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Mini Review

Direct Pulp Capping with Calcium-Based Materials: A Mini-Review

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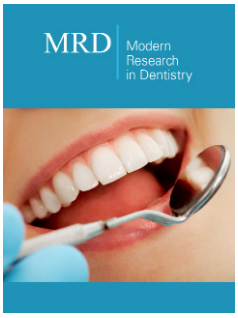

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Abstract

The dentin-pulp complex responds to injuries and harmful stimuli that affect the tooth by depositing dentin matrix in order to protect the pulp tissue, maintaining tooth vitality. However, maintaining vitality after pulp tissue exposure is still a challenge in dentistry. In this sense, the re-emergence of vital pulp therapies gained strength, especially due to its biologically minimally invasive approach. Among them, direct pulp capping is considered a low invasive technique based on the placement of a dental material directly on the exposed pulp site, facilitating the formation of a protective barrier and the maintenance of pulp vitality. Calcium hydroxide was the most used material for this purpose in the last decades. However, the development of new biocompatible materials, such as MTA and Biodentine, has being related with higher rates of clinical and radiographic success, reinforcing the effectiveness of this treatment. Despite that, more randomized clinical trials and histomorphological analysis of the newformed hard tissue are still needed to assess the quality of this treatment in the long term.

Introduction

The dentin-pulp complex is a biological complex composed by dentin and pulp tissues, which maintains an intimate structural, embryological and functional relationship. In this way, dentin and pulp are not considered isolated structures, but rather a complex in which tissue response mechanisms and its repercussions act as an integrated manner, maintaining a profound relationship throughout the life of the tooth. While the dental pulp has the essential function of forming the dentin matrix, the dentin, in turn, protects the pulp from external stimuli, coating it with a hard mineralized tissue [1-3].

The dentin-pulp complex vitality throughout a tooth's life contrasts with the loss of cellular enamel material after its eruption in the oral cavity. As an important consequence of this vitality, the dentin-pulp complex is able to respond to injuries and harmful stimuli that affect the tooth. When dentin is physically and/or chemically attacked, the pulp responds to these stimuli aiming to decrease dentin permeability through the formation of dentin matrix, as long as this tissue is not contaminated by bacteria and these stimuli do not exceed its repair capacity. The nature and magnitude of the response will reflect the extent of the lesion and the condition of the tissue in the complex [4-6].

The relationship between dentin and pulp starts in the tooth germ, when the first layers of dentin are deposited by odontoblasts that are recently differentiated from the dental papilla. Odontoblasts are post-mitotic cells organized as a layer of palisade cells along the interface between dental pulp and dentin [7]. Primary (developmental) dentin is formed by these cells during tooth development. In post-development, odontoblasts continue to deposit secondary (physiological) dentin slowly over the tooth lifetime [7,8] (Orchadson 2001). Tertiary dentin, in turn, is deposited in response to an injury or damage to dental tissues. It differs from the primary and secondary not only in its deposition rate, but also in its composition [9].

Several injuries can cause damage to the dentin-pulp complex. Among them, we can highlight the restorative procedures (cavity preparations and materials applied to the dentin), caries lesions and dental wear or trauma. In general, these stimuli can occur in small or large

extent and in low or high intensity, reflecting significantly on the type of tertiary dentin to be formed [10,11].

In this way, tertiary dentin can be subclassified as reactive or reparative. The reactive dentinal matrix is deposited by surviving odontoblasts that regulate its secretory activity in response to a relatively mild stimulus (of small extension and low intensity). In turn, the reparative dentin is secreted by a new generation of cells (odontoblast-like cells) differentiated from populations of progenitor stem cells. This process occurs in response to a stimulus of greater extension and intensity, culminating in the death of primary odontoblasts [11,12]. This process is more complex, since it requires initial recruitment of progenitor cells, signaling of cell differentiation and secretion of dentinal matrix [13,14].

After the recruitment and migration of stem and progenitor cells to the injury site, these cells begin to proliferate, expand, and then differentiate into odontoblast-like cells, under the influence of bioactive molecule signaling [15]. The odontoblastic cells synthesize organic matrix of type I and type V collagen and actively participate in its mineralization by secreting proteoglycans, glycoproteins and non-collagen proteins involved in nucleation and in the control of the growth of the mineral phase, such as: sialophosphoprotein dentin sialophosphoprotein), dentin matrix protein 1 (DMP-1, from dentin matrix protein1), alkaline phosphatase (ALP from English alkaline phosphatase) and osteocalcin (BGLAP from English bone gamma-carboxyglutamic acid-containing protein). All these components of the organic dentinal matrix will subsequently be mineralized, forming a reparative hard tissue [2,7].

The inflammatory process, caused by pulp injury, is responsible for inducing the repair process. The dentin-pulp complex reacts to the harmful stimulus through a combination of inflammation and mineralization. The balance between pulpitis and repair is essential to preserve pulp vitality. Thus, both processes must be in balance for the repair to take place. Otherwise, if the inflammatory response happens too intensely, the effects on the pulp tissue will be harmful, hindering the repair process and possibly leading to cell death. In cases of pulp tissue infection, the problem becomes even more serious. There will then be a need for balance between the inflammatory and repair processes, in order to favor the recovery of pulp tissue [9,16,17].

Traditionally, the management of deep carious lesions has been conducted with complete (or non-selective) removal of carious tissue, which can often lead to unintended pulp exposure and, consequently, endodontic treatment. However, management strategies for treating moderately exposed pulp have been changing in recent years. There is a resurgence of a tendency to avoid pulpectomy and return to vital pulp treatment techniques, such as partial or complete pulpotomy and direct pulp capping. These changes results of a better understanding of the repairing response of the dentin-pulp complex [18].

The success of restorative dentinogenesis depends on the adequate reestablishment of the morpho functional integrity of the dentin-pulp complex, making it capable of forming dentinal tissue in the site adjacent to the lesion, with a controlled inflammatory response. For this, the protection of the dentin-pulp complex through the application of specific materials between the pulp tissue and the restorative material can avoid additional damage caused by the surgical procedure, toxicity of the restorative materials and penetration of microorganisms due to infiltration [19-21].

The last few years have been marked by the development of new materials for this purpose, resulting in more predictable treatments from a clinical point of view. However, scientific evidence is still not consistent in relation to critical issues such as the prognosis of treatments, superiority between the materials used and quality of the newly formed bridge and underlying pulp tissue [18].

Direct Pulp Capping

Among the several trends in contemporary endodontics, we can highlight the development of biologically minimally invasive therapies, including the regenerative endodontic procedures and vital pulp therapy. Direct pulp capping is a less invasive approach to keep the exposed pulp vital [22].

As highlighted previously, the exposure of the pulp tissue places at risk the maintenance of the vitality of the dentin-pulp complex. This loss of vitality is even more serious when it affects teeth with incomplete rhizogenesis, where the development of the dental root is interrupted, resulting in tooth with shorter roots and thinner dentinal walls, which can lead to root fracture and loss of the element [23].

In general, there are three main causes for vital pulp exposure: caries injuries, mechanical factors and trauma. Caries exposure occurs when the carious lesion advances sufficiently towards the pulp tissue, exposing it even before the complete removal of the carious tissue. On the other hand, if exposure occurs during the preparation of a cavity free of caries, this is considered a mechanical exposure. This type of exposure usually occurs accidentally during tooth preparation. Traumatic exposure, in turn, is the result of trauma (such as during sports) capable of fracturing the coronal part of the tooth [24].

Treatment options for pulp exposure are pulpectomy followed by endodontic treatment, pulpotomy (partial or complete) and direct pulp capping.

Among them, direct pulp capping is considered the least invasive technique and is based on the placement of a dental material directly on the exposed pulp area in order to facilitate both the formation of a protective barrier [25-27] regarding the maintenance of pulp vitality [28,29].

Several factors can directly affect the results of direct pulp capping treatment. Among them, the patient's age and the clinical condition of the pulp related to the patient's symptoms are of importance. Younger patients tend to respond with a higher success rate than older patients [30,31]. This factor is probably related to the high metabolic rate and repair capacity of the youngest pulp. In addition, in general, the vital pulp can be classified into three clinical conditions: normal pulp, reversible pulpitis or irreversible pulpitis. Pulp capping is indicated in cases of normal pulp or

reversible pulpitis, when the patient has no clinical symptoms or when the symptoms disappear after the removal of the harmful stimulus [24].

The first direct pulp capping treatment was carried out in 1756 by Pfaff, using gold leaf [24]. Since then, several materials have been recommended for direct pulp capping [32,33]. Pulp capping materials are dental materials used to protect the exposed dentin-pulp complex and must promote pulp repair without causing damage to cells and the extracellular matrix, in order to maintain specialized connective tissue with normal characteristics, as well as promote the formation of dentin tissue [1,34].

Some properties are desired and considered essential for an ideal capping material, such as: ability to control infection; controlling inflammation; present adhesion to dentin, preventing infiltration; be easy to handle; promote the formation of dentin tissue; be biocompatible; and to be a biostimulator, which means to be able to modulate the pulp tissue response to aggression [17,35,36].

Currently, there are several materials available to be used in capping procedures. Among them, the most used and described in the literature are Calcium Hydroxide (CH), Mineral Trioxide Aggregate (MTA) and, more recently, tricalcium silicate-based material (Bio dentine) [24]. However, other materials, such as zinc oxide and eugenol cements [37] and photo-activated glass ionomer [38] have already been described.

Calcium hydroxide

Historically, CH has been described as the most used material for direct pulp capping procedures. It was introduced in dentistry in 1921 by Hermann and for several decades it was considered the "gold standard" of capping materials [39,40]. Chemically, CH is a strong base with an alkaline pH of 12.5 to 12.8. Its main action is based on ionic dissociation of the calcium (Ca^{+2}) and hydroxyl (OH^{-}) ions, guaranteeing its high pH that gives it excellent antibacterial properties, minimizing or eliminating the penetration of microorganisms and subsequent irritation of the pulp tissue, in addition to helping maintain the state of alkalinity of the exposed pulp tissue. These properties are essential to enable tissue formation [41,42].

When in contact with the exposed pulp tissue the CH induces a chemical injury caused by hydroxyl ions, causing an initial superficial necrosis [43]. This necrosis causes mild irritation and stimulates the pulp to repair, forming a dentin bridge of reparative dentin as result of cell differentiation, extracellular matrix secretion and subsequent mineralization by saturation of the zone with calcium ions [42,44-46]. However, studies have reported that the mineralized tissue barrier formed is discontinuous, of poor quality, and irregular requiring a long time for its formation, which enables microorganism's invasion and complications of the tissue repair [47,48]. In fact, CH has several disadvantages, such as inflammation of the pulp surface, which may present necrosis after capping, presence of tunnel defects in the dentin bridge, high solubility in oral fluids, lack of adhesion, degradation over time and, adding all these factors, the lack of an efficient seal of the underlying pulp against recurrent infections due to microleakage [49-51].

As a result of the disadvantages found in the use of CH, a significant number of materials have been tested and reported in the literature in the last two decades as alternatives to CH. These new classes of materials seem to have more promising results, justifying the return to the study of pulp capping materials by the endodontic community.

Mineral Trioxide Aggregate (MTA)

MTA was developed at the University of Loma (United States of America) and was first introduced in dentistry by Torabinejad in 1993, proposing a material for Para endodontic surgeries, with the main goal of promoting the sealing of communication between inside and outside environment. Nowadays, MTA is indicated in several clinical situations, for example: direct pulp capping, as endodontic cement, perforation repair, apical plugs for immature teeth and for coronary sealing after regenerative endodontic procedures [52]. MTA has been characterized as a bio stimulative or bioactive material, due to the fact that it promotes very favorable tissue reactions [53,54]. Bioactivity is a characteristic of a biomaterial to form mineral hydroxyapatite on its surface [55].

Chemically, the MTA consists of a powder (white or gray) composed of hydrophilic particles that, in the presence of water, solidify. This powder is formed by a mixture composed mainly of tricalcium silicate, tricalcium aluminate, tricalcium oxide, silicate oxide and bismuth oxide (which gives it radiopacity). Its handling consists of incorporation with distilled water, supplied by the manufacturers [56-58].

Its mechanism of action described in the literature is based on the principles that MTA forms CH that releases calcium ions, which favors cell adhesion and proliferation; creates an antibacterial environment by alkaline pH; modulates cytokine production; encourages the differentiation and migration of cells that will form an extracellular matrix to be mineralized; and forms hydroxyapatite or carbonated apatite on the surface in contact with the MTA, providing a biological seal [59]. Still, other factors that seem to favor the repair are its excellent sealing capacity, which makes marginal infiltration difficult; low solubility; and satisfactory radiopacity [53,54,60].

The literature has shown that pulp tissue responds favorably to MTA, with the deposition of a complete barrier of mineralized tissue, in a shorter formation time when compared to CH, with a minimal sign of inflammation to the tissue, maintaining the remaining pulp with normal characteristics. In addition, the success rate of pulp therapies using MTA has been superior to techniques using CH materials [61,62]. However, the main disadvantages of MTA have been described as the high rate of coronary gray discoloration, difficulty in handling, its high cost and its long setting time, resulting in high solubility at an early stage, which can lead to microleakage [63-65].

Cavalcanti et al. [66] evaluated the effect of different pulp-capping materials on the secretion of interleukin-1 beta (IL-1β) and interleukin-8 (IL-8) by migrating human neutrophils. They found that MTA caused significantly higher secretion of IL-β than CH. Then they concluded that in combination with all the other biological advantages of MTA described above, their results indicate that MTA could be considered the material of choice for dental pulp capping.

Tricalcium silicate based cement (Biodentine)

Biodentine (Septodont, Saint-Maur-des-Fosses, France) was launched in 2009 with the proposal of being a "dentine substitute" and has been frequently described in the literature as an extremely promising material, being the main representative of tricalcium silicate-based cements used in dentistry. The positive characteristics of Biodentine showed in the literature reviews are represented by its physical properties superior to those of other materials, better handling, excellent biocompatibility and a wide range of clinical applications, similar to those of MTA [67].

The material is available in the form of a capsule containing the ideal proportion of the powder for subsequent addition of the liquid. The powder composition is formed by tricalcium silicate, calcium carbonate and zirconium oxide (radio pacifier); while the liquid contains calcium chloride dihydrate, which acts as an accelerator, Areo and purified water. Both substances present in the liquid contribute to reduced setting times (from 10 to 12 minutes). In addition, the composition of the liquid accelerates the hydration reaction and reduces the amount of water needed for the mixture, providing adequate consistency, which also contributes to the easy handling of the mixture [68].

Biodentine is associated with a high pH (12) and the release of calcium and silicon ions, which stimulates mineralization and creates a "mineral infiltration zone" along its interface with dentin, providing a better seal. Caron et al. [69] found that Biodentine exhibits sealing properties superior to that of MTA. According to Rajasekharan et al. [70], as Biodentine overcomes the main disadvantages of MTA, it has great potential to revolutionize the different modalities of treatment in dentistry, especially after traumatic injuries. However, more long-term, high-quality clinical studies are needed for definitive conclusions. On the other hand, literature reviews and randomized clinical trials have shown that Biodentine and MTA show similar results in terms of success rates for either direct pulp capping or application after pulpotomy [71-73].

Recently Petta et al. [74] evaluated the osteogenic differentiation of human dental pulp stem cells in response to substances released by the pulp capping agents, Biodentine (BD), mineral trioxide aggregate (MTA) and two-paste calcium hydroxide cement (CHC), along with their physicochemical characteristics. They showed that BD was the most stable material and formed the higher number of mineralized nodules even when non-mineralizing cell culture medium was used. They concluded that BD presents physicochemical characteristics more conducive to pulp repair than those of MTA and CH.

Success rates

Although the Biodentine presents physical and biological chacteristics superior that those of CH and MTA, until now the success rates of these materials applied in clinical trials seems to be similar. Several studies in the literature have shown high success rates for pulp capping procedures, mainly through clinical and radiographic evaluations. Brizuela et al. [75] conducted a randomized clinical trial with permanent teeth with pulp exposure that were directly capped with CH, MTA or Biodentine. Follow-up clinical evaluations were performed at 1 and 3 weeks, 6 months and 1 year. In one week, patients presented 100% clinical success rates in all groups. Over time, it was possible to notice a few failure cases (especially in the CH group). There was no statistical difference between the materials.

Katge [76] compared the direct pulp capping procedure in the young pulp of permanent molars through clinical and radiographic evaluation. The selected patients had bilateral first molars with caries involvement. According to the split mouth design, patients were divided into Biodentine (right side) and MTA (left side) groups as capping materials. The evaluations after 6 and 12 months reported a 100% success rate for both materials used at both periods.

Parinyaprom et al. [77] also compared the success rates of direct pulp capping using MTA and Biodentine in permanent teeth with pulp exposure after 6 months, using clinical and radiographic evaluations to determine success. They found a success rate of 92.6% for MTA and 96.4% for Biodentine, with no significant difference. Gray discoloration was present in 55% of teeth capped with MTA. In the Biodentine group, no discoloration was observed.

Conclusion

The re-emergence of vital pulp therapies gained strength in dentistry, especially due to its biologically minimally invasive approach. Direct pulp capping, when well indicated, seems to be an effective alternative capable of maintaining the health and vitality of the dentin-pulp complex. Recently, the development of new biocompatible materials, such as MTA and Biodentine, has being related with high rates of clinical and radiographic success for this treatment. However more randomized clinical trials are still needed to assess the quality of this treatment in the long term. In addition, histomorphological analysis of the newformed hard tissue and adjacent pulp tissue would also be helpful to understand the predictability of the prognosis.

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