LITERATURE REVIEW

Pulp regeneration / revitalization in immature permanent teeth

Jiménez-Pascual, Sandra
Graduated in Dentistry from the Complutense University of Madrid (UCM). Student of the Master's Degree in Dental Sciences, UCM. Student of the Expert Course in Periodontal Clinic, UCM.

Gallardo-López, Nuria Esther
Medical specialist in Stomatology. Master's degree in Paediatric Dentistry. Specialist in Comprehensive Dental Care for Children with Special Needs. Tenured lecturer in Dentistry (UCM).

Mourelle-Martínez, María Rosa
Medical specialist in Stomatology. Paediatrician. Medical Specialist in Occupational Medicine. Master's degree in Paediatric Dentistry. Specialist in Comprehensive Dental Care for Children with Special Needs. Tenured lecturer in Dentistry (UCM).

Published in spanish Científica Dental Vol. 21. Nº 1. 2024
www.cientificadental.es

SUMMARY

Introduction. Treatment of affected immature teeth is a challenging procedure. Immature teeth have wide canals, thin dentin walls and open apices, in addition to being more prone to fracture and with a poor long-term prognosis. Revascularization of an immature tooth attempts to preserve the teeth as long as possible, but there are failures because it is difficult to achieve optimal disinfection of the root canal system.

Methods. An exhaustive search was carried out by consulting the electronic databases PubMed and Web of Science of the last 10 years, using keywords and eligibility criteria.

Results. The search process yielded 635 total articles. After applying filters, eliminating duplicates and selecting articles by title and abstract, only 27 were for the present study.

Conclusions. Pulp revitalization has high survival rates in the treatment of necrotic immature permanent teeth. Randomized clinical trials are needed to compare the effect of platelet-rich fibrin, platelet-rich plasma, and induced bleeding on the revitalization of a tooth with necrotic pulp. One of the main problems of pulp revitalization is coronal discoloration. Triple antibiotic paste is a very effective antimicrobial agent, but high concentrations could have a detrimental effect on stem cell survival.

KEYWORDS

Apical closure; Open apex; Immature teeth; Permanent teeth, Platelet-rich fibrin; MTA; Non-vital traumatized immature permanent; Pulp necrosis; Dental pulp regeneration.

- IME
- IBECS
- LATINDEX
- GOOGLE SCHOLAR

Post address:
María Rosa Mourelle Martínez,
Department of Clinical Dental Specialties.
Faculty of Dentistry, Complutense University of Madrid, Spain.
Plaza de Ramón y Cajal S/N,
28040, Madrid, Spain.
rmourelle@odon.ucm.es

Date received: 27 December 2023.
Date accepted for publication:
20 February 2024.

coem
Ilustre Colegio Oficial de Odontólogos y Estomatólogos de la Iª Región

INTRODUCTION

During childhood and adolescence, traumatic dental injuries are common, causing damage to the tooth and its supporting structures, including root fractures, bone loss, and tooth loss[1]. The loss of permanent teeth at an early age may result in arrested growth of the alveolar bone, thereby impeding subsequent aesthetic and functional reconstruction[2]. Given the increasing desire to preserve natural teeth, a tooth with a poor prognosis presents a new challenge for dentists[1].

The principal characteristic of young permanent teeth is incomplete root development. This results in an open apical foramen, thinner and more fragile root walls, an inadequate crown-root ratio, and an unformed root structure[3]. These particular characteristics of young permanent teeth mean that the required pulp treatments are different and should be as conservative as possible.

The management of affected immature teeth is among the most challenging procedures in endodontics. Owing to the fact that such immature teeth possess very wide canals, thin dentinal walls, and open apices, they present increased difficulty for the clinician during biomechanical preparation[1,3]. Furthermore, these are more prone to fracture and, therefore, have a poor long-term prognosis[3,4].

Traditionally, immature teeth diagnosed with necrotic pulp are treated by apexification with calcium hydroxide ($Ca(OH)_2$) or mineral trioxide aggregate (MTA)[5,6]. However, neither procedure allows for thickening of the root wall or continued root development[7]; consequently, these teeth become fragile and susceptible to fracture[5].

Regenerative endodontic procedures represent a novel therapeutic approach that promotes continued root growth in necrotic immature teeth, potentially preventing root fracture[5]. The revascularisation of a traumatised immature tooth seeks to preserve the teeth for as long as possible[2].

In pulpal revascularisation, the root canal is disinfected with antibiotics or antimicrobial agents[8]. Promotion of the blood clot is necessary following disinfection of the root canal system. In recent years, this promotion of the conventional clot (induced by over-instrumentation) has been replaced by the use of platelet-rich plasma or platelet-rich fibrin, which offer enhanced efficacy and a higher concentration of growth factors to promote dental bleeding[7].

However, a significant concern in teeth undergoing regenerative endodontic treatment is achieving optimal disinfection of the root canal system[6]. Although revascularisation is an increasingly utilised treatment, clinical failure rates in the revitalisation of immature teeth may reach up to 40%[8].

When pulp regeneration or revitalisation is performed, a significant proportion of cases fail. Therefore, it is necessary to identify the most effective techniques to undertake this treatment with minimal risk.

MATERIALS AND METHODS

Sources of information and search strategy

A comprehensive search was conducted to ensure that as many studies as possible were identified through electronic searching.

For the search strategy, the following electronic databases were consulted: 1) PubMed and 2) Web of Science, covering the past 10 years, using the following MeSH keywords: “apical closure”, “open apex”, “immature teeth”, “permanent teeth”, “platelet-rich fibrin”, “MTA”, “non-vital traumatised immature permanent”, “pulp necrosis”, “dental pulp regeneration”.

Boolean operators were used, such as: “immature” NOT “mature”, “permanent” NOT “temporal”, “Blood Clot” OR “Platelet-rich Fibrin”.

Eligibility Criteria

The selection of articles for this study was conducted by applying the following selection criteria (Table 1).

All identified articles were assessed according to the title, keywords, and abstract to exclude those not relevant to the review question.

Table 1. Inclusion and exclusion criteria.

Inclusion Criteria	Exclusion Criteria
- Publications from the last 10 years - Studies: • Conducted in young permanent teeth • In vivo • Using the revascularisation/ revitalisation	- Publications in languages other than Spanish or English - Studies with clinical follow-up of less than 3 months - Animal study

RESULTS

Selection of studies

The search process yielded a total of 635 articles. After applying the filter of "publications from the last 10 years", 135 articles were excluded, leaving 500 articles remaining. After removing duplicates in both databases (218 articles), a total of 282 publications remained.

The remaining publications were filtered for "randomised controlled trials" and "clinical trials". In PubMed, the search was reduced to 17 articles, while in Web of Science, it was reduced to 212, resulting in a total of 229 articles.

Following selection of the articles by title and abstract, 53 were chosen for full-text review. Twelve of these were excluded for being systematic reviews; three for

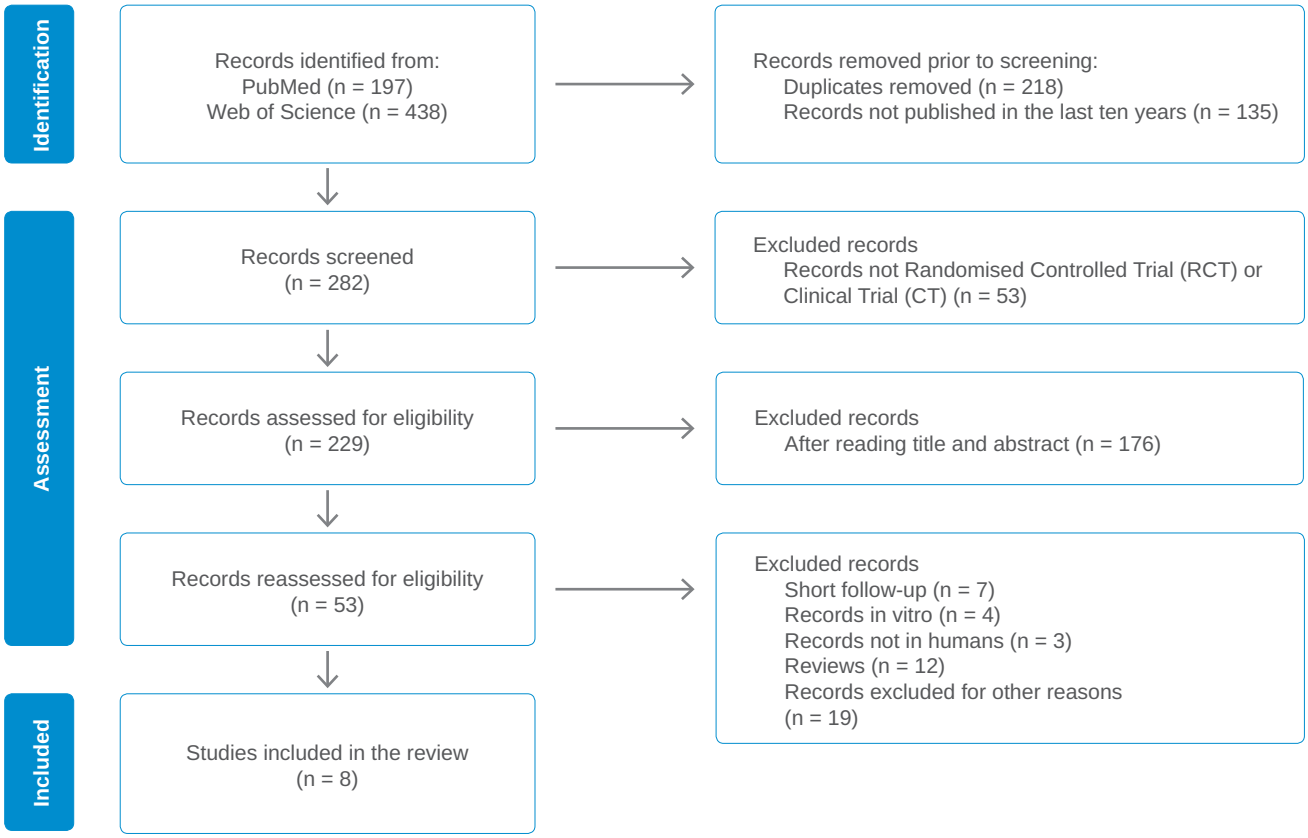

Figure. Flow diagram of the search conducted..

involving non-human samples; four of them, for being in vitro studies; seven, for having a follow-up period of less than three months; and the remainder, for other reasons. Thus, only eight were selected for full-text review, and all of these were included in the present study (Figure).

Characteristics of the studies

For this search, various types of studies were consulted, excluding, as previously mentioned, systematic reviews. Furthermore, sample size, case follow-up, and aetiology have also been considered (Table 2).

Patient characteristics

The sampling unit in these studies is the immature necrotic permanent tooth. A total of 227 immature necrotic permanent teeth are included The majority are maxillary incisors (193), although mandibular incisors (1), premolars (5), maxillary molars (3), and mandibular molars (25) have also been studied (Table 2).

Revascularisation technique

In half of the studies selected for this review, pulp revascularisation was performed by inducing bleeding (blood clot formation) (BC)[2, 8-10]. Only one study utilised platelet-rich fibrin (PRF)[11] and another employed platelet-rich plasma (PRP)[12]. The remaining two were conducted using platelet-rich fibrin in half of the sample, and in the other half, blood clot induction was performed[13,14] (Table 3).

Use of MTA

Of the eight studies selected for this review, five used MTA exclusively to create a coronal plug[2, 11-14].

Two other studies divided the sample into two groups, using MTA in one group and either Bioceramic Root Repair[8] or EndoSequence Bioceramic Putty[9] in the other. Only one study used NeoMTA Plus[10] (Table 3).

Intracanal medication

Triple antibiotic paste (TAP) was used in five studies[9,11–14]. Another study used TAP in half the sample and $Ca(OH)_2$ in the rest[10]. In one study, either $Ca(OH)_2$ or 2% chlorhexidine digluconate gel was used[8]. In the eighth study included in this review, tetracycline and triamcinolone were used as intracanal medication[2] (Table 3).

Table 2. Descriptive characteristics of the studies.

Author and year	Type of study	Sample size	Sample unit (tooth)	Cause of necrosis	Follow-up (months)
Bukhari S, 2016	Retrospective case series	28	21 anterior teeth, 5 premolars and 2 molars. 22 maxillary and 6 mandibular	Caries or trauma	7-31
Ragab RA, 2019	Randomised clinical trial	22	Incisors	Not specified	6 y 12
Mittmann CW, 2020	Retrospective study	16	Maxillary incisors	Trauma	22
Rizk HM, 2020	Randomised clinical trial	30	Maxillary incisors	Trauma	3, 6, 9 y 12
Wikström A, 2022	Prospective cohort study	75	Maxillary incisors	Trauma	≥ 24
Al-Qudah A, 2023	Prospective randomised clinical study	50	23 maxillary anterior teeth, 1 anterior mandibular tooth, 3 maxillary molars and 23 mandibular molars	Caries or trauma	3, 6, 12, 24 y 36
Kumar JK, 2023	Prospective clinical study	1	Maxillary incisor (11)	Trauma	12
Biradar N, 2023	Case series	5	Maxillary incisors	Not specified	12

Discolouration

Four studies reported the occurrence of coronal discolouration, either caused by MTA or after blood clot induction[2, 8, 11, 14]. Only one study reported the absence of coronal discolouration, coinciding with the use of NeoMTA Plus[10]. Three studies made no reference to the presence or absence of discolouration[9, 12, 13] (Table 3).

Failures / exclusion

A total of 54 treatments failed. Failures could be early or late[8]. The former (19) are characterised by an absence of bleeding on induction or failure to form a blood clot; whereas in the latter group (11 teeth), patients exhibited persistent clinical symptoms. Others failed due to severe resorption (3) or non-attendance at follow-up visits (1)[2].

Other unfavourable outcomes included root resorption (1 case), association with the sinus tract (1), sensitivity to percussion (2), and persistence or increase in the size of the apical radiolucency without symptoms (3)[10]. In some cases, failure was due to the need for additional treatment (3) or incomplete healing (4)[9] (Table 3).

DISCUSSION

Regenerative therapy has demonstrated excellent success rates[3] and has proven to be the technique offering the greatest benefit for the long-term management of non-vital permanent teeth[11].

Revascularisation is a promising approach for treating immature incisors, helping to restore sensitivity and promote apical closure[2], increase dentinal wall thickness[11] and at least preserve the alveolar bone in terms of socket preservation. Further studies are needed to determine the ideal conditions for revascularisation, such as trauma type, age, and apical foramen width[2].

The success of revascularisation is considered to depend on reducing bacterial load[18]. The main reported side effect was discolouration, seen only in damaged teeth. The most consistently observed radiographic finding was narrowing of the apical diameter[3]. Yang et al. (2022) followed up at 6, 12, 24, and 36 months, showing further radiographic evidence of healing in immature necrotic teeth[16].

Table 3. Description of clinical outcomes.

Author and year	Revascularisa tion technique	Intracanal medication	Sealing material	Discolouratio n	Failures / exclusions (teeth)
Mittmann CW, 2020	BC	Tetracycline and triamcinolone	MTA	Yes	4
Wikström A, 2022	BC	Ca(OH)2 or 2% chlorhexidine digluconate gel	MTA or Bioceramic Root Repair	Yes	30
Al-Qudah A, 2023	BC	Ca(OH)2 o TAP	NeoMTA Plus	No	7
Kumar JK, 2023	FRP	TAP	MTA	Yes	0
Biradar N, 2023	PRP	TAP	MTA	Not specified	0
Rizk HM, 2020	FRP o BC	TAP	MTA	Yes	6
Ragab RA, 2019	FRP o BC	TAP	MTA	Not specified	Not specified
Bukhari S, 2016	BC	TAP	MTA or EndoSequence Bioceramic Putty	Not specified	7

BC (blood clot);
MTA = Mineral Trioxide Aggregate
Ca(OH)2 = calcium hydroxide;
TAP = triple antibiotic paste
PRF = platelet-rich fibrin;
PRP = platelet-rich plasma

In a prospective study, Wikström et al. (2022) reported successful pulpal revitalisation, with resolution of clinical and radiographic signs and continued root development.

Continuous root development was observed in 60% of the teeth in which the procedure was performed, with failed cases being associated with the absence of bleeding (n=19) and persistent infections (n=11)[8], as well as crown fractures[19].

Use of MTA

In the study by Tawfeek et al. (2023) demonstrated that clinical and radiographic success, whether using NeoMTA or conventional MTA (WMTA), was 100%. Discolouration was detected in only one tooth with NeoMTA (9.1%) and in three teeth (27.3%) with MTA, but the difference between the groups was not statistically significant[15].

Similarly, Ajram et al. (2019) demonstrated that the regenerative endodontic technique is feasible and can be successfully performed using Ca(OH) and MM-MTA[5]. In the randomised clinical trial by Abuelniel et al. (2020), it was demonstrated that teeth treated with MTA exhibited significant discolouration from 6 to 18 months of follow-up. It was observed that 23 of the 25 teeth treated with MTA had developed discolouration at the 6-month follow-up visit[20].

The case series conducted by Hajizadeh et al. (2019), illustrated 12-month follow-ups of revascularisation in three necrotic immature teeth using MTA as a coronal barrier. The treatments were considered successful, as the teeth were functional, all unfavourable signs and symptoms were alleviated, and some degree of root development was achieved[17].

In the study conducted by Sajjad et al. (2022), 40 cases were treated with MTA and 32 were successful. A complete resolution of signs and symptoms was observed, with absence of periapical radiolucency, in most cases, elongation of root length, increased thickness of the root canal walls, and apical closure[21].

Use of platelet-rich fibrin, platelet-rich plasma, and stimulation of the blood clot

The randomised controlled trial (RCT) conducted by Rizk et al. (2020), demonstrated that the teeth in which platelet-rich fibrin was used (examined group) exhibited a statistically significant increase in radiographic root length and width, an increase in periapical bone density, and a reduction in apical diameter compared to the control group (in which bleeding was induced, resulting in the formation of a blood clot). At the end of the follow-up period, all treated teeth were negative in the sensitivity test. The control group exhibited greater coronal discolouration compared to the examined group[14].

In the prospective case series by Nawal et al. (2020), immature necrotic permanent maxillary anterior teeth (n=6) underwent pulp regeneration using platelet-rich fibrin. None of the teeth demonstrated improved responsiveness to pulp sensitivity tests at the end of the 5-year follow-up; however, all exhibited a reduction in apical diameter (mean of 30.96%), which was statistically significant. An increase in root thickness (40.20%) and root length (13.18%) was also observed[7].

Ragab et al. (2019) stated, in their RCT, that the use of platelet-rich fibrin is effective for controlling the placement of MTA at the desired level, with only slight pressure exerted on the MTA during placement; It is also stated, however, that the use of platelet-rich fibrin may not be necessary for pulp revitalisation in immature permanent anterior teeth[13]. Similarly, Sakthivel et al. (2020) confirmed that platelet-rich fibrin is an ideal biomaterial for regeneration[6].

In the RCT conducted by Rizk et al. (2020), they conducted a 12-month follow-up (n=24). Platelet-rich fibrin demonstrated a marginal increase in radiographic root length and width, periapical bone density, and a reduction in apical diameter. No statistically significant differences were observed when compared with the blood clot. The treated teeth did not respond to the sensitivity test at the conclusion of the study. The blood clot exhibited a statistically significantly greater degree of coronal discolouration compared to the platelet-rich fibrin group[14].

Ragab et al. (2019) stated, in their randomised clinical trial, that the blood clot was important for creating vital tissue within the empty sterile canals[13].

In the prospective clinical trial conducted by Markandey et al. (2022), a follow-up period of 12 to 24 months was conducted, yielding the following results: the use of a blood clot, platelet-rich plasma, and platelet-rich fibrin demonstrated similar potential for the healing of periapical lesions and apical closure, as well as for radicular wall thickness and root length in immature teeth[22].

Platelet-rich plasma is superior to platelet-rich fibrin and induced bleeding with regard to the healing of periapical wounds; however, they produce comparable outcomes in terms of lateral wall thickening, root lengthening, and response to vitality tests[23].

A disadvantage of platelet-rich plasma and platelet-rich fibrin techniques is that additional time is required to extract and centrifuge blood prior to its introduction into the root canals[23].

Canal disinfection

Sakthivel et al. (2020) confirmed that revitalisation of an immature necrotic infected tooth is possible under conditions of complete canal disinfection[6].

Biradar et al. (2023) once again demonstrated the role of antibiotics in creating a favourable environment for the growth of pulpal and periapical tissues; furthermore, they make particular mention of triple antibiotic pastes (TAP), which play an important role as intracanal medicaments in regeneration and revascularisation procedures[12]. Hajizadeh et al. (2019) stated that the concentrations of medicaments are important in achieving a balance between canal disinfection, the release of growth factors from the dentine matrix, and the survival/proliferation of stem cells from the apical papilla[17]. It should be noted that triple antibiotic paste is a highly effective antimicrobial agent; however, high concentrations of this mixture may have a detrimental effect on the survival of stem cells[24].

Ragab et al. (2019) stated, in their RCT, that ciprofloxacin and metronidazole in addition to sodium hypochlorite are effective in controlling infection, although in some cases an extension of the treatment period is required[13].

Adverse effects

Higher concentrations of antibiotic medications, as well as $Ca(OH)_2$, may cause adverse effects on the mechanical, physical, and chemical properties of radicular dentine; that is, it may negatively affect fracture resistance in the cervical third of the roots[25,26].

When used at high concentrations, antibiotic medicaments (TAP) may demonstrate superior antimicrobial properties compared to $Ca(OH)_2$. However, high concentrations of TAP have been associated with several complications, such as antibiotic resistance, high cytotoxicity, and discolouration of the teeth[10].

There is a low incidence of adverse effects. The most frequently reported drawback in the reviewed publications was tooth discolouration caused by MTA.

Endodontic regeneration failed in some cases due to discolouration and recurrent caries, crown fracture[4] or loss of the coronal restoration of the treated teeth[9].

CONCLUSIONS

According to this literature review, pulp revitalisation demonstrates high survival rates in the treatment of immature necrotic permanent teeth, with satisfactory clinical and radiographic outcomes.

Revascularisation facilitates improved apical closure, increased dentinal wall thickness, and greater root length. It also preserves the alveolar bone.

Randomised clinical trials are required to compare the effect of platelet-rich fibrin and induced bleeding on the long-term revitalisation of teeth with necrotic pulp and open apices. Platelet-rich plasma results in superior apical healing, with root lengthening and thickening of the dentinal walls.

Clinical and radiographic success can be achieved using either MTA or Ca(OH2). One of the principal challenges of pulp revitalisation is coronal discolouration. NeoMTA is a material that has demonstrated less discolouration compared to conventional MTA. Likewise, it has been shown that the use of platelet-rich fibrin results in less discolouration than induction of bleeding and clot formation.

Triple antibiotic paste is a highly effective antimicrobial agent; however, high concentrations may have a detrimental effect on the survival of stem cells.

Although current research in regenerative therapy is highly promising, its outcomes remain unpredictable due to the histological nature of the regenerated tissue. Consequently, further studies are required to assess the follow-up and efficacy of each of these treatments.

BIBLIOGRAPHY

1. Aminsobhani M, HafeziMotlagh K, Mahjourian, Qomi R. Management and saving a traumatized poor prognosis maxillary central incisor for 18 years: A patient-centered treatment. Clin Case Rep. 2023;11(9):e7905.
2. Mittmann CW, Kostka E, Ballout H, et al. Outcome of revascularization therapy in traumatized immature incisors. BMC Oral Health. 2020;20(1):207.
3. Jena D, Sabiha PB, Kumar NS,et al. Regenerative therapy for the permanent immature teeth: A long term study. An Original Research. J Pharm Bioallied Sci. 2023;15(Suppl 1):S127-S131.
4. Alobaid As, Cortes LM, Lo J, 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.
5. Ajram J, Khalil I, Gergi R, Zogheib C. Management of an immature necrotic permanent molar with apical periodontitis treated by regenerative endodontic protocol using calcium hydroxide and MM-MTA: A case report with two years follow up. Dent J (Basel). 2019;7(1):1.
6. Sakthivel S, Gayathri V, Anirudhan S, Roja RJS. Platelet-rich fibrin and collagen matrix for the regeneration of infected necrotic immature teeth. J Clin Transl Res. 2020;6(1):1-5.
7. Nawal RR, Utneja S, Sharma V, Yadav S, Talwar S. Long-term follow-up of traumatized immature necrotic permanent teeth treated with regenerative endodontic protocol using platelet-rich fibrin: A prospective case series. J Conserv Dent. 2020;23(4):417-421.
8. Wikström A, Brundin M, Romani Vestman N, Rakhimova O, Tsilingaridis G. Endodontic pulp revitalization in traumatized necrotic immature permanent incisors: Early failures and long-term outcomes-A longitudinal cohort study. Int Endod J. 2022;55(6):630-645.
9. Bukhari S, Kohli MR, Setzer F, Karabucak B. Outcome of revascularization procedure: A retrospective case series. J Endod. 2016;42(12):1752-1759.
10. Al-Qudah A, Almomani M, Hassoneh L, Awawdeh L. Outcome of regenerative endodontic procedures in nonvital immature permanent teeth using 2 intracanal medications: A prospective randomized clinical study. J Endod. 2023;49(7):776-785.
11. Kumar JK, Surendranath P, Eswaramoorthy R. Regeneration of immature incisor using platelet rich fibrin: Report of a novel clinical application. BMC Oral Health. 2023;23(1):69.
12. Biradar N, Ragulakollu R, Tej G, Bogishetty C, Gandham S, Vardhan P. Combination therapy of antibiotics and platelet-rich fibrin for apical closure: Case series. Int J Clin Pediatr Dent. 2023;16(3):541-546.
13. Ragab RA, Lattif AEAE, Dokky NAEWE. Comparative study between revitalization of necrotic immature permanent anterior teeth with and without platelet rich fibrin: A randomized controlled trial. J Clin Pediatr Dent. 2019;43(2):78-85.
14. Rizk HM, Salah Al-Deen MS, Emam AA. Pulp revascularization/revitalization of bilateral upper necrotic immature permanent central incisors with blood clot vs platelet-rich fibrin scaffolds-a split-mouth double-blind randomized controlled trial. Int J Clin Pediatr Dent. 2020;13(4):337-343.
15. Tawfeek HA, El-Bardissy AA, Abou El-Yazeed M, Youssef R, Abd Alsamad AM. Clinical and radiographic evaluation of NeoMTA versus conventional white mineral trioxide aggregate in revascularization of non-vital immature permanent anterior teeth (A randomized controlled trial). BDJ Open. 2023;9(1):17.
16. Yang YQ, Wu BL, Zeng JK, Jiang C, Chen M. Pulp revascularization on an adult mandibular right second premolar: A case report. World J Clin Cases. 2022;10(17):5833-5840.
17. Hajizadeh S, Youzbashi Zadeh R, Vatanparast N. Pulp revascularization in three immature permanent mandibular molars with necrotic pulps: A case series. Iran Endod J. 2019;14(4):301-305.
18. Barzuna Ulloa M, González Alfaro C. Revascularización en un molar inferior, con un tercio de formación radicular. Odontología Vital. 2019;(30):87-97.
19. Shimizu E, Ricucci D, Albert J, et al. Clinical, radiographic, and histological observation of a human immature permanent tooth with chronic apical abscess after revitalization treatment. J Endod 2013;39:1078-1083.
20. Abuelniel GM, Duggal MS, Kabel N. A comparison of MTA and Biodentine as medicaments for pulpotomy in traumatized anterior immature permanent teeth: A randomized clinical trial. Dent Traumatol. 2020;36(4):400-410.
21. Sajjad I, Sajid M, Munir B, Akhlaq H, Zehra T, Ahmed J. Success of revascularization of pulp in necrotic maxillary anterior immature permanent teeth. Pakistan Journal of Medical and Health Sciences. 2022;16(1):420-422.
22. Markandey S, Das Adhikari H. Evaluation of blood clot, platelet-rich plasma, and platelet-rich fibrin-mediated regenerative endodontic procedures in teeth with periapical pathology: a CBCT study. Restor Dent Endod. 2022;47(4):e41.
23. Shivashankar VY, Johns DA, Maroli RK, et al. Comparison of the effect of PRP, PRF and induced bleeding in the revascularization of teeth with necrotic pulp and open apex: A triple blind randomized clinical trial. J Clin Diagn Res. 2017;11(6):ZC34-ZC39.
24. Alfahadi HR, Al-Nazhan S, Alkazman FH, Al-Maflehi N, Al-Nazhan N. Clinical and radiographic outcomes of regenerative endodontic treatment performed by endodontic postgraduate students: a retrospective study. Restor Dent Endod. 2022;47(2):e24.
25. Yassen GH, Sabrah AH, Eckert GJ. Effect of different endodontic regeneration protocols on wettability, roughness and chemical composition of surface dentin. J Endod. 2015; 41:956-960.
26. Yassen GH, Vail MM, Chu TG, Platt JA. The effect of medicaments used in endodontic regeneration on root fracture and microhardness of radicular dentine. Int Endod J. 2013;46(7):688-695.