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REVIEW ARTICLE

Regenerative endodontic therapy for external inflammatory *lateral* resorption following traumatic dental injuries: Evidence assessment of best practices

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Abstract

Background: External inflammatory *lateral* resorption (EILR) following dental trauma is a severe complication that can lead to significant root loss and tooth extraction.

Objective: The aim of this project was to review current evidence in the literature on regenerative endodontic therapy (RET) for EILR following traumatic injuries and assess the best treatment practices.

Methods: Publications appearing in PubMed, from January 1, 2001 to January 9, 2022 were studied. Inclusion criteria were: (a) Publications in English; (b) Publications on RET and EILR; (c) Teeth subjected to dental trauma; and (d) Presence of intracanal bleeding and blood clots. Exclusion criteria were: (a) Conference proceedings; (b) Lectures; (c) Abstracts; and (d) Letters to editor; (e) Non-English publications.

Results: 355 publications were analysed. Nine met all inclusion criteria. In 10 (58.8%) teeth, triple antibiotic paste was used for an average of 26 days. Double antibiotic paste was used in 3 (17.6%) teeth for an average of 14 days. In 3 (17.6%) cases, calcium hydroxide ($Ca(OH)_2$) was used for 14 days and negative pressure irrigation was applied once on 1 (6%) tooth.

Discussion: Using RET to treat EILR has some advantages compared to long term $CA(OH)_2$ dressing. RET requires shorter dressing time compared to $CA(OH)_2$. This can significantly improve patient compliance. Additionally, in immature teeth, RET helps to arrest root resorption leading to continued root maturogenesis and revascularization. It is recommended that a meticulous follow-up should be conducted when RET is performed to assure early detection of treatment failure.

Conclusions: RET appears to be a good treatment modality producing biologic repair and improving prognosis in cases of EILR in post-traumatic tooth/pulp injuries. The key limitation of this study is that all publications included were either case reports or case series that usually tend to report successful outcome.

KEYWORDS

external, regenerative endodontic, revascularization, root resorption, root resorption dental injury

INTRODUCTION

Dento-alveolar trauma (DT) occurs more frequently during childhood and adolescence (Altay & Gungor, 2001; Lin et al., 2007, 2008). Prompt and appropriate management is essential to improve prognosis of the affected dentition (American Association of Endodontists, 2014; Andreasen et al., 2012; Bourguignon et al., 2020; Fouad et al., 2020; Levin et al., 2020). Treatment of a traumatized tooth requires comprehensive diagnosis, interdisciplinary treatment approach and rigorous monitoring during a long-term follow-up period. Lack of proper and timely treatment can result in complications and more involved treatment in the future (Lin et al., 2013; Schwartz-Arad & Levin, 2004). Factors affecting the prognosis of traumatic dental injuries include the nature and severity of the trauma of the tissues involved (pulp, dentine, cementum, periodontal ligament (PDL) and bone) and the time that elapsed from injury to treatment. (Lauridsen et al., 2012a, 2012b). Complications can appear shortly after the traumatic event or at any time afterwards, even years later (Lin et al., 2016).

Root resorption is a pathological process with a wide range of aetiological factors. These may include microbial, mechanical (i.e., impact injuries, pressure or orthodontic movement), chemical (i.e., caustic agents) and thermal (Rotstein et al., 1991) factors. External inflammatory resorption (EIR) involves an initial injury, followed by microbial contamination that in turn elicits an immune response resulting in root resorption (Fuss et al., 2003; Tronstad, 1988). Root resorption can be classified based on the location of the resorption (Trope, 2002b):

1. External inflammatory *apical* resorption. This EIR occurs around the root apices of teeth with inflamed/infected pulps. Generally, this type of resorption responds favourably to endodontic treatment. External apical inflammatory resorption was detected radiographically in only 19% of the teeth examined, while 81% of teeth demonstrated this type of resorption when examined histologically. Only 7% was diagnosed coincidentally (Laux et al., 2000).
2. External inflammatory *lateral* resorption. This type of resorption presents a distinct lateral wall (periradicular) resorption of the root and adjacent bone (Abbott, 2016). It is caused by microbial invasion of the dentinal tubules causing irritation of the periodontium, especially in areas where the cementum layer is disrupted. This can lead to clinical complications that affect the prognosis. Radiographically, it can be recognized by a bowl-like radiolucency observed in both the root and adjacent bone (Fuss et al., 2003; Tronstad, 1988; Figure 1). This type of root resorption may be difficult to differentiate from replacement root resorption with similar periradicular resorption of the cementum and dentine. However, this is rare (Figure 2). It has been reported that cone beam computed tomography is more accurate in detecting external inflammatory lateral resorption (EILR), even in its early stages (Patel & Saberi, 2015; Patel et al., 2014; Figure 3).

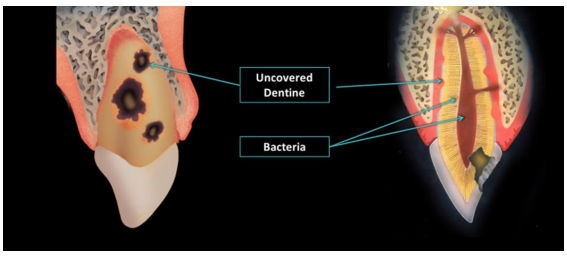

FIGURE 1 Graphical illustration of external inflammatory *lateral* resorption. Root canal and dentinal tubules are necrotic and infected, and inflammatory response with osteoclastic activity is apparent in the dentin and the bone. Uncovered dentine due to dental trauma (the original figure was published in Fuss et al., 2003 and revised accordingly).

The occurrence of EILR is rarer than external inflammatory *apical* resorption. A follow-up study showed that EIR with lateral root surfaces involvement comprised 3.5% of the total traumatic dental injuries, with an average patient age of 9.5 years (Lin et al., 2016). When diagnosing teeth with open apices, the occurrence was higher, reaching up to 23% (Lin et al., 2016; Soares et al., 2015). It is particularly prevalent in teeth that undergo avulsion and replantation, where it may occur in up to 61% of cases (Andreasen et al., 1995). A meta-analysis of root resorption following replantation of avulsed teeth found that external root resorption occurred in 51% of all cases, EILR in 23.2% and surface resorption in 13.3% (Souza et al., 2018).

The aetiology of root resorption involves two phases: injury and stimulation (Tronstad, 1988; Trope, 1998). Injury is related to non-mineralized tissues covering the root, mainly pre-cementum and pre-dentine (Chambers et al., 1985). In these cases, denuded mineralized tissue is colonized by multinucleated cells that initiate a resorption process. However, without further stimulation, the process ceases and repair with cellular cementum ensues (Bosshardt, 2005). This resorption, termed external surface resorption, occurs within 2–3 weeks following trauma. On occasion, if the area of the injured root surface is extensive, it can result in denuded dentine.

The continuation of the resorption process depends on stimulating factors, such as persistent inflammation and/or infection (Fuss et al., 2003; Tronstad, 1988). Severe trauma occurring anywhere along the root surface may result in EILR (Andreasen et al., 1995). This process involves

the presence of microorganisms in the root canal and dentinal tubules releasing lipopolysaccharides and peptidoglycans into the periodontium. As a result, macrophages, neutrophils, complement proteins and antibodies from B lymphocytes are secreted into the surrounding tissues (Jiang et al., 2002). These leukocytes promote the secretion of cytokine like IL-1, IL-6 and TNF-α, which increase the secretion of RANK-Ligand (RankL), thereby inducing differentiation of monocytes into osteoclasts/odontoclasts that resorb bone and dentine, respectively (Choi et al., 2005; Chung et al., 2006). Clinically, the teeth are usually asymptomatic in the early stages of the process, and resorption may sometimes be diagnosed at this stage by radiographs. However, as the process progresses, the teeth can become symptomatic and periradicular pathosis may develop. Radiographically, radiolucency may initially be observed on the external root surface, accompanied by resorption of the adjacent bone (Fuss et al., 2003; Figure 2).

Currently, guidelines regarding the recommended treatment for EILR following traumatic dental injury vary, mainly regarding the type of medication and its duration in the root canal system (Bourguignon et al., 2020; Cvek, 1992; Fouad et al., 2020). Therefore, the purpose of this investigation was to review the current literature on regenerative endodontic therapy (RET) for EILR following traumatic injuries and assess the best practices for treatment.

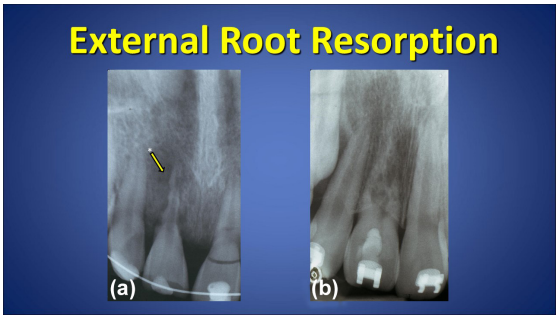

FIGURE 2 (a) Radiograph showing external inflammatory *lateral* resorption. Radiolucency is observed along the external root surface of the dentin and adjacent bone. (b) Radiograph showing external replacement resorption. No radiolucency is observed at the resorption site and bone fills the resorption lacuna.

METHODS

A search of publications appearing in the PubMed electronic database (nih.gov), from January 1, 2001 to January 1, 2022 was done using specific keywords (Table 1). Inclusion criteria were: (a) Publications in the English language; (b) Publications on regenerative endodontic treatment and EILR; (c) Teeth subjected to dental trauma; and (d) Presence of intracanal bleeding and blood clots. Exclusion criteria were: (a) Conference proceedings; (b) Lectures; (c) Abstracts; and (d) Letters to the editor (e) Non-English publications. The terms and combinations used in the search analysis are listed in Table 1.

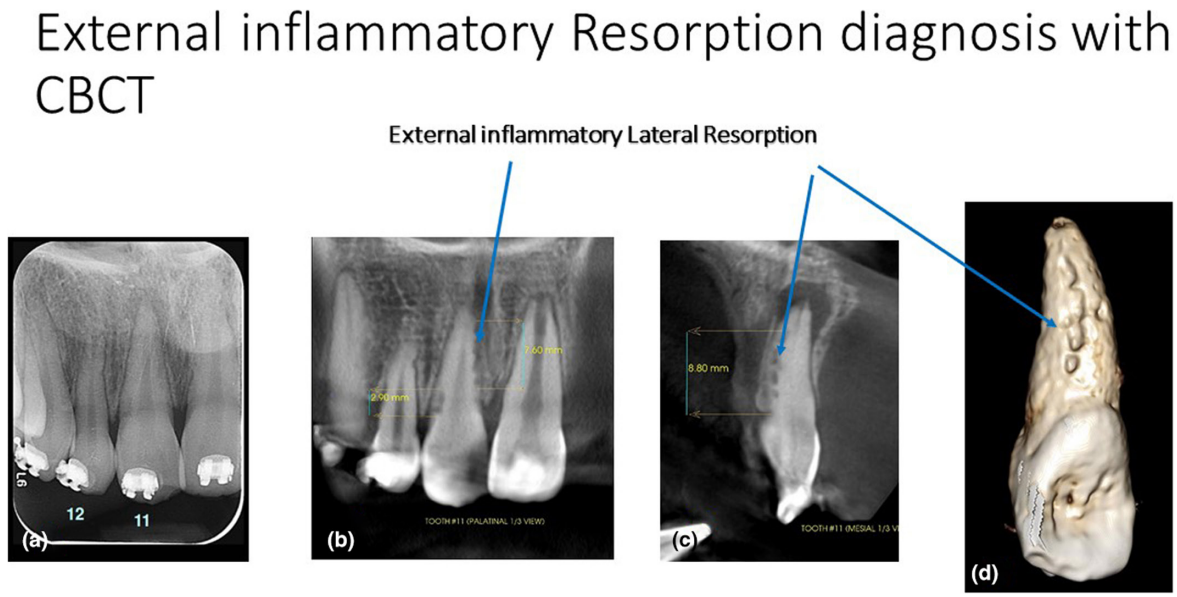

FIGURE 3 External inflammatory *lateral* resorption diagnosis with CBCT. Patient was referred to the endodontic department due to severe pain after lateral luxation. (a) Periapical X-ray taken 5 months after the dental trauma reveals periapical radiolucency in tooth number 11. (b) CBCT on coronary section reveals external resorption on the mesial and distal part of the root in tooth number 11. (c) CBCT on the sagittal section reveals external resorption on the palatal wall of tooth number 11. (d) Three dimension of the tooth shows the resorption of the root.

TABLE 1 Search strategy for PubMed

#30 AND #31
('2001/01/01'[Date – Publication]: '2022/01/09'[Date – Publication])
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Root Canal Preparation [MeSH Terms]
Root Canal Obturation [Mesh:NoExp]
Root Canal Therapy [Mesh:NoExp]
revascularization [Text Word] OR revascularization [Text Word] OR revascularization [Text Word] OR re-vascularisation [Text Word]
Regenerative Endodontic*[Text Word] OR Endodontic Regenerative [Text Word] OR Endodontics Regenerative [Text Word]
Regenerative Endodontics [MeSH Terms]
#10 OR #11
root resorption*[Text Word] OR resorption root [Text Word] OR resorptions root [Text Word]
root resorption [MeSH Terms]
#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8
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Tooth Luxation*[Text Word] OR Luxation Tooth [Text Word] OR Luxations Tooth [Text Word]
Dislocation Tooth [Text Word] OR Dislocations Tooth [Text Word] OR Tooth Dislocation*[Text Word]
Tooth Avulsion*[Text Word] OR Avulsion Tooth [Text Word] OR Avulsions Tooth [Text Word] OR Avulsed Tooth [Text Word] OR Tooth Avulsed [Text Word]
Tooth Avulsion [MeSH Terms]

A total of 355 relevant papers from PubMed were assessed using the Mendeley citation software (Mendeley). Additionally, a manual search was also conducted to fine-tune the search per the inclusion criteria. The data collected were analysed, detailed in a table and a descriptive statistical analysis performed.

RESULTS

Three hundred and fifty-five publications met the inclusion criteria. Of these, nine include RET for EILR, of which four were case reports and five were case series (Table 2). These nine publications included cases occurring in 17 teeth of 12 patients. RET was performed

TABLE 2 Studies characteristics of RET for EILR. Each line represents a single tooth treated

Study characteristics					Sample characteristics			Treatment and outcome				
Authors	**Gender**	**Country**	**Age**	**Tooth no.**	**Tooth stage**	**Trauma type**	**Time to resorption**	**Treatment**	**Blood clot**	**Dressing time**	**Follow-up**	**Outcome**
Miller et al. (2012)	M	USA	9	11	Immature	Avulsion	7 weeks	TAP[a]	Yes	6 weeks	18 months	[b]Healed
Santiago et al. (2015)	M	Brazil	9	11	Mature	UCF [i]+ Luxation (not specified in article)	12 months	TAP[a]	Yes	30 days	27 months	[b]Healed
	M		9	21	Mature	UCF [i]+ Luxation (not specified in article)	12 months	TAP[a]	Yes	30 days	27 months	[b]Healed
	M		9	41	Mature	Avulsion	3 months	TAP[a]	Yes	30 days	27 months	[b]Healed
	M		8	11	Mature	Avulsion	1 month	TAP[a]	Yes	30 days	15 months	[b]Healed
	M		8	21	Mature	Avulsion	1 month	TAP[a]	Yes	30 days	15 months	New periapical Radiolucency
Saoud et al. (2016)	F	Libya	7	21	Immature	Avulsion	6 weeks	TAP[a]	Yes	28 days	60 months	[b]Healed
	M		16	11	Mature	Uncomplicated crown fracture [i]	24 months	Metapest[c] for 2w. followed by TAP[a] 2w.	Yes	14 days	19 months	[b]Healed
Priya et al. (2016)	M	India	11	21	Mature	Avulsion	6 months	DAP[d]	Yes	14 days	12 months	[b]Healed
Chaniotis (2016)	F	Greece	7	31	Immature	Avulsion	6 months	Irrigated using 6% [e]NaOCl through the EndoVac negative pressure + [f]EDTA 17%	Yes	Single visit	24 months	[b]Healed
Tzanetakis (2018)	M	Greece	7	21	Immature	Intrusion	2 months	[g]$Ca(OH)_2$	Yes	2 weeks	30 months	[b]Healed
Lu et al. (2020)	F	China	9	21	Immature	Avulsion	4 months	[g]$Ca(OH)_2$	Yes	2 weeks	30 months	[b]Healed
	F		9	11	Immature	Extrusion	12 months	[g]$Ca(OH)_2$	Yes	2 weeks	18 months	[b]Healed
Yoshpe et al. (2020)	F	Israel-USA	12	21	Mature	Avulsion	24 months	TAP[a] + PRF[h]	Yes	3 weeks	24 months	[b]Healed
	F		9	11	Immature	Avulsion	6 months	TAP[a] + PRF[h]	Yes	3 weeks	12 months	[b]Healed
Chitsaz et al. (2021)	F	Iran	8	11	Immature	Avulsion	1 month	DAP[d] + PRF[h]	Yes	3 weeks	14 months	[b]Healed
	F		8	21	Immature	Complicated crown fracture	6 months	DAP[d] + PRF[h]	Yes	3 weeks	10 months	[b]Healed, s

[a]Triple antibiotics pastes & Platelet riche fibrine.

[b]Healed: '*Functional, asymptomatic teeth with no or minimal radiographic periradicular (apical) pathosis (radiolucency)*'.

[c]Iodoform+ Ca(OH).

[d]Double antibiotic pastes.

[e]NaOCl-sodium hypochlorite.

[f]EDTA-Ethylenediaminetetraacetic acid.

[g]$Ca(OH)_2$-Calcium hydroxide.

[h]PRF-Platelet-Rich fibrin.

[i]Uncomplicated crown fracture.

in 9 (58%) immature teeth and in 8 (42%) mature teeth. The average injury distribution age was 9.3 years for boys and 8.8 years for girls, with a total average age of 6.1 years. In 10 teeth (58.8%), Triple Antibiotic Paste (TAP) was used for an average duration of 26 days. One report described the use of Metapaste (MetaBiomed), a mixture of $Ca(OH)_2$ with Iodoform prior to the use of TAP (Bhat et al., 2003; Rafiee et al., 2016; Saoud et al., 2016). Double Antibiotic Paste (DAP) was used in 3 teeth (17.6%) for an average of 14 days. In 3 cases (17.6%), $Ca(OH)_2$ was used as intracanal medication for 14 days and in one tooth (6%), a single visit using negative pressure irrigation was described.

DISCUSSION

To date, *no review* has assessed the evidence of best practices of regenerative endodontics (RE) for the treatment of EILR.

Failure to identify EIR with lateral wall resorption in the early stages can lead to loss of the teeth involved (Andreasen, 1985; Heithersay, 2007; Schmidt & Stern, 1996), often at the early stages of puberty (Perez et al., 1991; Pissiotis et al., 2007; Sapir & Shapira, 2008). Ritter et al. (2004) showed that the continuation of root formation and revascularization occurs only if the root canal is bacteria-free (Saoud et al., 2016). Nonetheless, growing evidence supports the conclusion that RET can arrest EIR with dentine resorption on the *lateral* wall (Aggarwal & Singla, 2010; Priya et al., 2016; Santiago et al., 2015; Saoud et al., 2016; Utneja et al., 2012). Moreover, it has been shown that growth factors from the blood clot, and those embedded in dentine, are critical for the regenerative process by promoting biological healing (Galler et al., 2016; Yoshpe et al., 2020). Currently, there are no clear guidelines regarding the most predictable treatment for EIR on the *lateral* root surfaces following trauma. The therapy for EIR can be divided into prevention and treatment.

Prevention of EIR for teeth after severe trauma injury

In mature teeth affected by avulsion or intrusive luxation, root canal treatment should be performed and include dressing the root canal system with either antibiotic/corticosteroid paste (Ledermix® paste Lederle Pharmaceuticals), or $Ca(OH)_2$, for 1–4 weeks, followed by obturation (Fouad et al., 2020). In immature teeth, meticulous monitoring of pulp vitality and follow-up should be conducted in accordance with the International Association of Dental Traumatology (IADT) protocols (Bourguignon et al., 2020; Diangelis et al., 2012; Fouad et al., 2020). The use of antibiotic/corticosteroid paste (Ledermix® paste Lederle Pharmaceuticals) in mature teeth after avulsion was recently recommended by the IADT with the goal of preventing EIR with lateral root surface involvement. The paste, consisting of triamcinolone acetonide (1%) and demethylchlortetracycline calcium (3.21%) in a water-soluble cream, was found to be effective in preventing inflammatory root resorption with lateral root surface involvement in monkeys due to its ability to penetrate the dentinal tubules and affect the periodontium. It resulted in promotion of reparative cementum, and reducing inflammation damage due to corticosteroids (Pierce et al., 1988; Pierce & Lindskog, 1987; Trope, 2002a).

Treatment of EILR

When EILR is observed, there is no definitive method of treatment. Traditionally, based on Cvek's study, long-term $Ca(OH)_2$ has been the treatment of choice (Cvek, 1992). The recommendations for the duration of $Ca(OH)_2$ intracanal medication in EIR vary from 4 weeks (Darcey & Qualtrough, 2013) to several months. High success rates were reported following $Ca(OH)_2$ medication for 3–54 months, where the average duration was 24 months for immature teeth and 11 months for mature ones (Cvek, 1992). The treatment is assessed radiographically every 3 months until the PDL space is observed along the root (Cvek, 1992; Finucane & Kinirons, 2003). The low solubility of $Ca(OH)_2$ and buffering effect of the dentine prevent permeability of hydroxyl ions through the dentinal tubules thereby limiting antibacterial properties that can stimulate the healing process (Andreasen, 1970, 1985; Trope, 2002a) in the root canal (Fuss et al., 1989, 2002). Furthermore, the use of long-term $Ca(OH)_2$ dressing in immature teeth can lead to the formation of an apical stop (apexification) and non-maturation of the root apex, which in contrast can mature with RET.

Antibiotics have demonstrated better antibacterial effects by penetrating the dentinal tubules up to a depth of 500 μm, in comparison to $Ca(OH)_2$ alone that penetrates up to 200 μm (Fuss et al., 2002; Haapasalo & Orstavik, 1987). Antibiotics as intracanal medicaments have been found to be effective in disinfecting the root canal and dentine tubules (Haapasalo & Orstavik, 1987; Hammarström et al., 1986; Lin et al., 2003).

Iwaya et al. (2001) reported the first case of revascularization of a necrotic tooth, later termed RET (American Association of Endodontists, 2020). In 2013, the American Association of Endodontists (AAE) adopted a protocol (Banchs & Trope, 2004) as a guideline

for treatment of necrotic young immature permanent teeth, and published a statement and guidelines for RET in 2016 (Diogenes et al., 2016). One objective of RET is primary periapical healing, which is an indicator of RET success (Koç & Del Fabbro, 2020; Mohammadi, 2011). Additional benefits include an increase in the thickness of dentine walls, an increase in the length of the immature root and positive response to sensibility tests (Diogenes et al., 2016; Geisler, 2012). According to the protocol of the AAE (2021), each tooth should be irrigated with 20 ml of 1.5% sodium hypochlorite (NaOCl), dried with paper points, dressed with $Ca(OH)_2$ or low concentration of TAP (mixture of equal parts of three antibiotics—metronidazole, cefuroxime axetil and ciprofloxacin dissolved into a creamy paste consistency), or DAP (mixture of equal parts of two antibiotics – metronidazole and ciprofloxacin dissolved into a creamy paste consistency) for a period of 3 weeks. Irrigating with ethylenediaminetetraacetic acid (EDTA) as the final step before initiating bleeding has been found to be beneficial in the formation of new mineralized tissue (Galler et al., 2016). Thus, EDTA irrigation is recommended as a necessary part of the endodontic regeneration protocol. The growth factors released from the dentine may reach the open tubules in the resorbed areas of the root thereby enhancing proliferation and differentiation of stem cells of the surrounding bone and PDL, as well as those from the blood clot or blood combatants (platelet-rich plasma, platelet-rich fibrin) that arrest the resorption process (Galler et al., 2016).

The first study describing the arrest of EIR with lateral root surface involvement by means of RET using TAP as intracanal medication and apical blood clot to repair apical periodontitis and pulp was published in 2012 (Miller et al., 2012). Subsequently, other case reports and case series have been published (Table 2), providing ample evidence that RET might be an efficient tool for treating and arresting EIR (Aggarwal & Singla, 2010; Chitsaz et al., 2021; Miller et al., 2012; Priya et al., 2016; Santiago et al., 2015; Saoud et al., 2016; Utneja et al., 2012).

RET can be used as a treatment modality for EILR after trauma when prominent periradicular resorption is observed, with several advantages. First, compliance is improved by decreasing the number of visits to only one or two appointments, instead of multiple visits over an average of 24 months (Cvek, 1992). TAP was used for an average of 28 days and DAP and $Ca(OH)_2$ for an average of 14 days. In the second appointment, a blood clot was induced in the canal and covered by Mineral Trioxide Aggregate and a coronal sealing. In one case, the regenerative procedure was performed in a single visit in order to improve patient compliance. This was achieved by using a high concertation of 6% NaOCl, and irrigation by means of a negative pressure irrigation system, EndoVac™ system (Endo Vac, Axis/SybronEndo) minimizing the possibility of extrusion of irritants into the periapical tissues (Chaniotis, 2016). Second, in immature teeth, RET helps arresting root resorption and leading to continued maturogenesis and revascularization of the root. The use of traditional long-term $Ca(OH)_2$ in the root canal induces the formation of a calcified apical barrier. $Ca(OH)_2$ causes necrosis of Hertwig's Epithelial Root Sheath thereby inhibiting the continued formation of the root (Huang, 2009). Saoud et al. (2016) used RET to treat a mature tooth of a 16-year-old female who presented with combined internal and external root resorption that left very thin dentinal walls. Their rational was that the use of RET would, in addition to arresting the resorptions, facilitate thickening of the canal walls and consequently strengthening the root.

Since no comprehensive research on the use of the RET to treat resorptions has been done, there is a need for meticulous follow-ups. If RET fails to show a favourable effect in arresting EIR with lateral root surface involvement, the classic Cvek (1992) treatment should be performed.

Treatment following severe dental trauma can be divided to mature and immature teeth. In the case of immature teeth pulpal status must be stablished. If there is no sign of pulp necrosis only follow-up is indicated. When evidence of apical periodontitis and EILR exist, RET should be initiated immediately according to the AAE protocol. If no healing of the resorption sights is achieved long-term $Ca(OH)_2$ dressing should be applied followed by complete root canal treatment. If still there is no evidence of healing tooth extraction should be considered (Figure 4). In the case of severe trauma to mature teeth, the tooth should be dressed with $Ca(OH)_2$ for 1–4 weeks followed by root obturation. If signs of EILR appear obturation should be removed and RET initiated. After healing is observed follow-ups should be done for up to 5 years. If no healing is achieved long-term $Ca(OH)_2$ dressing should be applied followed by complete root canal treatment. If still there is no evidence of healing tooth extraction should be considered (Figure 5). 5 years follow-up is indicated after treatment termination.

The ESE protocol for RET recommends the use of non-condense $Ca(OH)_2$ in the root canal to improve disinfection. The use of $Ca(OH)_2$ as intracanal medication in the first appointment showed successes in arresting periradicular resorption and promoting healing (Lu et al., 2020; Tzanetakis, 2018). The combination of meticulous intracanal irrigation and disinfection, and the release of growth factors from the blood clot and those embedded in the dentin, have been shown to promote biological healing (Galler et al., 2016; Palma et al., 2017; Yoshpe et al., 2020).

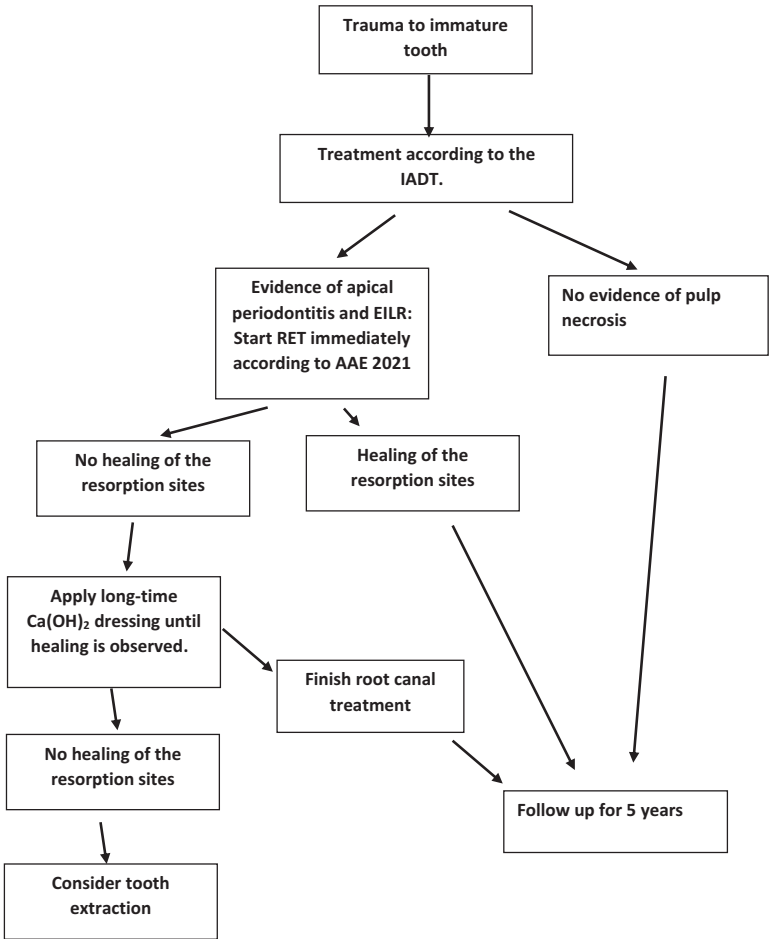

FIGURE 4 Flow chart treatment of immature teeth following trauma. IADT, International association of Dental Traumatology. RET, Regenerative endodontic treatment. EILR, External inflammatory lateral resorption. AAE, American association of endodontists protocols 2021.

Cvek's use of long-term $Ca(OH)_2$ dressing requires greater compliance on the part of the patient as well as the dental surgeon and is time-consuming since $Ca(OH)_2$ needs to be refreshed every 3 months (Cvek, 1992). Furthermore, it increases the risk of weakening the tooth due to its effect on dentin and the risk of a subsequent fracture (Andreasen et al., 2002). The use of RET can overcome these disadvantages.

Several limitations of the study and possible bias should be noted. First, all publications analysed were either case reports or cases series. Usually, such reports do not present treatment failures. Second, the search was limited only to publications appearing in PubMed Medline. It is plausible that additional publications concerning RET may exist in other literature search platforms. Third, the search was limited only to publication in the English language. It is possible that additional publications may have appeared in other languages.

CONCLUSION

EILR following traumatic dental injury is a serious complication. To date, there is no definitive protocol that aims to arrest EILR. RET was found to be a beneficial treatment modality that produces biologic repair and improves prognosis in cases of EILR in post-traumatic tooth/pulp injuries. Treatment with long-term $Ca(OH)_2$ has shortcomings. Recently, several publications have suggested the use of RET therapy to arrest EILR and obtain biologic repair.

AUTHOR CONTRIBUTION

Prof. Ilan Rotstein and Prof. Shaul Lin were responsible for conceptualization, data review and analysis and writing of the manuscript. Dr. Daniel Moreinos was responsible for editing and together with Dr. Dekel Wisblech for literature search and initial reviews.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data openly available in a public repository that issues datasets with DOIs.

ETHICS STATEMENT

The study did not require ethical approval.

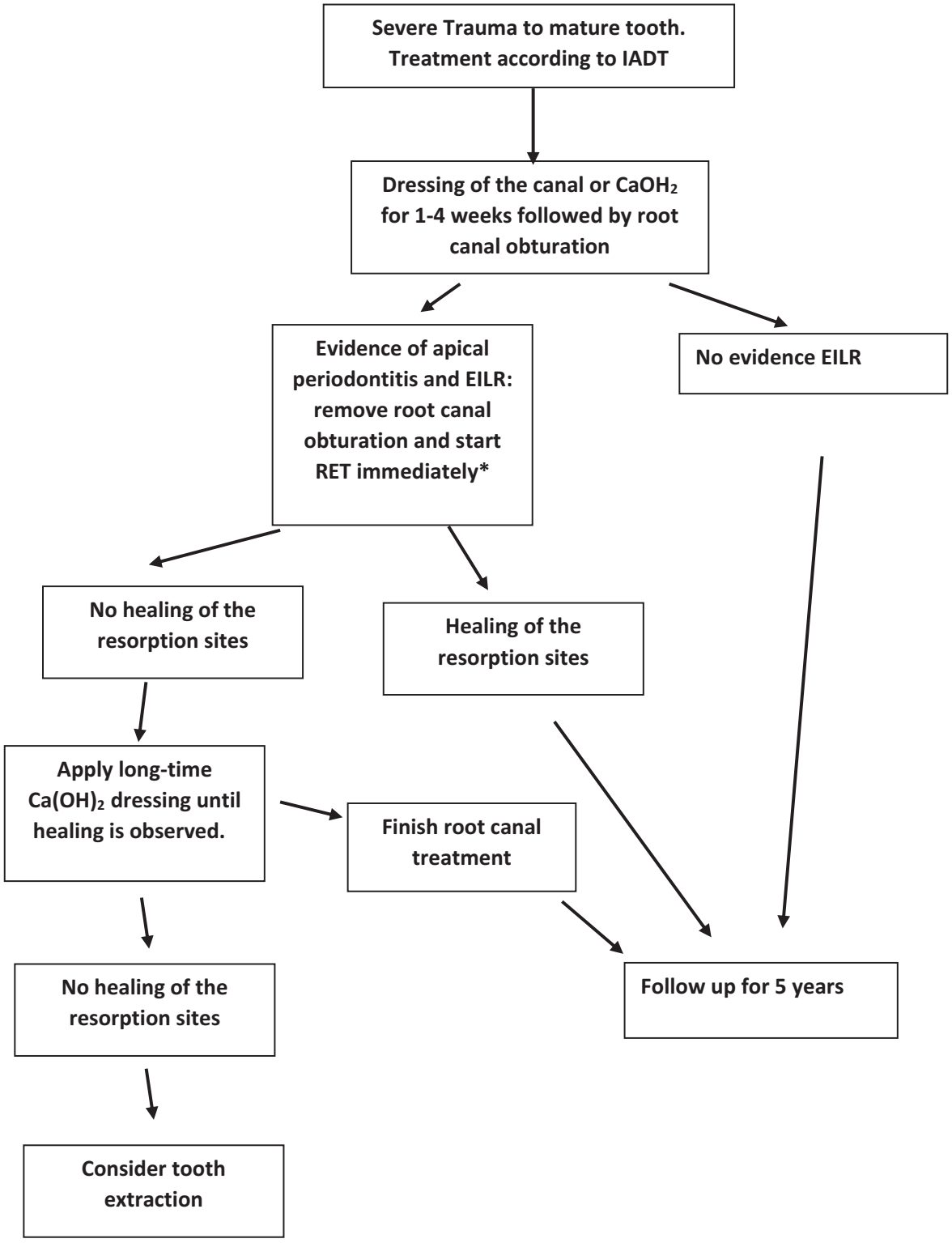

FIGURE 5 Flow chart treatment of mature teeth following trauma. EILR, External inflammatory lateral resorption. IADT, International association of Dental Traumatology; RET, Regenerative endodontic treatment.

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