities to regenerate.

Keywords: *pulp revascularization, pulp regeneration, pulp revitalization, regenerative endodontic procedures*

Introduction

Dental pulp is built of a densely innervated and vascularized loose network of connective tissue with different kinds of cells with unique roles like odontoblasts interspersed with more frequently encountered cells including fibroblasts, endotheliocytes, immunocytes, and stem/progenitor cells, together with an extracellular matrix consisting of fibrillar proteins as well as ground substance (1). Microbial, mechanical, physical, and chemical factors are strong enough to endanger it, resulting in alterations and inflammation of its vasculature, and causing pain which has been reported as excruciating and almost unbearable, making the patients seek dental care on a prompt basis (2).

Endodontics is that branch of dentistry concerned with the morphology, physiology, and pathology of the human dental pulp and peri-radicular tissues repeat (2). Clinical and technical management of diseases of these tissues is oftentimes very difficult due to the vastly varied anatomical nature of the pulpal space. Root canal treatment has been used to scavenge the diseased pulp and allow healing of the supporting tissues. In a small proportion of teeth, the creation of the apical root structure, Hertwig's Epithelial Root Sheath (HERS) may not be completed (causing an open apex) because of trauma or breach of the pulp by caries. In these scenarios, alternative techniques have been found, which regenerate a functional pulp tissue optimally (3). The promise and prospects of regenerative endodontic therapies in teeth with necrosis were initially investigated by Nygaard-Østby in 1961 (4) with limited success. In the past decades, interest has been replenished in regenerative endodontic procedures (REPs), which have been defined as ''biologically based procedures devised to predictably replace damaged, diseased, or missing structures, which includes dentine, root structures and cells of the pulp-dentine complex, with live viable tissues, preferably of the same origin, that restore the normal physiologic functions of the pulp-dentine complex'' (5, 6). REPs act with the perquisite that the root canal devoid of contamination together with a freshly stimulated blood supply can definitively restore vascularization, aiding in root completion (7, 8).

Shimizu described the regenerating process as the replacing of injured tissues by the similar parenchymal cells which existed before within the same tissue (9). Revascularization is a productive technique for inducing maturation in non-vital teeth with incompletely formed roots. It has been seen that these treatments accompanied with the use of plasma rich proteins can possibly enhance and speed up the process to attain the favored biological outcome of this regenerative technique (10).

While a desirable treatment option, there are not presently any randomized clinical studies on which to found decisions regarding therapy (11). Results have been mostly scarce, and the success of the procedure determined by two-dimensional radiography questioned. Moreover, causal factors behind necrosis, and its management can affect the outcomes. Few researchers are concerned about the variables which will have a major influence on the expected outcomes, like repair vs. regeneration, presence of viable cell populations, capacity to receive impacting vasculogenesis/angiogensis together with neurogenesis/re-innervation, the nature of the defective pulp or root originally, potential for complete sterilization of canal, tissue responses including mineralization of the pulpal space, and problems linked with clinical protocols and their use (3, 12-17). Therefore, although research into REP is getting heavy media attention within dentistry, there seems to be much speculation and absence of a clear vision as to where these attempts are headed and what will be the ultimate future of these procedures in tooth retention.

Methodology

This study is based on a comprehensive literature search conducted on September 21, 2022, in the Medline and Cochrane databases, utilizing the medical topic headings (MeSH) and a combination of all available related terms, according to the database. To prevent missing any possible research, a manual search for publications was conducted through Google Scholar, using the reference lists of the previously listed papers as a starting point. We looked for valuable information in papers that discussed the information about the difference between pulp revascularization and regeneration, their utilization, and outcomes. There were no restrictions on date, language, participant age, or type of publication.

Discussion

In the endodontic context, pulp revascularization is generally described as re-introduction of vascularity in the root canal system (18). Pulp regeneration, on the contrary, has not been accurately defined. Many new review papers on regenerative endodontics seem to describe pulp regeneration as the restoration of the pulp-dentin complex, which is still somewhat unclear (4, 19-21). Pulp regeneration cannot occur without revascularization or angiogenesis, but pulp

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revascularization, which refers to restoration of vascularity in the pulpal space but not invariably odontoblastic repopulation on dentinal surfaces (12). Even though blood vessels are necessary components of dental pulp, pulpal regeneration is regarded incomplete without an odontoblastic layer bordering the dentin-pulp interface. Pulp regeneration can also be thought as incomplete without nociceptors and sympathetic and parasympathetic nerve fibers, as well as interstitial fibroblasts and perhaps most crucially, stem/progenitor cells that help in replenishing all pulpal cells in the regenerated pulp when they go through apoptosis and turnover (12). Thus, it can be helpful to consider pulp revascularization as the process of inducing angiogenesis in endodontically treated root canal, and pulpal regeneration as process of restoring functional odontoblasts and/or nerve fibers additionally to pulp revascularization.

Some researchers question the idea gaining traction today about pulp revascularization, triggered through bleeding or triple antibiotic pastes, being the same as pulp regeneration which is considered a revolution among endodontists (22). Some researchers believe that pulp revascularization in the traditional endodontic context does not make use of the basics of tissue engineering, specifically stem cells, scaffolding as well as growth-related factors, and is different from new experimental research on pulp regeneration (23).

When it comes to revascularization of the vacant pulpal space in a tooth with open apex and pulpal necrosis, the ingrowth of connective tissue, certain vascular and neural elements and an osteocementum matrix has been observed in few cases, together with what appears to be radiographically a decrease in the pulpal space; in certain cases, root can lengthen due to HERS remnants. Even though some teeth have been retained using REPs, the potential for pulpal regeneration and dentinal production is highly disputed (24) in cases where there is an absence of residues of the dental papilla and HERS near the apical area of the unclosed apex, or the canal. Further, many researchers are of the opinion that teeth indicated for REP can be retained using other more traditional procedures like apexification (13). Nonetheless, neither procedure has been proven to be more optimal than the other in retaining teeth, though a regenerative procedure may cause root thickening and lengthening (13). One of the main benefits being attributed for using REP is the potential for making the root stronger with further deposits of hard tissue. It is not yet clear whether the hard tissue formed is dentin or an osteocementum kind of tissue and if it closely locks into the dentin to strengthen the root (14, 25-27). Essentially, some researchers question if the process has greater semblance to guided tissue repair as seen in periodontal repair instead of revascularization or regeneration (28), particularly more likely when total pathogen (gram negative bacteria species) eradication is not achievable, and subsequently, their lipopolysaccharides through bone sialoprotein gene expression, spur an osteocementum formation in the canal (29).

Regenerative procedures are an upcoming area in the medical field, especially in odontology, as the process can be looked into with the help of cone beam tomography or periapical radiography, as the root forming comprises hard tissue deposition and can be reviewed, gauged, and juxtaposed with previous examinations. In the recent past, some authors resisted attempting revascularizing, nonvital, immature teeth with infected pulp space, in spite of a few cases of success because of the perceived risks of attempting revascularization of an infected root canal. Hence, the conventional therapy of apexification induction with calcium hydroxide and mineral trioxide aggregate (MTA) or via operative endodontics for closing wide-open apices was always opted for as the first treatment choice. Although the interactions with human pulp derived stem cells are still vague (30, 31), due to the complex nature and information deficit, it is suspected that conventional pulpal cells that resist infection can grow rapidly under the impact of Hertwig's epithelial root sheath even during the inflammation stage; generating odontoblasts which have the ability to give rise to atubular dentin at the apex termination, triggering apexogenesis (32-34). The inflammation stage needs adequate blood supply in the periapex, for recruiting cells for defense against pathogens. Consequently, chemotactic factors are released, called cytokines and interleukins. Simultaneously, or one by one, they lead to inflammatory changes in some scenarios whilst limit them in others, regulating the process. Few classical cells are the mast cells, that, on getting prompted by etiological elements like neurotoxic bacteria, undergo multiplication and degranulate leading to inflammatory and vascular alterations (35, 36). Nonetheless, to promote healing and to enhance the revascularizing process, radicular infection needs to be eliminated.

Alternatively, a mechanism for developing the root may be related to stem cells from the apical papilla or the bone marrow stem cells residing in the alveolus. After instrumenting further than the territory of the root canal

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into the periapical area to induce bleeding, mesenchymal stem cells may transport from the bone to the canal, causing bone or dentin-like tissue formation *clinically (37, 38)*.

Similar and consistent outcomes in the endodontics are not always achieved. The pace of maturogenesis differs due to distinctive conditions of each case. A possibility of chronic necrosis my strip the pulpal tissue of remnants of viable cells and may lead to reduced capabilities to regenerate. Numerous reviews have declared it to be a revolutionary transition in the therapy for immature permanent teeth as well as being the next generation, from conventional seal creation methods using calcium hydroxide and mineral trioxide aggregate apexification to biologically based therapies (39, 40). However, many researchers are not firm proponents of REP (5, 14). One review made a statement that due to "the lack of long-term evidence to support the use of REP in traumatized teeth with open apices, revascularization-regeneration procedures should only be attempted if the tooth is not suitable for root canal obturation, and after apexogenesis, apexification or partial pulpotomy treatments have already been attempted and have a poor prognosis'' (5). There are other academicians who hold the opinion that results of revascularization continue to be difficult to predict, and the managing these teeth clinically is cumbersome, when they succeed, they offer are an upgrade to conventional therapy which leaves teeth with shorter roots and thinner canal walls predisposed to cracks.

One detected disadvantage has been a paucity of available proof on outcomes (4). Even though many case reports and few case series report favorable outcomes, these studies need to be regarded as a low level of evidence, especially since one of the main issues with interpreting case reports is that often only selected outcomes which have had success are published. Several such reports also only report outcomes restricted to bicuspids (32, 41-45). Till now, there seems to be only one prospective pilot study which assesses outcomes for anterior teeth (46). In that study, 14 infected nonvital immature incisors with infection were managed via REP post-trauma. Nevertheless, the researchers utilized nonstandardized images, several of which seemed to be of low quality and either with foreshortening or elongation. Even small alterations in angulation during pre-treatment and follow-up assessments can result in inconsistencies and inaccuracies while interpreting. Therefore, the utilization of nonstandardized radiographs to evaluate outcomes in REP, specifically to measure any addition in root length, has only made possible assessment qualitatively. Of recent, a geometrical imaging program (47) tried to minimize the potential variations in angulations between pre-treatment and follow-up images that allowed quantitative estimation of alterations in root length and dentinal wall thickness to be made. This method in theory allows to calculate the extent of any root maturation, which is an upgrade on previous qualitative assessments on outcome. The validity of using this method on anterior teeth has not been tested on teeth with trauma managed by REP.

A number of case reports have described successful outcomes when REP have been utilized for the treatment of infected immature teeth (32, 41, 48). It has been found that this regimen can allow apexogenesis, which is continued maturogenesis with closing of open apices as well as addition in root length and thickness of lateral dentin on root walls (47).

Quantitative evaluation through the use of imaging software which controls for angulation of preoperative and recall radiographs for changes in root length and dentin thickness appears to add validity to the biological changes that may take place after REP. Further, the significance that lengthier periods of follow up are needed is justified by observations of continuing root maturogenesis following 36 months.

Moreover, on the subject of materials used in REPs, antibiotic paste's component, minocycline has been shown as the main reason for discoloration (49). Also, many studies have shown that both gray MTA (50) and white MTA (51) can lead to discoloration postoperatively. sub-cementoenamel junctional administration of MTA was found to be challenging in some teeth, and in few cases, the material fails to develop a complete seal. Few difficulties in the placement of MTA can be avoided if a collagen matrix is used (51). A potential method for avoiding discoloration is to seal the dentinal walls of the access cavity with a dentin bonding agent (50). It is believed, without supporting evidence, that REPs are contraindicated in avulsed teeth (14). Many researchers are of the opinion that placement of MTA in the root canal of immature teeth going through resorption is contraindicated if there is a possibility that the tooth may require a root submergence procedure later. The recent review in Dental Traumatology (5) does seem timely because there does appear to be a lack of evidence and conflicting results as well as a paucity of prospective studies. However, it may be too strongly recommending that regeneration must only be tried as a final resort in treatment failure with a bad prognosis

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where apexogenesis, nonsurgical apexification, or obturation has already been tried. The beforementioned procedures are usually linked with good outcomes, so if these recommendations were followed, there would be lesser incidence where regenerative procedures would be indicated. Further, going for a regeneration post MTA apexification can be difficult, and there is no research or case study which reports a successful regenerative outcome after any of these procedures. The present authors recommend that if regeneration is to be attempted, they should be regarded as the first line of treatment for traumatized infected immature teeth. A greater incidence of incisor teeth cracks is seen in teeth treated via calcium hydroxide apexification where root maturation was arrested (52). This may be due to the fragile nature of remaining root structure, which may be complicated by the adverse impact of calcium hydroxide on radicular dentin strength (53). Even if REPs are utilized in incisor teeth, there is often only a minor fluctuation in the thickness of the dentin in the cervical and middle third radicular portions of the tooth, which continue being thin.

Conclusion

Though revascularization has only been introduced recently as part of REP, it has been found to be beneficial for teeth affected before reaching maturation as it allows the forming of root using a comparatively simple method and improves longevity for the teeth undergoing the treatment. Nonetheless, further research is needed for evaluating its efficacious over longer time periods and novel techniques. Studies so far have shown that pattern for maturing roots post REP is variable at assessment at 1.5 years, however in majority of patients, lesion in the periapex seemed to undergo resolution totally.

Disclosure

Conflict of interest

There is no conflict of interest

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Data availability

Data that supports the findings of this study are embedded within the manuscript.

Author contribution

All authors contributed to conceptualizing, data drafting, collection and final writing of the manuscript.

References

1. Okiji T. Pulp as a connective tissue. Seltzer and Bender's dental pulp. 2012:67-89.

2. Gutmann JL. Revascularization/Revitalization & Regeneration in Endodontics-Quo Vadis?

3. Hargreaves KM, Diogenes A, Teixeira FB. Treatment options: biological basis of regenerative endodontic procedures. Pediatric dentistry. 2013;35(2):129-40.

4. Murray PE, Garcia-Godoy F, Hargreaves KM. Regenerative endodontics: a review of current status and a call for action. Journal of endodontics. 2007;33(4):377-90.

5. Garcia-Godoy F, Murray PE. Recommendations for using regenerative endodontic procedures in permanent immature traumatized teeth. Dental Traumatology. 2012;28(1):33-41.

6. Silva L. Stem cells in the oral cavity. Studies on Stem Cells Research and Therapy. 2015;1(1):012-5.

7. Friedlander L, Cullinan M, Love R. Dental stem cells and their potential role in apexogenesis and apexification. International Endodontic Journal. 2009;42(11):955-62.

8. Versluis A, Kim H-C, Lee W, Kim B-M, Lee C-J. Flexural stiffness and stresses in nickel-titanium rotary files for various pitch and cross-sectional geometries. Journal of endodontics. 2012;38(10):1399-403.

9. Shimizu E, Jong G, Partridge N, Rosenberg PA, Lin LM. Histologic observation of a human immature permanent tooth with irreversible pulpitis after revascularization/regeneration procedure. Journal of endodontics. 2012;38(9):1293-7.

10. de Souza Araújo PR, Silva LB, dos Santos Neto AP, de Arruda JAA, Álvares PR, Sobral APV, et al. Pulp revascularization: a literature review. The open dentistry journal. 2017;10:48.

11. Torabinejad M, Nosrat A, Verma P, Udochukwu O. Regenerative endodontic treatment or mineral trioxide aggregate apical plug in teeth with necrotic pulps and open apices: a systematic review and meta-analysis. Journal of endodontics. 2017;43(11):1806-20.

 http://dx.doi.org/10.52533/JOHS.2022.21108

12. Mao JJ, Kim SG, Zhou J, Ye L, Cho S, Suzuki T, et al. Regenerative endodontics: barriers and strategies for clinical translation. Dental Clinics. 2012;56(3):639-49.

13. Lin J, Zeng Q, Wei X, Zhao W, Cui M, Gu J, et al. Regenerative endodontics versus apexification in immature permanent teeth with apical periodontitis: a prospective randomized controlled study. Journal of endodontics. 2017;43(11):1821-7.

14. Wigler R, Kaufman AY, Lin S, Steinbock N, Hazan-Molina H, Torneck CD. Revascularization: a treatment for permanent teeth with necrotic pulp and incomplete root development. Journal of endodontics. 2013;39(3):319-26.

15. Albuquerque M, Valera M, Nakashima M, Nör J, Bottino M. Tissue-engineering-based strategies for regenerative endodontics. Journal of dental research. 2014;93(12):1222-31.

16. Huang G-J, Garcia-Godoy F. Missing concepts in de novo pulp regeneration. Journal of dental research. 2014;93(8):717-24.

17. Song M, Cao Y, Shin S-J, Shon W-J, Chugal N, Kim RH, et al. Revascularization-associated intracanal calcification: assessment of prevalence and contributing factors. Journal of endodontics. 2017;43(12):2025-33.

18. Hargreaves KM. Cohen's pathways of the pulp: Elsevier; 2016.

19. Sun HH, Jin T, Yu Q, Chen FM. Biological approaches toward dental pulp regeneration by tissue engineering. Journal of tissue engineering and regenerative medicine. 2011;5(4):e1-e16.

20. Bansal R, Bansal R. Regenerative endodontics: a state of the art. Indian Journal of Dental Research. 2011;22(1):122.

21. Demarco FF, Conde MCM, Cavalcanti BN, Casagrande L, Sakai VT, Nör JE. Dental pulp tissue engineering. Brazilian dental journal. 2011;22:3-13.

22. Spångberg L. The Emperor's new cloth. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontics. 2009;108(5):643-4.

23. Hargreaves KM, Law A. The wrong emperor. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics. 2010;109(3):327-8.

24. Saoud TMA, Zaazou A, Nabil A, Moussa S, Aly HM, Okazaki K, et al. Histological observations of pulpal replacement tissue in immature dog teeth after revascularization of infected pulps. Dental Traumatology. 2015;31(3):243-9.

25. Wang Y, Zhu X, Zhang C. Pulp revascularization on permanent teeth with open apices in a middle-aged patient. Journal of endodontics. 2015;41(9):1571-5.

26. Dudeja PG, Grover S, Srivastava D, Dudeja KK, Sharma V. Pulp revascularization-it's your future whether you know it or not? Journal of Clinical and Diagnostic Research: JCDR. 2015;9(4):ZR01.

27. Antunes LS, Salles AG, Gomes CC, Andrade TB, Delmindo MP, Antunes LA. The effectiveness of pulp revascularization in root formation of necrotic immature permanent teeth: A systematic review. Acta Odontologica Scandinavica. 2016;74(3):161-9.

28. Diogenes A, Ruparel NB, Shiloah Y, Hargreaves KM. Regenerative endodontics: a way forward. The Journal of the American Dental Association. 2016;147(5):372-80.

29. Lertchirakarn V, Aguilar P. Effects of lipopolysaccharide on the proliferation and osteogenic differentiation of stem cells from the apical papilla. Journal of Endodontics. 2017;43(11):1835-40.

30. Lieberman J, Trowbridge H. Apical closure of nonvital permanent incisor teeth where no treatment was performed: case report. Journal of Endodontics. 1983;9(6):257-60.

31. Nevins A, Wrobel W, Valachovic R, Finkelstein F. Hard tissue induction into pulpless open-apex teeth using collagen-calcium phosphate gel. Journal of endodontics. 1977;3(11):431-3.

32. Banchs F, Trope M. Revascularization of immature permanent teeth with apical periodontitis: new treatment protocol? Journal of endodontics. 2004;30(4):196-200.

33. Heithersay GS. Stimulation of root formation in incompletely developed pulpless teeth. Oral Surgery, Oral Medicine, Oral Pathology. 1970;29(4):620-30.

34. Saad AY. Calcium hydroxide and apexogenesis. Oral Surgery, Oral Medicine, Oral Pathology. 1988;66(4):499-501.

35. Kamal R, Dahiya P, Palaskar S, Shetty V. Comparative analysis of mast cell count in normal oral mucosa and oral pyogenic granuloma. 2011.

 http://dx.doi.org/10.52533/JOHS.2022.21108

36. Silva L. A literature review of inflammation and its relationship with the oral cavity. Global Journal of Infectious Diseases and Clinical Research. 2015;1(1):1-7.

37. Krebsbach PH, Kuznetsov SA, Satomura K, Emmons RV, Rowe DW, Robey PG. Bone formation in vivo: comparison of osteogenesis by transplanted mouse and human marrow stromal fibroblasts. Transplantation. 1997;63(8):1059-69.

38. Gronthos S, Mankani M, Brahim J, Robey PG, Shi S. Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo. Proceedings of the National Academy of Sciences. 2000;97(25):13625-30.

39. Huang GT-J. A paradigm shift in endodontic management of immature teeth: conservation of stem cells for regeneration. Journal of dentistry. 2008;36(6):379-86.

40. Hargreaves KM, Giesler T, Henry M, Wang Y. Regeneration potential of the young permanent tooth: what does the future hold? Pediatric dentistry. 2008;30(3):253-60.

41. Chueh L-H, Huang GT-J. Immature teeth with periradicular periodontitis or abscess undergoing apexogenesis: a paradigm shift. Journal of endodontics. 2006;32(12):1205-13.

42. Jung I-Y, Lee S-J, Hargreaves KM. Biologically based treatment of immature permanent teeth with pulpal necrosis: a case series. Journal of endodontics. 2008;34(7):876-87.

43. Ding RY, Cheung GS-p, Chen J, Yin XZ, Wang QQ, Zhang CF. Pulp revascularization of immature teeth with apical periodontitis: a clinical study. Journal of endodontics. 2009;35(5):745-9.

44. Thomson A, Kahler B. Regenerative endodontics–biologically-based treatment for immature permanent teeth: a case report and review of the literature. Australian Dental Journal. 2010;55(4):446-52.

45. Iwaya Si, Ikawa M, Kubota M. Revascularization of an immature permanent tooth with apical periodontitis and sinus tract. Dental Traumatology. 2001;17(4):185-7.

46. Shah N, Logani A, Bhaskar U, Aggarwal V. Efficacy of revascularization to induce apexification/apexogensis in infected, nonvital, immature teeth: a pilot clinical study. Journal of endodontics. 2008;34(8):919-25.

47. Bose R, Nummikoski P, Hargreaves K. A retrospective evaluation of radiographic outcomes in immature teeth with necrotic root canal systems treated with regenerative endodontic procedures. Journal of endodontics. 2009;35(10):1343-9.

48. Lenzi R, Trope M. Revitalization procedures in two traumatized incisors with different biological outcomes. Journal of Endodontics. 2012;38(3):411-4.

49. Nosrat A, Homayounfar N, Oloomi K. Drawbacks and unfavorable outcomes of regenerative endodontic treatments of necrotic immature teeth: a literature review and report of a case. Journal of endodontics. 2012;38(10):1428-34.

50. Reynolds K, Johnson J, Cohenca N. Pulp revascularization of necrotic bilateral bicuspids using a modified novel technique to eliminate potential coronal discolouration: a case report. International endodontic journal. 2009;42(1):84-92.

51. Petrino JA, Boda KK, Shambarger S, Bowles WR, McClanahan SB. Challenges in regenerative endodontics: a case series. Journal of endodontics. 2010;36(3):536-41.

52. Cvek M. Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-percha. A retrospective clinical study. Dental Traumatology. 1992;8(2):45-55.

53. Andreasen JO, Farik B, Munksgaard EC. Long-term calcium hydroxide as a root canal dressing may increase risk of root fracture. Dental Traumatology. 2002;18(3):134-7.

 http://dx.doi.org/10.52533/JOHS.2022.21108