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Pulp Revascularization: Future Therapy of Tooth with Open Apex

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Abstract

Introduction: The endodontic management of necrotic permanent immature teeth is a challenge for the practitioner. These teeth are treated by apexification. However, because of the complications associated with this treatment, researchers have developed other therapies. Currently, a new technique called pulp revascularization has emerged. This technique allows the continuation of root completion thanks to a healthy tissue newly formed at the intra root canal level. Material and method: A literature search of articles dealing with pulp revascularization of immature permanent teeth was conducted using two types of search strategy, a literature search using keywords on databases and then a manual "bottom-up" search of references of previously identified articles. Results: 112 articles were identified based on inclusion and exclusion criteria. Discussion: This work showed that pulp revascularization is a new therapy that aims to restart root development on an immature permanent tooth. It is based on the principle of tissue engineering and uses the differentiation potential of stem cells. Conclusion: Currently, the literature values revascularization as it allows root development, sidewall thickening, apical closure and a decrease in periapical lesion and ensures a good sealing. Clinical and radiographic success rates appear to be encouraging, except that factors influencing treatment must be taken into consideration.

Keywords

Immature Tooth, Apexification Pulp Therapy, Pulp Revascularization

1. Introduction

Previously, the wide-open apex of the immature tooth was filled by apexification with calcium hydroxide or the mineral trioxide aggregate (MTA). This is due to

the cessation of root completion and the presence of thin and fragile root canal walls.

Currently, thanks to scientific research, we have discovered major advances in the field of tissue engineering, and the field of endodontics has not escaped it. This is where the notion of root canal revascularization of teeth with open apex began to find its indication one step at a time.

This new treatment is based on the removal and replacement of infected or inflamed pulp with new, mainly connective tissue by means of stem cell differentiation [1]. With this therapy, the immature tooth could continue its completion root, apical closure and allow the total elimination of the periapical bone lesion.

The main objective of this work, through a literature review on "Pulp revascularization", is to develop this new therapy for necrotic permanent immature teeth by describing not only its implementation and operating protocol but also its indications, its limitations, the different clinical procedures and the products used.

2. Materials and Methods

This literature review is a methodical type of literature review that was conducted in four stages:

2.1. Literature Search

A computerized literature search strategy on databases accessible via the Internet was established, notably PubMed (main search engine) which provided access to the Medline bibliographic database.

Also, an advanced search using Boolean equations and direct links to articles on a topic similar to the selected article was used during our search strategy. ScienceDirect and Google Scholar are search engines that were also explored.

To facilitate our computerized bibliographic search, targeted keywords were used: immature teeth, dental pulp regeneration, dental revascularization, dental triantibiotic, pulp dental stem, dental roots development, immature necrotic teeth, pulp revascularization, immature tooth treatments.

A manual literature search was also included in our search strategy. It consisted of a reading of all the articles found as well as a study of their bibliographies. It allowed us to collect a number of new articles that would have escaped the computer search.

-Selection of articles:

For the selection of articles, inclusion and exclusion criteria had to be respected. (**Table 1**)

2.2. Critical Reading

The selected articles were subjected to a critical methodical reading to retain only those with sufficient methodological quality, using different critical analysis grids.

Table 1. Inclusion and exclusion criteria.

Inclusion criteria	Exclusion criteria
-articles written in French and English, over a period from 2000 to 2015. -articles dealing with pulp revascularization therapy on immature teeth with necrotic/inflamed pulp. -Articles describing the operating protocol for this therapy. -Articles describing the different materials suitable for this therapy.	-articles describing the endodontic management of teeth with structural or shape abnormalities. -articles describing endodontic management on a mature deciduous or permanent tooth. -Articles describing traditional management of immature permanent teeth.

3. Results

After the literature search, 138 articles were identified as good for our work. The use of the inclusion and exclusion criteria cited above allowed us to retain 128 articles that could correspond to the topic studied.

From the 128 articles, we identified 117 by reading the title and abstract. And after the elimination of five articles that did not meet the inclusion criteria, 112 were retained for our topic.

Revascularization is a relatively new and forward-looking therapy for the treatment of immature permanent teeth with interrupted root development [2]. Regeneration of the dentin-pulp complex is targeted in this therapy for teeth with irritated pulp [3].

It is a therapy that requires the restoration of a blood supply. It describes the recolonization of a cavity by a neoformed tissue rich in blood vessels [4] [5] [6] [7].

The principle of this revascularization was inspired by the tetrad of tissue genes. The latter is based on four main elements: stem or progenitor cells, growth factors, a matrix that can control the development of this tissue and a favourable environment. [5] [8] [9]

Analysis of the articles on pulp revascularization revealed several clinical procedures, and comparison of these revealed a fairly similar sequencing of the steps:

-First step: Root canal disinfection and introduction of intra root canal medication (no longer used in recent years)

-Second step: Induction of the blood clot and placement of the capping material.

-Third step: Placement of the final filling.

Although the operating protocols are similar, the materials used in revascularization may vary from one practitioner to another.

During root canal disinfection, the removal of necrotic and/or infected tissue and microorganisms is an essential step in the success of the treatment prior to

final root canal filling. There are three different irrigation solutions that can be used in revascularization therapy (Table 2).

Regarding intra root canal medication, two main materials are used:

Calcium hydroxide:

Also called hydrated lime, first used by HERMANN in 1937, calcium hydroxide is a product widely used in endodontics for its chemical, antimicrobial, antiseptic, haemostatic, anti-inflammatory and anti-infectious actions.

Tri-antibiotic paste: TAP:

This is a classic-based paste developed by Sato et al in 1996 and optimized by Hoshino and coll in 1996, consists of three antibiotics: ciprofloxacin, metronidazole and minocycline. It comes in two main dosages. However, a study evaluating the viability of desmodontal fibroblasts tends to show that TAP is more cytotoxic than calcium hydroxide, cytotoxicitéy in relation to the presence of minocycline [10].

Despite the desired bactericidal effect, the clinical and biological use of this combination may present certain undesirable effects, such as: development of bacterial resistance [11], allergic reaction, as observed in animal studies [12], staining of the dental crown in humans [13], which is associated with the presence of minocycline. [14]

Once the blood clot is formed, it must be covered with a material that has certain biological and physico-chemical properties to ensure the capping. (Table 3)

According to articles on revascularization therapy, some advocate the use of calcium hydroxide as a capping material. At the same time, materials such as MTA, Biodentine or CEM (Calcium Enriched Mixture) have begun to be used. (Table 4)

4. Discussion

The analysis of all the articles dealing with the subject of revascularization, revealed two operating protocols with an identical principle, only the first time that differs.

Table 2. Advantages and disadvantages of the different irrigators used.

	Advantages	Disadvantage
Sodium hypochlorite	°wide-spectrum antibacterial action on spores, yeasts and viruses	°cytotoxicity proportional to its concentration 2.5% is the best concentration
EDTA	°removal of smear layer and mineral debris	°no action on organic debris decreased action on contact with sodium hypochlorite
Chlorhexidine	local antiseptic chemical safety broad-spectrum bactericide, antifungal	°reduced action on organic debris

Table 3. Properties of the ideal capping material according to specifications.

Biological properties	Physicio-chemical properties
	°tightness
°biocompatibility	°good mechanical resistance
anti-inflammatory action	°Compatibility with filling materials
anti-infective action	°radio-opacity
toxicity test	simple use
	°no staining of the teeth

Table 4. Table of advantages and disadvantages of different capping materials.

Material	Advantages	Disadvantages
Calcium hydroxide	°Bactericidal effect °Acidity neutralized °Local Haemostatic	°Resorbable °low resistance °Drought of the dentin cells
MTA	Marginal adaptation Biocompatibility °Low risk °Decrease in the number of treatment sessions	°Average clinical experience relatively high cost °Crown discoloration °long setting time (4 h)
Biodentine	°Decrease in the number of treatment sessions °Product for capping and at the same time temporary crown restoration °No crown discoloration °Good sealing Biocompatibility °Reduced setting time /MTA	°Water contamination slows the setting Lower cost °Not enough clinical experience at this time
CEM cement	Setting time less than 1 hour Handling in a wet environment possible Low failure rate	°Relatively high cost

4.1. Anesthesia

According to Wigler in 2013, anesthesia was justified when root canal exploration with a file or a gutta cone induced sensitivity. In this case, anesthesia without vasoconstrictors was recommended to minimize sensitivity and maximize the chances of having an adequate clot. [15]

4.2. Root Canal Disinfection

Although there are two different disinfection protocols, they have in common: the use of sodium hypochlorite with a concentration between 1.5% and 2% which avoids any risk of toxicity on the cells involved in the revascularization

and on the dentin [15] [16]. And the use of EDTA ensures demineralization of the dentinal root walls and facilitates the release of growth factors into the dentinal matrix. These promote the proliferation, survival and differentiation of stem cells [17].

Wang *et al.* recommended the use of 2% Chlorhexidine as the irrigation solution of choice when the practitioner decides to change the hypochlorite for its disadvantages.

At the end of the disinfection, it is necessary to introduce an intra-canal medication such as calcium hydroxide. According to Bystorm and Sundqvist in 1985, if the root canal remains empty between two sessions, the bacteria multiply rapidly and are able to regain their initial level. [11] [16] [18]

In addition, the literature has shown the interest of triple antibiotic paste as it is capable of eradicating endodontic pathologies by eliminating bacteria from the deep layers of root canal dentin [19]. The effectiveness of the combination of these three antibiotics has been shown in animal studies and has made it possible to sterilize 70% of the samples without instrumentation and without the use of disinfectant irrigation solution [20] [21] [22].

According to the literature, it is possible to use a macrolide combined with calcium hydroxide, or simply the hydroxide alone to reduce the clinical signs observed [19]. The use of minocycline is contrary to recommendations. Wiggler *et al.* in 2013, showed the possibility of using cephalosporin instead of minocycline as they had equivalent efficacy.

In conclusion, the studies show that calcium hydroxide and triple antibiotic paste allowed the elimination of a similar rate of bacteria >90%. [23]

The use of calcium hydroxide instead of antibiotics may be recommended in case of sensitivity to one of the antibiotics [24]. At present, it tends to be chosen more and more systematically as an intra-canal inter-sessional medication.

4.3. Induction of the Blood Clot

As soon as the symptoms of inflammation are resorbed, usually at the second visit, the central element of the revascularization procedure is the induction of bleeding into the root canal. In all protocols, it is reported that the formation of our blood clot is done by a deliberate apical overextension, using a large-diameter file, to induce intra-canal bleeding. It remains the primordial step for the success of this technique. But the formation of the bleeding remains unpredictable as it depends on the practitioner and the intra-canal medication.

It should be noted that the use of vasoconstrictors also influences bleeding and minimizes the chances of forming an adequate clot by constricting the vessels and reducing blood flow [25]. This clot forms in the apical 2/3 after about 7 to 10 minutes. [19] [26]

4.4. Capping Material

The literature highlights MTA, thanks to its chemical, biological and physical properties, also thanks to its ability to release calcium ions, in addition to its set-

ting in the presence of blood or water and its high biocompatibility. For a good seal, it has been recommended to place a 3 - 4 mm layer directly in contact with the blood clot, thus serving as a first filling layer [15] [27].

Nevertheless, due to its progressive degradation and poor sealing, MTA has been gradually replaced by Biodentin, which has the ability to complement the formation of the hard tissues of the tooth, and has certain advantages over MTA (properties identical to human dentin, absence of crown discoloration). Some authors who have used CEM have shown that its clinical indications are similar to MTA. They have also shown that this material has an antibacterial capacity comparable to calcium hydroxide and higher compared to MTA, a very good clinical decline similar to MTA [28].

5. Results of the Therapeutics

-Clinical results: clinically, revascularization allows a disappearance of clinical symptoms and a disappearance or healing of periapical lesions, despite the different disinfection protocols even in the absence of mechanical instruments [29]. As for the response to the vitality test, this is difficult to interpret, except that a response to the test affirms a neoformation of tissue in the root canal as well as a neo-innervation, whereas a negative response does not indicate the failure of this therapy [30].

-Radiological results: according to the results of this research it is deduced that pulp revascularization allows further root development, which means root lengthening and thickening. According to Lenzi and Tope in 2012, the physiological response following revascularization may vary from patient to patient. In fact, the initial stage of root completion and the duration of the follow-up of the patient affect the results. Thus, when this therapy is performed on teeth with fully developed roots, only apical closure is observed. For Chen *et al.* in 2012, the variations may also be qualitative; they reported five types of tissue responses following revascularization [16]:

- Type 1: increase in the thickness of the root canal walls and continued root development.
- Type 2: no significant root development but closure of the apices.
- Type 3: Continued root development with open apices.
- Type 4: severe calcification, with obliteration of the root canal space.
- Type 5: formation of a barrier of mineralized tissue in the root canal space between the MTA and the apex.

6. Conclusions

Regenerative endodontic procedures have become a part of the endodontic treatment spectrum except that in case of failure, apexification therapy will not always be possible especially if the coronal plug is the MTA.

Specialized clinicians need to know the procedure, the biological background, the advantages and disadvantages, the potential outcomes from a research-based

biological perspective and a pragmatic patient-centered perspective.

Currently, the literature values revascularization because it allows for root development, sidewall thickening, apical closure, as well as decreased periapical injury and good sealing.

At the same time, new biological perspectives aim at restoring pulp vitality by means of stem cells. However, these techniques are still complicated, uncertain, extremely expensive and, above all, the bioethical stakes are getting involved concerning the collection and use of these cells.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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