

Management of Non-Vital Open Apex in A Lateral Incisor Using Calcium Hydroxide and Reverse GP Cone Cold Lateral Compaction in A General Practice Setting

Haider Al-Saffar^{1*} and Stefan V.Stefanescu²

Abstract

Although dental trauma is poorly managed by general dental practices, it is important to follow appropriate steps to achieve optimal results. This case report outlines the management of non-vital immature teeth with calcium hydroxide and reverse Gutta Percha (GP) cone cold lateral compaction to achieving endodontic success. Even though it is a disputed technique, if proper conditions are provided, the root development continues to preserve a functionally fit and sound tooth on the arch of a young adolescence, avoiding extensive surgical and prosthetic procedures to replace a potentially compromised tooth. This case report highlights the beneficial effects of both calcium hydroxide and Chlorhexidine-dygluconate (CHX), which are far to be obsolete in the field of apexification or even regenerative dentistry as a whole. The 11 years old male presents post-traumatic necrosis in the upper left lateral incisor (tooth 2.2) which is dressed with calcium hydroxide, achieving the disinfection of the root canal, remission of the apical periodontitis and complete root formation 1 year later. The importance of the use of biocompatible materials as calcium hydroxide and CHX are emphasized in this case in which, although, no modern regenerative procedures and materials were used, the results are more than satisfactory. This report will look into the management of a non-vital immature lateral incisor with a reverse GP cone lateral compaction to achieving a successful apical and canal seal radiographically.

Keywords: Dental trauma; Endodontic; Root canal obturation; Apexification.

Introduction

About 90% of all dental traumas occur before the age of 20 [1]. This can have detrimental effects on the quality of life, regarding aesthetics, cost and time to

treat [2,3]. Young patients generally present with traumas to immature teeth [4]. Such teeth are presented with an open apex, and with any pulpal injury it can terminate root

¹Foxland Dental Surgery, 42 Foxland Road, Gatley, Cheadle, SK8 4QB, United Kingdom

²Dentist, Europa House, Europa trading estate, Stoneclough Road, Manchester, M26 1GG, United Kingdom

* **Corresponding Author:** Haider Al-Saffar, Foxland Dental Surgery, 42 Foxland Road, SK8 4QB, Stockport, United Kingdom

Accepted Date: 01-07-2021

Published Date: 03-03-2021

Copyright © 2021 by Al-Saffar H, et al. All rights reserved. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

formation. Therefore, immature teeth proved to be prone to fracture and having a poor prognosis [5-7]. Unfortunately, statistics have shown that 59% of dental trauma treatments in the UK are deemed inadequate [8]. That was put down to time constraints within a busy dental practice, practitioners' confidence and experience level, and the general census that a specialist environment for treatment was required [9].

In the retrospective clinical study by Cvek [6], the frequency of cervical root fractures was markedly higher in endodontically treated immature teeth than in mature teeth. It ranged in incidence from 28%–77%, according to the stage of root development. Thus, it is of utmost importance to correctly diagnose and treat the injury at onset for a predictable prognosis of the affected dentition [10]. In such scenarios, the accepted treatment protocol is usually the induction of root-end closure (apexification) before completing root canal obturation. Apexification is a procedure to promote the formation of an apical barrier, to close the open apex of an immature tooth with a non-vital pulp such that the filling materials can be contained within the root canal space [11]. Without the barrier, there is nothing against which the traditional Gutta Percha (GP) filling material can be condensed. Hargreaves et al. [12] used the term 'maturogenesis' to define the completion of root formation, whereas 'apexogenesis' was referred to as apical closure. New materials have emerged in the market for such purposes. But the most common material used which predictably has high success rates is calcium hydroxide, in the range of 79-96% [6]. Calcium hydroxide functions as a

potent disinfectant, early evidence has suggested osteoinductive properties [13]. Although this can take from 5.1-21 months to form [6,14-17]. Refreshing the calcium hydroxide paste usually takes place every 3 months [11]. Many factors play into achieving adequate apexification; such as patient (age) and dental factors (presence of symptoms or periradicular area, length of time since the tooth turned necrotic, tooth's stage of development), many of which orientates around patient's compliance and the frequency of calcium hydroxide dressing addition [18,19]. There is no universal protocol described in the literature, but most depend on the same principles: chemical disinfection of the canal without instrumentation and a tight bacterial seal of the access opening to prevent the ingress of bacteria. It has been shown that approximately 30% of immature teeth can fracture during or after treatment [20]. Thus, an ideal treatment approach for immature teeth with necrotic pulps and apical periodontitis would be to induce an endogenous mineralized structure within the canal space with the aid of surrounding tissues and cells to strengthen these teeth.

Predictors of a clinically successful apexification procedure include the absence of signs and symptoms of inflammation, radiographic evidence of resolution of periapical lesions, increased root length and canal wall thickness as a sign of continued root development [21].

Informed consent must be signed by the patients' parent(s)/ guardian(s), who must be informed that this procedure has no standardized guidelines, follow-up appointments are mandatory. The patient and parent/guardian also have to be

informed about consequences and potential risks, adverse effects, alternatives such as revascularization or extraction, advantages and prognosis. Risks that the treatment might fail to meet expected goals, for example, reduction or resolution of the apical lesion when present, continued root development with the reduction in the size of the apical foramen and deposition of additional hard tissue on the root canal walls need to be presented to the patient.

Case presentation

An 11-year-old male with no relevant medical history attended the dental practice after attaining an injury 3 days before his appointment. He had fallen on his upper anterior and was mainly complaining from tooth 2.2. The trauma resulted in a concussion. General examination and radiographs were taken followed by a trauma chart for the upper anterior; 2.2 presented as non-vital. Soft diet and monitoring were indicated as the finding could be transient to the trauma. The tooth was re-assessed a week later which shown to be vital and restored vascularisation. A month later the patient attained another concussion trauma to the same tooth, 2.2. A normal weekly review protocol was followed, but on the re-assessment appointment, the tooth had mild pain on percussion, buccal sinus, and radiographic finding of an immature apex (Figure 1 A-B).

It was explained to the patient and mother that since the tooth has become symptomatic, a root canal filling procedure has to commence by which an extirpation is necessary to achieve microbiological

control, periodical healing, apical closure and prevent root resorption.

The important steps that were undertaken are the removal of necrotic tissue and the subsequent root canal disinfection. Under rubber dam isolation (ColteneWhaledent, Alstatten, Switzerland) tooth's pulp chamber was opened using a round diamond bur (Komet Dental, Brasseler GmbH, Lemgo, Germany) at high speed under constant water cooling. Following cleaning and extension of the access cavity, the root canal was scouted with a size 10 K-file (VDW GmbH, Munchen, Germany).

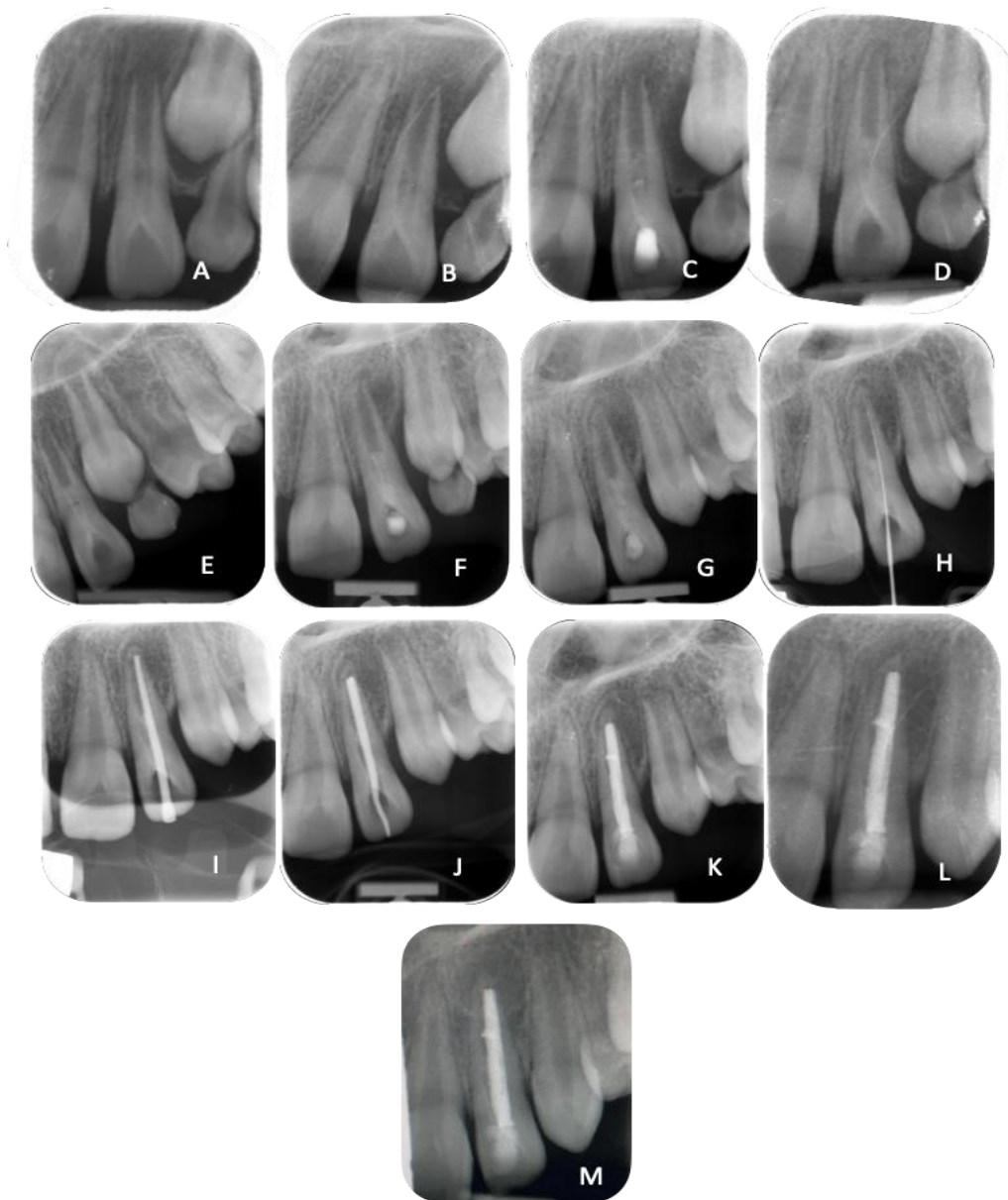
The mechanical treatment was completed with copious 2% CHX (Henry Schein, Melville, NY, USA) irrigation. CHX is recommended because of its antimicrobial activity and its substantivity; and the ability to extend antimicrobial action by interacting with the dentin [23]. In these cases mechanical cleaning might further weaken the already thin dentinal root walls [6], therefore a gentle brushing movement with Hyflex EDM OneFile size 25/~ (ColteneWhaledent, Alstatten, Switzerland) was carried out on the root canal walls, to disrupt the biofilm as suggested by Lin et al.[22]; the antimicrobial activity being assured by the irrigant.

Sodium hypochlorite (NaOCl) irrigation was avoided in this case because of the given size of the immature apical opening, as any NaOCl extrusion would likely to cause complications such as pain, swelling, tissue damage, and potential paraesthesia [24]. Also, the least effective concentration 5.25% proved to have a toxic effect on the periapical tissues [25].

After drying the canal with paper points size 25/0.06 (Sendoline AB, Taby, Sweden) Non-setting Calcium hydroxide paste (Calasept, Directa, UpplandsVasby, Sweden) was placed to the coronal portion of the root canal with a syringe-type carrier and then tamped down gently with the end of a paper point size 25/0.06 (Sendoline AB, Taby, Sweden) to the junction of the

middle and apical thirds of the root length. A double coronal restoration was placed, consisting in a zinc-oxide based cement (Cavit, 3M ESPE, St Paul, MN, USA), covered with a light-curing glass-ionomer cement (Riva, SDI, Bayswater, Victoria, Australia) that provides better sealing and resistance to wear as recommended by Abott [26].

Figure 1: A) the First presentation in March 2015. B) Second fall early June 2015. C) Review late July 2015. D) Re-dressing September 2015. E) Re-dressing November 2015. F) Re-dressing January 2016. G) Evidence of calcific apical barrier formation June 2016. H) WL determination. I) Tapered GP to WL. J) Reverse placement of tapered GP to working length. K) Post-Obturation radiograph with coronal seal. L) 6-month recall check-up. M) 12 months review.



A series of review appointments were scheduled once every 3 months to replace the calcium hydroxide apical dressing, take a periapical radiograph (Figure 1 C-F), and re-assess the formation of the calcific apical barrier.

15 months later, during the review, a tactile sensation of resistance was evident with paper point and radiographic evidence of the formation of the calcific apical barrier was seen (Figure 1 G).

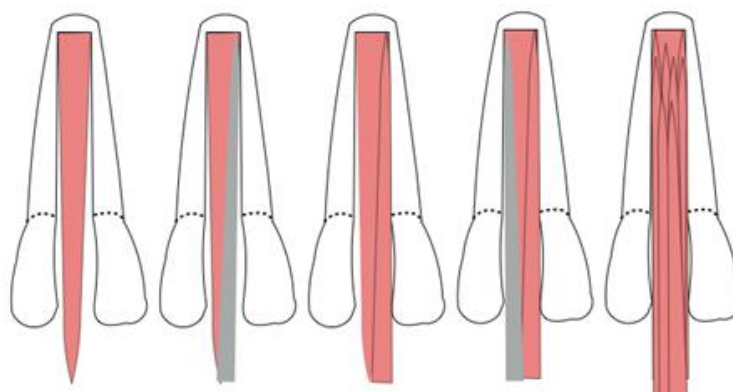
Figure 2: A) Pre-op photograph. B) Dressing. C) Isolation with floss ligature. D) Final composite.



A root canal obturation at this stage is indicated to seal the canal system definitively. A rubber dam isolation (ColteneWhaledent, Alstatten, Switzerland) (Figure 2 C) used with floss ligatures to optimally isolate tooth 2.2 and protect the patient's airways, followed by a diagnostic radiograph with ISO size 10 k-file (VDW, Munchen, Germany) in the canal to determine the working length (fig. 1 H). Root canal debridement was

completed meticulously using Hyflex EDM file (ColteneWhaledent, Alstatten, Switzerland) size 25/∼, paying more attention to the coronal and mid-third, without much compromising and weakening the dentine walls. Careful copious irrigation with NaOCl was used this time to disinfect the canal system with the aid of Ethylenediaminetetraacetic acid (EDTA) 17% solution (Calasept EDTA, Directa, UpplandsVasby, Sweden) to remove the smear layer.

Figure 3: Cold lateral compaction, following the reverse placement of the master tapered GP point. It is compacted against the canal wall with a spreader. An additional GP point is then normally placed into the void left by the spreader. The process is repeated until the canal is filled.



The canal's radiographic appearance appeared to be an irregular, wide, cylindrical shape and a flat apical region, which is very challenging to obturate with normal GP points (Figure 1 I). Therefore, a modified technique was used, combining ordinary cold lateral compaction and using the existing taper on the GP point to reversely place it in the canal then compacted with accessory GP points as

normal (Figure 3). This was further sealed using Guttaflow2 (ColteneWhaledent, Alstatten, Switzerland) to achieve a good 3D dimensional obturation. The final result was satisfactory, achieving a radiographical correct working length obturation with adequate condensation and coronal seal (Figure 1 J-K).

A 1 week follow up appointment was completed without any post-operative

complications. The patient was reviewed after 6 months and radiographic assessment was carried out (Figure 1 L), being recalled for yearly radiographic assessment to comply with endodontic treatment guidelines [27]. The patient attended the one-year review on which occasion a new periapical radiograph was taken confirming the healing and the stability of the obtained result (Figure 1 M).

Discussion

Three aspects are worth to be discussed related to this case: the chosen apexification procedure, the irrigant, and the obturation technique.

1. Calcium hydroxide is a highly alkaline compound and an antibacterial substance. It has a PH of 12.4-12.5 which is capable to break down living and necrotic tissues. Studies related to its dentine inductive and antimicrobial properties started in the '70s [28-34]. A further study about its role as a physical and chemical barrier; which prevents the proliferation of microorganisms in the root canal and prevents their ingress from the surrounding tissues was conducted [33]. It has been also reported recently about a novel and very fundamental property of Calcium hydroxide, which proved to increase the growth factor release from dentine²¹. For these reasons, calcium hydroxide has been long used as an "apexification agent" [35].

As for disadvantages, some hypothesized that it can induce uncontrolled calcification of the

canal space preventing the ingress of cells with an odontogenic potential, or being so alkaline that it is already toxic for the living cells [36]. The multiple visits during a long period (6-24 months) have been considered another aspect that might preclude its use [37]. Recent studies concluded that it undermines the mechanical strength of dentin having the property to break up the hydroxyapatite compounds in case of prolonged exposure to calcium hydroxide [6,33].

It was suggested that MTA might represent a better choice in achieving the apexification in 1 or 2 visits [38]. However, Andreasen et al. [16] proved that the use of calcium hydroxide for 14 days had no impact on dentine's fracture strength, signs of weakening being noticed only after 2 months of exposure. Recent procedures of apexification include the use of Mineral Trioxide Aggregate (MTA), which is a very biocompatible material that is going to be placed in contact with the apical tissues, thus kind of preventing the natural closure of the foramen as well as the increase in thickness and length of the root, making the tooth prone to fracture [15]. The advantage of using MTA is the reduced number of visits; the root canal is filled during the second visit, with gutta-percha. However, a recent systematic review and meta-analysis which compared MTA efficacy and calcium hydroxide in endodontic management of immature teeth, found no

significant difference between materials regarding clinical and radiographic success [39].

2. It has been proved that 3% NaOCl reduced the vitality of the living pulp cells to 60% and the 5.25% solution to less than 20%, therefore in the present study chlorhexidine-digluconate 2.4% was used for irrigation to disinfect the canal during the first visit when apex was open, NaOCl solution of 2.5% and EDTA 17% being used only during the last visit when apexification is satisfactorily achieved and the root filling was placed [40]. Although it was proved that CHX is cytotoxic thus it is not the best choice as an irritant, it has substantivity and in this case proved to be a good choice, allowing cells to keep depositing cement and dentine on contrary to previous findings when only apical closure was reported after a quite considerable time. It is well known the EDTA's effect in releasing growth factor from dentine during regenerative endodontic procedures, still, it hasn't been used in this case, and yet, there are evident signs that growth factor was released, proved by the continuous root development, most probably due to calcium hydroxide's activity which led to growth factor release [41].
3. Many obturation techniques can be used to achieve an adequate seal, but none will prevent 100% leakage in the long term [42,43]. These techniques have their advantages and disadvantages. Cold lateral compaction being the most common taught procedure and the

readily available of GP points in general dental practices, as opposed to other techniques and materials such as warm vertical condensation, thermo-mechanical technique, carrier-based systems, plastic techniques and apical barriers [44]. It is also arguable that the lateral compaction is advisable compared to the vertical one as regards to the lateral forces exerted on the thin root walls. In this case the clinicians' skills and the experience were of great importance. The present inverted cone technique is the author's invention, as an adaptation to the situation when we have to obturate a large root canal and there is no available vertical compaction device in the surgery.

As some statistical and outcome data on apexification, there is the study of Cvek [15] who reported on the outcome of 55 non-vital permanent incisors treated by apexification and noted that in 50 incisors there was healing and apical closure but no continued root formation 14–21 months post-treatment, whilst Alobaid et al. [44] found a higher success rate in apexification compared to revascularisation, 79% to 100% respectively, more adverse events in revascularisations than in apexification, 42% to 11% respectively, a statistically significant difference. He also found that of 31 cases treated, 19 with revascularisation, and 12 with apexification procedures, the biggest radiographic changes were recorded in a tooth in the apexification group. But on average, teeth within the revascularisation group showed a greater absolute change in width, but not in length, which is quite surprising. The

survival rate of regenerative endodontic therapy (100%) and MTA apical barrier technique (95%) were found to be greater than that of calcium hydroxide apexification (77%) in Jeeruphan's study [7]. Other authors reported that 96% is the frequency of periapical healing and apical barrier formation of non-vital immature teeth after calcium hydroxide treatment with a 5-year survival rate of 86%, which is indeed a very predictable outcome. However, if obturation was completed before achieving an apical barrier, the success rate would be less than 50% [18,46-49].

Although it is difficult or impossible to clinically determine the presence of surviving pulpal cells or to assess the ability of these cells to survive and differentiate, a factor that appears to be an indicator of that potential is the duration of the infection. It was hypothesized that the longer an infection exists, the lower the chances that pulp and stem cells required for regeneration will survive. Conversely, the longer the infection exists, the greater the probability that bacteria populating the dentinal tubules can be eradicated [36].

Under all the aspects this case is an example of managing immature teeth with apical periodontitis, raising some questions, and opening our understanding towards new approaches. Although no regeneration procedure or its proprietary material has been used, the achieved result is similar to those achieved using revascularisation. All the reports indicate a substantially greater change in the size of the roots, in regenerative procedures compared with revascularisation and even so, we have here a completely formed root. In the present

case, the length of the root changed spectacularly, a very unusual feature of apexification procedures. It is assumable that there were still plenty of living pulp and stem cells to continue the root development once conditions were created, i.e. the elimination of the bacterial factor. How is this possible? Probably, avoiding the use of NaOCl and EDTA during the first and review visits helped to lower the cytotoxic environment. Replacing it with CHX the antimicrobial effect was still reached. This cell activity seems to be independent of the calcium hydroxide's toxic effect which is supposed to have an inhibiting effect on living cells. In this case, calcium hydroxide was replenished every 3 months as described in the literature and still it seems not having such a devastating effect on the living cells (fibroblasts, odontoblasts, cementoblasts, stem cells). Calcium hydroxide's growth factor releasing property replaced the need for EDTA, which has the same property. No antibiotic paste was used either. If we look at the time necessary to achieve the wanted results, in this case, it is within the above-described time interval. The described procedure of root filling is an own developed procedure and although there are no clear guidelines on it, the outcome was more than satisfactory.

Dental trauma requires a systematic approach, to appropriately intervene when teeth become non-vital or resorption is identified. The guidance of the International Association of Dental Traumatology (IADT) is a very comprehensive and useful resource [50].

Conclusions

Even if such a procedure might not be the option of choice for the practitioners treating necrotic immature permanent teeth, its advantages cannot be overlooked:

1. The lack of dentine bridge formation that use to seal the pulpal space coronally;
2. MTA which also seals the pulp chamber in revascularization and impedes any possible retreatment, being no longer needed;
3. The ingrowths of a bony or dentine structure in the pulp space with the subsequent canal obliteration are prevented;
4. Less adverse events;
5. Although it needs more appointments, the procedure needs a similar time interval to achieve the expected changes in the root anatomy, having a comparable success rate to revascularization procedures,
6. Required fewer skills as being a less technique sensitive procedure.
7. The procedure allows access to the root canal and safe re-treatment in case of possible future complications or failures.

The conclusions are that the material used is as important as is the timing of the procedure and, highly likely, the age of the patient. In this case, the quick reaction of the clinician, who recognized the first signs of necrosis and subsequent apical periodontitis, was crucial in achieving this

References

1. Eilert-Petersson E, Andersson L, Sörensen S. Traumatic oral vs non-oral injuries. An epidemiological study during one year in a Swedish county. *Swed Dent J*. 1997;21(1-2):55-86.
2. Lindqvist KS, Brodin H. One-year economic consequences of accidents in a Swedish municipality. *Accid Anal Prev*. 1996;28(2):209-19.

outcome. There is a need for further studies to understand the processes and physiology of the apical papilla in such cases which might need rethinking the protocols to be used, as well as restoring calcium hydroxide, and CHX as leading materials in regenerative endodontics.

Clinical Relevance

The present case report opens a gate to understand the importance of monitoring such cases of trauma and promptly apply the necessary treatment. The patient's age and determination are of great importance to prognosis as well. Recall appointments have to be strictly attended. Calcium hydroxide is an extremely versatile material with properties still to be explored. Protocols need to be adapted to the patient's terrain and history of trauma.

Author's contributions

HA conducted clinical work. HA and SS drafted the manuscript; SS revised it critically. Both authors reviewed the case report and approved its final version.

Conflicts of interest

There are no conflicts of interest.

Acknowledgment

Authors declare that there are no commercial or financial conflicts of interest and that the research was funded out of personal income sources.

3. Glendor U, Halling A, Bodin L, Andersson L, Nygren Å, Karlsson G, et al. Direct and indirect time spent on care of dental trauma: a 2-year prospective study of children and adolescents. *Dent Traumatol.* 2000;16(1):16-23.
4. Navabazam A, Farahani SS. Prevalence of traumatic injuries to maxillary permanent teeth in 9-to 14-year-old school children in Yazd, Iran. *Dent Traumatol.* 2010;26(2):154-7.
5. Trope M. Treatment of the immature tooth with a non-vital pulp and apical periodontitis. *Dent clinics.* 2010;54(2):313-24.
6. Cvek M. Prognosis of luxated non-vital maxillary incisors treated with calcium hydroxide and filled with gutta-percha. A retrospective clinical study. *Dent Traumatol.* 1992;8(2):45-55.
7. Jeeruphan T, Jantararat J, Yanpiset K, Suwannapan L, Khewsawai P, Hargreaves KM. 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):1330-6.
8. Hamilton FA, Hill FJ, Holloway PJ. An investigation of dento-alveolar trauma and its treatment in an adolescent population. Part 1: The prevalence and incidence of injuries and the extent and adequacy of treatment received. *Br Dent J.* 1997;182(3):91-5.
9. Hamilton FA, Hill FJ, Holloway PJ. An investigation of dento-alveolar trauma and its treatment in an adolescent population. Part 2: Dentists' knowledge of management methods and their perceptions of barriers to providing care. *Br Dent J.* 1997;182(4):129-33.
10. Andreasen JO, Andreasen FM, Skeie A, Hjørting-Hansen E, Schwartz O. Effect of treatment delay upon pulp and periodontal healing of traumatic dental injuries—a review article. *Dent Traumatol.* 2002;18(3):116-28.
11. Rafter M. Apexification: a review. *Dent Traumatol.* 2005;21(1):1-8.
12. Hargreaves KM, Giesler T, Henry M, Wang Y. Regeneration potential of the young permanent tooth: what does the future hold? *Pediatr Dent.* 2008;30(3):253-60.
13. Mitchell DF, Shankwalker GB. Osteogenic potential of calcium hydroxide and other materials in soft tissue and bone wounds. *J Dent Res.* 1958;37(6):1157-63.
14. Dominguez Reyes A, Munoz Munoz L, Aznar Martin T. Study of calcium hydroxide apexification in 26 young permanent incisors. *Dent Traumatol.* 2005;21(3):141-5.
15. Cvek M. Treatment of non-vital permanent incisors with calcium hydroxide. I. Follow-up of periapical repair and apical closure of immature roots. *Odontol Revy.* 1972;23:27-44.
16. Andreasen JO, Farik B, Munksgaard EC. Long-term calcium hydroxide as a root canal dressing may increase risk of root fracture. *Dent Traumatol.* 2002;18(3):134-7.
17. Sheehy EC, Roberts GJ. Use of calcium hydroxide for apical barrier formation and healing in non-vital immature permanent teeth: a review. *Br Dent J.* 1997;183(7):241-6.
18. Mackie IC, Bentley EM, Worthington HV. The closure of open apices in non-vital immature incisor teeth. *Br Dent J.* 1988;165(5):169-73.
19. Finucane D, Kinirons MJ. Non-vital immature permanent incisors: factors that may influence treatment outcome. *Dent Traumatol.* 1999;15(6):273-7.
20. Kerekes K, Heide S, Jacobsen I. Follow-up examination of endodontic treatment in traumatized juvenile incisors. *J Endod.* 1980;6(9):744-8.
21. Galler KM, Buchalla W, Hiller KA, Federlin M, Eidt A, Schiefersteiner M, et al. Influence of root canal disinfectants on growth factor release from dentin. *J Endod.* 2015;41(3):363-8.
22. Lin LM, Shimizu E, Gibbs JL, Loghin S, Ricucci D. Histologic and histobacteriologic observations of failed revascularization/revitalization therapy: a case report. *J Endod.* 2014;40(2):291-5.
23. Haapasalo M, Shen Y, Qian W, Gao Y. Irrigation in endodontics. *Dent Clinics.* 2010;54(2):291-312.
24. Doherty MA, Thomas MB, Dummer PM. Sodium hypochlorite accident—a complication of poor access cavity design. *Dent Update.* 2009;36(1):7-12.
25. Stojicic S, Zivkovic S, Qian W, Zhang H, Haapasalo M. Tissue dissolution by sodium hypochlorite: effect of concentration, temperature, agitation, and surfactant. *J Endod.* 2010;36(9):1558-62.
26. Abbott PV. Medicaments: aids to success in endodontics. Part 2. Clinical recommendations. *Aust Dent J.* 1990;35(6):491-6.
27. European Society of Endodontology. Quality guidelines for endodontic treatment: consensus report of the European Society of Endodontology. *International Endodontic Journal.* 2006;39(12):921-30.

28. Shubich I, Miklos FL, Rapp R, Draus FJ. Release of calcium ions from pulp-capping materials. *Journal of Endodontics*. 1978;4(8):242-4.
29. Holland R, de Mello W, Nery MJ, Bernabe PF, de Souza V. Reaction of human periapical tissue to pulp extirpation and immediate root canal filling with calcium hydroxide. *J Endod*. 1977;3(2):63-7.
30. Cvek M. A clinical report on partial pulpotomy and capping with calcium hydroxide in permanent incisors with complicated crown fracture. *J Endod*. 1978;4(8):232-7.
31. Dow PR. The versatility of calcium hydroxide therapy: a case report. *J Endod*. 1979;5(9):274-6.
32. Piekoff MD, Trott JR. Apexification: report of case. *J Endod*. 1976 Jun 1;2(6):182-5.
33. Mohammadi Z, Dummer PM. Properties and applications of calcium hydroxide in endodontics and dental traumatology. *Int Endod J*. 2011;44(8):697-730.
34. Siqueira Jr JF, Lopes HP. Mechanisms of antimicrobial activity of calcium hydroxide: a critical review. *Int Endod J*. 1999;32(5):361-9.
35. Chueh LH, Huang GT. Immature teeth with periradicular periodontitis or abscess undergoing apexogenesis: a paradigm shift. *J Endod*. 2006;32(12):1205-13.
36. Huang GT. A paradigm shift in endodontic management of immature teeth: conservation of stem cells for regeneration. *J Dent*. 2008;36(6):379-86.
37. Kleier DJ, Barr ES. A study of endodontically apexified teeth. *Dent Traumatol*. 1991;7(3):112-7.
38. Torabinejad M, Chivian N. Clinical applications of mineral trioxide aggregate. *J Endod*. 1999;25(3):197-205.
39. Chala S, Abouqal R, Rida S. Apexification of immature teeth with calcium hydroxide or mineral trioxide aggregate: systematic review and meta-analysis. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011;112(4):e36-42.
40. Martin DE, De Almeida JF, Henry MA, Khaing ZZ, Schmidt CE, Teixeira FB, et al. Concentration-dependent effect of sodium hypochlorite on stem cells of apical papilla survival and differentiation. *J Endod*. 2014;40(1):51-5.
41. Galler KM. Clinical procedures for revitalization: current knowledge and considerations. *Int Endod J*. 2016;49(10):926-36.
42. Ng YL, Mann V, Rahbaran S, Lewsey J, Gulabivala K. Outcome of primary root canal treatment: systematic review of the literature—part 1. Effects of study characteristics on probability of success. *Int Endod J*. 2007;40(12):921-39.
43. Aqrabawi JA. Outcome of endodontic treatment of teeth filled using lateral condensation versus vertical compaction (Schilder's technique). *J Contemp Dent Pract*. 2006;7(1):17-24.
44. Darcey J, Roudsari RV, Jawad S, Taylor C, Hunter M. Modern endodontic principles part 5: obturation. *Dent Update*. 2016;43(2):114-29.
45. Alobaid AS, Cortes LM, Lo J, Nguyen TT, Albert J, Abu-Melha AS, et al. Radiographic and clinical outcomes of the treatment of immature permanent teeth by revascularization or apexification: a pilot retrospective cohort study. *J Endod*. 2014;40(8):1063-70.
46. Mackie IC, Worthington HV, Hill FJ. A follow-up study of incisor teeth which had been treated by apical closure and root filling. *Br Dent J*. 1993;175(3):99-101.
47. Tronstad L. *Clinical Endodontics: A Textbook*, edn. NY: Thieme. 2007.
48. Huang GJ. Apexification: the beginning of its end. *Int Endod J*. 2009;42(10):855-66.
49. Phillips JM, Srinivasan V. The management of non-vital immature permanent incisors. *Dent Update*. 2014;41(7):596-604.
50. International Association of Dental Traumatology (IADT).