Pulp revascularization: a literature review

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ABSTRACT

Permanent teeth with incomplete root formation are one of the greatest challenges of endodontic practice. These teeth need a type of treatment that is different from conventional endodontic therapy. The most common causes of incomplete root formation are: dental trauma and deep tooth cavity, both of which may lead to pulp necrosis. Teeth with incomplete root formation and pulp necrosis were usually treated by apexification. In other words, treatment comprised multiple sessions to replace calcium hydroxide-based root canal dressing and the fabrication of a MTA apical plug to create an apical barrier. Nevertheless, with this method, root dentin walls are thin and fragile. Thus, revascularization becomes a new treatment option that aims at promoting the completion of root formation, with invagination of a new connective tissue in the inner space of the pulp cavity. This study conducts a literature review comparing some case reports that focus on pulp revascularization in immature permanent teeth with pulp necrosis. Based on this review, it is reasonable to conclude that pulp revascularization is a feasible method for root maturation with thickening and, as a consequence, strengthening of young permanent teeth root walls.

Keywords: Pulp revascularization. Apexification. Blood coagulum.

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Introduction

Histologically speaking, whenever the root apex of a tooth does not have apical dentin covered by cementum; or, radiographically speaking, should the apical ending not reach Nolla's stage 10 (tooth with complete root apex), the tooth is diagnosed with incomplete root formation.[1] According to Nosrat et al,[2] treating immature teeth by means of pulp necrosis is a challenge for Endodontics.

A traumatic injury of an immature permanent tooth may lead to loss of pulp vitality and, as a consequence, interrupted root development mainly due to bacterial contamination caused by tooth cavity or traumatic injury.[3] As a result, the tooth is left with an open apex and poor crown-root ratio, given that it tends to have thinner-wall root subjected to a higher risk of fracture. Should an endodontic intervention be necessary, the clinician is about to face a difficult situation, since biomechanical preparation is complicated in these cases.[4]

Conventional treatment of young permanent teeth with incomplete root formation and pulp necrosis includes long-term application of calcium hydroxide to induce apexification.[5] According to Ding et al,[3] this treatment method has several disadvantages, namely: variable treatment time, patient's cooperation and increased risk of tooth fracture after long-term preparation. The MTA plug technique has also been employed to create an artificial apical barrier. Although those techniques prove to be clinically effective, they do not contribute to root strengthening. As a consequence, the absence of continuous root development leads to thin and fragile root dentin walls.[6]

A new concept of endodontic therapy for immature teeth with incomplete root formation and pulp necrosis has been introduced by Iwaya et al.[7] It consists of pulp revascularization, aiming at continuous root development; and invagination of a new connective tissue in the inner space of the pulp cavity. Revascularization has many advantages, among which is the reduction in treatment time, completed within one or two sessions after infection control; favorable cost/benefit, given that a few appointments and little additional material are necessary; and, last but not least, the greatest advantage of all: stimulus for complete root formation, which, as a result, provides root wall strengthening. According to Thibodeau and Trope,[5] as well as Keswani and Pandey,[8] the procedure involves root canal passive decontamination (with sodium hypochlorite, EDTA or chlorhexidine solution) and the use of intracanal dressing which, according to Shin etal,[9] Iwaya et al[10] and Cehreli et al,[11] may be formocresol, triple antibiotic paste (metronidazole, ciprofloxacin and minocycline) or calcium hydroxide paste. Thus, according to Nosrat et al,[2] in the absence of clinical signs and symptoms, treatment goes on by removing the paste and inducing bleeding of apical tissues with a sterile instrument. Once blood coagulum is formed, the root canal opening is sealed at the cervical third with the aid of a MTA barrier. The process of inducing blood coagulum to go into the root canal is justified by the studies conducted by Ostby.[12] The author observed that blood and blood coagulum were essential to form fibrous connective tissue inside an empty root canal. According to Nosrat,[2] the tissue formed in the root canal is not pulp and does not function as pulp tissue. This means that revascularization is similar, but not equivalent to regeneration during the process of wound repair.

Thus, this paper aims at conducting a literature review to assess a series of case reports, published between 1961 and 2013, about young permanent teeth with incomplete root formation and pulp necrosis treated by pulp revascularization.

Literature review

This literature review focuses on clinical cases which, according to some studies, would directly influence the basic criteria required for a successful revascularization treatment. We believe that this methodology increases one's understanding about the study. The extensive literature on pulp revascularization determined that discussions should be restricted to some factors commonly focused by *in vivo* studies and literature reviews. To this end, the following databases were used for research: MEDLINE, PubMed, BBO, LILACS, SciELO and the library archives of the School of Dentistry / Piracicaba (FOP-UNICAMP).

Root formation begins after enamel and dentin achieve the enamel-dentin junction. Tooth root development relies on the inner and outer epithelia of the enamel organ which are connected and apically immersed into the mesenchyme that surrounds them. The connection between both epithelia is known as Hertwig's epithelial root sheath. These cells induce differentiation of inner connective tissue cells into odontoblasts, responsible for depositing the first layer of root dentin. At this point, the continuity of the root sheath is disrupted, and its lower portion remains immersed into the mesenchyme, which induces differentiation of odontoblasts. From this point on, the epithelial rests of Malassez are formed. As odontoblasts differentiate to form the dentin, and as the sheath degenerates, dentin contacts the surrounding mesenchyme. The mesenchymal cells in contact with the dentin differentiate into cementoblasts to form the cementum that is deposited over the root dentin.[13]

According to Torneck,[14] at the beginning of root formation, initial dentin formation causes the disruption of Hertwig's epithelial root sheath, providing it with a lacy aspect in the area permeated by dental follicle. Complete root formation of permanent teeth happens three to five years after tooth eruption.

"Tooth with incomplete root formation", "immature apex", "open apex" or "young foramen" are terms that have been widely used to identify the endodontic processes in which root has not been completely formed.[15]

An open root apex occasionally results from extensive resorption of a mature apex after orthodontic treatment, from periapical inflammation or as part of trauma repair.[16]

In young patients, permanent incisors are commonly affected by traumatic lesions of which type and intensity might cause pulp alterations. The incidence of lesions, particularly those caused by falls, collisions and stumbles, is higher for individuals aged between 8 and 10 years old.[17]

According to Soares et al,[18] the apical constriction of a mature tooth, found near the CDC (cementum, dentin, canal) limit facilitates endodontic preparation and filling. However, the root canal of immature teeth with incomplete apexes is usually hourglass-shaped, with the diameter of the foraminal opening greater than the canal found in the cervical and middle thirds.

Completely formed teeth have a cone-shaped root canal with the major base towards the pulp chamber and the minor, towards the apical third. Conversely, teeth with incomplete root formation do not have the root completely formed. They have a frustum-shaped canal, with the major base towards the apical third. Thus, an open foramen does not provide anatomic buttress which, as a consequence, hinders filling,[15,16] given that biomechanical preparation cannot establish the "apical seat" necessary for gutta-percha cone placement. For this reason, there might be a risk of root canal overfilling (even if cones of greater diameter are used) due to the absence of a physical barrier that prevents condensation necessary to establish complete hermetic apical sealing.[1]

To overcome the aforementioned difficulties, several procedures have been used. All efforts should be made to preserve a vital pulp. Conventional treatment allows the physiological process of root formation (apexogenesis) to happen without further complications.[18] Pulp necrosis, on the other hand, requires especial endodontic intervention.

Traditionally, the absence of pulp vitality and presence of an open apex require an intervention that aims at promoting apexification. The procedure includes cleansing and filling the root canal with a temporary paste (calcium hydroxide monthly replaced) that stimulates the formation of calcified tissue in the apex. Nevertheless, calcium hydroxide-induced apexification has its limitations, for instance, the time required for the formation of an apical barrier (from 6 to 24 months for a porous barrier). Additionally, the technique does not promote complete root formation, but apical closing instead. In addition to the aforementioned technique, the method of placing an apical barrier composed of mineral trioxide aggregate (MTA) has also been used as buttress during condensation for definitive filling.[5,15,19]

Apexification procedures have some disadvantages, including the fact that root canal walls remain thin and that the finishing process of root development might not occur. As a result, teeth are more likely to fracture after endodontic treatment.[2]

Revascularization procedures are recommended to treat young permanent teeth with pulp necrotic tissue and/or apical periodontitis.[20] This method increases thickness of root canal walls as a result of hard-tissue deposition, and stimulates complete root development of young permanent teeth.[21]

According to Camp,[22] Shin et al,[9] Banchs and Trope,[23] Nosrat et al[2] and Chueh et al,[24] before endodontic treatment, correct pulp and periapical diagnoses are essential for teeth with incomplete root formation, since there is risk of pulp vitality loss. Diagnostic tests are essential for obtaining as much information as possible before exploring all treatment options.

Diagnosis starts with patient's complete medical history and the potential implications related to the treatment of choice. Patient's dental history and associated pain are useful to determine the conditions of the pulp.[9,21-24]

Aspects such as nature, type, length and distinction between provoked and spontaneous pain must be registered. Pain provoked by thermal, chemical or mechanical irritants usually suggests a minor degree of pulp inflammation which, most of the times, is reversible. Spontaneous pain, however, is commonly associated with extensive and degenerative irreversible pulp inflammation or necrosis.[22,24]

Medical as well as dental history is determined by a complete clinical examination. Areas of redness, swelling, fluctuation, tissue sensibility, dental cavity, defective restorations or fractured teeth are recorded. Crown discoloration, or parulis, might be indicative of pulp necrosis.[2-5,22,24]

Electrical and thermal pulp tests are limited due to variability in response. Occasionally, they might not be elucidative because, in teeth with incomplete root formation, the parietal layer of nerves is not completely developed and, as a consequence, the pulp responds less to those stimuli.[18,21-23] Furthermore, invalid data might be obtained as a result of less reliable responses (fearful child, conduct-related issues, lack of understanding or poor communication). Therefore, more sensitive methods and tools must be developed.[22,25] As a consequence, most diagnoses are made by observation of clinical symptoms and pathologic radiographic evidence.

Radiography is of paramount importance to the diagnosis of pulp pathologies in teeth with developing apex. Apical radiograph of high quality is used to assess root development, periapical radiolucency and root resorption.[2,6,9,21,22,24,26,27]

Given that revascularization occurs in immature teeth with open apex and pulp necrosis, this situation is frequently found in young patients. For this reason, patient's age is key to help immature teeth attain complete root maturation.

Most studies focusing on pulp revascularization analyze the clinical-radiographic results of treatment performed on immature teeth of patients aged between 6 and 16 years old.[2-5,6,9,12,21,23,24] Four researches also report tests conducted with 6-month young dogs.[12,28,29,30]

According to Chueh et al,[24] young children have great healing capacity and better potential of stem cell regeneration. Furthermore, immature teeth have faster apical bone healing and continuation of root development, which reveals the great potential for regeneration in young children's teeth.

Most case reports and studies reveal that lower premolars with pulp necrosis and upper incisors, which are more likely to fracture, are the type of teeth most commonly treated by revascularization.[3,4,5,9,23,24,28,31,32] However, two researches report revascularization of immature molars.[2,32] Radiographically speaking, these teeth have immature apex, large canal, parallel walls and open apex.[3,4,21,23,24]

These teeth are often diagnosed with chronic periapical abscess.[4,9,21,23] Recent studies reveal that revascularization is predictable in ideal conditions and with chemical decontamination of root surface.[2,4,21,23,24,32]

According to Nosrat et al,[2] Banchs and Trope,[23] Cotti et al,[4] Thibodeau and Trope,[5] Wang et al,[28] Ding et al,[3] Chen et al[21] and Shin,[9] the ideal conditions comprise root canal biomechanical preparation carried out after local anesthesia and isolation with rubber barrier. In case of remaining restorations or dental cavity, the barrier is removed and a cavity access is prepared with a fissured diamond bur and abundant water. The pulp chamber entrance is copiously irrigated with an auxiliary chemical substance. Root canal mechanical instrumentation is not carried out by the majority of revascularization treatment procedures not only because immature teeth have thin dentin walls and, for this reason, are more likely to fracture; but also because smear layer formation could obstruct dentin walls and tubules.[3,4,5,9,21,24] Therefore, chemomechanical preparation aims at cleaning, extending and shaping the root canal, since infection control promotes a favorable environment that allows pulp and periapical cells to participate in repair and regeneration.[21]

To this end, irrigation solutions are used in root canal irrigation-aspiration due to their minor viscosity coefficient and reduced superficial tension, requirements that favor increased jet reach, turbulence formation and liquid reflux towards a coronary direction, all of which allow a more effective root canal cleaning.

The literature reveals that some researchers use sodium hypochlorite irrigation similarly to conventional root canal preparation, which is widely used at different concentrations: 5.25% NaOCl,[2,3,4,21,23] 2.5% NaOCl,[24] 1.25% NaOCl,[5,28] 1% NaOCl + EDTA,[32] 6% NaOCl + saline solution + 2% chlorhexidine gluconate.[9] This is due to the potent antibacterial and proteolytic activity of sodium hypochlorite which dissolves organic material, eliminates microorganisms and removes necrotic tissue. Higher concentrations increase the effect of sodium hypochlorite, however, such efficacy is neutralized by the increase in toxicity, given that sodium hypochlorite leads to inflammatory response and severe damage when in contact with vital tissues.[32] Nevertheless, the cases reported to date reveal that the application of sodium hypochlorite do not produce any post-operative sequelae. Once the procedure is complete, the root canal is gently dried with sterile paper points.

Revascularization success depends on the absence of bacteria inside the root canal, since the new tissue ceases its development as bacteria are found in the root canal space.[30,33] Thus, the technique most commonly employed for revascularization includes the use of a triple antibiotic paste applied to complement canal decontamination. Several topical antibiotic combinations are able to decontaminate carious dentin and necrotic root canal. One of the combinations used is the triple paste composed of metronidazole, ciprofloxacin and minocycline. It has proved effective in fighting pathogens usually found inside the canal root system,[2-6,9,21,23,28] and in eliminating bacteria found deeper in the root dentin (which can survive even after endodontic treatment).

Sato et al[31] concluded that the combination between ciprofloxacin, metronidazole and minocycline enters the dentin tubules and eradicates bacteria from infected root dentin. This strongly suggests that root canal treatment allows infected root dentin to be decontaminated by the topical application of those drugs.

Considering that most bacteria found in deeper layers of infected root dentin walls are strict anaerobic, metronidazole was the first choice of antibacterial drug. It has been reported that metronidazole enters deeply into carious lesions, decontaminates lesions *in vivo* and spreads through the dentin. However, alone, it cannot neutralize all bacteria. For this reason, other drugs are necessary to sterilize infected root dentin. Therefore, ciprofloxacin and minocycline, combined with metronidazole, were necessary to decontaminate infected root dentin because, together, they generate fibroblasts that are viable for toxicity test and biocompatible with the tissues.[29]

On the other hand, calcium hydroxide and formocresol have also been effectively used as intracanal dressing, decontaminating the root canals of young permanent teeth with pulp necrosis and apical periodontitis/abscess during revascularization procedures.[3,4,6,21,23,24,26] Nevertheless, some authors describe that a retrospective evaluation of radiographic results reveal that revascularization with triple antibiotic paste significantly increases root wall thickness, greater than what is produced by calcium hydroxide or formocresol. Additionally, radiographic results reveal that disinfection by formocresol caused minor improvements in root length and thickness. Furthermore, a series of cases concerning revascularization treatment with calcium hydroxide as intracanal dressing reveal that a 10 to 29-month follow-up is necessary to judge radiographic evidence of root development.[2,6]

The polyantibiotic mixture is applied with a K-file #25 instrument, 3 mm shorter than the length radiographically estimated. Afterwards, the tooth is temporarily restored. After a period of time, the patient returns and the tooth is once more anesthetized with anesthetic without vasoconstrictor, which facilitates isolated and accessed bleeding. Subsequently, the antibiotic paste is removed by means of a new irrigation procedure and, afterwards, canal is dried with paper sterile points.

Apical tissues are irritated using a K-file #40 instrument, so as to obtain bleeding and blood coagulum formation inside the root canal, as well as to guide tissue invagination.[2-5,21,23,25,28,29,32] Blood coagulum consists of a fibrin network that functions as a path for cell migration, including macrophages and fibroblasts in the periapical region. Blood coagulum, however, not only forms an inactive scaffold, but it also provides growth and differentiation factors that are important for the process of repair.[2,3,5,28] Additionally, it contributes to tissue inner growth.[2-5,23,28]

In 1961, Ostby[12] reported that laceration in granulation tissue adjacent to the foramen might be beneficial to the process of repair. Moreover, blood has inherent antibacterial proprieties such as cells that develop into phagocytes. Blood invagination into the root canal might have two effects: destruction of remaining microorganisms and phagocytosis of necrotic remnants. Last but not least, the most important benefit: blood coagulum organization and the formation of fibrous tissue in the apical third.

Thus, it is safe to suppose that blood coagulum — inside the decontaminated and empty root canal space which contains growth factors derived from platelets, as well as growth factors derived from dentin walls — plays the role of a scaffold rich in proteins, crucial to a successful population, as well as to cell differentiation and root development.[2,3,5]

According to Ding et al,[3] during revascularization treatment, blood coagulum formation should remain until it reaches 3 mm below the level of enamel-dentin junction. Subsequently, an MTA plug is fabricated over the blood coagulum, preventing bacteria from entering into the root canal before revascularization. This procedure is performed to develop a coronary sealing against bacteria and to prevent potential root canal recontamination.[2-6,9,21,26,28] MTA has been used to promote effective pulp sealing. Oppositely to calcium hydroxide, it is biocompatible with adjacent pulp tissue and is able to induce pulp cells proliferation. Moreover, MTA is able to maintain a higher pH for long periods of time, in addition to having excellent marginal adaptation. It has also been used as coronary plug, due to the beneficial properties it has during therapy.[2,9,26]

Nosrat et al[2] also report that the use of CEM cement is an alternative to the cervical plug. This tooth-colored, water-based cement has the same clinical applications of MTA, but with a different chemical composition. The sealing capacity, cytotoxicity and biocompatibility of CEM cement are comparable to MTA. However, unlike the latter, the characteristics of CEM cement surface resemble the human dentin which is able to form hydroxyapatite, even in normal saline solution, in addition to promoting the differentiation into stem cells and inducing the hard tissue formation.

The MTA plug is usually protected by a glass ionomer layer, 2 mm thick, placed over the cement which, in turn, is covered by a resin barrier placed in the coronary portion to seal the tooth against potential infiltration.[2-5,21,23,28] Young permanent teeth submitted to this process should be clinically and radiographically preserved from 6 to 26 months.[2-6,9,21,23,26,28] Follow-up is necessary to verify whether the tooth had a good response to treatment, continued its root development in a physiological manner, and whether it is asymptomatic and with apex is closed, all of which represent a successful case of revascularization.

Final Considerations

Based on this literature review on revascularization, it is reasonable to conclude that:

» Apexification remains as the first choice of treatment for young immature permanent teeth with incomplete root formation and pulp necrosis.

» Revascularization is advantageous over apexification due to the number of sessions and, as a consequence, the treatment time required. Revascularization requires one to three sessions performed within a short period of time, approximately one or two weeks. Additionally, it is advantageous for increasing dentin wall thickness and favoring continuous root development.

» There are new possibilities (revascularization) for pulp treatment of young permanent teeth with open apex and pulp necrosis.

» Additional studies are warranted to further investigate the topic of revascularization, given that the benefits yielded by this technique are greater in comparison to the results achieved by apexification (thin root walls more susceptible to fracture).

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