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EVALUATE THE EFFECT OF REGENERATIVE ENDODONTICS ON TEETH WITH NECROTIC PULP: A SYSTEMATIC REVIEW AND META-ANALYSIS

Mohammad Gharishvandi Abraki¹, Baharan Arshadi Fard^{2*}, Salar Motamedi³,
Arash abbasi⁴, Maryam Rasooli⁵

¹Postgraduate Student, Department of Endodontics, School of Dentistry, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran.

²Postgraduate Student of Prosthodontics, Qazvin University of Medical Sciences, Faculty of Dentistry, Qazvin, Iran.

³Dental Research Center, Research Institute of Dental Sciences, School of Dentistry, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

⁴Faculty of Dentistry, Isfahan University of Medical Sciences, Isfahan, Iran.

⁵Postgraduate Student, Department of Endodontics, Dental School, Hamadan University of Medical Sciences, Hamadan, Iran.

*Corresponding Author: Baharan Arshadi Fard

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Abstract

Background and aim: the present study was conducted with the aim of investigating the effectiveness of REPs in adult teeth with pulp necrosis.

Method: all international databases, PubMed, Scopus, Science Direct, ISI, Web of Knowledge and Embase were examined, until March 2023 based on keywords related to the objectives of the study. The current study was conducted based on the PRISMA 2020 checklist, and Google Scholar search engine was also used to find related articles. The 95% confidence interval risk ratio was calculated using the fixed effect model. Stata/MP v.17 software was used to conduct the meta-analysis.

Result: After reviewing the abstracts of 181 articles, 32 articles were selected for full text review, of which three articles were included in the meta-analysis. Risk ratio of successful treatment outcome between regenerative endodontic procedures group and nonsurgical root canal treatment group was 0.05 (RR, 0.05 95% CI -0.05, 0.15; $p > 0.05$). significant difference between regenerative endodontic procedures group and nonsurgical root canal treatment group in terms of positive response to electric stimuli (RR, 1.59 95% CI 0.60, 2.59; $p > 0.05$).

Conclusion: Based on the present meta-analysis, regenerative endodontic procedures are a favorable treatment method compared to traditional methods in the treatment of necrotic adult teeth.

Keywords: Regenerative Endodontics, Necrotic Pulp, root canal treatment

Introduction

Regenerative endodontic procedures (REPs) is a biologic-based treatment modality for immature permanent teeth diagnosed with pulp necrosis. The ultimate objective of REPs is to regenerate the pulp-dentin complex, extend the tooth longevity and restore the normal function(1). Evidence shows that REPs can have favorable results in complete recovery of periapical tissues, thickening of the root canal wall(2, 3). Over the past years, REPs have generally been used in the treatment of immature teeth with pulp necrosis and apical periodontitis(4). Nowadays, with the increase of new treatment perspectives, the use of REPs in the treatment of adult teeth with pulp necrosis is observed(2). The findings of the studies show that REPs offer advanced biological properties and can be considered as an alternative method for conventional root canal treatment. Also, the evidence shows that comparing the two methods of REPs and traditional methods, there are favorable results in favor of REPs(5, 6). Furthermore, in a recent histological study, Arslan et al., 2019 showed that ingrowth of a vital tissue in the root canal system is possible after REP in mature teeth(7). The identified tissue was a combination of a fibrous bone and connective tissue with some vascular structures. Considering the novelty of using REPs in the treatment of adult teeth with necrosis, the number of studies(8-10) is very few and the results of the studies have not reached a consensus. Therefore, a study that summarizes the results of the studies and provides strong evidence is needed. Therefore, the present study was conducted with the aim of investigating the effectiveness of REPs in adult teeth with pulp necrosis.

Method

Search strategy

In the current study, all international databases, PubMed, Scopus, Science Direct, ISI and Embase were examined, searching until March 2023 based on keywords related to the objectives of the study. The current study was conducted based on the PRISMA 2020 checklist(11, 12).

Keywords and the MeSH terms:

((("Dental Implantation, Endosseous, Endodontic"[Mesh] OR "Root Canal Obturation"[Mesh] OR "Regenerative Endodontics"[Mesh] OR "Dental Pulp Diseases"[Mesh]) OR "Regenerative Endodontics/statistics and numerical data"[Mesh]) AND "Dental Pulp Necrosis"[Mesh]) AND "Tooth"[Mesh].

Eligibility criteria

Inclusion criteria: Only articles published in English, randomized clinical trials, no limit on sample size, and complete data.

Exclusion criteria: studies without control group, prospective and retrospective studies, case-control studies, cross-sectional studies, case series, case reports, in-vitro and reviews papers; animal studies and studies without full text access.

the Google Scholar search engine was used to search for articles and the PICO strategy to answer the research questions (Table 1).

Table1. PICO strategy.

PECO strategy	Description
P	Population: patient's teeth with necrotic pulp
I	Intervention: Regenerative endodontic procedures
C	Comparison: nonsurgical root canal treatment
O	Outcome: treatment outcome

Data collection

Two reviewers independently screened each record and each report was retrieved. All studies were selected based on inclusion and exclusion criteria. The specifications of samples of the selected studies were extracted based on a checklist that included 5 items, the items were: author's name, publication year, study design, sample size, mean of age, number of teeth, type of teeth.

Risk assessment

the quality of randomized control clinical trial studies was evaluated using the Cochrane Collaboration's tool(13). The scores of this tool are between 0 and 6, and higher score showed higher quality of study; the scoring of each item is 1 for low risk and 0 for high and unclear risk.

Data analysis

Meta-analysis was performed using STATA/MP. V17 software. Mantel-Haenszel methods are fixed-effect meta-analysis methods using a different weighting scheme that depends on which effect measure. 95% confidence interval for risk ratio with fixed effect model and Mantel-Haenszel method were calculated. Potential heterogeneity between studies was reported with the I^2 coefficient (low:50%<; moderate: 50%-75%; high:>50%).

Result

Study selection

In the initial search using keywords, 181 articles were found, and all references were entered into EndNote X8 software. Among these articles, 10 articles were duplicated, 8 articles were due to Records marked as ineligible by automation tools, and 7 articles were due to other reasons were removed and finally the abstracts of 156 articles were reviewed and 124 articles that did not meet the inclusion criteria were removed at this stage. The full text of 32 articles was fully reviewed by two blinded observers. Incomplete articles, without data, inconsistency with the objectives of the study were excluded 29 articles) and finally three articles were selected (Figure 1).

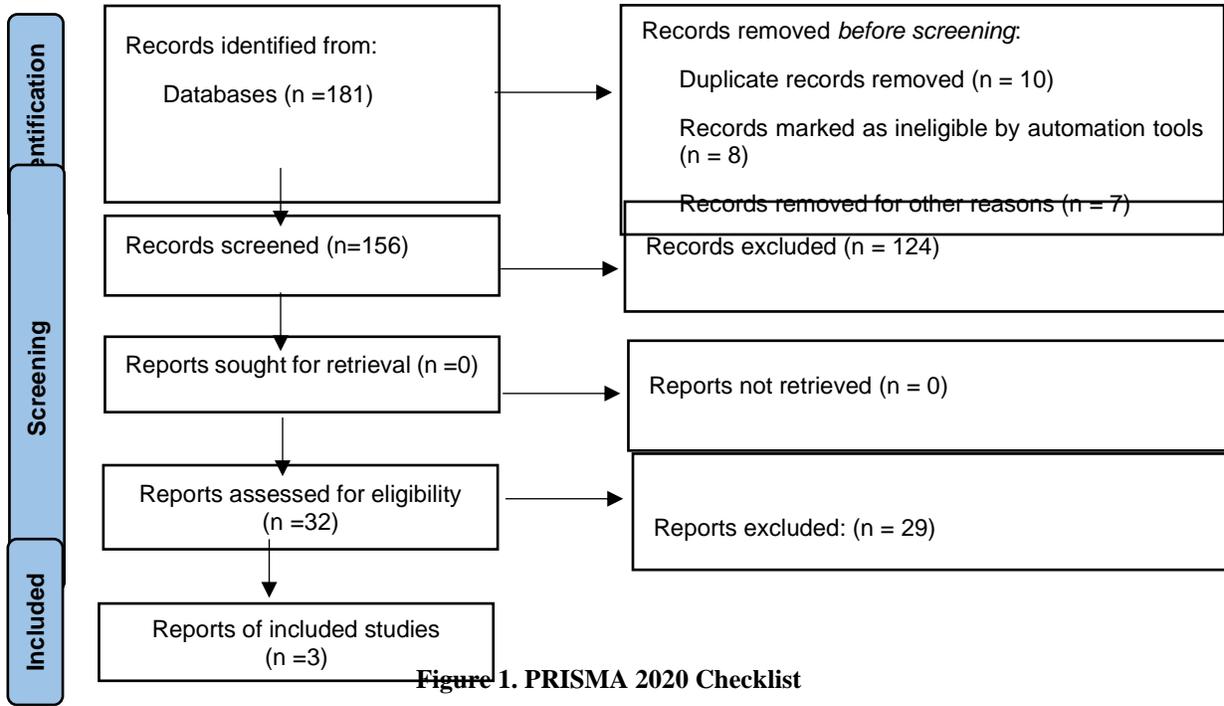


Figure 1. PRISMA 2020 Checklist

Study characteristics

A total of 112 patients included. Table 2 shows a summary of Data extracted.

Risk assessment

According to Cochrane Collaboration’s tool, all randomized clinical trial study had high quality (low risk of bias).

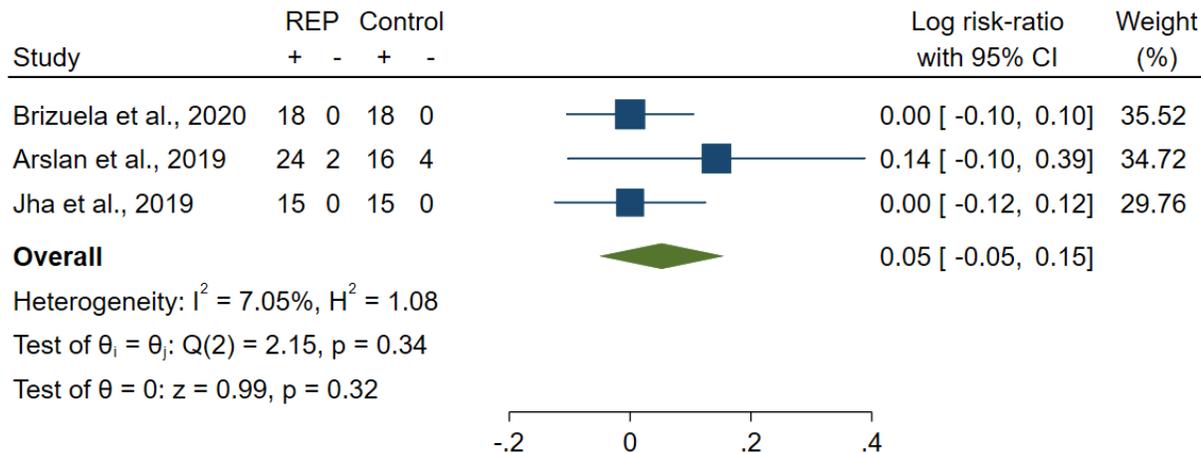
Table 2. Data extracted from studies selected for systematic review and meta-analysis.

Study. Years	Study design	Number of patients		Mean or range of age	groups		Number of teeth	Type of teeth
		male	female		intervention	control		
Brizuela et al., 2020 (9)	RCT	11	25	16-58	REP	nonsurgical root canal treatment	36	mature with apical lesions
Arslan et al., 2019 (8)	RCT	35	11	20.58	REP	nonsurgical root canal treatment	46	mature, necrotic with apical lesions
Jha et al., 2019 (12)	RCT	30		9-15	REP	nonsurgical root canal treatment	30	permanent mature with apical lesions

Table 3. Risk of bias assessment (Cochrane Collaboration’s tool)

study	Random sequence generation	allocation concealment	blinding of participants and personnel	blinding of outcome assessment	incomplete outcome data	selective reporting	Total score
Brizuela et al., 2020 (9)	+	+	+	+	+	+	6
Arslan et al., 2019 (8)	+	+	+	+	+	+	6
Jha et al., 2019 (12)	+	+	+	+	+	+	6

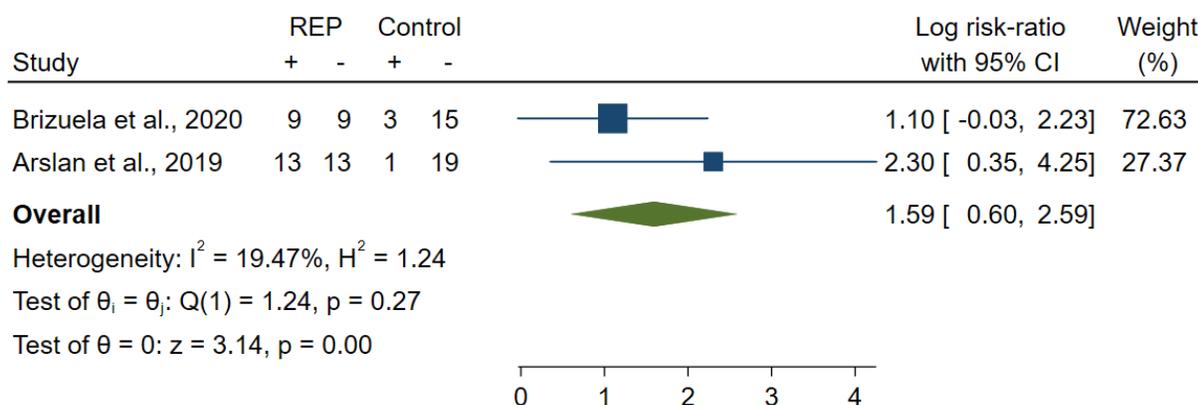
Risk ratio of successful treatment outcome between REP group and nonsurgical root canal treatment group was 0.05 (RR, 0.05 95% CI -0.05, 0.15; $p > 0.05$) with low heterogeneity ($I^2 = 7.05\%$; $P = 0.34$) (Fig.2). there was no significant difference between REP group and nonsurgical root canal treatment group in terms of successful treatment outcome ($p = 0.32$).



Fixed-effects Mantel-Haenszel model

Figure 2. forest plot showed successful treatment outcome between REP group and nonsurgical root canal treatment group

Risk ratio of positive response to electric stimuli between REP group and nonsurgical root canal treatment group was 1.59 (RR, 1.59 95% CI 0.60, 2.59; $p > 0.05$) with low heterogeneity ($I^2 = 19.47\%$; $P = 0.27$) (Fig.3). there was significant difference between REP group and nonsurgical root canal treatment group in terms of positive response to electric stimuli ($p = 0.00$).



Fixed-effects Mantel–Haenszel model

Figure 3. forest plot showed positive response to electric stimuli between REP group and nonsurgical root canal treatment group

Discussion

In the present study, an attempt has been made to investigate the effectiveness of REPs in the treatment of adult teeth with necrotic pulp and to be able to use it as an alternative treatment to traditional methods. The present meta-analysis showed that there was no statistically significant difference in the success rate of treatment with REP compared to traditional methods. Therefore, REP is favorable for restorative treatment results and is a good alternative option. The use of high-concentration detergents and the use of intracanal and pharmaceutical drugs are known as the most successful methods to achieve complete disinfection. However, biocompatibility considerations must be taken into account. In all the studies included in the present review, a 2-step disinfection protocol was performed, which did not differ significantly between each other. There were no differences between the selected studies in terms of treatment outcomes based on the drug used. In two studies, a calcium silicate material was used and in one study, mineral trioxide was used. Previous studies have shown that the use of these substances are effective in the results of treatment with REPs(6, 14). The use of single-rooted teeth can also affect the treatment results because it may potentially be an important drawback for creating REPs as a suitable alternative treatment option in cases of mature necrotic teeth with apical periodontitis. A study has shown that immature posterior teeth treated with REP(15, 16). According to the mentioned cases and the lack of clinical trial studies related to the purpose of the present study, the full acceptance of REPs as a suitable treatment option in all dental categories (anterior-posterior) with pulp necrosis requires more evidence. However, the findings of this study can help future studies. Consequently, REPs are a viable treatment option for clinicians when teeth with pulp necrosis and an apical hole up to 1 mm in diameter are to be endodontically managed. If these techniques are not qualified or considered unsuccessful, conventional root canal procedures can always be performed as an alternative. It is suggested that future clinical trial studies be conducted with a larger sample size, longer evaluation periods, and follow-up time.

Conclusion

Based on the present meta-analysis, REPs are a favorable treatment method compared to traditional methods in the treatment of necrotic adult teeth. More observations are needed to confirm the present results. Endodontists can use REPs as a treatment protocol; However, more clinical studies are needed and endodontists need to record their clinical observations in this regard.

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