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APEXIFICATION REVISITED

Dental Science

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ABSTRACT

Pulpal necrosis in permanent teeth with immature roots leads to development of roots which are very short, thin walled and an inadequate crown-root ratio, which overshadows their survival prognosis. Traditionally, the apexification procedure has consisted of multiple and long-term applications of calcium hydroxide to create an apical barrier to aid the obturation. Recently, artificial apical barriers such as those made with mineral trioxide aggregate (MTA) have been used in teeth with necrotic pulps and open apices. More recently, procedures referred to as regenerative endodontics have received much attention as an option for these teeth. This paper reviews the past, present and recent concepts used for apexification.

KEYWORDS

Apexification, non-vital immature tooth, MTA, Calcium Hydroxide, Biodentine, Blunderbuss Canal, Immature Root Apices

INTRODUCTION

Pulpal involvement as a consequence of trauma or caries in immature permanent teeth can trigger the loss of pulpal vitality as well as directly affect root development.[1] The completion of root development and closure of the apex occurs up to 3 years after eruption of the tooth.[2] The treatment of pulpal injury during this period provides a significant challenge for the clinician due to the lack of natural apical constriction and the thin root walls that are prone to fracture.[3]

To manage these teeth, apexification has long been the treatment of choice, enjoying considerable success in preserving damaged immature teeth.[4]

Successful apexification depends on the formation of a hard tissue barrier by cells that migrate from the healing periradicular tissues to the apex and differentiate under the influence of specific cellular signals to become cells capable of secreting a cementum, osteocementum or osteodentin organic matrix.[5]

Apexification can be achieved in two ways: (1) as a long-term procedure using calcium hydroxide dressing to allow the formation of a hard tissue barrier, or (2) as a short-term procedure creating an apical plug of MTA. Completion of endodontic therapy is delayed until root-end closure is completely achieved by apexification.[6]

APEXIFICATION

Definition:

American Association of Endodontists defined apexification as "a method to induce a calcified barrier in a root with an open apex or the continued apical development of an incompletely formed root in teeth with necrotic pulps".[7]

Etiology of open apex:

Hertwigs epithelial root sheath (HERS) responsible for determining the shape of the root surrounds the apical opening to the pulp and eventually becomes the apical foramen. Complete destruction of the HERS can arrest any further lengthening of the root, but previously differentiated odontoblasts and cementoblasts can complete apical closure. HERS forms the outline for the root and apex, but without a vital pulp, root development cannot continue to completion.[8]

Cvek's classification of open apex:

Cvek has proposed a classification for the degree of root formation and maturation which offers didactic radiographic characteristics with valuable clinical applications. Cvek's classification(figure 1) describes the five stages of root development.[9]

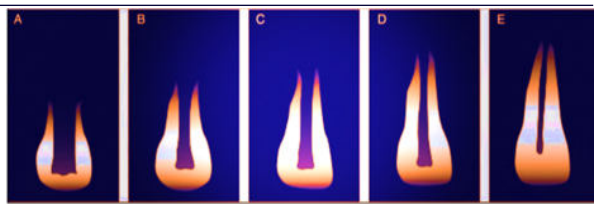

Figure 1 Stages of root development. A, B, C, D and E indicate stages 1, 2, 3, 4 and 5, respectively; 1= < 1/2 root length, 2= 1/2 root length,3= 2/3 root length,4= wide open apical foramen and nearly complete root length and 5= closed apical foramen and completed root development. (Adapted from Figure 1 from Cvek[9], p. 46)

OBJECTIVES:

Apexification procedure should induce root end closure (apexification) at the apices of immature roots or result in an apical barrier as confirmed by clinical and radiographic evaluation. Adverse post-treatment clinical signs or symptoms of sensitivity, pain, or swelling should not be evident. There should be no radiographic evidence of external root resorption, lateral root pathosis, root fracture, or breakdown of periradicular supporting tissues during or following therapy. The tooth should continue to erupt, and the alveolus should continue to grow in conjunction with the adjacent teeth.[10]

Diagnosis & Case assessment:

Accurate diagnosis is imperative prior to determining the treatment plan for teeth with underdeveloped roots. For this, careful assessment of pulp status is required. Radiographs are used to assess the maturity of the developing root and presence or absence of periradicular pathoses. Clinical evaluation should be based on history and clinical testing. Less reliable pulp testing data pose a special challenge in children.[8]

The clinical and radiographical assessment has to be done preceded by a comprehensive history of subjective symptoms and cause of the injury or duration of decay. Precise pain history explaining the duration, aggravating and relieving factors should be considered. The duration, nature of the pain, aggravating and relieving factors must be obtained. Duration of pain might vary, however pain that persist for more than a few seconds in a tooth with a vital pulp indicates irreversible pulpitis. If the pain is severe and spontaneous and lasts for more than a short duration of time, it indicates irreversible pulpitis, and the pulp has to be completely removed.[11]

Substantiation from objective tests is essential. These comprise visual examination, percussion testing and thermal and electric pulp testing.

The existence of a swelling or sinus tract denotes pulpal necrosis and acute or chronic abscess. If the tooth is tender on percussion and pain is throbbing in nature, it suggests that there is apical periodontitis, and there is inflammation in the periapical tissue. In the immature teeth, pulp vitality testing usually gives erratic response because the sensory plexus of nerves in the sub odontoblastic region is not well developed as root formation is incomplete, and any injury to it give unreliable responses. Over-dependence on the results of pulp vitality tests in immature teeth, especially the electric pulp testing is not suggested.[11]

Radiographic interpretation in these immature teeth with open apex can be challenging. In normal condition radiolucent area is present surrounding the developing apex of an immature tooth with a healthy pulp hence it is tricky to distinguish between this normal finding and a pathologic radiolucency due a necrotic pulp. Comparing the periapical region with that of the contralateral tooth may be useful. Although it is not possible to set up a close association between the results of these vitality tests and the histological diagnosis, an accurate clinical diagnosis of pulpal vitality can be made in majority of cases by merging the outcome of the history, examination and diagnostic tests. If the tooth is diagnosed as having a necrotic pulp, then apexification of the tooth is the treatment of choice.[11]

Working length determination:

Accurate canal length measurement is required to ensure complete canal debridement without over-instrumentation and over-extension of the obturation material. Extrusion of foreign materials might damage the periapical tissues including the remaining and vital HERS. Electronic apex locators are not accurate in immature teeth or teeth with wide open apices and radiographic determination of root length is recommended.[8] Despite radiographs being the key method of determining working lengths, several laboratory studies have investigated other methods including third generation EALs and paper point. [12]

Apical closure after apexification:

The radiographic aspect of the apical closure obtained after apexification treatment has been classified [Frank, 1966; Feiglin, 1985] in 4 clinical types (table 1) according to the presence or absence of the Hertwig epithelial sheath and its relationship with the apical residues of the pulp tissue.[13]

Table 1 Shows Classification Of Apical Closure After Apexification

Type 1	HERS and apical odontoblasts are still vital, the root will develop normally with a physiological process of apexogenesis.
Type 2	HERS is still vital but are missing vital odontoblasts, the root will lengthen without a physiological maturation of the apex.
Type 3	HERS and the odontoblasts are both non-vital, the healing can only take place with the formation of a cap of mineralised tissue produced by osteoblasts and cementoblasts activity at the apex.
Type 4	HERS and the odontoblasts are both non-vital, the healing can only take place with the formation of a cap of mineralised tissue produced by osteoblasts and cementoblasts activity at the coronal to the apex.

Materials Used For Apexification And Recent Advances

Before 1966, immature teeth with necrotic pulps were often extracted and the clinical management of a "blunderbuss" canal usually required a surgical approach for the placement of an apical seal into the often fragile and flaring apex, a procedure that is frequently difficult in uncooperative children. In 1961, Nygaard-Ostby suggested that during debridement of the canal if the endodontic file is taken beyond the apex and bleeding is initiated it may lead to vascularization of the canal which will cause the formation of apical barrier.[14] A number of investigators have demonstrated apical closure using an antiseptic paste as a temporary filling material following root canal debridement. Ball in 1964, successfully reproduced these results using an antibiotic paste.[15]

Some investigators believe that continuation of root apex development in nonvital teeth may be resumed by removal of the nonvital tissue and control of infection alone.[16] While some authors have suggested that debridement of the canal may lead to damage to the cells and should be done with utmost care if done at all.[17]

Although a variety of materials have been proposed for induction of apical barrier formation, Calcium Hydroxide has gained the widest acceptance. Various materials that have been recommended to induce apexification in teeth with immature apices, are described below.

Calcium Hydroxide (CH)

Calcium hydroxide is the most wildly accepted material used for apical barrier formation. It was first introduced by Kaiser in 1964, and he mixed it with camphorated parachlorophenol (CMCP) to induce apical closure.[18] His procedure was popularized by in 1966 by Frank, who described step by step procedure and four types of apical closure. Vehicles like saline, distilled water, and methylcellulose have also been suggested by Heithersay in 1970 to reduce the potential for cytotoxicity. Klein and Levy in 1974 explained the successful induction of an apical barrier using calcium hydroxide and Cresatin. When used as a root canal medicament, Cresatin has been proven to be less toxic than CMCP and showed a minimal inflammatory potential.

The calcium hydroxide paste used in Endodontics is composed of a powder, a vehicle, and an optional radiopacifier. Various biological properties and effects such as antimicrobial activity, tissue dissolving ability, inhibition of tooth resorption, and induction of repair by hard tissue formation have been attributed to this strong alkaline substance, which has a pH of approximately 12.5. The antimicrobial activity of calcium hydroxide is related to the release of hydroxyl ions, which are highly oxidant and show extreme reactivity. These ions cause damage to the bacterial cytoplasmic membrane, protein denaturation and damage to bacterial DNA.[11] The study by Barthel et.al[19] shows that CH is able to eliminate the ability of an E. coli Lipopolysaccharide to stimulate TNF-alpha production in peripheral blood monocytes, and it confirms the ability of CH to inhibit tooth resorption by reducing the lipo polysaccharide stimulated osteoclast formation[20] The high pH of calcium hydroxide may activate alkaline phosphatase activity, and the presence of a high calcium concentration may increase the activity of calcium-dependent pyrophosphatase, which plays an important role in the mineralization process.[8]

Non-vital immature teeth undergoing apexification are first disinfected with irrigants like sodium hypochlorite and chlorhexidine then the canal is packed with calcium hydroxide paste for further disinfection and inducing apical closure by the formation of an apical calcific barrier. Histologically, the calcified tissue that forms over the apical foramen has been identified as an osteoid or cementoid material. The normal time required to attain apexification is 6–24 months (average 1 year ± 7 months) however it can take up to 4years also. [6] The speed and location of barrier formation are influenced by the rate of change of calcium hydroxide and the degree of apical development prior to treatment.[21] Pre-treatment infection and /or presence periapical radiolucency at the start of the treatment may increase the barrier formation time.[22]

In dental literature there is different schools of thoughts are present as to what should be the duration of the calcium hydroxide dressing, and the decision appears to be empirical. According to Tronstad et al, refilling every 3–6 months is favored. Abbot[23] has suggested that calcium hydroxide should be replaced frequently so as to check the status of the barrier formation and also increases the speed of the calcific bridge that is formed. Cohen & Burns suggested refilling only if there is radiographic evidence of resorption of the paste. Chosack & Cleaton-Jones suggested that after initial root filling with calcium hydroxide, there was nothing to be gained by its replacement either monthly or after 3 months for at least 6 months.[24] The study by Finucane et al[21] found that the mean time to barrier formation was 34.2 weeks. Age may be inversely related to the time required for apical barrier formation.[11]

However, CH therapy has many disadvantages, including variability of treatment time, unpredictability of apical closure, reinfection, weakening of dentinal walls, cervical fracture and patient compliance. These shortcomings led to seek for alternative treatment modalities.[25]

Tricalcium phosphate (TCP)

Coviello and Brilliant[26] (1979) reported use of tricalcium phosphate as an apical barrier. The material was packed into the apical 2mm of canal against which gutta percha was condensed and treatment is achieved in one appointment.

Dentin chips

It was used to create an apical stop or matrix for the purpose of obtaining a biologic apical seal. Tronstad found that dentin chip plugs are well tolerated by the tissues and may act as an effective barrier in the apical part of the root canal.[27] A similar result was obtained in 1972 by Erausquin, who found that apical plugs formed by compressing radicular pulp and dentin chips in rat molar teeth resulted in a favorable tissue reaction.[14] Saunders studied the application of Nd:YAG pulsed

laser to dentin chips, hydroxyapatite, and low-fusing porcelain to produce a fused apical plug and found that this laser is unable to melt the dentin chips.[28]

Mineral trioxide aggregate (MTA)

It was first introduced in 1993 by Torabinejad et al[29] and received food and drug administration approval in 1998. MTA provides scaffolding for the formation of hard tissue and the potential of a better biological seal. MTA is a hydrophilic powder and consists of trisilicate cement. It was shown to have good biocompatibility, sealability and low solubility.[30] Various authors have reported clinical success using MTA for single visit apexification, report that MTA provides a viable alternative to achieve root closure in immature teeth or root fracture, even in cases with an open apex. MTA helps in the formation of bone and periodontium around its interface. A bonded restoration can be placed without any delay, thus reducing the possibility of root fractures. The time required for the formation of the barrier is significantly less in teeth treated with MTA compared to teeth treated with calcium hydroxide.[31] In one of the comparative studies, it was found that the mean time taken for barrier in MTA was 4.50 ± 1.56 months whereas for CH was 7.93 ± 2.53 months and the difference was statistically very significant. (p value- 0.0002).[32]

The major disadvantage of MTA is its manipulation due to which its placement in the wide apical area is difficult to achieve. A matrix can be used in apexification procedures against which MTA can be placed and condensed. Using a matrix prior to the placement of MTA avoids its extrusion, reduces leakage in the sealing material and allows favorable response of the periapical tissues. Several materials have been recommended to create a matrix, like hydroxyapatite-based materials, resorbable collagen, platelet-rich fibrin, absorbable suture and calcium sulphate.[33]

Biodentine

Biodentine is a new calcium silicate based cement of the same type as MTA. It exhibits physical and chemical properties similar to those described for certain Portland cement derivatives. Its biocompatibility has also been validated experimentally by Laurent et al.[34] Based on all its properties, Biodentine has been claimed to be a bioactive dentin substitute for the single visit apexifications. The main advantages of Biodentin over MTA include its ease of handling, high viscosity, shorter setting time (10 minutes), greater biocompactabilty, bioactivity, biomineralization and improved antimicrobial property, making it more suitable in clinical use.[35]

Calcium Phosphate Cement (CPC)

Calcium phosphate cement, one of the bioceramic material, has received a lot of research in due to their chemical similarity to bones and teeth. They are useful biomedical materials owing to their excellent biocompatibility and nontoxicity of their chemical components. The CPC powder consisted of tetracalcium phosphate (TTCP), $Ca(PO_4)_2O$, and dicalcium phosphate anhydrous (DCPA), $CaHPO_4$, when mixed with water at a powder : liquid ratio of 4:1, the paste hardened in about 30 minutes and formed hydroxyapatite. This cement has good handling characteristics when compared to MTA. CPC is inexpensive and also has antibacterial property, which is attributed to its high pH in the order of 12. Calcium phosphate cement showed osteoconductivity and was able to be resorbed and replaced by new bone.[36]

Freeze-dried bone

Bio-resorbable demineralized bone matrix (DMBM) is the protein component of bone and is widely used in various clinical conditions such as periodontal defects and oral and maxillofacial bone defects. Periodontal defects grafted with demineralized bone matrix allograft showed histologic evidence of regeneration of new bone and periodontium.[37] Demineralized freeze-dried bone compacted into the canal provides a biocompatible apical matrix. Rossmeisl et al. found freeze-dried dentin to be a biocompatible apical barrier against which guttapercha could be condensed.[14]

Platelet rich fibrin

Sometimes to reduce the chances of apical extrusion of the filling material, a matrix should be placed before placement of the filling material. Platelet-rich fibrin (PRF) developed by Choukroun and Dohan, contains strong fibrin membrane enriched with platelets and growth factors. It serves to accelerate the wound healing and also serves as internal matrix to condense MTA.[38] PRF contains leukocyte matrix, which includes cytokines platelet and stems cells within it, and they are biodegradable that help the epithelial cell to migrate. Growth factors are realized by PRF within a span of 1 - 4 weeks.[30] Woo et al. conducted an in vitro study in which combination of MTA and PRF showed synergistic effect on the stimulation of odontoblastic cell differentiation via the modulation of BMP/Smad signaling pathway.[38]

Bioaggregate

Recently, a modified version of MTA, the calcium silicate-based nanoparticles sized bioceramic BioAggregate (DiaRoot BioAggregate, Innovative BioCeramix Inc., Vancouver, BC, Canada) has emerged on the dental market. It contains nano sized particles of Aluminium, which is mixed with deionized water. Unlike MTA, BioAggregate does not contain aluminum oxide and bismuth oxide. Recent studies reported that BioAggregate is more biocompatible, better-sealing ability, higher fracture and acidic resistance than MTA.[39]

Enamel matrix derivative

A combination of MTA and enamel matrix derivative (EMD) promotes synergistically more rapid odontoblastic differentiation in human dental pulpal cells (HDPCs) than MTA alone.[40] Shariari et al. investigated the effect of the combination of EMD plus Bio-Oss on bone formation in calvarial defects in rabbits. The results of their study showed that using EMD plus Bio-Oss had synergistic effects on bone regeneration in bone defects. Also, it is demonstrated that EMD and Bio-Oss are biocompatible and osteoconductive. Several clinical studies carried out previously did not report any severe inflammation or histologic reaction. Based on the positive effects of EMD and Bio-Oss on bone regeneration and their biocompatibility, these materials can be considered for apexification.[41]

Recombinant amelogenin protein (RAP)

Amelogenin is an extracellular matrix protein that regulates the initiation and growth of hydroxyapatite crystals during mineralization of enamel and also directs the formation of cementum during embryonic root development. Recently, the capacity of the recombinant amelogenin protein (rM180) to act as an apexification therapy, to facilitate incomplete root apex formation in a dog model. Amelogenin-treated canals showed calcified tissue formation at the apical foramen that was functionally attached to bone by an oriented periodontal ligament in 89.2% of the specimens. Additionally, this treatment also induced pulp regeneration in 85% of the treated canals. Canals that showed no pulp regeneration still showed thickened root walls covered by an odontoblastic cell layer in addition to the closed apex, suggest that RAP can be used as novel apexification material, resulting in a thickening and strengthening of the canal walls, and achieving apical closure.[25]

Photobiomodulation (PBM) therapy

Photobiomodulation (PBM) therapy is a form of light therapy that utilizes non-ionizing light sources, including lasers, and promotes biostimulatory effects on different cell types, both in vitro and in vivo. Thus, PBM stimulates cell growth, increases cell metabolism, improves cell regeneration, promotes tissue response, and accelerates dentin regeneration after pulp exposure. In animal study by Zaccara et al, showed PBM therapy improved tissue response to apexification with MTA. Thus, PBM might be recommended as an adjuvant therapy to accelerate apical healing and the root development process.[42]

CONCLUSION

Immature teeth with necrotic pulp have a complicated treatment plan. Apexification aims at induction of an apical closure and continued development of root. Calcium Hydroxide is the gold standard material used for apexification. MTA has been proven to be successful. MTA is effective in treating immature permanent teeth with necrotic pulps with the advantage of reduced treatment time and more predictable barrier formation. Biodentine further gives the advantage of lesser setting time and hence facilitates single visit apexification. The shortcoming is similar to calcium hydroxide that the placement of an apical plug does not account for continued root development along the entire root length. Biodentine may be an efficient alternative to the conventional apexification materials. However techniques for one-visit apexification provide an alternative treatment option in these cases. Prospective clinical trials comparing these alternative techniques are required.

REFERENCES

(1) Lauridsen E, Hermann NV, Gerds TA, Kreiborg S, Andreasen JO. Pattern of traumatic dental injuries in the permanent dentition among children, adolescents, and adults. Dent Traumatol. 2012;28:358–63.
(2) Gawthaman M, Vinodh S, Mathian VM, Vijayaraghavan R, Karunakaran R. Apexification with calcium hydroxide and mineral trioxide aggregate: Report of two cases. J Pharm Bioallied Sci. 2013 Jul;5(Suppl 2):S131–4.
(3) 3Plascencia H, Díaz M, Gascón G, Garduño S, Guerrero-Bobadilla C, Márquez-De Alba S, et al. Management of permanent teeth with necrotic pulps and open apices according to the stage of root development. J Clin Exp Dent. 2017 Nov 1;9(11):e1329–39.
(4) Chala S, Abouqal R, Rida S. Apexification of immature teeth with calcium hydroxide or mineral trioxide aggregate: systematic review and meta-analysis. 2011;112(4):7.
(5) Ripamonti U, Reddi AH. Tissue engineering, morphogenesis, and regeneration of the periodontal tissues by bone morphogenetic proteins. Crit Rev Oral Biol Med 1997; 8:154 – 63.
(6) Paulindraraj S, Venkatesan R, Suprakasam S, Christopher A. Apexification-Then and Now: A Review. 2015;1(6):4.
(7) Ave NS. Glossary of Endodontic Terms. :48.
(8) Rotstein I, Ingle JI. Ingle's endodontics 7 [Internet]. 2019 [cited 2021 Jan 20]. Available from: http:// search. ebscohost. com/ login. aspx? direct= true& scope= site& db= nlebk&db=nlabk&AN=2175853
(9) Cvek M. Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-percha. A retrospective clinical study. Endod Dent Traumatol. 1992;8:45–55.
(10) Guideline on Pulp Therapy for Primary and Immature Permanent Teeth. Pediatr Dent. 2016 Oct;38(6):280–8.
(11) Rafter M. Apexification: a review. Dent Traumatol 2005; 21: 1–8.
(12) Determination of working length for teeth with wide or immature apices: a review. Int Endod J. 2012;9.
(13) Ballesio I, Marchetti E, Mummolo S, Marzo G. Radiographic appearance of apical closure in apexification: follow-up after 7-13 years. Eur J Paediatr Dent. :6.
(14) Torabinejad M, Abu-Tahun I. Management of teeth with necrotic pulps and open apices. :26.
(15) Ball JS. Apical root formation in non-vital immature permanent incisor. Report of a case. Brit Dent J 1964: 116: 166–167.
(16) Möller AJ, Fabricius L, Dahlen G, Ohman AE, Heyden G. Influence on periapical tissues of indigenous oral bacteria and necrotic pulp tissue.
(17) Das S, Das AK, Murphy RA. Experimental apexogenesis in baboons. Endod Dent Traumatol 1997: 13: 31–35.
(18) Kaiser HJ. Management of wide open apex canals with calcium hydroxide. Presented at the 21st Annual Meeting of the American Association of Endodontists, Washington DC April 17 1964.
(19) Barthel CR, Levin LG, Reisner HM, Trope M. TNF-alpha release in monocytes after exposure to calcium hydroxide treated Escherichia coli LPS. Int Endod J. 1997 May; 30(3): 155–9.
(20) Jiang J, Zuo J, Chen S-H, Holliday LS. Calcium hydroxide reduces lipopolysaccharide-stimulated osteoclast formation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2003 Mar;95(3):348–54.
(21) Finucane D, Kinirons MJ. Non-vital immature permanent incisors: factors that may influence treatment outcome. Endod Dent Traumatol 1999;15:273–7.
(22) Cvek M. Treatment of non-vital permanent incisors with calcium hydroxide. I. Follow-up of periapical repair and apical closure of immature roots. Odonotol Revy 1972; 23:27– 44.
(23) Abbott PV. "Apexification with calcium hydroxide.when should the dressing be changed? The case for regular dressing changes". Australian Endodontic Journal 24.1 (1998): 27-32.
(24) Mohammadi Z, Dummer PMH. Properties and applications of calcium hydroxide in endodontics and dental traumatology. International Endodontic Journal 2011;44: 697–730.
(25) Mounir MMF, Farsi JMA, Alhazzazi TY, Matar MA, El-Housseiny AA. Characterization of the apical bridge barrier formed following amelogenin apexification. BMC Oral Health. 2018 Dec;18(1):201.
(26) Coviello J, Brilliant JD. A preliminary clnical study on the use of Tricalcium Phosphate as an apical barrier. Journal of Endodontics, January 1979, volume 5, issue 1, pages6-13.
(27) Gutmann JL. Apical termination of root canal procedures—ambiguity or disambiguation? Evid-Based Endod. 2016 Jul 22;1(1):4.
(28) Saunders WP, Whitters CJ, Strang R, Moseley H, Payne AP, McGADEY J. The effect of an Nd–YAG pulsed laser on the cleaning of the root canal and the formation of a fused apical plug. Int Endod J. 1995;28(4):213–20.
(29) Lee SJ, Monset M, Torabinejad M: Sealing ability of a mineral trioxide aggregate for repair of lateral root perforations. Journal of Endodontics. November 1993, volume 19, issue II , pages 541-544.
(30) Ali SA, Zaman MMU, Mohammad N, Pavel SR, Islam KM, Hadiuzzaman M, et al. Recent Advancement in the Treatment of Open Apex: Materials and Technique. City Dent Coll J. 2012 Oct 21;9(2):25–30.
(31) Guerrero F, Mendoza A, Ribas D, Aspiazu K. Apexification: A systematic review. :4.
(32) Damle S, Bhattal H, Loomba A. Apexification of Anterior Teeth: A Comparative Evaluation of Mineral Trioxide Aggregate and Calcium Hydroxide Paste. J Clin Pediatr Dent. 2012 Apr 1;36:263–8.
(33) Goyal A, Nikhil V, Jha P. Absorbable Suture as an Apical Matrix in Single Visit Apexification with Mineral Trioxide Aggregate. Case Rep Dent. 2016 Dec 12;2016:e4505093.
(34) Laurent P, Camps J, About I. Biodentine(TM) induces TGF-β1 release from human pulp cells and early dental pulp mineralization. Int Endod J. 2012 May;45(5):439–48.
(35) De Rossi A, Silva LA, Gatón-Hernández P, et al. Comparison of pulpal responses to pulpotomy and pulp capping with biodentine and mineral trioxide aggregate in dogs. J Endod 2014;40(9):1362-1369.
(36) Deviprasad CS,Praveenag, KueiokoseMC, Rajeev A,Hari AA singlr visit apexification using calcium phosphate cement Cons Dent Endod J 2016; 1(2):46-49.
(37) Chhabra N, Singbal KP, Kamat S. Successful apexification with resolution of the periapical lesion using mineral trioxide aggregate and demineralized freeze-dried bone allograft. J Conserv Dent JCD. 2010;13(2):106–9.
(38) Joshi S, Palekar A, Pendyala G, Mopagar V, Padmawar N, Shah P. Clinical success of platelet-rich fibrin and mineral trioxide aggregate (MTA) or MTA-like agents in healing of periapical lesion in nonsurgically treated pulpless immature permanent teeth: A systematic review. J Int Soc Prev Community Dent. 2020;10(4):379.
(39) Tuloglu N, Bayrak S. Comparative evaluation of mineral trioxide aggregate and bioaggregate as apical barrier material in traumatized nonvital, immature teeth: A clinical pilot study. Niger J Clin Pract. 2016 Jan 1;19(1):52.
(40) Torabinejad M, Parirokh M. Mineral trioxide aggregate: A comprehensive literature review—part II: Leakage and biocompatibility investigations. J Endod 2010;36:190-202.
(41) Razavian H, Haerian A, Mosleh H. Novel Apexification Method In a Non-Vital Tooth With an Open Apex: A Case Report. J Dent Tehran Iran. 2014 May;11(3):371–8.
(42) Zaccara IM, Jardine AP, Mestieri LB, Quintana RM, Jesus L, Moreira MS, et al. Influence of photobiomodulation therapy on root development of rat molars with open apex and pulp necrosis. Braz Oral Res