Regenerative Endodontic Treatment or Mineral Trioxide Aggregate Apical Plug in Teeth with Necrotic Pulps and Open Apices: A Systematic Review and Meta-analysis

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Abstract

Introduction: A mineral trioxide aggregate (MTA) apical plug (MAP) and regenerative endodontic treatment (RET) have shown acceptable clinical outcomes. However, comparative studies are scarce. The aims of this study were to examine the level of evidence for both treatments, conduct a systematic review of the literature on MAP and RET, and run a meta-analysis on the survival and success rates of teeth treated with these procedures. **Methods:** Electronic searches were performed in MEDLINE, Web of Science, and the Cochrane Library. Two authors independently screened the titles and abstracts for eligibility. Subgroup analyses were performed on the clinical outcomes (ie, survival and success) of the procedures. **Results:** In all, 750 studies were identified, and 144 studies were subjected to qualitative synthesis. Ten randomized clinical trials were included in subgroup analyses. Most of the studies in both groups were case reports and case series (72% and 86% in MAP and RET, respectively). The overall level of evidence in both groups was low. The pooled survival rates were 97.1% (95% confidence interval [CI], 93.7–100) and 97.8% (95% CI, 94.8–100) for MAP and RET, respectively. The pooled success rates were 94.6% (95% CI, 90.2–99.1) and 91.3% (95% CI, 84.5–98.2) for MAP and RET, respectively. Very little heterogeneity was observed among the studies regarding survival and success rates ($I^2 < 50\%$, $P > .10$). There was no significant difference between the 2 groups regarding survival ($P = 1.00$) or success rates ($P = .58$). **Conclusions:** The existing literature lacks high-quality studies with a direct comparison of outcomes of MAP and RET. Randomized multicenter clinical trials with large sample sizes and long-term follow-ups are needed to address this gap in knowledge. (*J Endod 2017;*■:1–15)

Key Words

Immature tooth, meta-analysis, mineral trioxide aggregate apical plug, necrotic pulp, open apex, outcome, regenerative endodontic treatment, success, survival, systematic review

The preservation of natural dentition has long been the main objective in root canal treatment (1). Achieving this objective is more challenging in young patients presenting with immature necrotic teeth. Routine root canal treatment protocols to clean and obturate these teeth cannot be adequately performed because of immature roots. The current treatment options are apexification using long-term calcium hydroxide dressing, placing a mineral trioxide aggregate (MTA) apical plug (MAP), or regenerative endodontic treatment (RET) (2).

Several studies have shown that the long-term use of calcium hydroxide in immature teeth weakens the root structure (3, 4). In the MAP technique, placement of an MTA apical barrier facilitates achieving an apical seal, but it does not promote root development to prevent root fracture.

The intent of RET is to regenerate the pulp-dentin complex, which would promote root thickening and normal maturation of the root apex (2). There are 2 challenges yet to be resolved: a clinically applicable tissue engineering protocol for predictable regeneration of the pulp-dentin complex (5, 6) and an efficient disinfection protocol that eliminates infection completely and renders the microenvironment of the root canal space conducive to repopulation by stem cells (7–9). As a result, the histologic outcome of the treatment, type, and amount of newly formed tissue are unpredictable (10–17).

Clinical decisions about the best treatment option for the patient should be made based on specific scientific evidence after assessing its validity (18). A systematic review of the existing literature can provide an objective synopsis of the best available evidence to help dentists and their patients make these decisions. Systematic reviews are

> ### Significance
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> The treatment of immature teeth with pulp necrosis using an MTA apical plug or regenerative endodontic treatment results in high survival and success rates. The existing literature lacks high-level clinical studies comparing these 2 treatment modalities.

Review Article

inherently less biased, more reliable, and more valid than narrative reviews (19, 20). Comparative studies on the outcomes of different treatment strategies for teeth with pulp necrosis and open apices are very limited. Also, a search of the literature shows the absence of systematic reviews comparing the clinical outcomes of MAP with RET.

The aims of this study were as follows:

1. Examine the level of evidence for MAP and RET
2. Conduct a systematic review of the literature on MAP and RET
3. Run a meta-analysis on the survival and success rates of teeth with pulp necrosis and open apices treated either with MAP or RET

Materials and Methods

A systematic review protocol was developed following established guidelines (20). The methodology included formulating review questions using a patient population, intervention, comparison, and outcome framework; constructing a search strategy; defining inclusion/exclusion criteria; locating studies; assessing study quality; and extracting, interpreting, and analyzing data.

Formulating the Review Question

The patient population, intervention, comparison, and outcome framework was used to formulate the following questions:

1. In teeth with pulp necrosis and open apices, does RET compared with MAP result in better survival?
2. In teeth with pulp necrosis and open apices, does RET compared with MAP result in better success?

Inclusion Criteria

In this study, any organized attempt to revitalize a necrotic immature tooth to induce root development was considered as RET. If the clinician filled the apical part or the entire root canal space with MTA without the intention of revitalizing the tooth, the treatment was considered as MAP. Comparative, noncomparative, prospective, and retrospective clinical studies on immature teeth with pulp necrosis treated with RET (all different methods of disinfection, all types of scaffolds/growth factors/stem cells, and all types of sealing material) or MAP (all different methods of disinfection and obturation) published in English from June 1966 through November 2016 were included.

The exclusion criteria were as follows:

1. Studies that did not meet the previously mentioned inclusion criteria
2. Studies in which calcium silicate–based materials other than MTA were used for root canal filling in MAP group
3. Studies in which the outcome of interest (ie, survival and/or success rates) was not presented

Search Methodology

Electronic searches were performed in the MEDLINE database (via PubMed search engine), Web of Science, and the Cochrane Library to identify studies meeting the inclusion criteria. The search strategy was as follows (Appendix 1):

1. Teeth with immature roots and open apices
2. Pulp necrosis
3. MAP
4. RET
5. 1 and 2
6. 3 or 4
7. 5 and 6

In addition, the following alternative key words were used to optimize the search strategy: "immature teeth/open apex," "MTA apical plug/MTA apexification," and "regenerative endodontic treatment/tooth revascularization/tooth revitalization."

Study Selection

Two authors screened the titles and abstracts of all articles identified in the electronic search. Articles that did not meet the inclusion criteria were excluded upon reviewers' agreement. In case of disagreement between reviewers, a consensus was reached by a third reviewer who reviewed it independently and helped make the final decision about inclusion or exclusion. All remaining articles were subjected to a full-text review. A log of the excluded studies and the reasons for exclusion was prepared (Table 1). Agreement among reviewers for study inclusion was assessed with the Cohen kappa statistic. A threshold for substantial agreement was indicated at a level of 0.70.

Study Quality Rating

A 32-question data abstraction form for RET articles and a 28-question data abstraction form for MAP articles were developed. These abstraction forms had the same questions except for 4 procedure-related questions in the RET group about "type of scaffold," "source of stem cells," "application of growth factors," and "type of barrier over scaffold." From the abstracted information, an overall study quality rating score was developed. Based on criteria used in a systematic review by Torabinejad et al (1), each article was given a quality score with a maximum possible score of 17 points (61).

The quality of clinical trials was assessed using the Cochrane Collaboration's tool for assessing risk of bias (62). This tool assesses quality in 6 classifications with respect to risk of bias in sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other potential threats to validity (63).

The quality of observational studies (prospective and retrospective cohorts) was assessed using a modified version of the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies published by the National Institutes of Health (64, 65). In all, 11 criteria were assessed for each study: research question, study population, uniform eligibility criteria, sample size justification, timing of exposure assessment, sufficient time frame to see an effect, exposure measures, outcome measures, blinding of outcome assessors, follow-up rate >80%, and statistical analyses.

Clinical Outcomes

The average follow-up time in each study was calculated and extracted. Survival was defined as a retained tooth in the oral cavity at follow-up. Success was defined as a lack of clinical symptoms (ie, pain on percussion/palpation/function or sinus tract) and complete radiographic healing of the periapical lesion. Reduction in the size of the periapical lesion was classified as "uncertain." The rate of root development was extracted from RET studies. Root development was defined as increased root length, increased root thickness, or reduced apical diameter.

If the study sample was a pool of different clinical scenarios, attempts were made to extract the data and calculate the outcomes only for teeth with pulp necrosis and open apices. If this was not possible, the study was excluded from the analysis.

Data Analysis

A subgroup of level 1 studies (ie, clinical trials) was defined for each group (Table 2). The survival and success rates after MAP or RET were chosen as the appropriate summary statistics that allow