Revista da Faculdade de Odontologia de Porto Alegre

Different Techniques for the Treatment of Teeth with an Incomplete Root Development and Pulp Necrosis: A Systematic Review

Diferentes técnicas para o tratamento de dentes com rizogênese incompleta e necrose pulpar: uma revisão sistemática

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ABSTRACT

Introduction: The objective of this systematic review was to compare the apexification techniques of calcium hydroxide ($Ca(OH)_2$), or mineral trioxide aggregate (MTA), with the pulp regeneration technique, using cohort studies, and non-randomized and randomized clinical trials. **Methods:** The methodology was based on electronic research in the following databases: PubMed, MEDLINE, Google Scholar, SciELO, and LILACS. In addition, a manual search was carried out using the references that were listed in the articles found. **Results:** A total of

403 potentially eligible studies were found, with seven being included in the inclusion criteria of this systematic review. The seven studies involved a total of 312 teeth. The minimum time of a follow-up period was 12 months. The irrigation solution most used was sodium hypochlorite, for both of the apexification and revascularization techniques. The medication commonly chosen in the apexification groups was $Ca(OH)_2$, with antibiotic triple paste in the revascularization groups. The clinical rate of success in the groups treated with revascularization varied from 76% to 100%, while in the groups treated with apexification, it ranged from 68% to 100%. Only two studies reached a success rate equal to 100%. **Conclusions:** Variable levels of evidence were observed in relation to the treatments. However, it was confirmed that revascularization is an excellent option since its outcomes produced a greater gain of thickness and root length, besides developing a decrease in the apical foramen.

Keywords: Regenerative endodontics. Dental pulp necrosis. Apexification. Tooth apex. Periapical periodontitis.

RESUMO

Introdução: O objetivo desta revisão sistemática foi comparar as técnicas de apexificação, com hidróxido de cálcio ($Ca(OH)_2$) ou agregado trióxido mineral (MTA), com a técnica de regeneração pulpar, utilizando estudos coorte, ensaio clínico não randomizado e randomizado. **Métodos:** A metodologia foi baseada em pesquisa eletrônica nas seguintes bases de dados: PubMed, MEDLINE, Google Acadêmico, SciELO e LILACS. Além disso, foi realizada uma pesquisa manual utilizando as referências listadas nos artigos encontrados. **Resultados:** Foram encontrados 403 estudos potencialmente elegíveis, sendo sete incluídos nos critérios de inclusão desta revisão sistemática. Os sete estudos envolveram um total de 312 dentes. O tempo mínimo de um período de acompanhamento foi de 12 meses. A solução de irrigação mais utilizada foi o hipoclorito de sódio, para as técnicas de apexificação e revascularização. O medicamento comumente escolhido nos grupos de apexificação foi o $Ca(OH)_2$, com pasta tripla antibiótica

nos grupos de revascularização. A taxa clínica de sucesso nos grupos tratados com revascularização variou de 76% a 100%, enquanto nos grupos tratados com apexificação variou de 68% a 100%. Apenas dois estudos atingiram uma taxa de sucesso igual a 100%. **Conclusões:** Níveis variáveis de evidência foram observados em relação aos tratamentos. No entanto, confirmou-se que a revascularização é uma excelente opção, pois seus desfechos produzem maior ganho de espessura e comprimento radicular, além de diminuir o forame apical.

Palavras-chave: Endodontia regenerativa. Necrose da polpa dentária. Apexificação. Ápice dentário. Periodontite periapical.

INTRODUCTION

The regenerative endodontic protocol is an emerging alternative for the management of necrotic teeth that display an incomplete root development. Traditionally, dental elements that present apical periodontitis, thin and parallel walls, and an open apex, are treated by apexification[1]. Apexification can be conducted in one or multiple visits. This conventional method consists of successive exchanges of intracanal calcium hydroxide ($Ca(OH)_2$), in order to promote an apical calcific barrier[2]. However, this technique presents some limitations, specifically because it is a long-term therapy. This may compromise the patient's adherence to the treatment, which invariably lasts for more than 6 months, and it does not show any gain in dentin thickness, implying a fragility of the tooth. In addition, the prolonged use of $Ca(OH)_2$ may promote a weakening of the dentin[3,4]. Another apexification protocol is based on the use of of mineral trioxide aggregate (MTA), in order to make an artificial apical barrier that allows for root canal filling in the same session[5]. Although the clinical success of both variants of apexification is evident, these two protocols do not confer a dentin thickness gain, or a complete root development, resulting in a fragile and fracture susceptible tooth[6,7].

Recently, an alternative therapy to apexification has been used in clinical practice. This technique is called regenerative endodontic therapy and it

corroborates the viability of root formation and dentin thickness gain; consequently, there is a reinforcement of the root structure[8]. The initial concept of regenerative endodontics was proposed by Nygaard-Østby in the 1960s[9]. However, it was in the year 2000, based on two case reports, that regenerative endodontic activity aroused attention for its advantages. Thus began its introduction into clinical practice[6,10]. Banchs and Trope[7] suggested a protocol that recommended the disinfection with copious irrigation and a combination of three antibiotics as intracanal medication. After 26 days, over-instrumentation induce bleeding into the canal and a double seal of the coronal access should be carried out. The procedure produces a blood clot, which must be controlled at the cemento-enamel junction level.

The two aforementioned alternatives for the treatment of teeth suffering from pulp necrosis and an incomplete root development have demonstrated reliable clinical outcomes[1,7]. Regenerative endodontics is one of the most exciting advancements in dentistry nowadays, and it is constantly the subject of recent scientific research aiming to find the best treatment protocol. Although there are clinical considerations with emerging scientific evidence for the regenerative procedure[11], a broader discussion about each stage of the therapy should be carried out in order to consolidate an effective and unquestionable protocol for regenerative endodontics. Therefore, the main objective of this systematic review was to assess the best available evidence and to collect appropriate data, in order to evaluate the effectiveness of the techniques of apexification with $Ca(OH)_2$ or MTA, and of a pulp regeneration with a blood clot or injectable scaffolds, from cohort studies and clinical trials. In addition, a critical analysis of the available information will be made and the success rate of the techniques evaluated.

MATERIAL AND METHODS

Research Question

The research questions that guided the following literature review were: "Does the revascularization technique, with a blood clot only, a blood clot and

matrix, a blood clot plus a scaffold impregnated with a basic growth factor of fibroblasts, and a blood clot plus an absorbable collagen barrier, promote the best outcomes regarding periapical healing, an apical foramen closure, and an increased thickness in root length, with clinical success, if compared to the technique of apexification with $Ca(OH)_2$ or MTA, in human teeth with an incomplete root development and pulp necrosis?" and "Does revascularization demonstrate a higher survival rate in immature permanent teeth that exhibit necrotic pulp and an incomplete root development when compared to the apexification technique?".

These research questions were constructed according to the population, the intervention protocol, the comparison protocol, and the outcome (Population: human teeth with an incomplete root development and pulp necrosis; Intervention: pulp regeneration; Control: apexification with $Ca(OH)_2$ or MTA; Outcome: apical closure or root maturation, clinical and radiographic outcomes, clinical success rate and survival, an increase in length percentage and root thickness; Type of study: retrospective cohort, non-randomized and randomized clinical trial.

Strategy for the Identification and the Selection of Studies

The electronic databases that were used were PubMed, MEDLINE, Google Scholar, SciELO, and LILACS. The search strategy is described in Appendix 1 and the words used were identified from the keywords that were present in the articles that dealt with the subject, as well as the terms that were obtained from *MeSH* (*Medical Subject Headings* of the United States National Library of Medicine). In addition, a manual search was also performed on the references cited by the selected studies from the databases. The search and the selection of articles were carried out by two independent researchers (C.B. and C.J.), without any language restriction, in the period of May 2020. After the electronic search, the titles and the abstracts were evaluated according to the inclusion and exclusion criteria. The reading of the articles in full was carried out from those papers that met the inclusion criteria. Alternatively, in the cases of

studies with an insufficient amount of data in the title or in the abstract to establish a decision, a search was carried out in order to minimize the possibility of disregarding relevant research. The articles selected by both of the researchers were compared and when discrepancies were found, they were discussed. When necessary, a consensus was obtained from a third evaluator (M.C.B.).

Criteria for the Selection of Studies

Inclusion criteria

Retrospective cohort study, non-randomized and randomized clinical trial in human permanent teeth that displayed an incomplete root development and pulpal necrosis, subsequently comparing pulp revascularization techniques with a blood clot, a blood clot plus a scaffold that was impregnated with a basic growth factor of fibroblasts, and a blood clot plus an absorbable collagen barrier, when using the $Ca(OH)_2$ or MTA root apexification technique.

Exclusion Criteria

- Literature reviews, case reports, dissertations, theses, textbook chapters, and annals of congress;
- Deciduous teeth;
- Permanent human teeth with a complete root formation;
- Teeth without pulp necrosis;
- Apexification with other materials that were different from MTA and/or $Ca(OH)_2$.

Data Synthesis

The following information was analyzed and extracted from the studies: authors, year of publication, patient's age, inclusion criteria, irrigation protocol, the intracanal medication used and the time it remained intracanal, treatment protocol (apexification with $Ca(OH)_2$ or MTA and revascularization), follow-up period, sealing used, radiographic outcomes (changes in root length, canal wall thickness, apical diameter closure, plus other outcomes), and clinical outcomes.

RESULTS

Selection of studies

The research strategy found a total of 403 articles in the electronic databases, of which 204 articles were duplicates and they were excluded. After reading the titles and the abstracts, 186 studies were excluded, as they did not meet the inclusion criteria. With a complete reading of the texts, five articles were excluded because they also did not meet the inclusion criteria of this study. In the end, seven articles were included for this review, according to Figure 1. Table 1 presents the characterization of the articles that were included in this review.

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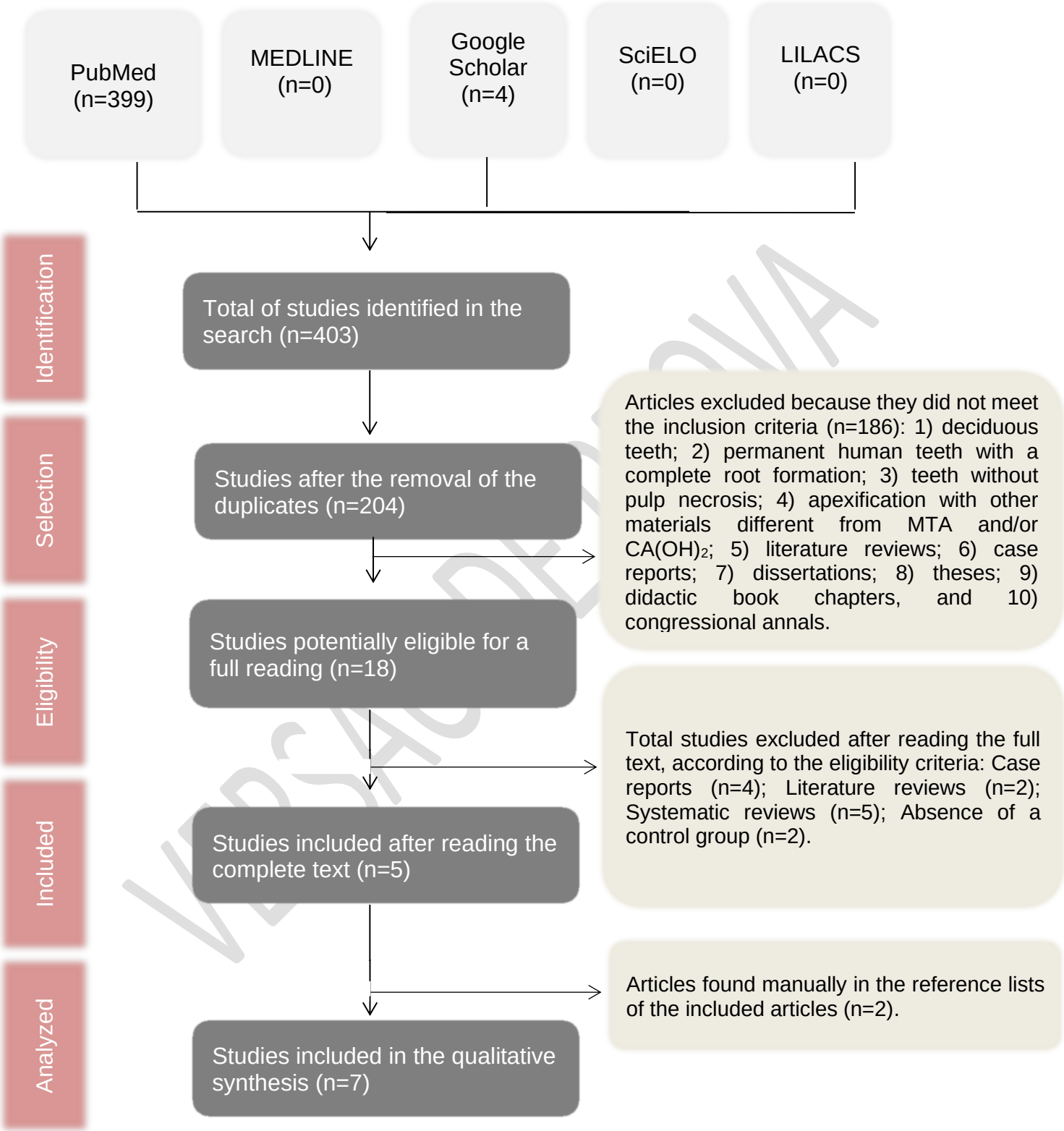

Figure 1: Flowchart of the search strategy for the identification and the selection of studies.

Board 1. Characteristics of the studies that met the inclusion criteria

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Author, year	**Type of study**	**Objective**	**Criteria for inclusion of patients**	**Patients / Type of teeth**	**Irrigation solution**	**Intracanal medication**	**Time of intracanal medication**	**Techniques**	**Sealing**	**Follow-up**	**Criteria evaluated in the result**	**Radiographic outcomes**	**Clinical outcomes**
Alobaid et al.[12], 2014.	Retrospective cohort study.	To evaluate and compare the clinical and radiographic outcomes of apexification ($Ca(OH)_2$ and MTA apical barrier) and the treatment of revascularization of immature nonvital permanent teeth. In addition, to try to identify the patient factors that may be important to achieve the success of these procedures.	Subjects should be between 6 and 16 years; The tooth should be immature (stage 1-4 according to the criteria of Cvek[13]); After the protocol of apexification or revascularization, the final restoration should have been performed; Follow-up of the patient for at least 3 months after the treatment.	31 treated teeth (19 revascularizations and 12 apexification, being 5 cases of MTA, and 7 cases of $Ca(OH)_2$).	REG group - Variable concentrations of NaOCl, chlorhexidine, and/or EDTA. APEX group with $Ca(OH)_2$ – "standard irrigator" (did not report which one). APEX group with MTA – "standard irrigator" (did not report which one).	REG group - antibiotic triple paste (ciprofloxacin, metronidazole, and minocycline), or double paste (ciprofloxacin and metronidazole), or $Ca(OH)_2$. APEX group with $Ca(OH)_2$ - $Ca(OH)_2$. APEX group with MTA - $Ca(OH)_2$.	Not included.	REG group - blood clot induction (although this was not achieved in all cases) + MTA. APEX group with $Ca(OH)_2$ - $Ca(OH)_2$ exchanges. APEX group with MTA - MTA plug + gutta-percha obturation.	REG group - MTA + composite resin. APEX group with $Ca(OH)_2$ – composite resin. APEX group with MTA - not included.	Average follow-up time of 17 months and a recall rate of 63%.	Adverse events were defined as any event that involved the treated tooth during the treatment, or during the follow-up period, and this was classified as 1. Mild: No need for additional endodontic treatment. 2. Moderate: There was a need for additional endodontic treatments due to pain, swelling, or fistula. 3. Severe: The tooth needed to be extracted. Preoperative radiographs were evaluated by the study investigators regarding the presence or absence of periapical radiolucency, the stage of root development, and for signs of reabsorption. Postoperative radiographs were evaluated for the presence or absence of periapical radiolucency, for signs of reabsorption, intracanal calcification, apical calcification, and root length and width. In the cases where periapical radiolucency was present preoperatively, the postoperative images were evaluated in order to determine whether the radiolucency appeared larger or smaller on the follow-up images.	In the REG group, only 1 case with a persistent periapical pathology was identified, which was higher than at the beginning of the treatment. All of the other cases in the study were classified as cured, based on the resolution or on the lower appearance of periapical radiolucency. External resorption was observed in 4 cases, all in the REVASC group; however, in 3 of the 4 cases, the reabsorption appeared similar on the pre- and postoperative radiographs. Apical calcification was observed in 6 cases of the REG group and in 1 case of the APEX group. Only in the cases of the REG group, an intracanal calcified barrier (3 cases) and a canal obliteration (2 cases) were observed. In terms of the radiographic changes, the width measurements showed 1.4% - 3.2% for the APEX group versus 10.2% - 4.0% for the REG group. However, none of the radiographic outcomes measured (width, length, or apical diameter) were statistically different. The cases treated with REG generally showed greater differences between the treatment groups (1.4% variation in the width and in the apical diameter measurements). The APEX $Ca(OH)_2$ group showed a greater increase in the root length. In terms of clinical significance, a 20% increase in length or width of the root was noted.	During the follow-up period, most of the cases survived. The case in which the tooth was extracted belonged to the REG group and this resulted from a re-traumatism that led to a fracture of the treated tooth. Most of the cases were considered a clinical success (27/31, 87%), with 15 cases (79%) in the REVASC group, and 12 cases (100%) in the APEX group. Of the four teeth from the REG group that were considered as a failure, 3 were re-infected and 1 was re-traumatized; they were extracted as previously described. The differences between the groups regarding survival and clinical success were not statistically significant. With regard to adverse events, 8 cases were observed in the REG group versus 1 in the APEX group. In the REG group, 4 cases were classified as mild, 3 cases as moderate, and 1 case as a severe adverse event. There was only one in the APEX group and it was classified as mild. When comparing the risks for the occurrence of an adverse event, a slightly higher risk was found for an adverse event that occurred after the revascularization treatment than after the apexification treatment.

Board 1. Characteristics of the studies that met the inclusion criteria

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Author, year	**Type of study**	**Objective**	**Criteria for inclusion of patients**	**Patients / Type of teeth**	**Irrigation solution**	**Intracanal medication**	**Time of intracanal medication**	**Techniques**	**Sealing**	**Follow-up**	**Criteria evaluated in the result**	**Radiographic outcomes**	**Clinical outcomes**
Bose et al.[14], 2009.	Retrospective cohort study.	To determine the estimates of the radiographic success of the clinical endodontic regenerative procedures.	Immature permanent necrotic teeth with or without periapical pathology that were submitted to the endodontic regeneration procedures, as performed by dentists around the world.	54 cases of teeth that were treated with endodontic regeneration. They were subdivided into 3 groups: triple antibiotic paste, $Ca(OH)_2$, and formocresol. 40 control cases (20 treated with the apexification technique with MTA, and 20 treated with conventional non-surgical endodontic treatments).	REG group - NaOCl. Other groups were not applicable.	The teeth that were submitted to revascularization were subdivided into 3 groups: triple antibiotic paste, $Ca(OH)_2$, and formocresol. The control group consisted of 20 cases that used MTA for the apexification procedures, and 20 cases that were submitted to non-surgical endodontic treatments.	Not applicable.	Not applicable.	Not applicable.	Not applicable.	The development of the root length was evaluated, as well as the development of the dentinal wall thickness in the apical third of the root. Two secondary analyzes were performed. First, it was evaluated whether any time-related changes in the outcome measures could be detected, such as a percentage increase in the root length and an increase in the root wall thickness over time. Second, the authors radiographically observed whether the placement of $Ca(OH)_2$ had any influence on the result in relation to its location in the coronal half of the root canal system, or when it was placed beyond the coronal half (i.e., in the apical half of the root canal system).	The regenerative endodontic treatment with the triple antibiotic paste produced a significant increase in the dentinal wall thickness when compared to the control groups with MTA and the conventional non-surgical endodontic treatment group ($p < 0.001$). The treatments with $Ca(OH)_2$ ($p < 0.05$) or formocresol ($p < 0.05$) resulted in a significantly greater change in the dentinal wall thickness when compared to the non-surgical endodontic treatment group, but no differences were observed between these drugs and the apexification group with MTA. Finally, the antibiotic triple paste produced significantly greater differences in the dentinal wall thickness when compared to the $Ca(OH)_2$ or formocresol groups ($p < 0.05$ for both).	Not applicable.

Board 1. Characteristics of the studies that met the inclusion criteria

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Author, year	**Type of study**	**Objective**	**Criteria for inclusion of patients**	**Patients / Type of teeth**	**Irrigation solution**	**Intracanal medication**	**Time of intracanal medication**	**Techniques**	**Sealing**	**Follow-up**	**Criteria evaluated in the result**	**Radiographic outcomes**	**Clinical outcomes**
Chen and Chen[15], 2016.	Retrospective cohort study.	To radiographically compare the size of the periapical lesions after the treatments of immature permanent teeth with an incomplete root development (apexification treatment or regenerative endodontic treatment).	Absence of systemic diseases, pulpal necrosis in the premolar caused by the fracture of dens evaginatus (DE), radiographic findings with an immature apex accompanied by apical lesions, and clinical follow-ups that continued for more than 1 year. Cases that involved retreatment or traditional endodontic treatments were excluded.	38 teeth (17 treated with REG and 21 treated with APIC); this comprised of 18 cases using $Ca(OH)_2$ and 3 cases using MTA.	REG group – 2.5% NaOCl. APEX group with $Ca(OH)_2$ – not included. APEX group with MTA - not included.	REG group – $Ca(OH)_2$. APEX group with $Ca(OH)_2$ - $Ca(OH)_2$. APEX group with MTA – not included.	Not included.	REG group – a blood clot + MTA. APEX group with $Ca(OH)_2$ - $Ca(OH)_2$ exchanges. APEX group with MTA – an apical sealing with MTA + gutta-percha obturation.	REG group – GIC + composite resin. APEX group with MTA – GIC + composite resin. APEX group with $Ca(OH)_2$ + gutta-percha.	12 months.	The apical lesions were radiographically quantified and scored according to the periapical index (PAI) (Ørstavik et al.[16]), with a PAI score of 1 indicating a normal periapical structure; PAI score of 2 indicating small changes in the bone structure; PAI score of 3 indicating changes in the bone structure with some mineral loss; PAI score of 4 indicating periodontitis with a well-defined radiolucent area; PAI score of 5 indicating severe periodontitis with exacerbating characteristics.	Both treatments exhibited considerable success rates and there were no statistically significant differences between the two treatments for the PAI scores in the follow-up period of 1, 3, 6, and 12 months ($p > 0.05$). However, within 3 to 6 months, the regeneration treatment showed a tendency to eliminate the apical lesions more rapidly than did the apexification treatment ($p < 0.1$). In addition, the stages of root development in the test teeth showed no significant statistical differences in the final treatment outcomes.	Not applicable.

Board 1. Characteristics of the studies that met the inclusion criteria

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					First visit			Second visit					
Author, year	**Type of study**	**Objective**	**Criteria for inclusion of patients**	**Patients** **Type of teeth**	**Irrigation solution**	**Intracanal medication**	**Time of intracanal medication**	**Techniques**	**Sealing**	**Follow-up**	**Criteria evaluated in the result**	**Radiographic outcomes**	**Clinical outcomes**
Jeerup han et al.[17], 2012	Retrospective cohort study.	To compare the outcomes of the treatments of apexification with $Ca(OH)_2$, apexification with MTA, and revascularization, in immature teeth with nonvital pulp, and to establish a standard protocol.	All of the dental charts of the patients receiving treatments on a permanent immature tooth attended the Department of Dentistry and Endodontics at the Department of Pediatric Dentistry of Mahidol University, Bangkok, Thailand, between 1997 and 2009. The teeth that met the following criteria were selected: immature permanent teeth that were to be treated by apexification with Ca (OH) 2, by apexification with MTA, or by the technique of revascularization. Presence of preoperative, postoperative, and follow-up radiography of at least 6 months after the completion of the treatment; Record the signs and the symptoms of preoperative and follow-up visits.	61 teeth (22 cases of APEX with $Ca(OH)_2$, 19 cases of APEX with MTA, and 20 cases of REG).	REG group – 2.5% NaOCl. APEX group with $Ca(OH)_2$ - not applicable. APEX group with MTA - not applicable.	REG group – antibiotic triple paste (metronidazole, ciprofloxacin, and minocycline) APEX group with $Ca(OH)_2$ - $Ca(OH)_2$. APEX group with MTA – This was performed in one session, without the use of an intracanal medication.	REG group - mean of 28.85 ± 13.08 days. APEX group with $Ca(OH)_2$ - mean of 17 ± 12.6 months. APEX group with MTA - 0 days.	REG group – a blood clot + matrix (CollaPlug®; Zimmer Dental, Carlsbad, CA, USA) was placed on the blood clot that formed below the cement-enamel junction. APEX group with $Ca(OH)_2$ – successive exchanges of $Ca(OH)_2$. APEX group – MTA plug + gutta-percha obturation.	REG group – not applicable. APEX group with $Ca(OH)_2$ - not applicable. APEX group with MTA – GIC + MTA + composite resin.	Average of 21.15 + - 30.47 months.	The outcomes of the treatments were evaluated when taking into account the survival and success rates. Survival was defined as the retention of the tooth in the arch at the time of the postoperative recall. Although many factors may have contributed to the lack of survival, this study considered only the cases of catastrophic fractures, deeming them as non-repairable. Success was defined according to the criteria as described by Friedman and Mor[18], which consists of the following categories: Healed: clinical characteristics (subjective and objective) and normal radiographic findings, without radiolucency; Healing: reduced periapical radiolucency and a normal clinical presentation; Disease: an increased or persistent radiolucency (without change), even with a normal clinical presentation, or with clinical signs or symptoms present, regardless of the radiographic presentation.	The analysis of the radiographic outcomes showed a significant effect ($p < 0.0001$) for the treatment of REG in the total width of the root in the apical third. The treatments of the immature teeth with the REG protocol produced significantly increased root width percentages (28.2%) when compared to the APEX with MTA (0.00%) treated teeth, or the APEX with $Ca(OH)_2$ treated teeth. There were no statistically significant differences between the APEX group with $Ca(OH)_2$ and the APEX group with MTA. The groups differed significantly ($p < 0.001$) in the root length. The teeth that were treated with the REG procedure showed a significantly greater percentage increase in the root length (14.9%) when compared with the teeth that were treated in the APEX group with MTA (6.1%), or in the APEX group with $Ca(OH)_2$ (0.4%) ($p < 0.01$ for both of the comparisons). In this study, the REG procedure was associated with significant increases in both the root length and in the root thickness when compared to the APEX group with $Ca(OH)_2$ and the APEX group with MTA, as well as experiencing excellent survival rates.	In terms of dental survival, the REG group presented similar survival rates of the teeth (20/20 teeth [100%]) when compared to the teeth that were treated in the APEX group with MTA (18/19 teeth [95%]). Both of these treatments produced higher survival rates ($p < 0.05$) when they were compared to the teeth treated in the APEX with $Ca(OH)_2$ group (17/22 teeth [77%]). The teeth that were treated with the REG protocol had healing rates (16/20 cases [80%]) that were similar to the treated teeth in the APEX with MTA group (13/19 [68%]) and in the APEX with $Ca(OH)_2$ group (17/22 [77%]).

Board 1. Characteristics of the studies that met the inclusion criteria

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Author, year	**Type of study**	**Objective**	**Criteria for inclusion of patients**	**Patients** Type of teeth	**Irrigation solution**	**Intracanal medication**	**Time of intracanal medication**	**Techniques**	**Sealing**	**Follow-up**	**Criteria evaluated in the result**	**Radiographic outcomes**	**Clinical outcomes**
Lin et al.[19], 2017.	Randomized clinical trial.	To compare the outcomes of the regenerative endodontic treatment with the apexification treatment in immature permanent teeth with pulp necrosis and apical periodontitis.	Patients between 8 and 16 years; pulp necrosis, defined by a negative response to the temperature test with cold and the electric pulp test; radiographic evidence of an immature tooth with a single canal and an open apex greater than 1 mm in diameter with the presence of periapical radiolucency; the tooth involved had dens evaginatus or a history of trauma. The exclusion criteria were a patient with a systemic disease, patients allergic to the antibiotics used in the study, a vital tooth, a tooth with periodontal disease, a tooth with more than 1 canal, and radiographic evidence of a root fracture.	118 teeth (38 APEX and 80 REG).	REG group – 1.5% NaOCl, physiological saline solution at 0.9% and 20 mL 17% EDTA. APEX group – 1.5% NaOCl, physiological saline solution at 0.9% and 20 mL 17% EDTA.	REG group – triple antibiotic paste (ciprofloxacin, metronidazole, and clindamycin hydrochloride). APEX group – $Ca(OH)_2$.	REG group – 3 weeks. In the cases where the patient remained in pain, this medication remained for 3 weeks, totaling 6 weeks. APEX group – 1 week.	REG group – a blood clot + an absorbable collagen barrier + MTA. APEX group – Vitapex paste (paste used for the treatment of deciduous teeth based on iodoform and $Ca(OH)_2$ with a viscous vehicle) + GIC. When an apical barrier became radiographically evident, the canal was obturated with gutta-percha.	REG group – GIC and composite resin. APEX group – composite resin.	12 months.	The treatment success was defined as the elimination of symptoms, the disappearance of apical radiolucency, an increase in root length, and\or a decrease in the apical foramen. The failure cases were determined when one of the following factors was present: the presence of clinical symptoms (pain, swelling, or fistula), no change in the size of the root or the apical foramen, the recurrence of apical periodontitis, or external root resorption.	In the REG group, the root length reached 81.16% in all of the cases, while the root thickness was 82.60%; this was while 65.21% of the cases presented an apical closure. In the APEX group, only 9 cases (26.47%) presented an increased root length, no case presented an increase in the root thickness, and 28 cases (82.35%) presented an apical closure due to the formation of a calcification barrier. When compared with the APEX group, the REG group showed a significant increase in the root length and in the thickness, with a smaller decrease in the apical foramen size. Complications, such as calcifications in the ERG group, were recorded in 26 teeth. In the cases of successful REG, discoloration and calcification were the two main complications. A total of 30 REG cases presented discoloration. This occurred mainly in the first 3 months after the treatments, while diffuse calcification was found in 26 of the REG cases, with most of them occurring in the 6-month follow-up period.	After one year of follow-up, all of the teeth survived and they were asymptomatic. The REG and APEX groups achieved comparable outcomes regarding a resolution of the symptoms and apical healing. Etiology had an impact on the REG result, and the cases of "dens evaginatus" presented a better prognosis than did the cases of trauma after the REG treatments. Complications, such as discoloration in the REG group, were recorded.

Board 1. Characteristics of the studies that met the inclusion criteria

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					First visit			Second visit					
Author, year	**Type of study**	**Objective**	**Criteria for inclusion of patients**	**Patients** Type of teeth	**Irrigation solution**	**Intracanal medication**	**Time of intracanal medication**	**Techniques**	**Sealing**	**Follow-up**	**Criteria evaluated in the result**	**Radiographic outcomes**	**Clinical outcomes**
Nagy et al.[20], 2014.	Non-randomized clinical trial.	To evaluate the regenerative potential of permanent immature young necrotic teeth after the following treatment protocols: MTA apical plug, a regenerative endodontic protocol with a blood clot, a regenerative endodontic protocol with a blood clot, and an injectable scaffold impregnated with a fibroblast growth factor.	Only patients who did not continuously use medications were included in this study.	36 anterior nonvital immature maxillary teeth with or without signs, and/or symptoms of periapical pathology (12 APEX MTA, 12 REG, and 12 REG FGF). The patients' ages ranged from 9 to 13 years.	REG group – 10 ml of 2.6% NaOCl, followed by a sterile saline solution. APEX group with MTA - 10 ml of 2.6% NaOCl, followed by a sterile saline solution. REG FGF group - 10 ml of 2.6% NaOCl, followed by a sterile saline solution.	REG group – antibiotic triple paste (metronidazole, ciprofloxacin, and doxycycline). APEX group – antibiotic triple paste (metronidazole, ciprofloxacin, and doxycycline). REG FGF group - antibiotic triple paste (metronidazole, ciprofloxacin, and doxycycline).	REG group – 3 weeks. APEX group – 3 weeks. REG FGF group – 3 weeks.	REG group – a blood clot + MTA. APEX group – MTA plug + gutta-percha obturation. FGF group – a blood clot + hydrogel + MTA.	REG group – MTA + composite resin. APEX group – composite resin. REG FGF group – MTA + composite resin.	18 months.	The clinical evaluation of pain and/or of swelling and the standardized radiographic evaluation considered an increase in root length, an increase in root thickness, a decrease in the apical diameter, and an alteration in periapical bone density. 7 patients were excluded from the study; this was due to an inadequate adherence and an inability to remember (3 from the MTA group, 2 from the REG group, and 2 from the FGF group). The recall percentages for the MTA, REG, and FGF groups were 75%, 83%, and 83%, respectively.	As for the decrease in the apical diameter, there were no significant differences between the REG and the FGF groups at 3, 6, 12, and 18 months. The MTA group was significantly different from the REG and the FGF groups at 12 and 18 months, presenting a greater apical foramen. Regarding the periapical bone density, a significant improvement was observed after 12 months of follow-up in all of the groups; however, there were no significant differences between all of the groups during the whole of the follow-up period. The REG and FGF groups showed a progressive increase in the root length and in the width, with a decrease in the apical diameter. The regenerative endodontic procedure allowed for the continuous development of the roots in the teeth with necrosis. The use of an artificial hydrogel and a growth factor of the basic fibroblast growth factor was not essential for the repair.	The clinical and radiographic examination during the follow-up period showed signs and symptoms of failure in 3 of the 29 cases (2 cases in the FGF group, and 1 case in the REG group). The success rates for the MTA, REG, and FGF groups were 100%, 90%, and 80%, respectively, in relation to the clinical criteria (pain and swelling), and the radiographic data (compression, thickness, bone density, and the apical diameter decrease). The regenerative endodontic procedure allowed for the continuous development of the roots in the teeth with necrotic pulp. The use of artificial hydrogel scaffolds and the basic fibroblast growth factor were not essential for the root repair.

Board 1. Characteristics of the studies that met the inclusion criteria

(conclusão)

					First visit			Second visit					
Author, year	**Type of study**	**Objective**	**Criteria for inclusion of patients**	**Patients** Type of teeth	**Irrigation solution**	**Intracanal medication**	**Time of intracanal medication**	**Techniques**	**Sealing**	**Follow-up**	**Criteria evaluated in the result**	**Radiographic outcomes**	**Clinical outcomes**
Silujjai and Linsuwanont[21], 2017	Retrospective cohort study.	To evaluate the clinical and the radiographic outcomes of apexification and revascularization in immature permanent nonvital teeth and to analyze the factors that influenced the outcome of the treatments.	The dental charts of the patients who attended the endodontic post-graduation clinic from 2008 to 2014. They were investigated for cases of nonvital immature permanent teeth that were treated by MTA apexification or revascularization. The cases with at least 1 year of follow-up were selected, with adequate clinical and radiographic data that was preoperative, intraoperative, and postoperative. Patients between 8 and 46 years.	43 teeth (26 cases of APEX and 17 cases of REG).	REG group – NaOCl from 1.5% to 2.5% and 17% EDTA. APEX group with MTA - 2.5% NaOCl.	REG group – antibiotic triple paste (metronidazole, ciprofloxacin, and minocycline) APEX group – $Ca(OH)_2$.	REG group – not included. APEX group – not included.	REG group – a blood clot + MTA. APEX group – MTA plug + gutta-percha obturation.	REG group – MTA + composite resin. APIC MTA group – composite resin.	It ranged from 12 to 96 months.	The radiographic evaluation included the presence, the absence, or the increase in the apical radiolucent lesion size, also with changes in the root developmental stage, according to Cvek[13]. This evaluation also included a measurement of the root development, in terms of the root length and the radicular dentine thickness. The evaluation of the clinical outcomes (modified Friedman and Mor[18]) consisted of the success or failure of functional retention. Success was defined as follows: a normal radiographic appearance, or with reduced apical radiolucency, combined with a normal clinical presentation (without any clinical signs, such as pain, and the radio without radiolucency. The failures were defined as follows: a radiolucency that emerged or persisted without change, even when the clinical presentation was normal, or the presence of signs or symptoms, even when the radiographic presentation was also normal. Functional retention was defined as follows: the clinical presentation was normal, whereas radiolucency may have been absent or present (newly emerged or persisting).	The mean percentage change in the root length increase was 9.51% in the REG group and 8.55% in the APEX with MTA group. Interestingly, the revascularization treatments showed varying degrees of root length increase that ranged from 4% to 58%. A fracture was the main cause of failure of the APIC teeth. All of the teeth in the failed REG group had signs and symptoms of persistent apical periodontitis. The REG group produced a significantly increased root width (mean = 13.75%) when compared to the APEX with MTA group (3.30%).	The success rates of the APEX and REG groups were 80.77% and 76.47%, respectively, and the functional retention rates were 82.76% and 88.24%, respectively. The APEX and REG groups provided a reliable outcome in aspects of the resolution of the disease and in tooth functional retention. The treatments did not provide predictable and satisfactory root development.

APEX Group: Group submitted to the apexification procedure
REG Group: Group submitted to the endodontic regeneration procedure

APEX with $Ca(OH)_2$ Group: Group submitted to the calcium hydroxide apexification procedure
APEX with MTA: Group submitted to the mineral trioxide aggregate apexification procedure
REG FGF Group: Group submitted to the regenerative procedure with a blood clot and an injectable scaffold
FGF Group: A blood clot and a scaffold injection (regenerative endodontic protocol)
EDTA: Ethylenediaminetetraacetic acid
NaOCl: Sodium hypochlorite
GIC: Glass ionomer cement

Type of study

Most of the studies included in this systematic review were of a retrospective cohort (n = 5)[12,14,15,17,21]. Meanwhile, the study by Lin et al.[19] was a randomized clinical trial and the study by Nagy et al.[20] was a non-randomized clinical trial.

Type of teeth

The seven studies involved a total of 312 teeth. The teeth most commonly treated were premolars (n = 139)[15,17,19], followed by central incisors (n = 99)[17,19,20]. Some studies did not report on the specific teeth covered, with a total of 74 unspecified teeth[12,14,21].

Age

In the studies analyzed, the age of the patients ranged from 06 to 46 years, with three studies not reporting on the age of the individuals[14,15,17].

Follow-up time

There was great variability in the follow-up periods between the studies included in this review. However, most of the studies had a minimum period of 12 months, except for the study by Nagy et al.[20], which was followed up in four moments, or that is, at 3, 6, 9, and 12 months. Jeeruphan et al.[17] had an average follow-up time of between 21.15 and 30.47 months. The maximum follow-up time was 96 months, according to the study by Silujjai and Linsuwanont[21]. One article did not report on the follow-up period[14].

Disinfection protocol

As for the root canal disinfection protocol for the revascularization technique, sodium hypochlorite (NaOCl) was used in concentrations ranging from 1.5 to 2.6%, except for in the study by Alobaid et al.[12] who did not report on the concentrations of NaOCl, chlorhexidine, and/or ethylenediaminetetraacetic acid

(EDTA). The study by Silujjai and Linsuwanont[21] used 17% EDTA for the NaOCl sequence, while the study by Lin et al.[19] used 17% EDTA plus 0.9% physiological saline solution. In the study by Nagy et al.[20], for both of the revascularizations, they used 10 ml of 2.6% NaOCl, followed by a sterile saline solution. The study by Bose et al.[14] only used NaOCl, not to mention the concentration.

As for the groups in which the apexification technique was chosen, four studies did not present or record the irrigating solution that was used for the disinfection procedure[12,14,15,17]. While the studies by Lin et al.[19] and Silujjai and Linsuwanont[21] used NaOCl of between 1.5% and 2.5%, and the study by Lin et al.[19] used NaOCl with 0.9% physiological saline solution, followed by 20 mL of 17% EDTA. The study by Nagy et al.[20] used 10 ml of 2.6% NaOCl, followed by sterile saline for the apexification group with MTA.

Intracanal medication

Six studies[12,14,17,19-21] used an antibiotic triple paste as an intracanal medication in their revascularization groups. However, there was a variation between them regarding the composition of the medication. The study by Bose et al.[14] did not report which drugs constituted the paste. All the remaining studies used two drugs in common, which were ciprofloxacin and metronidazole, with only the third element varying. The studies by Alobaid et al.[12], Jeeruphan et al[17] and Silujjai and Linsuwanont[21] chose minocycline, while Lin et al.[19] chose clindamycin hydrochloride and, finally, Nagy et al.[20] used doxycycline. Chen and Chen[15] chose to use $Ca(OH)_2$ in the revascularization group, not reporting their choice in the apexification group.The medication commonly chosen in the apexification groups was $Ca(OH)_2$[12,15,17,19-21].

Time of intracanal medication

The time of medication varied from 3 to 6 weeks for the revascularization groups[17,19,20], while four studies did not report on the time of medication[12,14,15,21]. In the group that chose for the apexification technique, three studies varied the

time between 1, 3, and 4 weeks, respectively[17,19,20], and four articles did not describe the time of medication that they adopted[12,14,15,21].

Revascularization technique

In the revascularization technique, all of the studies chose to induce the formation of a blood clot. However, the study by Bose et al.[14] did not inform on the technique of revascularization.

Radiographic outcomes

According to the study by Chen and Chen[15], there were no differences between the two techniques regarding the periapical index scores (PAI). This periapical index quantifies the apical lesions in radiographic images. In addition, the stages of root development did not show a statistically significant difference after both of the treatments. On the other hand, Alobaid et al.[12] concluded that there was a difference between the groups regarding the root width (1.4% ± 3.2% for apexification versus 10.2% ± 4.0% for revascularization). In this study, a total of four cases (27%) were observed out of a total of 17 cases in the revascularization group, versus one out of a total of 15 in the apexification group; thus, there was a change of 20% or more out of any of the radiographic outcomes (width, length, and the area of the apical foramen). However, none of the radiographic outcomes showed a statistically significant improvement between the groups. In addition, it was also observed that among the 17 patients who were submitted to revascularization, three patients had a pulp canal obliteration (17.6%).

The studies by Alobaid et al.[12] and Lin et al.[19] also showed that in their radiographic outcomes, a greater root length and thickness was achieved in the group that used the revascularization technique when in comparison to the apexification group. Silujjai and Linsuwanont[21] demonstrated that the revascularization technique provided significantly greater percentage changes in root width when compared to the apexification technique with MTA. Likewise, Jeeruphan et al.[17] also demonstrated that the revascularization protocol

significantly improved the root width (28.2%) when compared to the apexification protocol with MTA (0.00%) and with $Ca(OH)_2$ (1.52%). These authors also observed that the revascularization protocol significantly improved the root length (14.9%) when compared to the teeth treated with MTA (6.1%) or $Ca(OH)_2$ (0.4%) in the apexification protocol. Between the apexification groups, there were no statistically significant differences. For Bose et al.[14], the outcomes showed that regenerative endodontic treatment with antibiotic triple paste and with $Ca(OH)_2$ for the root canal disinfection produced significant improvements in the root length when compared to the apexification groups with MTA and formocresol.

The triple antibiotic paste also produced larger differences in the root wall thickness than did the $Ca(OH)_2$ or formocresol groups, and the $Ca(OH)_2$ inserted position influenced the radiographic outcomes. The study by Nagy et al.[20] was the only study in all of the groups to quantify the bone density, showing significant improvements after 12 months of follow-up. After a monitoring period of 18 months, most of the cases presented radiographic evidence of periapical healing. The revascularization groups with a blood clot that were associated with an injectable scaffolding showed a progressive increase in the length and the width of the root, but with a decrease in the diameter of the apical foramen. However, the use of an injectable scaffolding was not essential for the root repair.

Clinical success

One study did not report on the clinical success rate[14]. The study by Chen and Chen[15] reported that both treatments exhibited considerable success rates, presenting no statistically significant differences. For the studies that quantitatively measured the success rate, there was an approximation between the findings[12,17,20,21]. The success rate in the groups that were treated with the revascularization technique ranged from 76% to 100%, while in the groups that were treated with apexification, it varied between 68% and 100%. Only the studies by Lin et al.[19] and Nagy et al.[20] achieved a success rate equal to 100%.

Few studies reported on any adverse events. The study by Alobaid et al.[12] observed a higher incidence in the revascularization group (42%) when

compared to the apexification group (11%). According to the study by Chen and Chen[15], the main complication of apexification was a tooth fracture (14.3%). In three cases, two had cervical fractures and one presented an apical fracture. The mean time to the occurrence of any complication was 1.7 years after the treatment. The study by Lin et al.[19] reported that after one year of follow-up, all of the teeth were asymptomatic, and the revascularization and apexification groups achieved comparable outcomes when in relation to the resolution of the symptoms. In addition, the authors observed that the etiology of necrosis had an impact on the outcome of revascularization and that the cases of "dens evaginatus" had a better prognosis than did the cases of trauma. They also observed other complications, such as discoloration in the revascularization group.

Survival rate

The studies by Bose et al.[14], Chen and Chen[15], Nagy et al.[20], and Silujjai and Linsuwanont[21], did not report on the survival rates. The study by Lin et al.[19] reported a 100% survival rate in both of the treatment groups, while the study by Jeeruphan et al.[17] presented a rate of 100%, but only in the revascularization group. The MTA and $Ca(OH)_2$ apexification groups had 95% and 77% survival rates, respectively. However, the study by Alobaid et al.[12] presented a survival rate of 100% in the apexification group, while in the revascularization group, the survival rate was equal to 95%.

Coronal sealing

The study by Bose et al.[14] did not report on the method used for coronal sealing in the groups that adopted the revascularization technique, or in the groups that adopted the technique of apexification. The study by Jeeruphan et al.[17], which was subdivided into three groups, that is, the revascularization group, the apexification group with MTA, and the apexification group with $Ca(OH)_2$, reported only on sealing in the apexification group with MTA, in which they used glass ionomer cement (GIC) and composite resin.

The studies of Chen and Chen[15] and Lin et al.[19] also adopted GIC when it was associated with a composite resin, but only in the revascularization groups. This was while in the apexification groups, Lin et al.[19] adopted only a composite resin, whilst Chen and Chen[15] used GIC and composite resin for the apexification group with MTA and gutta-percha for the apexification group with $Ca(OH)_2$. Alobaid et al.[12] and Nagy et al.[20] used MTA when associated with composite resin for the sealing in the revascularization groups, with only a composite resin in the apexification groups. Finally, the study by Silujjai and Linsuwanont[21] used MTA and composite resin for sealing in the revascularization group, and only MTA in the apexification group.

DISCUSSION

Permanent teeth with necrotic pulp and with an incomplete root formation are traditionally treated using the method of apexification with MTA or with Ca(OH)2. Both variations of the technique, despite demonstrating substantial clinical outcomes, also present disadvantages such as: reduction of root resistance mediated by calcium hydroxide, little gain in root thickness and length, teeth more susceptible to fracture, and the requirement for excellent patient compliance due to the need for several visits scheduled for many months[17]. In this sense, regenerative endodontic procedures are an alternative to conventional treatment with scientific evidence that shows satisfactory clinical outcomes from the continuation of the rhizogenesis process and gain in dentin thickness[22]. However, this technique imposes clinical challenges and its success is related to predictors of prognosis, which must be taken into account[23-26].

Considering the studies included in this literature review, there was great variability in the patients' age, which ranged from 06 to 46 years old[12,19-21]. All of these studies showed satisfactory clinical outcomes. However, the study by Silujjai and Linsuwanont[21] was the one with the lowest success rate. It is believed that this can be explained by the age group of patients included in the study (up to 46 years old). This line of reasoning is supported by the results of the studies by Estefan et al.[27] and Cai et al.[28], which demonstrated that the closer the tooth

age to the eruption time, the greater the potential of dental pulp regeneration. In addition, regeneration procedures on teeth with larger apical diameters demonstrate greater increase in thickness, length and apical narrowing of the root[27,29]. Therefore, the size of the radiographic apical opening of the pre-treatment can be considered as a factor that contributes to the success of revascularization, with the ideal opening being greater than 1.1 mm[30]. Of the seven articles that were inserted in the systematic review, only one added apical foraminal openings larger than 1 mm in diameter as inclusion criteria[19].

As for the protocol for root canal disinfection in the cases of revascularization technique, the included studies that mentioned concentration used NaOCl as irrigant, which ranged from 1.5 to 2.6%[15,17,19-21]. Alobaid et al.[12] used NaOCl and chlorhexidine as an irrigating solution. However, they did not mention the concentrations, nor did they report whether there was a difference in the results depending on the irrigant of choice.

The disinfection of the root canal system is essential for tissue regeneration and for the procedure to be successful[31,32], so there is a need for decontamination with antimicrobial irrigators[33,34] and the use of intracanal medication[35]. According to Hoshino et al.[32], antibiotic triple paste, which is composed of minocycline, metronidazole, and ciprofloxacin, has proved efficiency in eliminating the endodontic pathogens both in vitro and in vivo. Considering the included studies, Alobaid et al.[12], Jeeruphan et al[17] and Silujjai and Linsuwanont[21] used the combination of these three antibiotics. Lin et al.[19] chose clindamycin hydrochloride, and Nagy et al.[20] used doxycycline instead of minocycline. However, all studies obtained considerable success rates, regardless of the combination chosen. Among the studies that mentioned the time of use of the intracanal medication, it varied from 3 to 6 weeks in the revascularization groups[17,19,20]. This period of intracanal medication seems to be adequate for clinical success, since Ghabraei et al.[36] demonstrated that it takes only 7 days to eliminate Enterococcus faecalis from dentinal tubules in the apical half of the root canal up to 40 microns (μ) depth.

An empty and disinfected intracanal environment does not allow for the growth of regenerated tissues, thus it requires a scaffold to support the undifferentiated cells[37,38]. Several authors have suggested the induction of a blood clot, which would act as a support for the migration of the pluripotent cells. This would result in a biological framework, rich in growth factors, allowing for favorable support, in order to provide the appropriate conditions for the differentiation and the growth of tissue into the pulp space[7,39-41]. Other methods that serve as a framework have been used and have been suggested in the literature, such as platelet-rich plasma (PRP) and platelet-rich fibrin (PRF)[42-44]. PRF is a non-thrombosed autologous fibrin mesh that serves as a reservoir for the slow release of the growth factors over a period of 7 to 14 days. PRP, on the other hand, exhibits a sudden release of the growth factors in approximately 7 to 14 hours[45]. However, there is still no consensus among authors on the best technique. According to Duggal et al.[42], no additional benefit was found when compared to the use of a blood clot. Naggy et al.[20] consolidated the findings of Duggal et al.[42] when stating that the use of an artificial hydrogel scaffold, or a scaffold impregnated with the basic fibroblast growth factor, was not essential for the repair.

The compatibility of the material of choice for the coronal plug is vital to allow for the survival of the stem cells and for the regeneration of new tissues, which are sensitive to the conditions of the intracanal environment[46]. The MTA is considered the recommended material for regenerative procedures[47]. Of the articles included in this review that mentioned the material used, MTA was the material of choice[12,15,19-21]. Although all have obtained considerable results, current scientific evidence demonstrates that Biodentine® is also an excellent alternative for this purpose. According to Aly et al.[48], in a study without significant difference in the results, Biodentine® obtained a higher clinical success rate and provided an increase in root length higher than with MTA, suggesting a greater chance of maintaining the dental element. In this context, Biodentine® should be considered for a regenerative therapy.

The proservation period and the survival rate are extremely important to determine the success of revascularization. The success rate in the groups treated with revascularization ranged from 76% to 100%[12,17,20,21]. Silujjai and Linsuwanont[21] had the lowest success rate (76.46%) and observed cases of failure up to three years after the completion of treatment with revascularization. This demonstrates that supervision shorter than this period can compromise the success rate. This can also explain the high success rate (100%) observed by Lin et al.[19] and Nagy et al.[20], whose follow-up period was 12 and 18 months, respectively. Regarding the survival rate, only three studies mentioned it[12,17,19]. In all studies, the survival rate was around 100% both in revascularization and apecification. This indicates that an adequate disinfection is probably the most important factor in the clinical success and in the survival of the dental elements submitted to these procedures, corroborating with the findings of Lui et al.[49], which show the importance of eliminating persistent microorganisms, due to their ability to remain viable in dentinal tubules, hindering regeneration and repair processes. Failure in apecification is usually caused by tooth fracture, which results in tooth extraction[21].

As already mentioned, the primary purpose of the revascularization technique is root maturation. However, in some cases, even if a complete root development is not achieved, success can be considered when there is a resolution of pain, infection, and periapical pathology, in addition to demonstrating the long-term retention of the dental element[50]. Chen and Chen[15] observed that in the revascularization technique, even with the presence of a persistent periapical lesion, continuous root development occurred. Silujjai and Linsuwanont[21] corroborated this finding since they observed two cases of revascularization that were classified as a failure, in which the periapical lesions increased. However, there was an extension of the root length and width. Other authors have also demonstrated considerably greater percentage changes in root length and width when compared with the apexification group with MTA or $Ca(OH)_2$, ensuring superiority in the revascularization technique when considering root development[14,21,51,52]. Alobaid et al.[12] observed an increase in

the length and width of the root process through the technique of revascularization. However, this was without statistically significant differences with the apexification technique, probably due to the small sampling.

Although the revascularization procedure has numerous advantages, there are also unwanted effects resulting from the technique. Alobaid et al.[12] evidenced in their results that there were three cases of intracanal calcified barrier formation and two cases of obliteration. Chen and Chen[15] also demonstrated that 17.6% of the cases that were treated with the revascularization technique, presented pulp canal obliteration. Lin et al.[19] reported on intracanal calcification, external resorption, and coronary discoloration, as being adverse effects, most of which became evident in a 6-month period.

CONCLUSION

Based on the data listed in this literature review, pulp revascularization proves to be a technique with high predictability and clinical success. Thus, the regenerative endodontic procedure can be considered as the treatment of choice for teeth with incomplete rhizogenesis and pulp necrosis. In addition, in case of failure of the revascularization procedure, which usually occurs due to the persistence of microbials in the root canal system, the apecification technique may still be the treatment of choice, thus increasing the survival rate of the dental element.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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APPENDIX 1: SEARCH STRATEGY

Population: “necrotic immature permanent teeth” OR "immature teeth" OR "immature permanent teeth" OR “necrotic immature permanent tooth” OR "immature tooth" OR "immature permanent tooth" OR "incomplete root formation" OR “immature necrotic permanent” OR “open apex”.

Intervention: “pulp revascularization” OR “apexogenesis” OR “apexogeneses” OR “regenerative endodontic technique” OR “regenerative endodontic procedures” OR “pulp revitalization” OR “regenerative endodontic therapy” OR "regenerative endodontic" OR "regenerative endodontic treatment" OR "guided tissue regeneration" OR "dental pulp regeneration" OR "regenerative endodontic procedure" OR "regenerative pulp" OR "regenerative endodontics" OR "apexification" OR “stem cell therapy” OR “pulp revitalization therapy” OR “pulp like tissue regeneration” OR “regenerative endodontic protocols”, OR "triple antibiotic past" OR " double antibiotic paste" OR "tri-antibiotic paste" OR "triple antibiotics".

Control: “apexification” OR “apexifications” OR “calcium hydroxide apexification” OR “mineral trioxide aggregate apical barrier techniques” OR "mineral trioxide aggregate apical barrier".

Outcomes: “root maturation” OR “endodontic clinical success” OR “root development” OR “endodontic success” OR “root thickness” OR “radiographic success” OR “functional development” OR “apical closure” OR “root-end development” OR “apical repair” OR “radiographic repair” OR “absence of periapical radiolucent” OR “reduction in spontaneous pain” OR “reduction in sinus

tract” OR “increase in root length” OR “root length increase” OR “root canal thickness” OR “thickening of the root” OR “clinical outcomes”.

Type of study: “retrospective studies” OR “retrospective study” OR "cohort study" OR "cohort studies" OR "prospective cohort study" OR "prospective cohort studies" OR "studies, retrospective" OR "study, retrospective" OR "studies, cohort" OR "study, cohort" OR "concurrent studies" OR "studies, concurrent" OR "concurrent study" OR "study, concurrent" OR "Closed Cohort Studies" OR "Cohort Studies, Closed" OR "Closed Cohort Study" OR "Cohort Study, Closed" OR "Study, Closed Cohort" OR "Studies, Closed Cohort" OR "Analysis, Cohort" OR "Cohort Analysis" OR "Cohort" OR "Cohort Analyses" OR "Historical Cohort Studies" OR "Cohort Study, Historical" OR "Historical Cohort Study" OR "Study, Historical Cohort" OR "Studies, Historical Cohort" OR "Cohort Studies, Historical".