

UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL
FACULDADE DE ODONTOLOGIA
PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA
DOUTORADO EM CLÍNICA ODONTOLÓGICA/ODONTOPEDIATRIA

GABRIEL FERREIRA NICOLOSO

MANEJO DE DENTES PERMANENTES COM RIZOGÊNESE
INCOMPLETA E NECROSE PULPAR

PORTO ALEGRE
2017

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Tese apresentada ao Programa de Pós-Graduação em Odontologia, Nível Doutorado, Universidade Federal do Rio Grande do Sul, como pré-requisito final para a obtenção do título de Doutor em Clínica Odontológica – Odontopediatria.

Linha de pesquisa – Biomateriais e técnicas terapêuticas em Odontologia

Orientador: Prof. Dr. Luciano Casagrande

PORTO ALEGRE
2017

CIP - Catalogação na Publicação

Nicoloso, Gabriel Ferreira
Manejo de Dentes Permanentes com Rizogênese
Incompleta e Necrose Pulpar / Gabriel Ferreira
Nicoloso. -- 2017.
48 f.

Orientador: Luciano Casagrande.

Tese (Doutorado) -- Universidade Federal do Rio
Grande do Sul, Faculdade de Odontologia, Programa de
Pós-Graduação em Odontologia, Porto Alegre, BR-RS,
2017.

1. Dentes permanentes com rizogenese incompleta.
2. Revascularizacao da polpa. 3. Endodontia
regenerativa. 4. Apicificacao. I. Casagrande,
Luciano, orient. II. Título.

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INCOMPLETA E NECROSE PULPAR

Tese apresentada para obtenção do título de doutor no Programa de Pós-Graduação em Odontologia da Universidade Federal do Rio Grande do Sul e avaliada pela banca examinadora formada por:

Porto Alegre, 25 de Agosto de 2017

Dr. Luciano Casagrande (Orientador)

Dra. Patrícia Maria Poli Kopper Mora

Dr. Carlos Alexandre Souza Bier

Dra. Stefanie Bressan Werle

Dra. Fabiana Soares Grecca Vilella (Suplente)

AGRADECIMENTOS

Aos coautores do artigo, Tatiane da Silva Dal Pizzol, Francisco Montagner, Roberta Kochenborger Scarparo e Jonas de Almeida Rodrigues, pela parceria para desenvolvimento do trabalho.

À Gabriela Goldenfum, pela disponibilidade e parceria durante a elaboração do artigo.

Aos professores da disciplina de odontopediatria, pela amizade e acolhimento durante o período de doutorado.

Aos meus colegas de mestrado e doutorado, pela amizade durante todo período.

À Universidade Federal do Rio Grande do Sul e demais professores da instituição, pela qualidade de ensino proporcionada durante todo período.

Aos Coordenadores do Programa de Pós-Graduação, Cassiano Kuchenbecker Rösing e Fabrício Mezzomo Collares, pelo apoio recebido e pela condução de um programa de excelência.

Ao Professor Dr. Fernando Borba de Araújo, pela amizade, carinho e ensinamentos desde a especialização e durante todo período de doutorado.

Ao Professor Dr. Luciano Casagrande, pela amizade, conselhos, apoio, ensinamentos e exemplo de profissionalismo, educação e ética.

Aos meus amigos, por me apoiarem em todos os momentos.

À minha família, pelo apoio, carinho e amor incondicional.

À Deus, pela vida.

RESUMO

A perda da vitalidade pulpar, em consequência de injúrias traumáticas, lesões cáries profundas e malformações dentárias, pode interromper o desenvolvimento radicular em dentes permanentes jovens. O tratamento endodôntico em dentes com rizogênese incompleta constitui-se num desafio ao clínico para a realização de tratamentos convencionais, devido principalmente à dificuldade de debridamento das paredes dentinárias e do adequado selamento apical. Além disso, em função das paredes dentinárias delgadas e uma proporção coroa-raiz inadequada, a ocorrência de fraturas no trans e pós-operatório não é um evento raro. Existem diferentes estratégias terapêuticas para o manejo destes dentes com rizogênese incompleta, incluindo os procedimentos de apicificação e revascularização da polpa. O objetivo desta tese foi revisar sistematicamente a literatura para avaliar a efetividade dos procedimentos de apicificação e revascularização da polpa em relação aos desfechos clínicos, radiográficos e de retenção dentária. Dois revisores de maneira independente revisaram a literatura e avaliaram os artigos. A busca foi realizada na literatura via PubMed/MEDLINE e Embase até junho de 2017 para selecionar estudos de caso-controle e coorte. Um total 231 artigos foram localizados nas bases de dados, dos quais 3 permaneceram após a aplicação dos critérios de elegibilidade. Após a seleção dos artigos, os dados de cada estudo foram coletados e o risco de viés avaliado. Foram obtidas estimativas de efeito comparando o sucesso clínico e radiográfico e retenção dentária entre o *plug* apical de agregado de trióxido mineral (MTA) versus revascularização da polpa (BC) e hidróxido de cálcio (CH). As duas meta-análises comparando tanto o MTA vs BC para os desfechos clínicos e radiográficos ($Z=0.164$, $p=0.869$, $RR=1.010$, $95\%CI:0.895-1.140$, $I=0\%$) e retenção dentária ($Z=0.855$, $p=0.393$, $RR=1.050$, $95\%CI:0.939-1.173$, $I=0\%$) ou MTA vs CH para os desfechos clínicos e radiográficos e retenção dentária ($Z=-1.596$, $p=0.110$, $RR=0.816$, $95\%CI:0.635-1.048$, $I=0\%$) não demonstraram diferenças estatisticamente significativas. Todos estudos incluídos na revisão sistemática foram considerados de alta qualidade metodológica. Em conclusão, a técnica de revascularização da polpa, por possibilitar o desenvolvimento radicular adicional, deve ser a primeira opção de tratamento em dentes permanentes com rizogênese incompleta que apresentem proporção coroa-raiz inadequada, entretanto, o *plug* apical de MTA parece apresentar resultados mais fidedignos em relação ao sucesso em geral, e assim, nos casos de dentes permanentes que apresentem proporção coroa-raiz satisfatória, esta técnica de ser a primeira opção de tratamento.

Palavras-chave: Dentes permanentes com rizogênese incompleta, Revascularização da polpa, Endodontia regenerativa, Apicificação

ABSTRACT

The loss of pulp vitality, as a consequence of traumatic injuries, deep carious lesions and dental malformations, may interrupt the root development in young permanent teeth. The endodontic treatment in immature teeth constitutes a challenge to the practitioner to perform conventional treatments, mainly due to difficulty of dentinal walls debridement and adequate apical sealing. In addition, due to the thin dentinal walls and inadequate crown-root proportion, occurrence of trans and postoperative fractures is not a rare event. There are different therapeutic strategies to manage these immature teeth including apexification and pulp revascularization procedures. The aim of this thesis was to systematically review the literature to evaluate the effectiveness of apexification and pulp revascularization procedures regarding the clinical, radiographic and tooth retention outcomes. Two reviewers independently performed the screening and evaluation of articles. The literature was screened via PubMed/MEDLINE and Embase databases until June 2017 to select case-control and cohort studies. A total of 231 articles were retrieved from the databases, in which only 3 remained after the eligibility criteria. After the selection of the articles, the data of each study was extracted and bias risk assessed. Pooled-effect estimates were obtained comparing the clinical and radiographic success and retention rates among the mineral trioxide aggregate (MTA) apical plug vs pulp revascularization (BC) and calcium hydroxide (CH). The two meta-analysis comparing either MTA vs BC for clinical and radiographic outcomes ($Z=0.164$, $p=0.869$, $RR=1.010$, $95\%CI:0.895-1.140$, $I=0\%$) and tooth retention rates ($Z=0.855$, $p=0.393$, $RR=1.050$, $95\%CI:0.939-1.173$, $I=0\%$) or MTA vs CH for clinical and radiographic outcomes and tooth retention rates ($Z=-1.596$, $p=0.110$, $RR=0.816$, $95\%CI:0.635-1.048$, $I=0\%$) showed no statistically significant differences. All studies included in the systematic review were classified as high quality. In conclusion, the revascularization treatment, as it allows additional root development may be the first treatment option in immature necrotic permanent teeth that have inadequate crown-root ratio, however, the MTA apical plug seems to provide more predictable outcomes regarding the overall success, and thus, in cases of permanent teeth having adequate crown-root proportion, it should be the first treatment option.

Keywords: Immature permanent teeth, Pulp revascularization, Regenerative endodontic treatment, Apexification

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INTRODUÇÃO

Lesões traumáticas extensas ou cáries profundas podem resultar em danos a polpa dental, levando a pulpite irreversível ou necrose pulpar. Em dentes permanentes imaturos com necrose pulpar, o processo de formação radicular é interrompido, deixando paredes dentinárias frágeis e ápices sem a completa formação, o que pode resultar, nos casos severos, em fraturas radiculares e necessidade de extrações dentárias (CVEK, 1992; RAFTER, 2005).

Devido às particularidades anatômicas dos dentes com rizogênese incompleta e a dificuldade de um preciso diagnóstico das condições pulpares, a terapia endodôntica representa um desafio ao cirurgião-dentista. Tratamentos endodônticos com o objetivo de induzir a formação de uma barreira apical de tecido mineralizado (apicificação) ou a continuação da formação radicular (revascularização da polpa) estão indicados em dentes necróticos imaturos (RAFTER, 2005; NAGY et al., 2014). As alternativas de tratamento, atualmente, resumem-se em: apicificação através de trocas de hidróxido de cálcio ou a técnica do tampão apical de MTA; e revascularização da polpa através de terapias endodônticas de revascularização/revitalização com a técnica da indução do coágulo ou a utilização de *scaffolds* à base de concentrados de plaqueta (PRP) ou fibrina (PRF).

As técnicas de apicificação em dentes com rizogênese incompleta e necrose pulpar constituem-se em opções não cirúrgicas para o tratamento endodôntico. Estas consistem no preparo do canal radicular, desinfecção através de soluções irrigadoras, medicação intracanal, e obturação final do conduto com cones de guta percha. A apicificação pode ser realizada através de trocas periódicas de Hidróxido de Cálcio, com intuito de fechamento do ápice prévio para posterior obturação, ou através da técnica do tampão apical de MTA que permite a obturação imediata (DAMLE et al., 2012; BONTE et al., 2015).

A apicificação com o uso de hidróxido de cálcio possui algumas desvantagens, como a variabilidade no tempo de tratamento, sendo necessárias múltiplas visitas durante um período relativamente longo (média de doze meses), onde são feitas trocas da medicação e frequentes acessos ao canal, tornando ainda mais frágeis as paredes do conduto radicular e a coroa do dente, o que aumenta o risco de fratura (ANDREASEN et al., 2002; BATUR et al., 2013). Uma alternativa para apicificação tradicional é a colocação de uma barreira artificial no ápice radicular, de maneira a evitar o extravasamento do material de preenchimento durante a obturação. Atualmente, o material de escolha utilizado como plug apical é o Agregado de

Trióxido Mineral (MTA), devido a sua alta capacidade de vedação e biocompatibilidade. Esta técnica apresenta algumas vantagens em relação à apicificação tradicional envolvendo trocas de hidróxido de cálcio: menor tempo de procedimento, possibilidade de obturação radicular na mesma sessão em que o MTA é colocado no terço apical do canal radicular e diminuição do risco de fraturas radiculares (SIMON et al., 2007; BONTE et al., 2015). Entretanto, nenhuma das técnicas apresenta a possibilidade de promover a continuação do desenvolvimento radicular adicional (SHABAHANG; TORABINEJAD, 2000; JEERUPHAN et al., 2012).

Técnicas alternativas à apicificação tem sido propostas (GALLER et al., 2016). Segundo a Associação Americana de Endodontia (AMERICAN ASSOCIATION OF ENDODONTICS, 2017), a endodontia regenerativa ou revascularização da polpa é a primeira opção de tratamento em dentes com rizogênese incompleta e necrose pulpar que possuem um desenvolvimento radicular incompleto e fechamento apical incompleto, devido à possibilidade de continuação do desenvolvimento radicular, o que promove o fortalecimento das raízes nestes dentes. Esta técnica consiste basicamente na desinfecção do canal radicular através de soluções irrigadoras e medicação intracanal seguida da indução de coágulo com ou sem a utilização adicional (ou de maneira independente) de *scaffolds* à base de concentrados de plaqueta (PRP) ou fibrina (PRF) e, posterior restauração com resina composta (CONDE et al., 2016).

Independentemente da técnica a ser realizada no tratamento de dentes permanentes com rizogênese incompleta e necrose pulpar, os objetivos devem ser a remissão de sinais e sintomas clínicos e reparo ósseo periapical. Quando da realização das técnicas de revascularização da polpa, os objetivos secundários e terciários constituem-se no desenvolvimento radicular adicional (aumento de espessura e comprimento da raiz) e o restabelecimento da vitalidade pulpar, respectivamente (AMERICAN ASSOCIATION OF ENDODONTICS, 2017). Entretanto, além destes objetivos durante a realização de ambas as técnicas (apicificação e revascularização), e principalmente no tratamento de pacientes jovens, a retenção destes dentes deve ser considerada um desfecho importante, devido a impossibilidade de realização de implantes dentários em pacientes menores de 18 anos, no caso de insucesso dos tratamentos propostos.

Ensaio clínicos randomizados e estudos de coorte têm demonstrado altas taxas de sucesso clínico e radiográfico para as técnicas de apicificação e revascularização (PRADHAN et al., 2006; EL MELIGY; AVERY, 2006; DAMLE et al., 2012; JEERUPHAN et al., 2012; ALOBAID *et al.* 2014; NAGY et al., 2014; BEZGIN et al., 2015; BONTE et al., 2015;

NARANG et al., 2015; SILUJJAI & LINSUWANONT, 2017). Entretanto, este número elevado de artigos publicados, a falta de acesso e tempo disponível de clínicos gerais e pesquisadores pode dificultar a implementação da melhor evidência na prática clínica (GRIMES;SCHULZ, 2002). Desta maneira, quando existe um número elevado de artigos publicados em um determinado tema sem consenso na literatura sobre o melhor tratamento, revisões sistemáticas são de extrema importância para compilar os resultados dos artigos publicados e estabelecer um guia prático da melhor evidência disponível no momento. Recentemente, uma revisão sistemática de ensaios clínicos randomizados (NICOLOSO et al., 2017) concluiu que a técnica de apicificação através do tampão apical de MTA parece promover melhores taxas de sucesso clínico e radiográfico em comparação as demais técnicas endodônticas para o manejo de dentes permanentes com rizogênese incompleta e necrose pulpar. Entretanto, a maioria dos artigos incluídos nesta revisão foram considerados de alto e moderado risco de viés, avaliaram um pequeno número de pacientes durante um período curto de acompanhamento, e não avaliaram a retenção dentária como desfecho clínico. Vale ressaltar que embora, ensaios clínicos randomizados produzam um alto nível de evidência para a prática clínica em relação à superioridade de um tratamento em relação ao outro, estas situações controladas, muitas vezes, acabam limitando a extrapolação dos resultados para a população em geral (VAN DE SANDE et al., 2016). Portanto, além de revisões sistemáticas de ensaios clínicos randomizados, que são de extrema importância para determinar a eficácia de um determinado tratamento em comparação aos demais, a realização de revisões sistemáticas de estudos observacionais, principalmente de estudos de coorte, são necessárias para determinar a efetividade dos tratamentos em situações que permitem uma extrapolação mais fidedigna.

Desta maneira, justifica-se a realização de uma revisão sistemática com estudos observacionais (estudos de caso-controle e coorte), que avaliem um número maior de pacientes em um período maior de acompanhamento em situações não controladas, para determinar a efetividade dos tratamentos endodônticos em dentes permanentes com rizogênese incompleta e necrose pulpar. Portanto, o objetivo desta tese foi revisar sistematicamente a literatura para avaliar a efetividade dos procedimentos de apicificação e revascularização da polpa em relação aos desfechos clínicos, radiográficos e retenção dentária.

ARTIGO

Artigo formatado nas normas de *International Journal of Paediatric Dentistry*

Fator de Impacto – 1.532

Qualis Odontologia – A1

Managing immature necrotic permanent teeth based on the effectiveness of endodontic treatments: a meta-analysis of observational studies

Running title: Managing immature necrotic teeth

Gabriel Ferreira Nicoloso, DDS, MS^a, gfnicoloso@gmail.com

Gabriela Goldenfum, DDS^a gabigolden@hotmail.com

Tatiane da Silva Dal Pizzol, MS, PhD^b, tatiane.silva@ufrgs.br

Francisco Montagner, DDS, MS, PhD^c, francisco.montagner@ufrgs.br

Roberta Kochenborger Scarparo, DDS, MS, PhD^c, roberta.scarparo@ufrgs.br

Jonas de Almeida Rodrigues DDS, MS, PhD^a jorodrigues@ufrgs.br

Luciano Casagrande, DDS, MS, PhD^a, luciano.casagrande@ufrgs.br

^aSchool of Dentistry, Post-Graduate Program in Pediatric Dentistry, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre - RS, Brazil.

^bFaculty of Medicine, Post-Graduate Program in Epidemiology, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre - RS, Brazil.

^cFaculty of Medicine, Post-Graduate Program in Endodontics, Federal University of Rio Grande do Sul (UFRGS), Porto Alegre - RS, Brazil.

Keywords: Immature permanent teeth, Pulp revascularization, Regenerative endodontic treatment, Apexification

Corresponding author:

Luciano Casagrande

Department of Oral Surgery and Orthopedics, Pediatric Dentistry, Federal University of Rio Grande do Sul

Ramiro Barcelos 2492, Bom Fim, Porto Alegre, RS 90.035-003, Brazil

Telephone: 0XX(51) 3308 5493

E-mail: luciano.casagrande@ufrgs.br; luciano.casagrande@gmail.com

Abstract

Background: Immature necrotic permanent teeth due to fragile dentine walls and inadequate crown-root proportion are difficult to manage with convectional endodontic treatments.

Aim: We aimed to systematically review the literature to assess whether pulp revascularization procedures are more effective than apexification ones regarding the clinical, radiographic and tooth retention outcomes.

Design: The literature was screened via PubMed/MEDLINE and Embase databases until June 2017 to select case-control and cohort studies that compared pulp revascularization and apexification based on the clinical, radiographic and tooth retention outcomes. Two reviewers independently performed screening and evaluation of articles. A total of 231 articles were retrieved from the databases, in which only 4 were selected for full-text analysis. After the exclusion criteria, 3 studies remained on quantitative and qualitative analysis. Pooled-effect estimates were obtained comparing clinical and remission of periapical radiolucency outcomes and tooth retention rates among MTA vs calcium hydroxide (CH) and pulp revascularization (BC).

Results: The two meta-analysis comparing either MTA vs BC for clinical and remission of periapical radiolucency outcomes ($Z=0.164$, $p=0.869$, $RR=1.010$, $95\%CI:0.895-1.140$, $I=0\%$) and tooth retention rates ($Z=0.855$, $p=0.393$, $RR=1.050$, $95\%CI:0.939-1.173$, $I=0\%$) or MTA vs CH for clinical and remission of periapical radiolucency outcomes and tooth retention rates ($Z=-1.596$, $p=0.110$, $RR=0.816$, $95\%CI:0.635-1.048$, $I=0\%$) showed no statistically significant differences. All studies were classified as high quality.

Conclusions: More studies are desirable to evaluate whether additional root maturation may strengthen the roots, and therefore, increase tooth retention over time. We observed that pulp

revascularization procedures in immature necrotic permanent teeth are equally effective to MTA apexification, providing an advantage of additional root maturation.

Prospero Register: CRD42017070058

Introduction

Pulp necrosis in children or adolescents may arrest tooth development, resulting in inadequate crown-root proportion, wide-open apex and thin dental walls^{1,2}. These features make endodontic treatment difficult, and the protocols for cleaning, shaping and filling root canals must be adapted^{3,4}. Traditionally, the endodontic treatment strategy for immature teeth with pulp necrosis is the apexification using long-term intracanal medication with calcium hydroxide, aiming to stimulate the formation of an apical calcified barrier. Placement of mineral trioxide aggregate apical plugs may also be performed, reducing the number of treatment sessions. These techniques are not likely to favor root development, keeping fragile dentine walls and inadequate crown-root proportion^{3,5}. Depending on the stage of root development, treatment duration, or even delay of seeking treatment, these immature teeth become prone to fracture, eventually leading to extraction⁵⁻⁷, thus affecting function, esthetic and self-esteem in young patients.

More recently, other clinical approaches, named as “regenerative endodontics”, “pulp revascularization” or “revitalization” procedures have been suggested, concerning the possibility of inducing root development, which is expected to improve the strength of the root, and thus tooth retention. The European Society of Endodontology (ESE) statement indicates that “pulp revitalization” is an alternative to apexification in properly selected cases, since a growing body of evidence shows the clinical feasibility of this approach⁸. According to the American Association of Endodontics (AAE)⁹, these protocols are the first treatment option for immature necrotic permanent teeth that has incomplete root development (length) as well as incomplete apical closure. It consists basically of root canal chemical disinfection with both irrigating solution and intracanal medication, followed by blood clot induction and placement of restoration¹⁰. The other available alternatives, i.e calcium hydroxide apexification and MTA

apexification, would be indicated especially when those immature teeth present more developed roots^{11,12}.

Regardless of the treatment performed, its success should be the remission of clinical signs and symptoms, resolution of periapical radiolucency¹² and tooth functional retention, which is especially important when dealing with young patients. Tooth retention is important because before the age of eighteen, these young patients may not choose to have dental implants if needed as a proper maxillary and mandibular bone development is necessary. Hence, as long as these teeth remain asymptomatic, regardless of periapical radiolucency, they should be considered successful.

Recently, a systematic review of randomized clinical trials¹² reported that MTA apexification seems to produce overall better clinical and radiographic (resolution of periapical radiolucency) outcomes in comparison to other endodontic treatments. However, most of the included articles were considered of moderate and high bias risk, evaluated a low number of patients over a short period of time and did not assess tooth retention. In general, although clinical trials provide strong evidence on decision making in regard to different treatments, these controlled settings provide high internal validity but low external validity, which make difficult extrapolation of results to daily clinical practice¹³. On the other hand, case-control and cohort studies (observational studies), regardless its inherent limitations, provide scenarios frequently observed in most practitioners' clinics. Therefore, it is pertinent to systematically screen the literature with observational studies to draw some conclusions on the effectiveness of these endodontic treatments in immature necrotic permanent teeth that could guide practitioners' decisions.

To date, there is no systematic review including a meta-analysis that screened the literature for case-control and cohort studies based on clinical and radiographic outcomes and

tooth retention of immature necrotic permanent teeth. Therefore, we aimed to systematically review the literature for observational studies to assess whether pulp revascularization procedures in immature necrotic permanent teeth are more effective than apexification ones regarding the clinical and radiographic outcomes and tooth retention rates.

Materials and Methods

Protocol and registration

This systematic review was reported according to the MOOSE (Meta-Analysis of Observational Studies in Epidemiology) study guideline¹⁴, which were registered at the International Prospective Register of Systematic Review (PROSPERO) database (CRD42017070058).

Focused PICO/PECO question

The following focused question was developed in accordance with the recognized Patient, Intervention/Exposition, Comparison and Outcome (PICO/PECO) format: “Are revascularization procedures more effective than apexification ones regarding the clinical, radiographic and tooth retention outcomes in the management of immature necrotic permanent teeth?”, where the Population were patients with immature necrotic permanent teeth; the Intervention/Exposition was pulp revascularization procedures; the Comparison was apexification procedures; and the Outcomes were clinical and radiographic success and functional retention of treated teeth.

Search strategy

A comprehensive literature search was conducted on MEDLINE via PubMed database up to June 16th, 2017. The following search strategy were used to explored the MEDLINE via PubMed database: ((((((((((immature teeth) OR immature tooth) OR immature dentition) OR

immature permanent teeth) OR immature permanent tooth) OR immature permanent dentition) OR young permanent teeth) OR young permanent tooth) OR young permanent dentition)) AND (((((((((((pulp revascularization) OR pulpal regeneration) OR pulp revitalization) OR root canal revascularization) OR root maturation) OR regenerative endodontic*) OR regenerative endodontic therapy) OR regenerative endodontic treatment*) OR regenerative endodontic procedure*) OR blood clot) OR platelet-rich fibrin) OR platelet-rich plasma)) AND (((((((((((calcified barrier) OR apical closure) OR root end formation) OR root apex closure) OR apical plug) OR MTA plug) OR apexification[MeSH Terms]) OR apexification*) OR mineral trioxide aggregate) OR calcium hydroxide).

Also, a search was conducted on Embase up to June 16th, 2017. On this database the following search strategy were used: 'immature teeth' OR 'immature tooth' OR 'immature dentition' OR 'immature permanent teeth' OR 'immature permanent tooth' OR 'immature permanent dentition' OR 'young permanent teeth' OR 'young permanent tooth' OR 'young permanent dentition' AND ('pulp revascularization' OR 'pulpal regeneration' OR 'pulp revitalization' OR 'root canal revascularization' OR 'root maturation' OR 'regenerative endodontic*' OR 'regenerative endodontic therapy' OR 'regenerative endodontic treatment*' OR 'regenerative endodontic procedure*' OR 'blood clot'/exp OR 'blood clot' OR 'platelet-rich fibrin' OR 'platelet-rich plasma') AND ('calcified barrier' OR 'apical closure' OR 'root end formation' OR 'root apex closure' OR 'apical plug' OR 'mta plug' OR 'apexification'/de OR apexification* OR 'mineral trioxide aggregate'/exp OR 'calcium hydroxide'/exp OR 'calasept' OR 'calcium hydroxide' OR 'calxyl' OR 'hypocal' OR 'limewater' OR 'pulpdent'. The results of searches of these two databases were cross-checked to locate and eliminate duplicates.

Eligibility criteria

The inclusion criteria of this review were: (1) Study design: observational studies (case-control and cohort design); (2) Participants: patients with immature necrotic permanent teeth; (3) Intervention: revascularization procedures; (4) Comparison: apexification procedures; (5) Outcomes: have assessed success by clinical and radiographic outcomes and functional retention of treated teeth; and (6) articles published in English.

On the other hand, articles were excluded based on the following criteria: (1) teeth presenting pulpitis and vital pulp therapy; (2) teeth with previous treatment to necrosis; (3) follow-up time of less than three months; (4) clinical protocol for each proposed treatment incomplete, e.g., in CH apexification, should have performed the root canal obturation with gutta-percha after the calcified barrier induction; or, in pulp revascularization cases, should have performed blood clot induction or used platelet rich plasma (PRP) or platelet rich fibrin (PRF) followed by MTA coronal seal and placement of restoration.

Study selection and data collection

Two reviewers (G.F.N. and G.G.) independently screened all of the titles and abstracts retrieved by the electronic search. Perfect agreement between reviewers in the study selection process was obtained, with a kappa score of 1.0. Afterwards, the full-text articles of the previous included studies were independently assessed by the same authors to apply the previous established exclusion criteria and those that fulfilled all the criteria were included in the qualitative and quantitative synthesis. Additionally, all references of the included studies were manually screened for potentially relevant articles. Any possible discrepancies encountered during this process, were resolved between the reviewers, and if a disagreement still persisted, the judgment of a third reviewer (L.C.) was considered decisive.

Data regarding the included studies were also independently extracted by the reviewers (G.F.N. and G.G.) based on a previously defined protocol in a specific form in the Microsoft

Office Excel 2007 software (Microsoft Corporation, Redmond, WA, USA). The data extracted included: type of study, year of publication, country, type of teeth (anterior or posterior teeth), number of patients and treated teeth, age of patients, etiology and diagnosis of pulp necrosis, presence of periapical lesion at the beginning, type of intervention, type of irrigant solution and intracanal medication, number of successful cases (clinically, radiographically and tooth retention rates), increase in root length and width, calcified barrier formation, crown discoloration, reasons for failures and follow-up of observed cases.

Outcome measures

The primary outcomes measures were the clinical and remission of periapical radiolucency (primary radiographic outcome) outcomes and tooth retention rates of different endodontic treatments employed during the management of immature necrotic permanent teeth. Secondary outcome of interest was based on root maturation (secondary radiographic outcome) – increase in root length and width during the follow-up measurements, formation of a calcified barrier and crown discoloration (crown staining). To the clinical and remission of periapical radiolucency as well as the tooth retention rate, the success or failure was considered in a dichotomous way, based on the author's criteria previously defined in each study.

Quality assessment of the included studies

Two blinded reviewers (G.F.N. and G.G.) independently assessed the methodological quality of the included studies according to the Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses¹⁵, which was adapted for the design of the included studies. It is based on a 'star system', in which a study is judged on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of either the exposure or outcome of interest for case-control or cohort studies, respectively. We considered the threshold between “high” and “low” quality studies as being

seven stars, i.e., if and study received seven or more stars it was considered to be of “high” quality. There was no disagreement between the reviewers in this process.

Statistical methods for the meta-analysis and assessment of heterogeneity

The meta-analysis was conducted using Comprehensive Meta-Analysis Software version 3.3 (Biostat, Englewood, NJ) using random-effect models and presented as forest plot with 95% CI. Pooled-effect estimates were obtained by comparing the failure rate between groups. A *p-value* <0.05 was considered statistically significant (Z test). Statistical heterogeneity of the treatment effect (experimental endodontic treatment vs control) among studies was assessed using Cochran’s Q test, with a threshold *p-value* of 0.1, and the inconsistency I^2 test, in which values between 25-50% were considered indicative of low heterogeneity, between 50-75% moderate and greater than 75% of high heterogeneity.

Results

Study selection

Study selection flow diagram is shown in Figure 1. The literature search conducted yield 231 articles. After duplicates were removed (11 coincided from either PubMed/MEDLINE or Embase), 220 studies remained in which we applied the inclusion criteria upon titles and abstracts yielding a number of 4 articles. Afterwards, the references of these articles were manually searched from potential relevant articles, but none were identified. Then, the full-text articles were assessed and the exclusion criteria were applied upon these articles. One study¹⁶ was excluded because the clinical proposed treatment protocol was incomplete, i.e., most of revascularization cases remained with intracanal medication for outcome evaluation. Therefore, a total of 3 studies^{1,2,6} were included in the quantitative and qualitative analysis.

Studies characteristics

Characteristics of each included study are summarized in Table 1. All of the included studies were retrospective cohorts. Publication year ranged from 2012 to 2017. Two of the three included studies were carried out in Thailand^{1,2} and one in the United States⁶. Either anterior or posterior teeth were assessed for the outcomes of interest, with or without periapical lesions in the beginning of the study. Trauma was main cause of endodontic treatment in immature necrotic permanent teeth, followed by dens invaginatus and caries. The diagnosis of pulp necrosis and outcome assessment were made by clinical and radiographic evaluation in all of the included studies. A total of 135 teeth were evaluated in the cohort studies with a follow-up (mean) ranging from 1 to 4 years.

All revascularization cases among included studies were performed with a rubber dam isolation. The authors did not state clearly if either calcium hydroxide apexification or MTA apexification were performed under rubber dam isolation or not, with the exception of one study² that reported all endodontic treatments being performed using rubber dam. The usual irrigating solution used for revascularization cases was sodium hypochlorite (various concentrations), followed by EDTA in some cases⁶, or in all cases². Only one study² stated clearly that 2.5% sodium hypochlorite was used for MTA apexification. One study¹ used triple antibiotic paste in all revascularization cases; another study⁶ used triple antibiotic paste, double antibiotic paste or calcium hydroxide as intracanal medicament; and Silujjai & Linsuwanont² used either triple antibiotic paste or calcium hydroxide.

Considering the clinical remission of periapical radiolucency outcomes, revascularization with blood clot induction was statistically similar to MTA apexification in all included studies, and calcium hydroxide apexification was either similar or inferior to revascularization and MTA apexification according to Jeeruphan *et al.*¹ and Alobaid *et al.*⁶, respectively.

None of the included studies assessed the formation of a calcified barrier as an outcome of interest. Alobaid *et al.*⁶ was the only study that reported crown discoloration (crown staining) as an adverse event of revascularization procedures. The authors⁶ observed that 2 out of 19 teeth (10.5%) treated by revascularization presented crown discoloration, whereas none of the teeth treated with apexification procedures had this adverse event. The increase in root length and width was statistically significant only in one study¹ favoring revascularization cases. Alobaid *et al.*⁶ did not find a statistically significant difference amongst treatment strategies and Silujjai & Linsuwanont² only observed a statistically significant increase in root width for revascularization compared to MTA apexification. On the other hand, when tooth retention was the outcome of interest, only one study reported¹ inferior rates for calcium hydroxide apexification in comparison to revascularization or MTA apexification.

Regarding the reasons for failures, two studies^{1,2} reported root or tooth fracture as the main cause of failure in apexification cases. Two studies^{2,6} stated that for revascularization cases the most common reasons for failure was reinfection or persistent infection.

Quality assessment of included studies

The results of the quality assessment using the Newcastle-Ottawa Scale (NOS) for verifying the quality of nonrandomized studies are presented in Table 2. The scores were seven in one study⁶ and eight in two studies^{1,2}. Thus, all studies included in this systematic review presented high quality. In all studies the patients were reviewed retrospectively for inclusion, which may account for some risk of bias in case selection. Alobaid *et al.*⁶ reported that the stage of root development was different from revascularization and apexification cases, which might contribute for some differences in the outcomes, especially in the quantitative analysis, such as increase in root width and length, and then received only one star in the ‘comparability domain’.

Meta-analysis

The comparisons were performed considering MTA as the control treatment, because in a previous published systematic review, it exhibited overall better clinical and radiographic (remission of periapical radiolucency) success¹². Two independent meta-analysis were performed to evaluate whether calcium hydroxide (CH) apexification or pulp revascularization (blood clot (BC) induction) present either better success rates (clinical success and remission of periapical radiolucency) or tooth retention rates in comparison to MTA apexification.

Regarding the first meta-analysis (Figure 2) that compared MTA apexification to BC revascularization in regard to the clinical and remission of periapical radiolucency outcomes ($Z = 0.164$, $p = 0.869$, $RR = 1.010$, 95% CI: 0.895 to 1.140, $I = 0\%$) and retention rates ($Z = 0.855$, $p = 0.393$, $RR = 1.050$, 95% CI: 0.939 to 1.173, $I = 0\%$), there was no statistically significant difference between the groups.

The second meta-analysis (Figure 3) that compared MTA apexification to CH apexification regarding the clinical and remission of periapical radiolucency outcomes and retention rates ($Z = -1.596$, $p = 0.110$, $RR = 0.816$, 95% CI: 0.635 to 1.048, $I = 0\%$), there was no statistically significant difference between the groups. In this meta-analysis both clinical and remission of periapical radiolucency outcomes and retention rates were the same, as the number of teeth considered as successful were similar in both analysis. Although Alobaid *et al.*⁶ reported success and tooth retention rates for CH and MTA apexification, it did not effectively affect the risk ratio calculation, as a pre-requisite to be included in the statistical analysis is to have reported, at least, one failure between treated groups.

Discussion

Summary of findings

We observed that pulp revascularization procedures in immature necrotic permanent teeth are equally effective to MTA apexification regarding the clinical and remission of

periapical radiolucency outcomes and tooth retention rates. According to our meta-analysis there is no statically significant difference between MTA apexification and pulp revascularization. However, based on the individual results of included studies in this systematic review, there is a tendency that the MTA apexification provides a greater chance of clinical success and periapical healing in immature necrotic permanent teeth.

Comparison of results with previous studies

To our knowledge, this is the first systematic review including a meta-analysis that screened the literature regarding the clinical and radiographic outcomes and tooth retention rates for immature necrotic permanent teeth in order to assess whether there is one endodontic procedure that is more effective in nonrandomized studies (cohort and case-control design), which would make the extrapolations more reliable to general practitioners. Kahler *et al.*¹⁷ screened the literature for nonrandomized studies assessing clinical and radiographic successes among endodontic treatments in immature permanent teeth; however, some information should be pointed out. The authors included a prospective clinical study⁴ and a retrospective study¹⁸ that compared unpublished and published case reports in their analysis. Moreover, they included in the tooth retention rate analysis (which should have compared successful cases of revascularization and apexification), the study of Saoud *et al.*¹⁹ that evaluated only revascularization procedures, which may overestimate the functional retention for revascularization. The authors did not perform a meta-analysis to assess the clinical and radiographic outcomes and retention rates. It should also be highlighted that recently a retrospective cohort study² evaluating MTA apexification and pulp revascularization over 5 years was published. Hence, it seems reasonable to update the literature with more strict criteria to assess whether apexification or revascularization procedures is more effective regarding the clinical and radiographic successes and retention rates.

All the included studies in this systematic review evaluated MTA apexification as a treatment option, reporting a clinical success and periapical healing rates of 80.77%², 94.70%¹ and 100% (only considered clinical success)⁶. In controlled scenarios (randomized clinical trials), the successes were 93.33% for periapical healing and 100% for clinical success according to Bonte *et al.*⁷, and 100% for clinical success and periapical healing according to other authors^{4,11,20-22}. On the other hand, the clinical success and periapical healing rates of pulp revascularization (evaluating only blood clot induction) were 76.47%², 79% (only considered clinical success)⁶, and 100%¹. In clinical trials, the clinical success and periapical healing rates were 90% according to Nagy *et al.*⁴ and Benzin *et al.*²³. Narang *et al.*²² found a 100% of clinical success and 60% of success in periapical healing (two out of five teeth exhibited 'fair' periapical healing - criteria used by the authors). Thus, despite the controlled or non-controlled scenarios, there is a tendency that the MTA apexification provides more predictable outcomes in immature necrotic permanent teeth in short (1.5 years) or long (5 years) periods of preservation.

Despite its advantages, MTA apexification has some inherent limitations, such as the difficulty of placement and cost. Additionally, it did not allow the possibility of additional root maturation^{4,22}. On the other hand, pulp revascularization provides the possibility of root maturation, especially dentinal wall thickening²⁴ that might strengthen these thin and fragile dentinal walls, diminishing the incidence of root fracture observed either in calcium hydroxide⁷ or MTA apexification². One point to be discussed is the proper disinfection of the root canal in these procedures, as most causes of failure are due to persistent infection or reinfection of root canals^{2,6}.

Recently, Diogenes *et al.*²⁵ evaluated the concentrations of disinfection solutions and intracanal medicaments. The authors reported that irrigation with 1.5% NaOCl followed by 17% EDTA and the intracanal medicaments either with TAP in concentrations of 0.1-1mg/ml or Ca(OH)₂ with 1mg/ml provide a higher survival of SCAP (stems cells of apical papilla) that

may play an important role on root maturation. However, most of the studies^{1,2,6} did not use this proposed concentration, and thus, it seems that they may be harming the cells from apical papilla precluding a potential benefit of root maturation. Therefore, there is still a necessity of further investigation on this topic, as most of the failures observed in those studies were due to lack of controlling infection within the root canals. It seems that higher concentrations of either irrigating solutions or intracanal medicaments may favour root canal disinfection but may diminish the survival of the SCAP²⁵.

Regarding the root maturation (increase in root width and length), Jeeruphan *et al.*¹ found a statistically significant difference in both width and length favoring pulp revascularization in comparison to calcium hydroxide and MTA apexifications. Silujjai & Linsuwanont² found only a significant difference in root width (compared only BC to MTA apexification). Alobaid *et al.*⁶ did not observed a significant difference among revascularization and CH or MTA. In controlled situations, Narang *et al.*²² observed increase in root length and width in blood clot (BC) revascularization but did not observed any increase for MTA apexification. Nagy *et al.*⁴ besides the statistically significant difference observed for BC in comparison to MTA, also observed a significant increase of 1.2 ± 0.5 (11.8 ± 4.9) and 0.32 ± 0.12 (12.7 ± 4.7) in length and thickness from baseline, respectively. Thus, it seems that there is actually an additional gain, mostly in root width, however, whether this increase in truly from dentin deposition or cementum-like and bone-like tissue^{26,27} needs further investigation.

There are some drawbacks regarding the pulp revascularization procedures, such as root canal obliteration²³, crown staining^{23,28,29}, impossibility of post cementation and difficulty of blood clot induction in some cases. Canal obliteration indeed might make the future endodontic procedure more difficult if the revascularization procedure has failure over time. However, it is not recommended to perform any re-intervention unless the treated tooth become symptomatic³⁰.

Crown discoloration (crown staining) may be an undesirable outcome, especially in young patients (teenagers) where esthetic is considered of utmost importance, being related to either the placement of minocycline or MTA (as a coronal plug). Alobaid *et al.*⁶ observed this adverse event in 2 out of 19 teeth (10.5%) treated with revascularization; however, as the authors used various types of intracanal medication (including TAP with minocycline) the cause of crown discoloration remains uncertain. On the other hand, in controlled settings, Bezgin *et al.*²³ reported that 12 of 20 teeth (60%) treated with revascularization procedures presented crown discoloration. The authors²³ reported that this adverse event was caused by MTA placement, despite the use of white MTA instead of grey MTA as a coronal plug. The fact that white MTA may induce crown discoloration is likely to be related to the interaction of its bismuth oxide with the collagen present in dentin³¹.

Apexification procedures may present more favorable results regarding crown discoloration; however, revascularization may benefit more the pediatric patients because it allows for strengthening the roots. Hence, clinicians should balance the importance of the outcomes for each procedure, once inadequate crown-root proportion may enhance the risk of crown or root fractures diminishing tooth retention over time. Moreover, there are some alternatives that attempt to diminish crown discoloration, such as, sealing the pulp chamber with dentin bonding agent before placement of TAP or MTA²³, replacement of the bismuth oxide present in the white MTA for other components³¹ or use of biocompatible MTA-like cements³².

Another point of discussion is related to the choice of calcium hydroxide (CH) or mineral trioxide aggregate (MTA) for apexification procedures. According to our second meta-analysis (Figure 3), both procedures had similar success and tooth retention rates, however, Jeeruphan *et al.*¹ observed a success of 77.3% for CH and 94.7% for MTA, and the failures were related to catastrophic fractures. It is well known that longer periods of calcium

hydroxide exposure may increase dentin brittleness over time^{33,34} and might be related to an increased risk of root fracture even in controlled scenarios⁷. Therefore, it seems that despite the similar outcomes for both treatments, MTA might be the best option because more teeth have been extracted when treated with calcium hydroxide.

In young patients, the functional retention of immature necrotic permanent teeth is more important than a specifically clinical success or periapical healing. It should be considered that asymptomatic teeth retained to the age of eighteen even with periapical lesions (radiographically) should be considered a successful treatment, because at this age patients could choose to have dental implants if necessary. All of the included studies^{1,2,6} evaluated the retention rates of treated teeth. When it was compared to the overall success (86%, 116/135 teeth), the retention rate raised 4% among all treatments performed (retention rate, 90%, 124/138 teeth), which should be considered an important outcome. It is noteworthy that more studies are desirable to evaluate what additional root maturation represents to root strengthen, and consequently, the functional retention over time. It is likely that over longer periods of follow-up, young patients with immature teeth reinforced by an increase in root width and length, may be benefited with an actual increase in tooth survival. Moreover, one must speculate that pulp revascularization procedures should be the first treatment option, where there is an inadequate crown-root ratio, rather than apexification ones in immature necrotic permanent teeth, because it offers the possibility of a second non-invasive treatment (MTA apexification) if the revascularization case present failure over time.

Strengths of study

The present study has several strengths. It may be the first meta-analysis that evaluated the clinical and remission of periapical radiolucency outcomes and tooth retention rates among nonrandomized studies, which make clinical extrapolations more reliable. Contrasting to our

previous systematic review of randomized clinical trials¹² that included only studies with moderate and high bias risk, this current review included only studies with “high” quality. Also, the included studies performed their outcomes assessment over longer periods of follow-up. The comprehensive search was conducted in two databases, and the references of included studies were crosschecked for additional studies. We reported this review according to the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) guidelines. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies was used. We also evaluated the possible heterogeneity of included studies using the I^2 test, but none was observed ($I^2 = 0\%$ in all meta-analysis). Therefore, strict criteria were used to report this systematic review, which strengthen our results contributing to the establishment of a guide to general practitioners.

Limitations of study

Some limitations have to be considered. We included only three studies in this systematic review with a total of 135 immature necrotic permanent teeth. There is still a need of a greater sample size to establish whether there is a more effective treatment in these teeth. There are some inherent limitations of the included observational studies, such as the risk of bias when collecting the data as it was screened retrospectively and lack of randomization of patients designated to the treatments. Another limitation may be related to our inclusion criteria of articles published only in English language. However, according to Moher *et al.*³⁵ the exclusion of non-English language articles might not be a limitation on the results of meta-analysis.

Implications for future researches

Although pulp revascularization procedures may increase root length and width some attempts should be made to use standards methods to quantify the real gain in root development,

as some X-ray distortions may overestimate its increase. Also, there is still a need of establishment of proper concentrations for root canal disinfectants that could enhance the survival of SCAP, but also reduce the microbial load and the risk of reinfection, allowing for periapical healing.

Conclusions

According to our meta-analysis there is no statistically significant differences between MTA apexification and revascularization procedures, which makes no endodontic procedure more effective in terms of clinical and remission of periapical radiolucency outcomes and tooth retention rates. However, pulp revascularization provides the possibility of additional root maturation, especially increase in root width, which could benefit young patients with early stages of root development, as it is likely to increase the tooth retention over time. Thus, it might be reasonable to, in patients with inadequate crown-root ratio, choose pulp revascularization as the first option of treatment in the management of immature necrotic permanent teeth, as these teeth present thin and fragile dentin walls, which may increase the possibility of root fracture. Nevertheless, MTA apexification seems to provide more favorable and predictable outcomes in terms of success over time, and thus, in cases where there is enough root development, it might be the best treatment option. More clinical studies are necessary to further investigate some topics of the apexification and revascularization procedures.

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Table 1. Detailed characteristics of the included studies in the systematic review

Study	Jeeruphan <i>et al.</i>	Alobaid <i>et al.</i>	Silujjai & Linsuwanont
Type of study	Retrospective Cohort	Retrospective Cohort	Retrospective Cohort
Year	2012	2014	2017
Country	Thailand	United States (US)	Thailand
Type of teeth*	Anterior and Posterior	Anterior and Posterior	Anterior and Posterior
Patients (number)	BC: 20 CH: 19 MTA: 22	*	BC: 17 MTA: 26 (28****)
Teeth (number)	BC: 20 CH: 19 MTA: 22	BC: 19 CH: 7 MTA: 5	BC: 17 MTA: 26 (29***)
Age of patients	BC: 12.9 ± 5.07 years CH: 10.5 ± 3.85 years MTA: 14.6 ± 6.17 years	BC: 8.8 ± 1.6 years CH: 9.8 ± 2.0 years MTA: 9.8 ± 2.0 years	8-46 years
Etiology of pulp necrosis	Trauma (59%), Dens evaginatus (32.8) and Caries (8.2%)	Trauma (77.4%), Caries (12.9%), Anatomic anomalies (9.7%)	Trauma (46.51%), Dens evaginatus (41.86) and Caries (11.63%)
Diagnosis of pulp necrosis	Clinically and Radiographically	Clinically and Radiographically	Clinically and Radiographically
Periapical lesion at the beginning	Either present and absent	Either present and absent	*
Type of Intervention	BC, CH and MTA	BC, CH and MTA	BC and MTA
Type of Irrigant Solution	BC: 2.5% NaOCl CH and MTA*	BC: various concentrations of NaOCl, Chlorhexidine, and/or EDTA CH and MTA*	BC: 1.5-2.5% NaOCl and 17% EDTA MTA: 2.5% NaOCl
Type of Intracanal Medication	BC: TAP (ciprofloxacin, metronidazole and minocycline) CH and MTA*	BC: TAP (ciprofloxacin, metronidazole and minocycline), double antibiotic (ciprofloxacin, metronidazole), and/or calcium hydroxide CH and MTA: calcium hydroxide	BC: either ciprofloxacin, metronidazole and minocycline or calcium hydroxide MTA: calcium hydroxide
Number of clinical successful cases	BC: 100% (20/20) CH: 77.3% (17/22) MTA: 94.7% (18/19) (BC = MTA > CH (p<0.05))**	BC: 79% (15/19) CH: 100% (7/7) MTA: 100% (5/5) (BC = MTA = CH (p=0.09))**	BC: 76.47% (13/17) MTA: 80.77% (21/26) BC = MTA (p>0.05)
Number of periapical healing successful cases	BC: 100% (20/20) CH: 77.3% (17/22) MTA: 94.7% (18/19) (BC = MTA > CH (p<0.05))**	*	BC: 76.47% (13/17) MTA: 80.77% (21/26) BC = MTA (p>0.05)
Retention rate	BC: 100% (20/20) CH: 77.3% (17/22) MTA: 94.7% (18/19) (BC = MTA > CH (p<0.05))**	BC: 95% (18/19) CH: 100% (7/7) MTA: 100% (5/5) (BC = MTA = CH (p=0.4))**	BC: 88.24% (15/17) MTA: 82.76% (24/29***) BC = MTA (p>0.05)
Increase in root length (percentage)	BC: 14.9% CH: 0.4% MTA: 6.1% (p<0.001)**	*	BC: 9.51% ± 18.14% MTA: 8.55% ± 8.97% BC = MTA (p>0.05)
Increase in root width (percentage)	BC: 28.2% CH: 1.52% MTA: 0% (p<0.0001)**	BC: 10.2% ± 4.0% CH and MTA*	BC: 13.75% ± 19.91% MTA: -3.30% ± 14.14% BC > MTA (p<0.05)
Calcified barrier formation	*	*	*
Crown discoloration	*	BC: 2/19 (10.5%) CH and MTA: 0/12 (0%)	*
Reasons for failures	CH and MTA: catastrophic fracture deemed nonrestorable	BC: 3 teeth became reinfected and 1 tooth was retraumatized and extracted	BC: 3 teeth showed persistent infection and 1 tooth was reinfected MTA: 2 teeth had vertical root fracture, 1 teeth had horizontal root fracture and 2 teeth had unrestorable tooth fracture
Follow-up (mean and SD)	BC: 21.15 ± 11.70 months CH: 27.32 ± 30.47 months MTA: 14.21 ± 7.84 months	BC: 14 ± 8.5 months CH: 21.8 ± 12.0 months MTA: 21.8 ± 12.0 months	BC: 35 ± 21.76 months MTA: 49 ± 31.09 months

Authors did not state clearly; * According to authors (p value); * Authors stated that 3 patients were unable to attend the recall visits but provided information that teeth were functional with no symptoms; **** Two patients (which did not attend the recall visits) had 3 MTA apexified teeth; Abbreviations: CH: Calcium Hydroxide apexification; MTA: Mineral Trioxide Aggregate apexification; BC: Blood Clot revascularization; TAP: Triple Antibiotic Paste

Table 2. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies

Study	Jeeruphan <i>et al.</i>	Alobaid <i>et al.</i>	Silujjai & Linsuwanont
1. Selection			
1.1. Representativeness of cohorts	*	*	*
1.2. Selection of cohorts			
1.3. Ascertainment of treatment regimen	*	*	*
1.4. Demonstration that the outcome of interest was not present at start of study	*	*	*
2. Comparability			
1. Comparability of cohorts on the basis of the design or analysis (Age *; other controlled factors *)	**	*	**
3. Outcome			
3.1. Assessment of outcome	*	*	*
3.2. Was follow-up long enough	*	*	*
3.3. Adequacy of follow-up	*	*	*

Figure 1. Flowchart of study selection

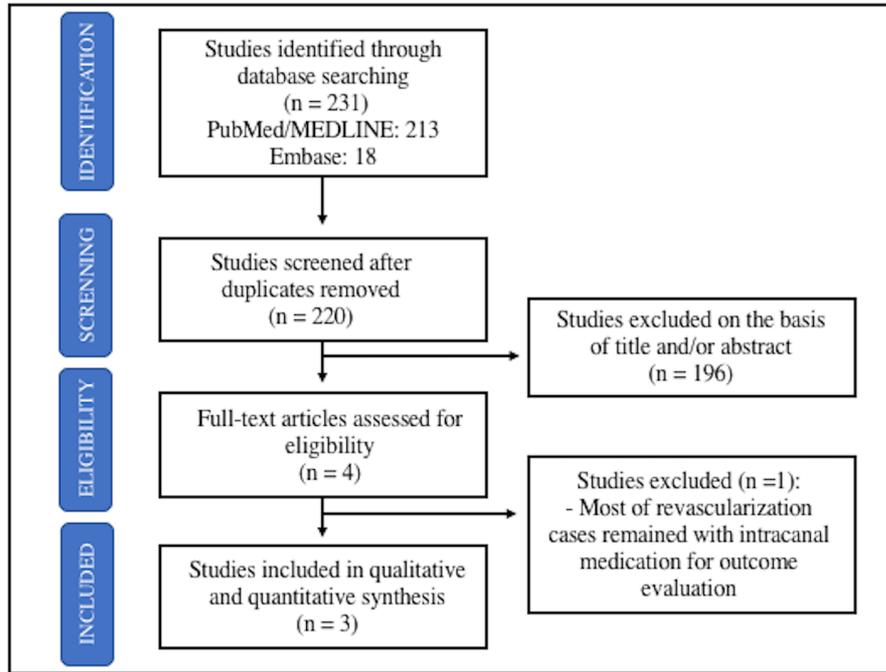


Figure 2. Forest plots of (A) clinical and radiographic success and (B) retention rates when MTA apexification was compared to pulp revascularization.

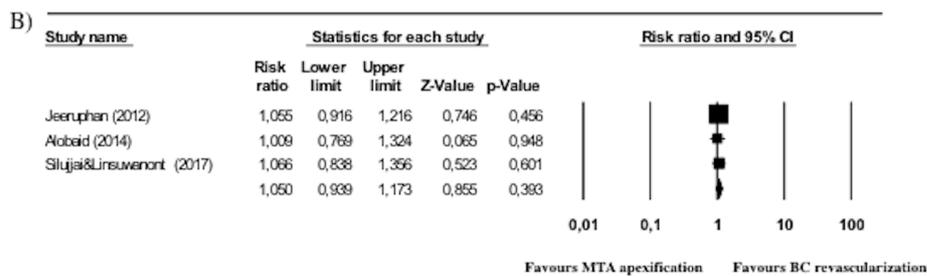
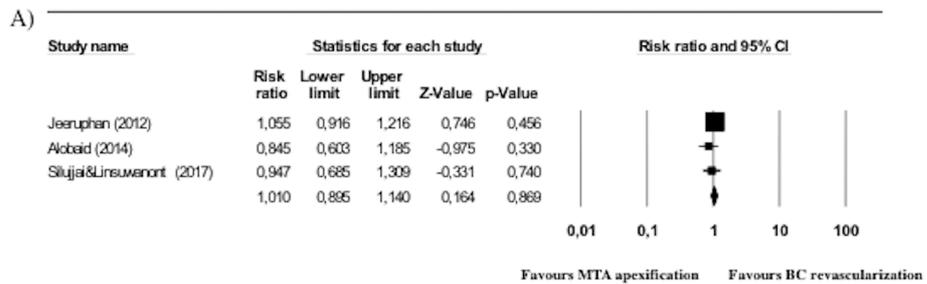
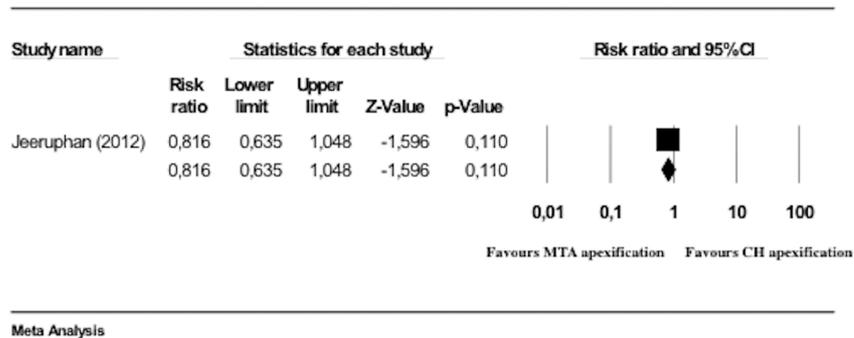


Figure 3. Forest plot of clinical and radiographic success and retention rates when MTA apexification was compared to CH apexification.



Why this paper is important to paediatric dentists

Immature necrotic permanent teeth due to fragile dentine walls and inadequate crown-root proportion are difficult to manage with conventional endodontic treatments. Paediatric dentists should know what protocol is more effective in each case to manage these immature teeth on their clinics.

Disclosure Statement:

The authors deny any conflict of interest.

CONSIDERAÇÕES FINAIS

Baseado nos resultados da revisão sistemática de estudos observacionais apresentada nesta tese, e nos resultados previamente observados na revisão sistemática de ensaios clínicos randomizados (NICOLOSO et al., 2017), o procedimento de apicificação através do *plug* apical de MTA parece apresentar as melhores taxas de sucesso clínico e radiográfico no tratamento de dentes permanentes com rizogênese incompleta e necrose pulpar. O procedimento endodôntico de apicificação através do *plug* apical de MTA apresenta maior eficácia clínica e radiográfica em relação aos tratamentos de apicificação com trocas de hidróxido de cálcio e revascularização de polpa através da indução do coágulo com ou sem a utilização adicional (ou de maneira independente) de *scaffolds* à base de concentrados de plaqueta (PRP) ou fibrina (PRF) (NICOLOSO et al., 2017).

Em situações não controladas, o procedimento endodôntico de apicificação com *plug* apical de MTA apresenta efetividade clínica e radiográfica e taxa de retenção similar a técnica de revascularização da polpa, conforme observado na meta-análise de estudos observacionais. Vale ressaltar que a técnica de revascularização apresenta a possibilidade de formação radicular adicional, principalmente o aumento da espessura radicular, o que beneficia pacientes jovens com dentes em estágios iniciais de desenvolvimento radicular, devido ao fortalecimento destas raízes, e possivelmente aumenta a taxa de retenção dentária. Assim, em pacientes que apresentem dentes com rizogênese incompleta e necrose pulpar com proporção coroa-raiz inadequada, a técnica de revascularização constitui a melhor opção de tratamento, devido à presença de paredes dentinárias finas e frágeis o que aumenta o risco de fratura radicular. Entretanto, em dentes permanentes com rizogênese incompleta e necrose pulpar que apresentem desenvolvimento radicular avançado, a técnica de apicificação através do *plug* apical de MTA deve ser a primeira opção de tratamento.

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