Biomaterials Journal
http://www.biomatj.com
Online ISSN: 2812-5045

Type of the Paper (Review Article)

Pulp therapy related materials

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Citation *Menna S. Gaber . Pulp therapy related materials . Biomat. J., 1 (5),1 – 10 (2022)*

https://doi.org/10.5281/znodo.5829408

Received: 26 April 2022

Accepted: 30 May 2022

Published: 31 May 2022

Abstract: The primary objective of pulp therapy is to stimulate the remaining pulp to regenerate to maintain its vitality. Therefore maintaining the integrity and health of the teeth and their supporting tissues affected by caries, traumatic injury, or other causes especially in young permanent teeth with immature roots.
Therefore in order to preserve the tooth, dental pulp regeneration and preservation can be achieved by pulp therapy that can be classified into; Pulp Capping (Vital pulp therapy) and Whole Pulp regeneration (Non-vital therapy)

Keywords: *pulp capping,pulp regenerations,pulp capping materials,calcium hydroxide,MTA*

I- Pulp Capping:

The main goal of pulp capping is to promote the pulpal tissue to heal by revascularization and the deposition of tertiary dentin, which increases the distance between the injury and the pulp.

Vital pulp therapy is only recommended for teeth that are asymptomatic, or which exhibit only minimal inflammatory symptoms. The idea of vital-pulp therapy has been greatly enhanced with the introduction of various pulp capping materials.(2)

Pulp capping is classified into:

1) Indirect Pulp Capping: A pulp capping agent is placed over the remaining thin layer of dentin above the pulp chamber.

2) Direct Pulp Capping: A protective biomaterial (called pulp capping agent) is placed directly over the exposed pulp.

3) Pulpotomy: When dental pulp exposure is large, or the pulp is infected, all of the coronal pulp must be removed, and direct pulp capping will subsequently be performed adjacent to the root pulp. A pulp capping agent is placed over partially removed coronal pulp tissue. (2)

Requirements of ideal pulp capping materials:

1. Stimulate reparative dentin formation.

2. Maintain pulpal vitality.

3. Antibacterial effect.

4. Adhere to dentin and restorative material.

5. Resist forces during placement and the life of the restoration. 6. Radiopaque.

7. Fluoride release.(3)

The first documented pulp-capping treatment was conducted in 1756 by Pfaff, using gold foil. Since then, many agents have been recommended for direct pulp capping. (2)

1.Calcium Hydroxide:

In 1930, Hermann discovered that calcium hydroxide is effective in repairing an exposure site. Since then, calcium hydroxide has been used with clinical success for facilitating the formation of reparative dentin along with the maintenance of vital pulp, the induction of mineralization and the inhibition of bacterial growth. Calcium hydroxide has been the gold standard for pulp capping. (4)

Mechanism of action:

Ca(OH)2 release calcium (Ca) and hydroxyl (OH) ions upon dissolution.

• Calcium ions react with carbon dioxide in the tissues, forming calcium carbonate. It can also increase the action of pyrophosphatase enzyme that increases energy utilization. Therefore, stimulating DPSCs (dental pulp stem cells) differentiation and dentin-bridge formation.

• Hydroxyl ions produce high pH of approximately 12. Therefore, provides excellent antibacterial properties as it neutralizes lactic acid from bacteria and damages the bacterial cytoplasmic membrane.

The regenerative effect of Ca(OH)2 is due its alkaline PH that solubilize dentine matrix stimulating the release of pro-angiogenic growth factors as vascular endothelial growth factor (VEGF), transforming growth factor β (TGF-β), platelet-derived growth factor (PDGF) and fibroblast growth factor (FGF) from it. These growth factors promote the migration and proliferation of (DPSCs) and periodontal ligament stem cells (PDLSCs). (5)

Three histologic zones under Ca(OH)2 are formed: -

Zone of obliteration: The pulp tissue immediately in contact with the calcium hydroxide is usually completely distorted because of the caustic effect of the drug. This zone consists of debris, dentinal fragments, hemorrhage, blood clot, and particles of calcium hydroxide. (6)

Zone of coagulation necrosis: A weaker chemical effect reaches the subjacent, more apical tissues and results in a zone of coagulation necrosis and thrombosis, also called layer of 'firm necrosis'. (6)

Zone of demarcation: A line of demarcation develops between the deepest level of the zone of coagulation necrosis and the subjacent vital pulp tissue. Exposed human dental pulp will heal with hard tissue bridging. (6)(7)

Advantages:

• Antibacterial properties

• High pH stimulates fibroblasts so promotes healing and repair. • Neutralizes low pH of acids.

• Inexpensive and easy to use.(5)

Disadvantages:

1.It has been reported that 89% of dentin bridges formed by calcium hydroxide cement contained tunnel defects. These tunnel defects fail to provide a permanent barrier and long-term biological seal against bacterial infection.

2. Dissolution which may lead to the formation of a dead space and microleakage. 3.Does not adhere to dentin or resin restoration.

4.May degrade during acid etching.

5.Associated with primary tooth resorption.(5)

2. Bonding Agents:

Dental adhesive systems were suggested for use as an indirect pulp capping material to overcome the disadvantages of calcium hydroxide as they produce superior adhesion. (3)

Disadvantages:

1. Unpolymerized monomer can cause cytotoxic effects in pulp cells 2. Absence of calcific bridge formation. (3)

Mechanism of action:

Adhesive resins could stimulate the release of pro-angiogenic factor as VEGF from the dentin matrix but decrease the release of FGF and has no effect on PDGF therefore it cannot induce the formation of an acceptable tertiary dentine bridge.(2)

3. Lasers:

Pulp capping therapy using lasers results in good prognosis for the tooth however, the sealing of exposed pulp with one of the dental materials after laser treatment is still required. Laser of different wavelengths is used. For Example: CO_2, Diode and Nd: YAG lasers.

Mechanism of action:

Sterile field is provided by the bactericidal effect of the laser. Area of coagulation is created by a superficial necrosis, with an underneath area of reversible damage, this stimulates odontoblasts to produce reparative dentin.(8)

Advantages:

1. The beam does not contact the tissue; therefore, an incision can be made without mechanical trauma to pulpal tissue.

2.Haemostatic and coagulant effect and stimulate the formation of secondary dentin.

Disadvatages: Technique sensitive and causes thermal damage to pulp in high dose. (8)

4.Zinc oxide eugenol: was introduced for direct pulp-capping.

Disadvantages: Chronic inflammation and a lack of pulp healing were observed, with no dentin bridge formation.

It was reported that eugenol is toxic, and zinc oxide eugenol resulted in high interfacial leakage.(4)

5. Resin Modified Glass Ionomer(RMGIC):

• Successful results of RMGIC as indirect pulp capping agents. As it was reported that it provides an excellent bacterial seal and fluoride release. (6)

• On the other hand not used in direct pulp capping as it irritates pulpal tissue leading to chronic inflammation and also there is failure of dentin bridge formation. (6)

6.Glucocorticoids combined with antibiotics:

In the 1970s, were frequently used in an attempt to control pulpal pain and suppress pulpal inflammation. Reports of poor wound-healing and even pulpal necrosis emerged, so steroids are no longer used for direct pulp capping. (4)

7.Growth factors, such as bone morphogenetic proteins (BMP) and transforming growth factors (TGF) induced reparative dentin formation. However,these growth factors are not adequately therapeutic, since they produce a porous osteodentin with tunnel defects. (4)

8.Extracellular matrix (ECM)

Extracellular matrix dentin molecules, for direct pulp-capping such as bone sialoprotein (BSP), matrix extracellular phosphoglycoprotein (MEPE), amelogenin and dentin phosphophoryn, have been shown to induce reparative dentin. Capping with ECM molecules is extremely promising, producing a reparative mineralized tissue with structural properties better than those produced

in the presence of calcium hydroxide. Among these, amelogenin is suggested to be most promising as a direct capping material. (4)

9.Calcium-silicate-based materials

9.1.Mineral trioxide aggregate (MTA), In the 1990s, Torabinejad and White introduced MTA which is basically a hydraulic Portland cement or calcium silicate. MTA has been used clinically with success rates similar to those achieved with calcium hydroxide.

Two types of MTA were available: White and Gray MTA. The gray version is due to the addition of iron (tetracalcium aluminoferrite). Tooth discoloration has been reported with the use of gray MTA. Therefore the use of white MTA has generally been recommended.(9)

• **The original MTA**, ProRoot MTA Gray was marketed in 1998 and was composed of 75% Type I Portland cement, 20% bismuth oxide and 5% calcium sulfate dihydrate.

The Portland cement is composed of approximately 55 wt% tricalcium silicate ($3CaO•SiO_2$), 19 wt% dicalcium silicate ($2CaO•SiO_2$),10 wt% tricalcium aluminate ($3CaO•Al_2O_3$), 7 wt% tetracalcium aluminoferrite ($4CaO•Al_2O_3•Fe_2O_3$), 2.8 wt% magnesium oxide, 2.9 wt% sulfate and 1.0 wt% free calcium oxide.

• .**ProRoot MTA White** was introduced in 2002 and differs from its predecessor in composition, *i.e.*, the elimination of tetracalcium aluminoferrite and an increase of calcium silicates. (9)

MTA without tetracalcium aluminoferrite is more popular, and many products are marketed worldwide: ProRoot MTA White, MTA Angelus White, White MTA Plus, MM-MTA, MTA, Tech BioSeal MTA.

The mechanism of action of MTA is similar to that of calcium hydroxide. The calcium hydroxide produced as a by-product of hydration of MTA is leached out and causes necrosis when in contact with the pulp. When MTA powder is mixed

with water at the time of application, calcium silicates in the powder hydrate to produce a calcium silicate hydrate gel and calcium hydroxide, as shown below:

$2[3CaO•SiO_2]+6H2O→3CaO•2SiO_2•3H_2O+3Ca(OH)2$

$2[2CaO•SiO_2]+4H2O→3CaO•2SiO_2•3H_2O+Ca(OH)2$

Thus, MTA can be described as a calcium-hydroxide releasing material and, therefore, is expected to present various properties similar to those described above for calcium hydroxide.(4)

The advantages of MTA

1. Its sealing ability, biocompatibility, bioactivity and capacity to promote mineralized tissue formation

2.MTA is suggested to be superior to calcium hydroxide due to its more uniform and thicker dentin bridge formation, less inflammatory response and less necrosis of pulpal tissue.

3.An antibacterial effect of MTA is controversial as reviewed by Parirokh and Torabinejad. MTA showed an antibacterial effect on some of the facultative bacteria but no effect on any of the strictly anaerobic bacteria. (4)

• Hydrophilic as it sets in moisture.

Disadvantages of MTA

• Expensive.

• Poor handling characteristics.

• Long setting time: Reported setting times have shown variations: (50 min, 4 h) (70 and 175 min) for the initial and final setting times, respectively. A long setting time may be inconvenient to both dentist and patient, because it requires two visits. Moreover, it may increase the risk of bacterial contamination.

• MTA cannot bond to dentin. Therefore, there is a risk of bacterial leakage, which could lead to failure of endodontically treated teeth.

• Tooth discoloration has been reported with the use of gray MTA, therefore the use of white MTA has generally been recommended in the esthetic zone.

9.2.Modified MTAs and MTA-like materials

Some modified MTAs overcoming the drawbacks of the original MTA are available, and most of them aimed to shorten setting time by modifying the composition or particle size of the powder.

In Angelus White MTA (setting time, 15 min), calcium sulfate was removed and calcium oxide was added to tricalcium silicate, dicalcium silicate, tricalcium aluminate and bismuth oxide.

In MM-MTA, calcium carbonate was added; in Tech BioSeal MTA, calcium chloride and montmorillonite were added; and the powder in MTA Plus was more finely ground.

MTA-like materials were marketed after 2006. They are not composed of Portland cement, which is manufactured from minerals of natural origin, but consist of synthetic calcium silicates as the main components and are aluminum-free. The difference in origin of calcium silicates is clearly

demonstrated in the release of metal ions from the set materials. In Angelus MTA and MM-MTA, which are based on Portland cement, a large amount of aluminum and trace amounts of arsenic, beryllium, cadmium and chromium were detected, but in DiaRoot and Bioaggregate based on synthetic calcium silicates, no metals were detected except a trace amount of aluminum.

9.2.1.BioAggregate, marketed in 2006, consists of

Tricalcium silicate

Dicalcium silicate

Tantalum pentoxide (radiopacifier)

Calcium phosphate monobasic.

Silicon oxide

Calcium phosphate reacts with part of the calcium hydroxide produced from setting (hydrating) calcium silicates, and during the reaction, hydroxyapatite and water are formed. The water thus produced contributes to the hydration reaction speed. Silicon oxide also reacts with calcium hydroxide by the so-called pozzolanic reaction ; is a measure for the reaction rate between a pozzolan [1]and Ca^{2+} or calcium hydroxide ($Ca(OH)_2$) in the presence of water and thus contributes to setting time. The setting time is within 4 h at a normal optimal powder/ liquid ratio (1 g/0.38 mL water).

[1](siliceous and aluminous materials which, in themselves, possess little or no cementitious value but which will, in finely divided form and in the presence of water, react chemically with calcium hydroxide (Ca(OH)2) at ordinary temperature to form compounds possessing cementitious properties)

9.2.2.Biodentine launched in 2009, contains tricalcium silicate, calcium carbonate and 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 shortened 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. 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.

Advantages:

• Dentin bridge formation.

• Antibacterial action.

• Excellent marginal adaptability.

• Shorter setting time, better handling characteristics and higher mechanical properties compared to MTA therefore it can be considered an interesting alternative to MTA and Ca(OH)2

9.2.3. Endo Sequence Root Repair Material (ERRM):

• Recently, a new bioceramic material has been introduced to the market. It is composed of calcium silicate, monobasic calcium phosphate, zirconium oxide and tantalum oxide and fillers.

• It require no mixing because it is available as paste in syringes or in a putty form. They are composed of nano- sphere particles that can penetrate into dentinal tubules and set using their moisture.

Mechanism of action:

• ERRM promoted the vascularization, migration and differentiation of DPSCs through the release of VEGF and BMP growth factors from dentin matrix.

Advantages:

• Excellent sealing ability.

• Highly biocompatible.

• Dentin bridge formation.

• Hydrophilic and antibacterial effect. (12)

The major advantage of this material is improved handling characteristics over MTA. This novel ready-to-use bioceramic materials shows promising results in dental pulp repair application than $Ca(OH)_2$ and MTA. Further studies are needed to evaluate their long term performance in clinical uses. (12)

9.2.4. Resin-modified MTA cement

TheraCal LC is a light curing, resin-modified calcium-silicate-filled single paste, containing calcium oxide, calcium silicate particles (type III Portland cement), strontium glass, fumed silica, barium sulphate, barium zirconate and resin consisting of Bis-GMA and polyethylene glycol dimethacrylate. (10)

Advantages:

• Higher calcium releasing ability and high mechanical properties than either MTA or $Ca(OH)_2$.

Stimulates hydroxy apatite and secondary dentin bridge formation. • Light polymerization prevents the material to be washed out. Disadvantages:

Severe inflammation as unpolymerized monomers can exert toxic effects to the pulp. (10)

9.2.5. Calcium-enriched mixture (CEM):

- It has been recently introduced as a hydrophilic tooth-colored cement.
- The CEM cement powder is composed of calcium oxide, calcium sulfate, phosphorus oxide, and calcium silicate as major elements.
- CEM is alkaline cement (pH~11) that releases calcium hydroxide during and after setting. Advantages:
- This cement is biocompatible and induces formation of cementum, dentin, bone and periodontal tissues.
- Antibacterial effect comparable to Ca(OH)2 and superior to mineral trioxide aggregate (MTA) and sealing ability similar to MTA.
- Its clinical applications include pulp capping, pulpotomy and perforation repair.
- **10. Propolis:**

• It is a natural extract of honey bees from different kinds of plants. The main chemical classes present in propolis are flavonoids and phenolics. It contains some elements (zinc and iron) that are important for collagen synthesis.

Mechanism of action:

Stimulate the release of transforming growth factor (TGF) from dentin matrix which is important for the differentiation of odontoblasts.

Advantages:

• Antioxidant, antibacterial, antifungal, antiviral and anti-inflammatory. (11) Disadvatages:

Moderate pulpal inflammation with partial dentinal bridge formation.

11. Enamel matrix derivative (EMD):

• Emdogain (EMD) is enamel matrix derivative of Hertwig's epithelial root sheath during tooth development. It plays important role in enamel mineralization and periodontal tissue formation.

• The biomaterial is an injectable gel solution consisting of enamel matrix proteins (amelogenin), water and a carrier (propylene glycol alginate).

Mechanism of action:

• It was suggested as a possible pulp capping material due the presence of amelogenin in its composition which promotes odontoblast differentiation. However it was suggested that it could be preferable material for periodontium regeneration as it can stimulate the periodontal cells to release VEGF.(3)

Disadvantages: The high cost of these biomaterials, its poor sealing qualities and no effective formation of hard tissue barrier are still considerable drawbacks. (3)

II- Whole Pulp Regeneration:

Regenerative endodontics aims to replace necrotic pulp tissue with regenerated pulp-like tissue especially in young patients with immature teeth. Pulp regeneration components:

1. Stem Cells

2. Growth factors (Morphogenic Signaling Molecules)

3. Scaffolds: Scaffolds are three dimensional structures that provide matrix for cells attachement. Also can be used to deliver growth factors. Several scaffolds have already been proposed. For example, injectable hydrogels have several features that make them attractive for dental pulp tissue engineering purposes.

Pulp regeneration mechanism:

Two strategies can be applied towards dental pulp regeneration: cell transplantation and cell homing. (13)

a) Cell transplantation:

In this method, *exogenous* stem cells are loaded (seeded) onto scaffolds either incorporated with signaling molecules or not.

***b)* Cell homing:**

Scaffolds impregnated with signaling molecules are injected into root canals to induce migration, proliferation and differentiation of *endogenous* stem cells around the root apex through enlarged apical foramen. (13)

However, cell-based therapy faces many obstacles in clinical translation because complex procedures need to be followed, such as tooth extraction, pulp extirpation, in vitro cell culture, selection of stem cells, ex vivo cell expansion, storage and shipping. Also, there are other risks of immune rejection, pathogen transmission and tumorigenesis during engraftment. Despite its scientific validity, dental pulp regeneration using cell transplantation is unlikely to be economically viable or competitive with current RCT. (13)

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