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OUTCOME OF ATTEMPTED REVASCULARIZATION: A NARRATIVE LITERATURE REVIEW.

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ABSTRACT:

Revamping the blood circulation to facilitate root canal development has been a breakthrough in pulp revascularization. This approach is mainly recommended for teeth with incomplete root formation or open apex, as an alternative to the apexification treatment. Apexification is the introduction of calcium hydroxide paste or Calcium Silicate Cements within the root canal system for a given duration to achieve a physiological barrier. Calcium Hydroxide can potentially weaken the root, attributing to its hygroscopic properties and the proteolytic activities. Therefore this lead to advent of MTA and biodentine with superior handling and sealing properties. Subsequently, there has been a progressive research on choice of treatment modalities that aim to complete maturation of immature teeth.

Keywords: Pulp revascularization, continuous Root development, Physiological Root Development, Disinfection, Endodontics.

1. INTRODUCTION

Conventional endodontic treatment involves various techniques for the chemical-mechanical preparation of root canal to eliminate the microbiota and is often challenging due to the intricate nature of the root canal system. (1) However, this process demands adequate stepwise strategy for completing treatment in immature teeth with open apex. (2) The challenge is attributed to the thin radicular dentin in incompletely formed apex, which does not allow for intensive filing of the root canal system and is prone to fracture during extensive mechanical preparation. (3) Due to incomplete formation of the plexus of Raskow, the tooth does not respond adequately to pulp sensibility and pulp sensitivity test. Preserving the vitality of a tooth is of utmost importance to maintain its responsiveness or the tactile response as an "alert" signal in the presence of pathogenic stimuli and proprioception. (4) Once a tooth loses its innervation and vascularization, it becomes more susceptible to various lesions and fracture. The maintenance of dental vitality enhances the tooth's defenses. Although materials such as MTA and Biodentine provide adequate seal when placed properly but fail to promote physiological root length, (5) thereby causing fracture in the long run. With an open communication between the apex and the periradicular dentin, (6) the obturation material has the risk of inflammation the periradicular tissue. (7,8)

Trauma at the developing stages of the tooth is the most common reason for the lack of complete root formation. (9) Further complicated by systemic infections hindering mineral deposition or by disruption of the blood flow. (10) This work aims to conduct a literature review on pulp revascularization as a treatment modality for open apex and assess its efficacy as a Regenerative Endodontic Procedure. (11)

Pulp revascularization is providential approach in regenerative endodontics as it promotes continued root growth, increased thickness of radicular dentin, apical closure further reducing the risk of root fractures. (12) The concept of revascularization is based on the apical pulp tissue's ability to survive in unfavorable necrotic conditions and proliferate under favorable conditions. In addition to the term "revascularization," (11,13) the concept of pulp revitalization has been employed to describe the generation of vital tissue within the root canal (14). However, using this definition may introduce a conceptual conflict, as the pulp tissue possesses distinct histological features that may not be accurately reproduced by the invaginated tissue originating from periapical tissues. (15,16)

The technique utilizes and induces the stem cells found in dental structures such as apical papilla, pulp and periodontal ligament to stimulate dentin-pulp regeneration. (16) Preservation and the promotion of stem cells within dental structures is very crucial for clinical success. (17) In cases of long standing large periapical lesions, deep caries, or trauma maintenance of stem cell viability can be questionable. (18)

There are two distinct types of stem cells: embryonic stem cells and adult stem cells, also known as postnatal cells. (19) In the context of pulp revascularization, the focus is primarily on mature stem cells, which house at different locations within the dental structure, including the pulp, apical papilla, and periodontal ligament. These clonogenic cells exhibit rapid differentiation and possess the capability to stimulate dentin-pulp regeneration on differentiation.

The three key factors for successful revascularization are- 1. Proper Disinfection of the Root canal (20) 2. Adequate matrix to promote the growth of the stem cells 3. Impervious seal of the access cavity. An ideal scaffold provides platform that binds and promotes the stem cells, has growth factors and undergoes self-degradation overtime. The three types of scaffold are - 1. Blood Clot 2. Plasma Rich Fibrin 3. Plasma Rich Platelet. (21)

Although induction of blood clot is easy within the root canal system with no additional procedure such as drawing of the blood needed but it has lesser growth factors in comparison to PRP or PRF. Platelet-rich plasma (PRP) is three dimensional first generation scaffold that is derived autologously having higher concentration of platelets. It was first introduced by Whitman et al in 1997. (22) These platelets release significant growth factors such as transforming growth factors, vascular endothelial growth factors, platelet derived growth factor, epidermal growth factors, fibroblast growth factors, matrix metalloproteinases 2 and 9, insulin-like growth factors etc. The mentioned growth factors promote healing and favor enhanced stem cell multiplication and differentiation. (23)

Platelet rich fibrin is a second generation which was first used by Choukroun et al in 2001 (24). Unlike PRP it does not have addition of bovine thrombin, comparatively easier preparation and does not require chemical manipulation of blood, making it an autologous leukocyte-platelet rich fibrin matrix. (25) As additional thrombin is not added, the risk of suffering from immunological reaction is eliminated.

Whilst most studies recommend a two-visit approach, some propose a single-session method which also demonstrated root-end development. Clinical cases presented in studies highlight successful outcomes, emphasizing the utmost importance of effective infection control.

Root Canal Disinfection

The initial phase of treating infected root canals in endodontics involves disinfection, achieved through the application of chemical substances and mechanical instrumentation. However, when dealing with immature teeth, mechanical removal of microorganisms is not advisable due to the delicate nature of the thin root walls. Therefore, decontamination is limited to the use of irrigant solutions and intracanal medication. It is preferred to use saline solution followed by 0.5-1% diluted sodium Hypochlorite. In between disinfection using triple antibiotic paste is preferred. (26)

INTRACANAL MEDICAMENT

Root canal medicaments play a vital role in creating a bacteria-free environment for successful revascularization. The most potent intracanal medicament used in the field of endodontics include calcium hydroxide and triple antibiotic paste. The microbiological niche in a traumatized immature teeth with infected necrotic pulp was similar to that of mature teeth infected with apical periodontitis (Nagata et al 2014)

Calcium Hydroxide is an effective medicament due to its high alkaline pH 12.5-12.8, causing an unfavorable environment for the bacteria to thrive. The antimicrobial potential of calcium hydroxide does not seem to be very promising and is weak. In vitro studies have shown increased attachment of human Apical cells to root dentin with calcium hydroxide rather than TAP (Kitikuson and Srisuwan 2016). Prolonged exposure of the radicular dentin to calcium hydroxide has shown to weaken the dentin. However in an in vitro study conducted by Kahler et al 2018 demonstrated no significant difference in strength of radicular dentin when placed for a period of 9 months. Authors concluded that the root fracture after placement is related to the stage of the root development rather than time period for which it is used. (27)

The use of Triple Antibiotic Paste for the disinfection of the root canal was first described by Hoshino et al and Sato et al. The synergistic effect obtained on combination of different antimicrobial agents aids in polymicrobial infection control. (28) Use of triple antibiotic paste containing Minocycline, Ciprofloxacin and Metronidazole is advocated for disinfection in teeth with immature pulp. (29) Modified triple Antibiotic paste, containing doxycycline is used instead of minocycline (30). The recommended use of TAP is at a given concentration of not greater than 1mg mL⁻¹ (AAE 2016) to prevent damage to the stem cells of the apical papilla. However Augmentin when placed within the infected canal has shown to eradicate

nearly 100% of microorganisms invitro (Baumgartner and Xia 2003).However , intracanal medicaments and irrigating solution completely do not eliminate the biofilm within the root canal system. Therefore mechanical debridement in such cases is essential but the same cannot be applied in open apex situation due to thin walls.

EDTA (Ethylenediaminetetracetic acid) is a chelating agent used to remove the smear layer in routine root canal therapy and release Growth factors from the Dentinal Matrix.(31)Use of EDTA has shown to release growth factors in regenerative Therapy(Galler et al 2015).Use of EDTA exposes the binding site for attachment of newly formed tissue (Yamauchi et al). A final rinse with EDTA before placement of the blood clot is advised as it conditions dentine for migration,adhesion and differentiation of the apical papilla to odontoblast like cell.

Irrigant Solutions

The most commonly used chemical substances worldwide for endodontic purposes are sodium hypochlorite (NaOCl) and chlorhexidine. NaOCl demonstrates antimicrobial efficacy against a broad spectrum of endodontic pathogens , with concentrations ranging from 0.5% to 6%.(26) In the context of pulp revascularization, more concentrated solutions, particularly 2.5% and 6%, are preferred to achieve clinical success. Despite their satisfactory antimicrobial properties, these substances are not biocompatible, impacting the survival of dental pulp stem cells and their ability to adhere to dentinal walls.(32)

MTAD, introduced by Torabinejad et al. , is composed of 3% thiosulfate, 4.25% citric acid, and 0.5% polysorbate.(26,33) Considering the pivotal role of stem cells in both revascularization and regeneration, studies have assessed the cytotoxicity and interference of various chemical substances in stem cell adhesion . (34)Sodium hypochlorite (NaOCl), chlorhexidine (CHX), Aquatine Endodontic Cleanser (AquatineEC), Morinda CitrifoliaTM (MCJ), sterile saline, EDTA, and MTAD were evaluated individually and in combination. NaOCl and CHX exhibited cytotoxic effects, resulting in a decrease in dental pulp stem cell adherence to dentinal walls. Interestingly, the presence of a smear layer did not influence this adherence.(32,35)

In comparison to NaOCl and CHX, Aquatine^{CTM} showed lower toxicity to dental pulp stem cells and facilitated cell adherence to root walls .However, further research is needed to comprehensively understand its properties and potential application in regenerative endodontics.(36,37)

Root Canal Medicaments

Pulp revascularization is most effective in an environment free of bacteria, necessitating a thoroughly cleaned and disinfected root canal system before cell colonization can take place. The root canal system infection comprises multiple bacterial species, making it unlikely that a single antibiotic can combat these microorganisms to establish a sterile environment. Researchers observed that the combination of three antibiotics (Metronidazole, Ciprofloxacin, and Minocycline) successfully eliminated bacteria colonizing the dentin surface. Furthermore, this antibiotic paste proved effective in eradicating bacteria within the deep layers of dentin.(37)

The antibiotic paste, containing 400 mg Metronidazole, 250 mg Ciprofloxacin, and 50 mg Minocycline, is prepared in a propylene glycol vehicle to achieve a creamy consistency. (38)Application methods include the use of a Lentulo spiral drill, syringe, or manual files. Despite promising outcomes, the antibiotic paste may exhibit certain side effects, such as crown discoloration attributed to the presence of minocycline, a semi-synthetic tetracycline effective against both Gram-positive and Gram-negative bacteria. However, it remains uncertain whether minimizing the contact time with minocycline could prevent discoloration, as visible crown discoloration is observed after just 24 hours.(39)

Concerns related to the development of microbial resistance represent another relevant factor associated with the use of the triple antibiotic paste. However, as of now, there is no consensus on this assertion, and it is merely speculated that applying this paste to root canals may decrease the likelihood of developing resistant bacteria.

Recent studies have explored the use of calcium hydroxide in pulp revascularization, demonstrating clinical and radiographic success. These studies indicate that dressing root canals with calcium hydroxide can solubilize bioactive molecules, including growth factors from the human dentin matrix, likely stimulating mesenchymal pulp cells to differentiate into odontoblast-like cells. Comparatively, studies by Bose et al. revealed that both calcium hydroxide and triple antibiotic paste were effective in supporting the pulp-dentin complex. Notably, these positive outcomes were observed when calcium hydroxide insertion was limited to the cervical third of the root canal.(40)

Pulp revascularization typically involves a two-session procedure. In the initial session, root canals are thoroughly cleaned using chemical substances and irrigated copiously, followed by the application of intracanal medication for a three-week period. After this interval, a blood clot is induced and sealed with Mineral Trioxide Aggregate (MTA) and composite resin.

While most studies advocate for the therapy to be conducted in two separate sessions, Shin et al. [39] demonstrated a single-session pulp revascularization approach. This method involved root canal decontamination with 6% sodium hypochlorite, sterile saline solution, and 2% chlorhexidine, without mechanical instrumentation. The procedure was completed with MTA/composite resin sealing, leading to documented root-end development and increased width of the dentin walls.

In a 2013 study by Forghani et al., a case involving a 9-year-old patient with localized swelling and pain during chewing was presented. Clinical examination revealed coronary fractures on both maxillary upper central incisors, with the upper right central incisor diagnosed as pulp necrosis with an acute periapical abscess. The upper left central incisor was diagnosed with irreversible pulpitis. Both fractured teeth had immature apices, and radiographic findings indicated a radiolucent periapical lesion around the apex of the right central incisor.

In another study from 2013, Jadhav et al. evaluated and compared apexification induced by revascularization with and without platelet-rich plasma (PRP) in non-vital immature permanent anterior teeth. The patient, a healthy 10-year-old boy, had upper anterior teeth fractured three years prior. Endodontic treatment was initiated but not concluded. PRP, prepared fresh, was introduced into the root canal of the maxillary left central incisor using a sterile collagen sponge, leading to a comprehensive evaluation and comparison of apexification outcomes.

2. DISCUSSION

Effective infection control is a critical factor for the success of pulp revascularization. In numerous experiments outlined in this review, the widely used medication was the three-antibiotic paste (TAP), comprising metronidazole, ciprofloxacin, and minocycline. Metronidazole, an antiprotozoal, antibacterial, and antihelminthic nitroimidazole agent, is particularly noteworthy in endodontics. It disrupts the energy metabolism of anaerobes, impeding the replication, transcription, and repair processes of their DNA. The presence of anaerobic conditions in root canals implies more resistant infections. Therefore, the addition of ciprofloxacin, effective against a broad spectrum of gram-negative and gram-positive bacteria, enhances the efficacy of the paste. Importantly, there is currently no known cross-resistance between ciprofloxacin and the endodontic microflora. Minocycline, a broad-spectrum tetracycline antibiotic, offers a wider spectrum than other members of the group.

Regenerative procedures are an emerging field in health sciences, particularly in dentistry. These procedures can be monitored using computer cone beam tomography or traditional and digital periapical radiographs. The root formation process, involving hard tissue deposition, can be tracked, measured, and compared to previous examinations.(41)

Historically, there was resistance among some authors to attempting revascularization in infected, nonvital, immature teeth. This reluctance was rooted in the uncertainty surrounding the concept, as there was a perceived risk in attempting to revascularize an infected root canal. Consequently, the traditional approach of inducing apexification with calcium hydroxide, mineral trioxide aggregate, or surgical endodontic procedures to seal wide-open apex teeth was commonly chosen as the primary endodontic intervention.

3. CONCLUSION

In conclusion, pulp revascularization emerges as an effective approach for immature teeth, promoting relatively straightforward root formation and potentially improving the prognosis for treated teeth. However, continued research is essential to assess long-term efficacy and explore new approaches in regenerative endodontics.

Conflict of Interest

The authors confirm that this article content has no conflict of interest.

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