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Pulp capping materials

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Abstract: Dental pulp-capping is done to preserve vital teeth when the pulp is exposed due to caries, trauma or instrumentation. Various materials are used as pulp-capping agent. The development of materials, techniques and knowledge of the dentin-pulp complex has gradually affecting its results positively. Nowadays, there are many direct and indirect pulp capping materials. Some, present for more than 50 years, like calcium hydroxide. Others, such as Biodentine or MTA, which are very recent, show promising results.

Keywords: Calcium hydroxide; dentinal bridge; biodentine; mineral trioxide aggregate; theracal LC; propolis; stem cells.

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Introduction

Direct and indirect pulp capping, with their different materials and clinical protocols, has been used for years to maintain the pulp health and vitality and stimulate odontoblasts to form reparative dentin. Direct pulp capping is used when the pulp is visibly exposed (vital pulp exposure), it might be either pathogenic exposure (due to caries) or accidental exposure (trauma, during tooth preparation or caries removal). Indirect pulp capping is usually used in deep cavity preparations, with or without caries remaining, which are close to the pulp but with no visible exposure. The objectives of any pulp capping procedure are to manage bacteria, arrest any residual caries progression, stimulate pulp cells to form new dentin, and provide a biocompatible and durable seal that protects the pulp from bacteria and harmful agents.[1]

Historically, the first pulp capping procedure was performed in 1756, by the Phillip pfaff, who packed a small piece of gold over an exposed vital pulp to promote healing. However, the success of the pulp capping procedure greatly depends upon the circumstances under which it is performed and the prognosis depends upon the age, type, site and size of pulp exposure. In addition to this the pulp capping material should have the following ideal properties like: [2]

- Induce reparative dentin formation.
- Maintain the pulp vitality.
- Release fluoride to prevent secondary caries.
- Bactericidal or bacteriostatic.
- Adhere to dentin.

- Adhere to restorative material.
- Resist forces during restoration placement and during the life of restoration.
- Be Sterile.
- Preferably be radiopaque.
- Provide proper bacterial seal. [3]

Pulp capping materials

1- Calcium hydroxide

In 1920 calcium hydroxide was introduced by Hermann as root canal filling material. To prove that it was a biocompatible material, between 1928 and 1930 he studied the vital pulp reaction to calcium hydroxide. Since then, calcium hydroxide has been recommended by several authors for direct pulp capping and has been considered the "gold standard" of direct pulp capping materials for several decades, against which new materials should be tested. [2]

Forms and composition

Calcium hydroxide cements are supplied in a visible light–cured system and a two-paste system. A catalyst paste containing calcium hydroxide, zinc oxide, and zinc stearate in ethylene toluene sulfonamide reacts with a base paste containing calcium tungstate, calcium phosphate, and zinc oxide in glycolsalicylate to form amorphous calcium. Visible light–cured calcium hydroxide preparations have demonstrated clinical success and may be less susceptible to hydrolysis. [5]

There is a list of well-known advantages to calcium hydroxide that have caused it to receive this acceptance. Calcium hydroxide has excellent antibacterial properties. One study found a 100% reduction in microorganisms associated with pulp infections after one-hour contact with calcium hydroxide. Most importantly, calcium hydroxide has a long term track record of clinical success as a direct pulp-capping agent in periods of up to 10 years. [3]

However, several disadvantages and limitations have been existed with the use of calcium hydroxide material such as extensive dentin formation obliterating the pulp chamber, high solubility in oral fluids, lack of adhesion, providing poor seal, low strength and degradation after acid etching. In addition, necrosis of the adjacent pulp tissue and inflammation of the contiguous tissue when calcium hydroxide is applied directly to pulp tissue. [3]

Another criticism of calcium hydroxide is the appearance of so-called "tunnel defects" in reparative dentin formed underneath calcium hydroxide pulp caps. A tunnel defect has been described as a patency from the site of the exposure through the reparative dentin to the pulp, sometimes with fibroblasts and capillaries present within the defect. However, other researchers have found that the quality of reparative dentin improves as the bridge gets thicker, and that many times, the tunnel defects are not patent with the pulp. It appears that tunnel defects are not a common finding in human studies involving direct pulp capping with calcium hydroxide. There are fewer studies that note observing tunnel defects and more studies that do not observe tunnel defects. [2, 3]

Mechanism of action

Traditionally, it has been believed that calcium hydroxide's high pH causes irritation of the pulp tissue, which stimulates repair via some unknown mechanism. In recent years, this "unknown mechanism" may have been explained by the release of bioactive molecules. It is known that a variety of proteins are incorporated into the dentin matrix during dentinogenesis. Of particular importance to the topic of pulp capping is that at least two of these proteins, Bone Morphogenic Protein (BMP) and Transforming Growth Factor-Beta One (TBF-β1), have demonstrated the ability to stimulate pulp repair. Furthermore, calcium hydroxide is known to solubilize these proteins from dentin. The release of these bioactive molecules as a significant mediator in pulp repair following pulp capping. [3]

2- Glass Ionomer (GI) / Resin-Modified Glass Ionomer (RMGI)

GI/RMGI is also cytotoxic when in direct cell contact. Glass ionomer provides an excellent bacterial seal and shows good biocompatibility when used in close approximation but not in direct contact with the pulp, fluoride release, and coefficient of thermal expansion and modulus of elasticity similar to dentin. Although there is, lack of dentin bridge formation, high solubility and slow setting rate. RMGIC as direct pulp capping agent exhibited chronic inflammation and lack of dentin bridge formation; whereas the calcium hydroxide control groups showed significantly better pulpal healing.[2, 6]

3- Adhesive systems

Adhesive systems were suggested for use as a potential direct pulp capping agent approximately 12–15 years ago. All components of adhesive systems have been shown to be cytotoxic to pulp cells, especially with increasing duration of contact with the pulp. Toxicity is seen in both multi- and single-component adhesive systems, and the unpolymerized components are more toxic than the well polymerized adhesive. [7, 2]

Some animal studies found that mechanical pulp exposures capped with adhesives generally resulted in pulp healing. A number of studies of primate, non-contaminated, mechanical pulp exposures capped with adhesive systems generally resulted in healing comparable to calcium hydroxide. However, this outcome changes when the results are examined from studies of bacteria-contaminated mechanical pulp exposures in primates. These contaminated exposures capped with adhesives resulted in poor pulp healing compared to calcium hydroxide. [7, 2]

When the results of human pulp-capping studies are reviewed, the conclusions become very different than what would have been deduced from animal studies. Calcium hydroxide provided significantly improved pulpal repair compared to adhesive systems, regardless of whether it was an etch-and-rinse or self-etch system. [7]

There are several possible explanations for these poor outcomes in human studies. First are the direct cytotoxic effects that adhesives have on pulp cells. Next is the difficulty in obtaining an adequate seal to protect against bacterial contamination. This poor seal may be due to one or more reasons. The placement of acid directly onto the mechanically exposed pulp may aggravate the bleeding process, which, in turn, makes application of the pulp capping material in a dry field very difficult. The increased moisture at the pulp cap site reduces polymerization of the adhesive. Then, resin components reduce the pulp's immune response, making it less likely that the pulp will be able to defend itself against bacterial contamination. [7]

Finally, adhesives result in chronic inflammation, even in the absence of bacteria; inflammation is a poor environment for pulp healing.

4- Mineral Trioxide Aggregate (MTA)

In recent years a new cement , mineral trioxide aggregate (MTA), developed in the 1990s by Torabinejad and his coworkers at Loma Linda University (California), has become available as a root canal repair material and for direct pulp capping. MTA is primarily calcium oxide in the form of tricalcium silicate, dicalcium silicate and tricalcium aluminate. Bismuth oxide is added for radiopacity, MTA is considered a silicate cement rather than an oxide mixture, a so its biocompatibility is due to its reaction products. The primary reaction product of MTA with water is Calcium Hydroxide, and so it is actually the formation of calcium hydroxide that provides MTA's biocompatibility. As a result, many of the advantages and potential mechanisms of action for MTA are similar to Calcium Hydroxide, including its antibacterial and biocompatibility properties, high pH, radiopacity and its ability to aid in the release of bioactive dentin matrix proteins. However, an antibacterial effect of MTA is debatable, MTA showed some of the facultative bacteria but no effect on any of the anaerobic bacteria. The antimicrobial activity of MTA may not be as strong as those of traditional Calcium Hydroxide based cements and sealers. [8]

MTA can provide more leakage-proof because of its sealing ability. MTA is suggested to be superior to Calcium Hydroxide due to its uniform and thicker dentin bridge formation, less inflammatory response and less necrosis of pulpal tissues. There are some differences between MTA and Calcium Hydroxide. First, MTA comes in two colors, white and grey. The grey version is due to the addition of iron. Another significant difference is the fact that MTA provides some seal to tooth structure. [8]

The disadvantages of MTA include long setting times approximately 2 hours and 45 minutes. Setting time of MTA Gray is shorter than that of MTA White. A long setting time may be inconvenient to both dentist and patient, because it requires direct pulp-capping with MTA in two visits: application of MTA in the first visit and seating of the permanent restoration over the sufficiently hardened MTA in the second visit. Moreover, it may increase the risk of bacterial contamination. Another disadvantage of MTA poor handling "sandy" feeling mixture produced by the coarse particles of Pro Root and water is difficult to be delivered to the required site and hard to condense adequately which can be affected by the particle size and distribution as well as by the shape of the MTA powder. Tooth discoloration has been reported with the use of gray MTA in direct pulp capping and therefore the use of white MTA has generally been recommended in the esthetic zone. However, tooth discoloration associated with white MTA was also described in case reports in endodontic treatments. Tooth color change was reported to be induced by both gray and white MTA. Several factors were reported to contribute to tooth discoloration by white MTA: contamination with blood, contact with sodium hypochlorite, the presence of light and oxygen. The possible involvement of the radio pacifier bismuth oxide in the discoloration is postulated. The reason and mechanism of tooth discoloration are not fully understood and remain to be investigated. MTA is very expensive, one gram of MTA powder costs approximately the same as 24 grams of calcium hydroxide base/ catalyst paste, making MTA much less cost effective per use. [2, 8]

5- Calcium phosphate Compound

Calcium phosphate (CP) cements have been used for repairing bone defects. They are reportedly good candidates for osseous augmentation due to their biocompatibility, moldability and osteoconductivity. Thus, there have been many dental trials investigating the use of these materials on periodontal defect. In addition, many studies have shown that CP cements stimulate pulp and can induce the formation of reparative dentin. Researchers also showed the superior physical properties of calcium phosphate cements compared to calcium hydroxide. However, CP cements were observed to have limitations, including long setting times and low compressive strength, when used alone as pulp-capping agents. [2, 9]

Recently, fast-setting α-tricalcium phosphate (TCP) based cement was developed experimentally to overcome the disadvantage of conventional CP cements. According to manufacturer, it was developed not only for endodontic use, including pulp therapy, root-end filling, and perforation repair, but also for periodontal/surgical use, such as in osseous regeneration, which has been considered a primary application of CP cements. In other words, in addition to setting time, α-TCP cement may be more advantageous in variety of clinical applications compared to MTA. [9]

The α-TCP has a similar odontogenicity to MTA both in vitro and in vivo, whereas it has a much quicker setting time. However, α-TCP showed inferior physical properties including solubility and compressive strength. The α-TCP is potentially suitable for use as an effective pulp capping material. However, long-term clinical evaluation is required with respect to the use of α-TCP. [9]

Alpha-tricalcium phosphate and Tetracalcium phosphate (4CP) set then convert to hydroxyapatite. In contrast to calcium hydroxide, tetracalcium phosphate cement induced bridge formation with no superficial tissue necrosis and significant absence of pulp inflammation. [2]

6- Biodentine

New bioactive cement was recently launched in the dental market as a dentin substitute. It shares both its indications and mode of action with calcium hydroxide, but does not have its disadvantages.[10]

It is formed of Tricalcium silicate, calcium carbonate, oxide, and zirconium oxide (radiopacifier) in the powder, which is mixed with calcium chloride solution containing modified polycarboxylate instead of water. Both substances in the liquid contribute to shorten setting times (from 10 to 12 min). Calcium chloride accelerates the hydration reaction, and polycarboxylate reduces the amount of water required for mixing by providing proper consistency, which also contributes to easy handling of the mixture. Calcium carbonate in the powder is expected to act as a nucleation site in the hydrating mass, enhancing the hydration and leading to faster setting. Biodentine sets in approximately 10-12 minutes. Bio dentine was reported to have efficacy similar to that of MTA in direct capping over mechanically exposed pulp. Complete dentinal bridge formation, an absence of inflammatory pulp response and layers of well-arranged odontoblasts and odontoblast-like cells were observed after 6 weeks. [8]

Biodentine stimulates release of transforming growth factor beta (TGF-β) from pulpal cells, stimulating reparative dentin formation in a very short period of time. Particular growth factors from the TGF-ß family have the ability to initiate odontoblast differentiation and hence produce tertiary dentine by cell signaling. [2, 8]

Another study of indirect pulp capping on rat molars concluded that Biodentine was able to stimulate (thick and dense) reactionary dentine formation, which stopped after about three months when a sufficient dentine barrier was formed. Studies conducted to test Biodentine for application as a direct pulp capping agent and for pulpotomy showed that it was well tolerated even when in direct contact with the pulp. It was even suggested that the quality of dentine bridges formed were better than those formed by calcium hydroxide alone. Used for pulp capping, the material offers certain advantages over calcium hydroxide: It is stronger mechanically, less soluble and produces tighter seals. [2]

7- TheraCal LC

Is a light cured, resin modified calcium silicate filled liner designed for use in direct and indirect pulp capping, as a protective base/liner under composites, amalgams, cements, and other base materials. TheraCal LC performs as an insulator/barrier and protectant of the dental pulpal complex. The proprietary formulation of TheraCal LC consists of tricalcium silicate particles in a hydrophilic monomer that provides significant calcium release making it a uniquely stable and durable material as a liner or base. Calcium release stimulates hydroxy apatite and secondary dentin bridge formation. The material might be very attractive for clinicians because of its ease of handling. Unlike other calcium silicate-based materials, TheraCal LC is resin-based and does not require any conditioning of the dentine surface. The material can be bonded with different types of adhesives directly after application. [2, 11]

8- Emdogain (EMD)

EMD is enamel matrix derivative secreted from Hertwig's epithelial root sheath during porcine tooth development. It is an important regulator of enamel mineralization and plays an important role during periodontal tissue formation. It stimulates the regeneration of acellular cementum, periodontal ligaments, and alveolar bone. EMD contains bone morphogenetic proteins (BMP) like molecules and BMP expressing cells. BMP like molecules in EMD promote odontoblast differentiation and reparative dentin formation. It was concluded that amount of hard tissue formed in EMD treated teeth was more than twice that of the calcium hydroxide treated control teeth. [2, 12]

9- Propolis

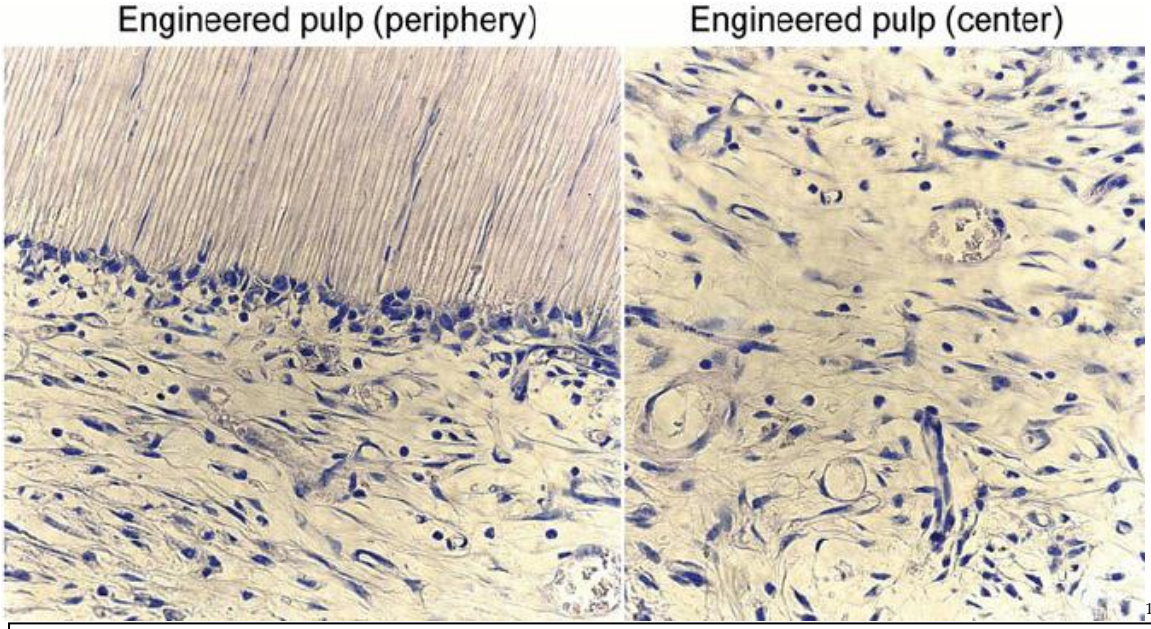
Propolis, a resinous material collected by honey bees, has been used as a traditional anti-inflammatory and anti-bacterial medicine for many centuries. Propolis is composed of 50% resin and vegetable balsam, 30% wax, 10% essential and aromatic oils, 5% pollen and 5% other various substances, including organic debris depending on the place and time of its collection. The constituents of Propolis vary widely due to climate, season and location; so its chemical formula is not stable. The most important pharmacologically active constituents in Propolis are flavonoids, which are well-known plant compounds that have antioxidant, antibacterial, antifungal, antiviral, and anti-inflammatory properties. [13]

It is used as indirect pulp capping paste when mixed with Zno powder and this showed similar effect of Zno and eugenol as secondry dentin formation. In direct capping with this paste showed no pulp degeneration and formation of protective layer. It contains flavonoids, phenolics, iron, zinc and other various aromatic compounds. propolis was compared propolis to MTA histologically in human dental pulp and showed similar bridge formation .[2, 13]

10- Dental pulp stem cells (DPSCs) and Stem cells from Human Exfoliated Deciduous Teeth (SHED)

Stem cells are unspecialized cells that continually reproduce themselves and can differentiate into specialized cells of one or more types. Stem cells can be divided into two major classes: embryonic/fetal stem cells and adult stem cells. Dental-derived stem cells are one of adult stem cells used as the cell sources for tissue engineering and regenerative medicine. Dental pulp stem cells (DPSCs) from permanent teeth are able to regenerate a dentin-pulp like complex that is composed of mineralized matrix with tubules lined with odontoblasts and fibrous tissue containing blood vessels in an arrangement similar to the dentin-pulp complex found in normal human teeth. Stem cells from human exfoliated deciduous teeth (SHED) are highly proliferative, clonogenic cells capable of differentiating into a variety of cell types including neural cells, adipocytes and odontoblasts.[14]

Nakamura S et al. (2009) used mesenchymal stem cells for clinical application in tissue engineering and regenerative medicine. In this study, they compared the proliferation of SHED, DSPCs and Bone Marrow Derived Mesenchymal Stem Cells (BMMSCs). They concluded that SHED has got significantly higher proliferation rate than that of DSPCs and BMMSCs and this could be a desirable option as a cell source for therapeutic applications, as shown in figure 1. [2, 14]



[15]

Figure 1. Dental pulp engineered with stem cells from human exfoliated deciduous teeth (SHED). SHED were seeded into tooth slice/scaffolds and transplanted into the subcutaneous space of immunodefi cient mice. After 21 days, the tooth slices were retrieved, fi xed, demineralized, and prepared for standard histology. Photomicrographs of hematoxylin/eosin- stained tissue sections (× 400) depicting the periphery and the central portion of the dental pulp-like tissue formed in the pulp chamber of these tooth slices.

Zhuang et al. also embedded Dental stem cell-derived extracellular vesicles (DSC-EVs) in the root fragment enriched with BMMSCs and observed dentine formation after 12 weeks of subcutaneously transplantation in nude mice. Besides the rodent models, DSC-EVs combined with treated dentin matrix (TDM) also presented the potential of dentin formation in a pulp exposure model of miniature pig, suggesting DSC-EVs loaded in TDM as a

promising strategy for pulp-capping therapy.Despite the obvious effects in vivo, the detailed molecular action of DSC-EVs in dentinogenesis remains unclear, calling for further mechanistic studies.[16]

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