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Regenerative Endodontic Effectivity In Cases of Necrotic Immature Permanent Teeth Treatment (*Literature Review*)

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Abstract

Introduction: Pulp necrosis in immature permanent teeth results in incomplete root development with short roots and thin dentinal walls that can lead to fracture. Apexification, the main treatment, did not increase the length and thickness of the root canal wall, making the teeth susceptible to fracture. Regenerative endodontic treatment uses a tissue engineering triad that allows the root to continue developing, increases the dentinal wall thickness, and restores the tooth's vitality to prevent fracture. **Purpose:** This literature review aimed to examine the effectiveness of regenerative endodontics in treating necrotic immature permanent teeth and which component is the most commonly used and effective. **Methods:** The literature review uses Google Scholar, DOAJ, Science Direct, and Pubmed data for the last five years, calculated from 2018 to 2023. The journals used fit with the inclusion and exclusion criteria, then analyzed using the Case Report Statement and Checklist and summarized to obtain data on the effectivity of regenerative endodontic treatment in necrotic immature permanent teeth. **Results:** This literature review successfully synthesized 18 Case Reports from journals that performed endodontic regeneration treatment on immature permanent teeth with necrosis using various components. **Conclusion:** Regenerative endodontic treatment using NaOCl with concentrations ranging from 1% to 2,5 %, EDTA 17% as irrigation solutions together with $Ca(OH)2$ as an intracanal medicament and blood clot as a scaffold proven to effectively eliminate disease, induce bone healing, and restoring the vitality of necrotic immature permanent teeth.

Keywords: Immature permanent teeth; necrotic teeth; regenerative endodontic

Introduction

Pulp necrosis is a condition that occurs when the pulp of the tooth dies, the blood vessels are gone, and the nerve is no longer in function.[1] Basic health research of the Republic of Indonesia 2018 showed that 57.6% of Indonesians have dental and oral problems, including pulp necrosis.[2] Pulp ecrosis in young permanent teeth has a prevalence of 39.5%.[3] Suwartini stated that pulp necrosis in the young permanent tooth with an open apex was caused by tooth decay (12.9%), trauma (33.8%), and dens invaginatus (25.9%), where this condition can cause the root formation to stop, so the root of the tooth becomes short, the walls are thin and susceptible to fractures.

Apexification and artificial apical barrier applications with MTA (Mineral Trioxide Aggregate) or Bio-dentine have been suggested to treat necrotic immature permanent teeth.

The treatment can induce the formation of mineral tissue in the apical area to cause apical closure but does not increase the dentin thickness in the root or the length of the root, so it can cause the tooth to fracture.[4,5] According to Suwartini, new alternative treatments are needed to treat young permanent teeth with necrosis to avoid the risk of fractures.[2] The American Association of Endodontists recommends endodontic regeneration to treat necrotic immature permanent teeth.[4,6] Gutiérrez et al. suggested that endodontic regeneration has a success rate ranging from 94% to 98%. It induces continued root development and increases the thickness of dentin, thus preventing fractures.[7] Alasqah et al. stated that teeth treated with endodontic regeneration have a 100% survival rate compared to those treated by apexification at 77%.[8]

Regenerative endodontic is a procedure that involves the use of ingredients that can help heal and repair the pulp dentin complex after removing diseased or infected tooth tissue by utilizing the tissue engineering triad, stem cell, scaffold, and bioactive growth factor, thus enabling the development of the roots and surrounding tissue.[9.10] The endodontic regeneration procedure is carried out by inserting irrigation solution and antimicrobial agent into the root canal to remove the necrotic and infected pulp tissue. After the necrotic and infected pulp is removed, induction of bleeding is performed on the apical to form a blood clot containing residues of vital pulp to enhance revascularization.[11] Arsyad et al. (2021) stated that endodontic regeneration can restore the vitality of non-vital teeth.[9]

Regenerative endodontics shows promising potential in pulp tissue regeneration in necrotic immature permanent teeth. Based on the description above, the author is interested in reviewing further “Regenerative Endodontic Effectivity in Cases of Necrotic Immature Permanent Teeth Treatment” in the form of a literature review using data from previous case reports.

Methods

The literature review was made using Pubmed, Science Direct, Google Scholar, and Semantic Scholar data for the last five years, calculated from 2018 to 2023. The articles used are in accordance with the inclusions and exclusions criteria in Table 1 and Table 2, which are then analyzed for bias assessment using the Case Report Statement and Checklist (CARE) to obtain the data of regenerative endodontic treatment in necrotic immature permanent teeth.

Table 1. Inclusion criteria and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Case report journal.	Case report of an individual with mature permanent teeth.
Case report of an individual with necrotic immature permanent teeth, incomplete root development, and open apices.	Treated with regenerative endodontic procedure followed by less than 6-months follow-up.
Treated with regenerative endodontic procedure followed by a minimum 6-months follow-up.	
Regenerative endodontic results assessed based on radiographic examination.	

Table 2. Data search strategy

Inclusion Criteria	Population	Intervention	Comparison	Outcome
Keyword	Immature Necrotic Permanent Tooth	Regenerative Endodontic Treatment	-	Continued Root Development, Increase Dentin Thickness, Apical Closure
Original Word	-	Stem Cells, Growth Factor, Scaffold, Platelet-Rich Fibrin, Platelet-Rich Plasma	-	-
Controlled Vocabulary	-	Endodontic Regenerative, Regenerative Endodontics, Regeneration Endodontic, Regenerative Endodontic Therapy,	-	Open Apex, Blunderbuss, Thin Dentinal Walls

	Revascularization Procedure, Pulp Regeneration Procedure	

Results

Article search results through Pubmed, Science Direct, Google Scholar, and Semantic Scholar data for the last 5 years obtained 18 case report journals that discuss regenerative endodontic treatment with various components. Regenerative endodontics in cases of immature permanent teeth treatment with different components in 18 journals showed satisfactory results. The treatment eliminates the disease and induces bone healing in 17 of 18 journals. Fifteen of 18 journals also showed that regenerative endodontics induce continued root development, and 2 of them showed that regenerative endodontics restore the vitality of the necrotic immature permanent teeth. A total of four journals utilized sodium hypochlorite (NaOCl) as an irrigation solution. Of these, three employed a concentration of 1.5%, while one used a concentration of 5.25%. Additionally, eleven journals used NaOCl at concentrations ranging from 1% to 2.5%, along with ethylenediaminetetraacetic acid (EDTA). Out of these eleven, ten journals utilized EDTA at a concentration of 17%, and one journal used it at a concentration of 20%. Furthermore, one journal used a combination of NaOCl at 2.5% and chlorhexidine at 2%. Another journal exclusively used chlorhexidine at 2%. Finally, one journal employed a mixture of NaOCl at 1.25%, EDTA at 17%, and pure chlorine dioxide (ClO_2) at 0.12%.

The most widely used intracanal medications were $Ca(OH)_2$ in 8 journals, TAP in 3 journals, combination of $Ca(OH)_2$ and TAP in 3 journals, combination of $Ca(OH)_2$ with Chlorhexidine 2% and DAP in 1 journals, combination of $Ca(OH)_2$ and $Ca(OH)_2$ with Chlorhexidine 2% in 1 journals, and MTAP in 1 journals. 15 Journals used blood clots as scaffolds, and three journals used alternative scaffolds other than blood clots, two of them used Platelet-Rich Fibrin (PRF), and 1 of them used Concentrated Growth Factor (CGF).

Discussions

The regenerative endodontic procedure is an alternative treatment of necrotic immature permanent teeth. The presence of bacterial residues on a third apical of the tooth may lead to failure in this procedure. Root canal disinfection is a decisive factor in regenerative endodontic procedures. It can create a room free from the contamination of bacteria and other microorganisms that optimize the process of stem cell regeneration. Mechanical debridement is difficult to perform on immature permanent teeth due to the thin dentinal wall and open apices. Chemical debridement using irrigation solutions and intracanal medications is much better to use in this situation.[32]

NaOC1 is the most used irrigation solution, either alone or with another irrigation solution. Based on research from Seraj et al. (2018), Asgary et al. (2022), and Gandhi et al. (2023) showed that NaOC1 1.5% as an irrigation solution has good effectiveness in eliminating disease and induced bone healing as well as induced continued root development.[34,44,47] Other research by John et al. (2019) showed that NaOC1 5.25% also gave the same effectiveness, but NaOC1 in high concentration has a risk of reducing the dentin elasticity module.[12,37] Ajram et al. (2019) stated that a low concentration of NaOC1 was effective to remove the necrotic tissue, has a great antimicrobial effect, and does not cause cytotoxicity to stem cells in apical papilla.

Another commonly used irrigation solution is EDTA. Alasqah et al. stated that EDTA can maintain stem cell survival and proliferation in the apical papillae and facilitate their attachment to the dentinal walls of the root canal.8 EDTA is generally used after irrigating using NaOC1 because the chelating effect of EDTA can increase the antibacterial ability of NaOC1. Hence, it can penetrate better on the dentine tubule. Previous research showed that 1 to 2.5% NaOC1 and 17% EDTA as irrigation solutions were effective in eliminating disease and induced bone healing, with 7 of them successfully inducing continued root development, and 2 of them succeeded in restoring tooth vitality. Another research by Ajram et al. with NaOC1 2,5% and EDTA 20% also gave the same result. [8,29,33,35,38,39,40,41,42,43,45]

Roy et al. demonstrated that a 2.5% sodium hypochlorite (NaOCl) solution and 2% chlorhexidine as irrigation solutions can effectively treat disease and promote bone healing, although they do not stimulate continued root development. In contrast, Alsofit et al. found that 2% chlorhexidine without intracanal medication was ineffective in eliminating the disease, even though it could encourage continued root development. Furthermore, Jamet et al. (2023) noted that chlorhexidine is cytotoxic to cells, which may inhibit regeneration processes.

Polyak et al. (2023) in his research showed that NaOC1 1,25%, 0,12% hyperpure chlorine dioxide (ClO_2), and EDTA 17% as an irrigation solution solution has good effectiveness in eliminating disease and induced bone healing as well as induced continued root development. Hyperpure chlorine dioxide (ClO_2) has antimicrobial properties, low toxicity, and does not interfere with the survival of PDLSC.[46]

Several intracanal medicaments commonly used in regenerative endodontic procudere were Ca $(OH)_2$, TAP, and DAP. Based on 8 research by Ajram et al. (2019), Lu et al. (2020), Kaur et al. (2021), Lorono et al. (2022), Hosseini et al. (2022), Alencar et al. (2022), Polyak et al. (2023), and Gandhi et al. (2023) showed that $Ca(OH)_2$ as an intracanal medication has 100% effectiveness in eliminating disease and induced bone healing as well as induced continued root development. Alasqah et al. (2020) stated that $Ca(OH)_2$ is capable of neutralizing lipopolysides produced by anaerobic bacteria and induces continous root development. [8,29,35,39,41,43,45,46]

Research by Natera et al. Seraj et al., and Roy et al. highlights the effectiveness of TAP (triple antibiotic paste) as an intracanal medication in eliminating infection and promoting bone healing. However, only Seraj et al. reported that TAP also supports continued root development.[11,33,34] Natera et al. found that using high concentrations of TAP can cause cell death in the apical papilla, preventing root development.[33] To avoid such damage, the AAE recommends using TAP at concentrations between 0.1-1 mg/mL. Roy et al. noted that TAP can cause tooth discoloration due to the minocycline component. [11] To address this, Asgary et al. replaced minocycline with penicillin G in a modified TAP (MTAP), which effectively eliminates infection, promotes bone healing, and supports continued root development.[44] Additionally, alternatives like Ca(OH)2 and DAP (double antibiotic paste) can prevent tooth discoloration.[11]

John et al. and Alasqah et al. investigated the sequential use of Ca(OH)2 in the first visit and TAP in the second. Both studies demonstrated effectiveness in infection elimination, bone healing, and root development, with Alasqah et al. also reporting restored tooth vitality. [8,37] In contrast, Hristov et al. found that using TAP first and Ca(OH)2 second only eliminated infection and promoted bone healing, but did not support root development due to patient non-cooperation, which hindered the regeneration process. Alternating two different intracanal medications aims to optimize root canal disinfection and ensure proper regeneration. [39]

Leite et al. demonstrated that regenerative endodontic treatment on two teeth, one using $Ca(OH)_2$ combined with 2% chlorhexidine and the other using DAP as intracanal medications, effectively eliminated disease, promoted bone healing, supported continued root development, and restored tooth vitality.[38] Similarly, Mohammadi et al. found that using $Ca(OH)_2$ in the first visit, followed by $Ca(OH)_2$ combined with 2% chlorhexidine in the second visit, effectively eliminated disease and promoted bone healing. However, it did not support continued root development. Mohammadi explained that combining $Ca(OH)_2$ with 2% chlorhexidine enhances its antimicrobial properties. [42]

Fifteen studies, including those by Natera et al. (2018), Seraj et al. (2018), Ajram et al. (2019), John et al. (2019), and others up to Polyak et al. (2023), showed that using a blood clot as a scaffold was 93% effective in eliminating disease and promoting bone healing. Of these, 11 studies demonstrated that blood clots also supported continued root development, with two studies further reporting the restoration of tooth vitality. Kim et al. (2018) explained that blood clots as scaffolds contain platelet-derived growth factors and mesenchymal stem cells, which play a role in regenerating pulp tissue. [6,8,11,33,34,35,36,37,38,39,40,41,43,44,45,46]

Mohammadi et al. (2021) and Hosseini et al. (2023) found that Platelet-Rich Fibrin (PRF) as a scaffold was effective in eliminating disease and promoting bone healing, though only one study reported its ability to support continued root development. [29,42] Kumar et al. (2023) explained that PRF aids tissue formation, epithelial migration, and increases the release of growth factors. [5] Gandhi et al. (2023) demonstrated that Concentrated Growth Factor (CGF) as a scaffold was effective in eliminating disease, promoting bone healing, and supporting continued root development. CGF is rich in growth factors that enhance the proliferation and differentiation of osteoblastic cells. [47]

An analysis of 18 studies identified the most commonly used components in regenerative endodontic treatment for necrotic immature permanent teeth: NaOCl (1–2.5%) and 17% EDTA as irrigation solutions, $Ca(OH)_2$ as an intracanal medication, and a blood clot as the scaffold. Low-concentration NaOCl minimizes adverse effects on stem cells and preserves dentin elasticity, while 17% EDTA, used after NaOCl, supports stem cell survival, proliferation, and adherence to root canal walls. It also prevents smear layer formation and facilitates the release of growth factors. Blood clots, containing platelet-derived growth factors and mesenchymal stem cells, can effectively regenerate pulp tissue. Alternatives like PRF and CGF can optimize regeneration but are more expensive.

Conclusion

Regenerative endodontic treatment for necrotic immature permanent teeth is optimal and highly effective in eliminating disease, promoting bone healing, and supporting continued root development. The most commonly used components in regenerative endodontic treatment for such cases include NaOCl at concentrations between 1% and 2.5% and 17% EDTA as irrigation solutions, Ca $(OH)_2$ as an intracanal medication, and blood clots as scaffolds.

Further research is needed to explore alternative components in regenerative endodontic treatment to identify options that may be more effective than the current standards of NaOCl (1%–2.5%), 17% EDTA, Ca $(OH)_2$, and blood clots as scaffolds.

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