

# **Current Approaches in Pulp Capping: A Review**

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# **Abstract**

The aim of this review article was to evaluate the effects of different materials such as calcium hydroxide, mineral trioxide aggregate, bioceramics, biodentine, endosequence root repair material, light cured tricalcium silicate cement used for maintaining the vitality of the pulp in direct and indirect pulp capping.

**Keywords:** Pulp capping materials, MTA, calcium hydroxide, biodentine, bioceramics

# **INTRODUCTION**

The purpose of pulp treatments after pulp perforation is to ensure that the pulp tissue recovers and maintains its vitality and functionality. Vital pulp treatment procedures involve the application of protective materials directly or indirectly on to the pulp after eliminating local irritants.<sup>1,2</sup> In vital pulp treatment techniques, the aim of the direct pulp capping is to place a medicament over the exposed pulp surface and stimulate reparative dentin formation and healing by inducing odontoblast-like cells.<sup>3</sup>

There are 3 vital factors for the success of vital pulp treatments:

1) Ensuring the control of infection by removing harmful elements from the environment,

2) Stimulation of pulp dentinogenic response by applying a biomaterial,

3) Preventing bacterial microleakages by forming a good plug/closure.<sup>3</sup>

**Pulp capping:** Vital pulp treatment is applied to teeth which have been traumatized (malocclusion, attrition, abrasion, erosion, mechanical trauma) or have deep caries lesions in order to maintain pulp vitality. The most applied vital pulp treatment procedure is pulp capping.<sup>1</sup>

**Indirect pulp capping:** During indirect treatment procedures, it is necessary to avoid excessive approaches and secondary irritations which may endanger the vitality, function and health of the tooth. Pulp perforations which may occur during the cavity preparation, especially

during the complete removal of deep caries, result in prolongation of the treatment and adversely affect the chance of recovery.<sup>4</sup>

Indirect pulp capping is a complex treatment method in teeth with deep carious lesions, in which the remaining dentin tissue is covered with a biocompatible material in order to prevent pulp exposure which may occur during mechanical trauma or caries removal. Indirect pulp treatment is applied in the presence of a deep caries lesion which is close to the pulp, when there is no pulp degeneration symptoms.<sup>5</sup> During the caries removal process, the affected dentin (firm but colored dentin) in the area adjacent to the pulp is not removed.<sup>6</sup> The tooth is then restored with a material which can prevent microleakages.<sup>5</sup>

#### **Indications for Indirect Pulp Capping**

There should be no spontaneous pain in the tooth. It may just be sensitive to cold. Radiographic examination should not reveal any apical pathology. There should be no pain on percussion and palpation. The vitality of the tooth should be determined by using an electrical pulp test.<sup>6</sup>

#### **Expected Results in Indirect Pulp Capping Treatment**

1. Neutralization: Hardening of acidic, infected, softened dentin with a decrease in caries microflora.

2. Protecting the pulp by reducing inflammation and improving blood circulation.

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Copyright© 2024 The Author. Published by Galenos Publishing House on behalf of Cyprus Turkish Medical Association. This is an open access article under the Creative Commons AttributionNonCommercial 4.0 International (CC BY-NC 4.0) License. 3. Stimulation of fibroblasts, undifferentiated mesenchymal cells and odontoblasts.

4. Maintaining the vitality of the pulp.<sup>4</sup>

# **Direct Pulp Capping**

The aim of this treatment in deep caries is to preserve the pulp tissue in a healthy way. In cases where the pulp has not lost its dentin stimulating factor and is not infected, perforated or injured by trauma or during cavity preparation, the process of stimulating the pulp-dentin complex and promoting the repair of dentin by covering it with a biocompatible chemical is called "Direct pulp capping". It is a form of treatment mostly applied to permanent teeth.<sup>6</sup>

# **Direct Pulp Capping Indications**

There should be no spontaneous pain in the tooth. The tooth should respond normally to thermal tests and it has to be vital. The tooth should not be painful on percussion and palpation. No apical pathology should be seen on radiographic examination. The size of the exposure area should be as large as the needle tip (less than 0.5 mm in diameter). Exposure of the pulp should occur without trauma. If pulp exposure occurs due to trauma, treatment should be made in less than 24 hours after exposure and the exposed area should be less than 0.5 mm. Bleeding in the perforated area should be under control within 3-5 minutes. The exposed area should be uncontaminated and dry. Tissue damage in the tooth should be at a level which can be restored after vital pulp treatment and a hermetic seal should be provided in the cavity.<sup>6</sup>

#### **History of Materials Used in Direct Pulp Capping**

It was reported that the first pulp capping was performed by Pfaff in 1756 using "gold foil".<sup>7,8</sup> Since then, different kinds of materials have been recommended to be used in direct pulp capping. In 1930, Hermann reported that calcium hydroxide was an effective agent in repairing the exposed pulp surface. Long-term studies have pointed out some drawbacks of calcium hydroxide and it is being replaced by new materials at present.<sup>6-8</sup>

#### **Properties of pulp capping materials:**

The materials used in the treatment of direct and indirect pulp capping must have some common properties:

1. Stimulate reparative dentin and should be tissue friendly,

2. Should not irritate the pulp, the effect on the pulp should be superficial and the pulp should be able to maintain its vitality,

- 3. Bactericidal or bacteriostatic. They must have an antiseptic effect,
- 4. Show alkaline reaction,
- 5. Neutralize the acids due to caries,
- 6. pH of the materials should be equal to the pH of the pulp,
- 7. Be able to bond to dentin,
- 8. Be able to bond to the restorative material,
- 9. Must be able to withstand the forces during and after the restoration,
- 10. Must be sterile,
- 11. Should be radiopaque,

12. Should not allow bacteria to pass through into pulp,

13. Should not have any harmful effects on human body or in the surrounding area locally.<sup>4,8</sup>

# **Materials Used in Pulp Capping**

#### **Pastes Containing Calcium Hydroxide**

Calcium hydroxide has been used in dentistry since the 1920s and is a strong base material with a high pH of 12.<sup>9</sup> It can dissolve in water in small amounts by releasing  $Ca^{2+}$  and OH ions. The high pH caused by the OH- ions provides an excellent antimicrobial effect and prevents the penetration of bacteria into the pulp. In addition, high pH causes irritation in the pulp tissue and creates a superficial 3-layered necrosis area on the exposed pulp surface. It also stimulates the formation of mineralization against this necrotic area. It also provides calcium which will be a source of mineralization with the  $Ca^{2+}$  it contains.<sup>9</sup>

The common disadvantages of calcium hydroxide are its weak dentine adhesion, mechanical instability (low mechanical resistance), dissolution in oral fluids over time (1-2 years), deterioration of its structure after acid etching, presence of multiple tunnels in repair dentin, increased inflammation in clinical use and its toxic effect on pulp cells. These adversely affect the long-term success of the treatment. The dissolution of calcium hydroxide over time causes microleakages in the restoration. Thus, bacteria can reach the pulp and pulp necrosis occurs.<sup>6,10</sup>

# **Zinc Oxide Eugenol Cements**

Zinc oxide eugenol is a sedative and pain-relieving material that, when applied to dentin, reduces the metabolism of microorganisms and limits the diffusion of toxic products to the pulp, thereby eliminating the signs of pulpal inflammation. It is frequently used in dentin cavities due to its effectiveness against bacterial leakage.<sup>11</sup>

Additionally, Zander and Glass<sup>12</sup>, suggested zinc oxide eugenol for use in direct pulp capping. However, chronic inflammation, failure of pulp healing and dentin bridge formation have been observed.<sup>12</sup>

# **Adhesive Systems**

Theoretically, primers of self-adhesive systems decalcify the inorganic structure and simultaneously prevent the precipitation of dried demineralized dentin by infiltrating the collagen fibrils. Self-adhesive systems prevent microleakages between the restoration and the tooth. Studies report that the presence of bacteria in the pulpal healing, cavity walls or pulp chamber cause failures. If microleakages can be prevented and the presence of bacteria can be controlled, the pulp can heal on its own.<sup>6,10</sup>

### **Glass Ionomer and Resin Modified Glass Ionomer Cements**

It is used in indirect pulp coatings due to its tight sealing (antimicrobial property), bonding and biocompatibility to dentin, and its fluoride release effect. Its main disadvantages are being cytotoxic to pulp tissues, poor physical properties, high solubility and slow hardening. Due to its cytotoxicity, it causes chronic inflammation and wide necrotic zones in the pulp.<sup>6</sup>

# **Polycarboxylate Cements**

When this cement is used together with potassium nitrate (KNO $_{\textrm{\tiny{\textit{3}}}}$ ), a desensitizing agent, it can be used as an effective liner or temporary cement in deep caries lesions. However, its antibacterial effect and dentin bridge formation is insufficient. It can chemically bond to tooth structures.<sup>6</sup>

# **Calcium Hydroxide**

# **Soluble Calcium Hydroxide**

In the past, calcium oxide powder was applied directly onto the pulp tissue and the formation of calcium hydroxide was observed as a result of the contact of the powder with the pulpal fluid. However, this practice does not continue today. One study which was carried out by Eleazer et al.<sup>13</sup>, has shown that an infectious response develops in the pulp with the direct application of calcium hydroxide powder. Komabayashi et al.<sup>7</sup> stated that, instead of calcium hydroxide powder, paste forms of calcium hydroxide powder maybe used for pulp capping. Some disadvantages of soluble calcium hydroxide have been reported such as; incomplete hardening, resorption over time, and porosities in the newly formed dentin which may cause microleakages.<sup>7</sup>

# **Calcium Hydroxide Cement**

Due to the disadvantages of soluble calcium hydroxide  $[Ca(OH)_2]$ described above, cement-type calcium hydroxide was developed and has been frequently used in clinical practice since the 1960s. The trade name of the most popular cement is Dycal. It consists of a catalyst and a base mixed in a ratio of 1:1.7

However, one study showed that Ca(OH), cannot be fully bonded to dentin, dissolves over time, and many tunnel defects were observed in the dentin bridge formed close to the material.<sup>14</sup>

In another study using canine teeth, mineral trioxide aggregate (MTA) was found to be more successful in terms of dentin bridge formation. There are dentin tubules in the dentin bridge formed under the MTA, but these tubules do not have continuity, their ends are blocked and closed to bacterial passage. However, the tubular dentin bridge formed under calcium hydroxide is continuous with the existing lateral dentinal tubules. In addition, in that study, inflammation and bacterial infiltration were not observed when MTA was applied, while both chronic inflammation in the coronal pulp and gram-positive cocci were detected in 4 samples in the calcium hydroxide group.<sup>15</sup>

A similar study performed on maxillary third molars showed that after direct capping using calcium hydroxide, mild inflammation rich in lymphocytes and mild hyperemia were observed under the dentin bridge. While these findings were not observed in the MTA group in the same study, a thicker dentin bridge formation was observed under the MTA. According to the results of that study, it was reported that MTA has superior properties compared to calcium hydroxide.<sup>16</sup>

In another study in which different materials were evaluated in terms of their antibacterial properties in direct pulp capping, researchers reported that the MTA group had the highest bacterial inhibition in terms of *S. mutans*, but Dycal showed the highest antibacterial property in 3 different bacterial types. The researchers reported that the antibacterial property of calcium hydroxide is related to its ability to release hydroxyl ions.<sup>17</sup> The success of calcium hydroxide, which

has been accepted as the "gold standard" for many years, especially as a direct capping material, is well known.<sup>18</sup> Today, the gold standard has changed and MTA is used more than calcium hydroxide in clinical studies.<sup>19</sup>

#### **Mineral Trioxide Aggregate**

MTA was developed as a bioactive material in the early 1990s and was aimed to be used as a retrograde filling material. It was first mentioned in the dental literature in 1993.<sup>20,21</sup> The main MTA, ProRoot grey MTA (Dentsply), was introduced in 1998. It contains 75% type 1 Portland Cement, 20% Bismuth Oxide and 5% calcium sulfate dehydrate.7 The main component of MTA is Portland cement. However, unlike Portland cement, MTA also contains bismuth oxide. In addition, the particles in MTA are smaller and more uniformly shaped. MTA contains less heavy toxic metals and has a longer working time.<sup>20</sup>

The mechanism of action of MTA is similar to that of calcium hydroxide. Calcium hydroxide appears as a by-product of the hydration of MTA as a result of its contact with the pulp tissue and causes necrosis. When MTA powder is mixed with water during application, calcium silicate powders in the powder hydrate to form hydrated calcium silicate gel and calcium hydroxide. Accordingly, MTA can be considered as a calcium hydroxide releasing material and it is expected to have all the properties described for calcium hydroxide.7

Biocompatibility, good sealing ability, bioactivity and triggering the formation of mineralized tissue are said to be the advantages of MTA.7,20 Pulp tissue has a natural tissue repair ability which can form reparative dentin. The healing of pulp tissue occurs as a result of the arrival of stem/progenitor cells to the damaged area and differentiation into odontoblast-like cells after proliferation. Reparative dentin often ends with a fibrodentin matrix composed of a tubular and/or irregular cuboidal cells.20 In addition, it has been observed that the reparative dentinogenesis resulting from MTA application is more pronounced and consistent compared to calcium hydroxide.<sup>21</sup> While MTA was used only in a gray color until 2002, a new version was introduced [white MTA (WMTA)] to meet patients' aesthetic expectations. MTA is now classified into two different categories as either traditional gray MTA or WMTA. The main differences are the amounts of  $Al_2O_3$ , MgO and FeO.<sup>21</sup> In addition to all these, WMTA does not contain iron.<sup>22</sup>

#### **Bioceramics**

Bioceramics are biocompatible ceramic compounds. They are compatible with various chemicals. Bioceramics exhibit excellent biocompatibility due to their biological properties similar to hydroxyapatite. Bioceramics have the ability to induce a regenerative response by forming different compounds during hydration. Bioceramics consist of a porous powder containing 1-3 nm nanocrystals and this property prevents bacterial adhesion.<sup>23</sup> The reason why bioceramics are widely used in dentistry and biomedicine is that they are more inert than metals. Over the past two decades, interest has turned to bioceramic materials. Biomaterials can form close bonds with hard tissues as well as induce physiological function. Bioceramics are now used in the living body for different purposes. They can be divided into two as "bioinert" or "bioactive" ceramics, depending on their interaction with tissues. Oxides, such as alumina or carbon compounds, are inert bioceramics as they experience little or no chemical change when in prolonged contact with a physiological environment.<sup>24</sup>

#### **Biodentine**

Biodentine is a tricalcium silicate-based dentin restoration material obtained from Portland cement. Many silicate-based materials have been developed in order to eliminate the difficulties which may be experienced due to the long setting time of MTA. Among them, Biodentine is a material consisting of powder and liquid and it can be used instead of damaged dentin (Biodentine; Septodont, Saint Maur de Fosses, France). It has a reduced curing time (12 min), strengthened mechanical properties and ease of application (high viscosity). It is used as an alternative to MTA.11,25,26 Biodentine is a calcium silicatebased bioactive material with the same usage areas as MTA. Since it has mechanical properties similar to dentin, it is a material which can be preferred in treatments which require the regeneration of the dentinpulp complex. This material, which has a positive effect on vital pulp cells, induces tertiary dentin formation and provides reparative dentin production when it comes into direct contact with the vital pulp.<sup>6,11,25</sup> In a study carried out by Poggio et al.<sup>27</sup> in 2014, the biocompatibility of Biodentine was compared with pulp capping materials such as Dycal, MTA Angelus and ProRoot MTA. According to their study, Biodentine and MTA-based materials showed less cytotoxicity than Calcium Hydroxidebased materials, and it was reported that the Biodentine material may be the best pulp capping material among these materials. $27$ 

#### **Endosequence Root Repair Material**

This is a root canal filling material designed mainly for endodontic treatment. It contains calcium silicate, monobasic calcium phosphate, zirconium oxide, tantalum oxide, thickening agents and special fillers.<sup>6</sup> It is a stable and ready-to-use material, having high mechanical bond strength, high pH, radiopacity, and hydrophilic hardening properties. $28$ 

#### **Light Cured Tricalcium Silicate Cement**

This material, which is marketed as an alternative to light-cured calcium hydroxide-based pulp coating materials, contains 45% white mineral material (type 3 Portland cement), 10% white radiopaque material, 5% white hydrophilic thickening agent (fumed silica barium zirconate) and approximately 45% resin. The resin content consists of both hydrophobic monomers (UDMA, BisGMA, TriEDMA/TEGDMA) and hydrophilic monomers (HEMA, PEGDMA). Due to its resin content, this material has good physical properties. It can induce the formation of apatite crystals with its calcium fluoride content. Tricalcium silicate material is biocompatible and has properties which induce the differentiation of human pulp cells similar to calcium hydroxide.<sup>6,29</sup> In addition, it is formulated to reduce microleakages by providing good bonding to composites by using light-cured tricalcium silicate-based materials as linings under composite restorations.<sup>30</sup>

In the study conducted by Cengiz and Ulusoy<sup>26</sup> in 2016, the bond strengths of Theracal and Biodentine materials were compared with restorative materials and it was reported that the Theracal material achieved a stronger bond. Accordingly, the success of the capping treatment will be positively affected.<sup>26</sup>

In another study by Camilleri<sup>31</sup> in 2014, the setting reactions of Theracal and Biodentine materials were compared. It was determined that the calcium ion release resulting from the setting reaction is much higher in Biodentine.<sup>31</sup>

In another study, Biodentine and Theracal were compared and it was reported that Theracal could not produce calcium hydroxide, and it used the water necessary for its hydration by diffusion of the water in

the environment. It is also thought that resin monomers may cause adverse reactions in the pulp.<sup>32</sup>

#### **Calcium Phosphate**

Calcium phosphate containing materials are biomedical materials with excellent biocompatibility and non-toxic properties because of their chemical compounds. Calcium phosphate cements are bioactive synthetic materials and the most frequently used ones are hydroxyapatite and tricalcium phosphates. These types are generally preferred because of their osteoconductivity, crystallographic structure and chemical structure similar to skeletal tissue.<sup>33</sup> Calcium phosphate cement is a self-curing bioactive material consisting of powder and liquid. Al-Sanabani et al.<sup>34</sup> said that it was developed by Brown and Chow in the 1980s. Calcium phosphate, which is a material superior to pure calcium hydroxide due to its self-curing feature, appropriate compressive strength and biocompatibility, has the potential to be used in direct or indirect pulp capping applications for dentin regeneration.<sup>35</sup> In one study, calcium hydroxide was compared with calcium phosphate for the potential of dentin bridge formation in the primary teeth of pigs. It was reported that calcium phosphate can form a more regular, faster and thicker dentin bridge compared to calcium hydroxide.<sup>29</sup>

However, as tricalcium phosphate could not completely prevent microleakages due to its porous structure, bacterial infiltration was encountered. For this reason, there are also researchers who recommend not to use it for pulp capping.<sup>6</sup>

#### **Calcium-Rich Mixture (CEM)/New Endodontic Cement**

Calcium-rich mixture (CEM) is a tooth-coloured water-based cement. It consists of calcium-containing compounds such as calcium oxide, calcium carbonate, calcium phosphate, calcium silicate, calcium sulfate, calcium hydroxide, and calcium chloride. These substances stimulate the formation of hard tissue and are not cytotoxic. Its antimicrobial and sealing properties are similar to calcium hydroxide. Although its chemical content is different from MTA, its clinical applications are similar. It is considered as an alternative to MTA as it hardens in a shorter time, is more fluid, has less film thickness, can be easily shaped and does not cause tooth discoloration.<sup>11,36</sup>

In a study comparing MTA and CEM, it was stated that CEM gave better pulpal results than MTA, although it was not statistically significant. The mean dentin bridge thickness of the CEM group was found to be higher than that of the MTA group, and the layer formed by odontoblast-like cells was observed more frequently in the CEM group. It was reported that the high content of the calcium compounds of this cement provides a rich pool of calcium and phosphorus ions. These elements are also used as part of the natural hydroxyapatite production of pulp cells. $37$ In another similar study, after CEM and MTA applications, a thicker dentin bridge was formed under the CEM and less pulp inflammation was observed. More tubular formations were observed in the dentin tissue formed under CEM, but no statistically significant difference was found between the materials.<sup>38</sup> In another study in which MTA and CEM were compared, it was reported that CEM material could be a vital pulp treatment material as successful as MTA.<sup>36</sup>

Zarrabi et al.<sup>38</sup> examined MTA and new endodontic cement (NEC) in human dental pulp and reported that both materials were biocompatible and formed dentinal bridges. However, NEC formed a thicker dentinal bridge and caused less pulp inflammation compared with MTA.<sup>38</sup>

# **Growth Factors and Proteins**

Growth Factors are natural polypeptide hormones. They regulate key cellular events in tissue repair, such as cell proliferation, chemotaxis, differentiation and matrix synthesis, by binding to their specific receptors. They are involved in mitogenesis, migration, matrix synthesis and remodulation during tissue repair.<sup>33,39</sup> Growth factors can act as signaling molecules which modulate cell behavior by mediating intracellular communication. Growth factors are polypeptides or proteins which bind to specific receptors on the surface of target cells. They can initiate the intracellular signaling cascade and behave in an autocrine or paracrine manner. This can send signals to the cell nucleus and stimulate the genetic structure which will change the behavior and activity of the cell.<sup>33,40</sup>

# **Enamel Matrix Protein (Emdogain-EMD)**

Enamel matrix derivative (EMD) is a bioactive molecule, the major component of which is amelogenin. This is released from preameloblasts to enable the differentiation of odontoblasts in the dental papilla during odontogenesis. It is derived from developing pig teeth, which resemble human enamel protein. The main component of EMD is amelogenin.<sup>41</sup> It has been reported that EMD potentiates alkaline phosphatase (ALP) activity and the release of bone matrix proteins in osteoblasts. It has been stated that amelogenin and amelin proteins participate in the differentiation of odontoblasts and the subsequent dentin formation during dentinogenesis. EMD induces endothelial cells of pulp capillaries and odontoblasts to produce a hard tissue barrier on the exposed pulp. EMD-enhanced ALP activity and bone morphogenetic protein expression in osteoblasts and dentin matrix protein go first to the site to strengthen the condition of the injured pulp and the production of repair dentin. This material was found to be clinically resistant because it contains amelogenin and amelin, which are defined as auto-proteins by the body's defense system, and it has been reported that it does not show any allergic or immunological reactions during 10 years of use.<sup>42</sup>

When EMD gel is applied to the exposed pulp, it induces the formation of dentin-like hard tissue. However, it is reported that when applied alone, Emdogain gel is ineffective in the formation of hard tissue due to its dissolution in propylene glycol alginate gel and it cannot provide a leak-proof seal. When used in combination with MTA, the differentiation of pulp cells into odontoblast-like cells is faster than when MTA alone is used. Therefore, it is not recommended to be used alone.<sup>6,11</sup>

In one study on miniature pig teeth, the success of calcium hydroxide and Emdogain materials in creating dentin bridges in direct pulp capping was compared. Hard tissue formation in teeth treated with Emdogain was reported to be 2 times greater than in calcium hydroxide for the 2 and 4 week results.<sup>41</sup>

#### **Transforming Growth Factors**

Transforming growth factor (TGFs) are a structurally and functionally related family isolated from healthy and neoplastic tissues. The two best-characterized types are TGF-alpha  $(α)$  and TGF-beta  $(β)$ . TGF- $β$  is a dimeric polypeptide linked by covalent bonds and has three different structures: TGF-β1, TGF-β2, TGF-β3, TGF-β4 is a multifunctional growth factor and it can be synthesized by many tissues, but bone and platelets are its main source. The three best-known iso-types of TGF-β in mammals, TGF-β1, TGF-β2, and TGF-β3, are reported to be involved in embryonic differentiation and development. It has been reported

that the activity of TGF-β is observed in the dental papilla and stellate reticulum in odontogenesis in mammals.<sup>40,43,44</sup>

#### **Bone Morphogenetic Proteins**

In 1965, Marshall Urist determined that a demineralized bone matrix induces bone formation when placed subcutaneously. The ability to form a demineralized bone matrix has been attributed by Urist to a protein called "Bone Morphogenetic Protein."45 It has been shown that bone morphogenetic proteins and recombinant human bone morphogenetic proteins stimulate osteodentin and subsequent tubular reparative dentin formation in pulp capping and amputation treatment in the absence of inflammation, but this success cannot be achieved in the presence of inflammation. In pulp capping, it has been reported that recombinant human proteins form repair dentin by protecting the pulp in a healthy way without wasting the deep pulp tissue.<sup>45</sup>

# **Insulin-Like Growth Factor**

Insulin-like growth factors (IGF) belong to the family of single-chain serum proteins. They are important regulators of cell proliferation and cell differentiation in various cells (osteoblast, fibroblast). Two separate polypeptides belonging to this family have been identified: IGF-1 and IGF-2. IGF-1 and IGF-2 are growth factors which are biochemically and functionally similar to insulin. IGFs are synthesized by many tissues such as the liver, smooth muscle, and the placenta.<sup>40</sup> It has been reported that dentin bridge and tubular repair dentin formation, which completely covers the exposed pulp, has been observed in capping treatments with IGF-1.<sup>44</sup>

# **Propolis**

It is an antimicrobial and anti-inflammatory agent consisting of resins collected by honey bees from cracks in trees and leaf buds. The most effective pharmacological component in propolis are flavonoids. Flavonoids are plant compounds with antioxidant, antibacterial, antifungal, antiviral and anti-inflammatory properties. Stimulation of TGF-β release and collagen synthesis of pulp cells are promising for their use in pulp coatings.<sup>6,46</sup>

# **Iloprost**

Prostacyclin (PGI2) is a potent vasodilator which increases angiogenesis and cellular differentiation by stimulating the release of vascular endothelial growth factor (VEBF), and it is also involved in bone remodeling. An increase in bone mass was observed in animals whose PGI2 synthesis was triggered. Osteoblasts produce PGI2 in response to growth factors, and both osteoblasts and osteocytes release PGI2 in response to mechanical loading. In addition, PGI2 induces VEBF in a large number of cells. VEGF stimulation triggered by PGI2 also increases endothelial cell proliferation and angiogenesis. Iloprost is a long-acting PGI2 analog used in the treatment of pulmonary hypertension. Iloprost is also used clinically in order to prevent bone necrosis. It has been reported that circulating endothelial cells and their progenitors increase in patients receiving iloprost infusion.<sup>11,47</sup>

When the effect of iloprost on the blood flow of dental pulp was examined, there was no significant difference with CaOH<sub>2</sub> in the first 24 hours, however, it was reported that blood flow increased significantly in samples treated with iloprost within 72 hours. This increase is thought to be effective in maintaining pulp vitality and the formation of the dentin bridge.<sup>47</sup>

In an *in vivo* study with iloprost in rats, it was found to be successful in forming tertiary dentin. Although the material is a long-acting PGI2 analogue, it has a short half-life in the lungs. Therefore, it is important to adjust the amount to be applied. $47$ 

# **Laser Applications**

Komabayashi et al.<sup>48</sup> said that, Melcer et al. first proposed the use of  $CO<sub>2</sub>$ lasers in direct pulp capping. They pointed out that laser applications improve the formation of tertiary dentin on the dentin surface and above all, provide sterilization. Melcer reported successful direct pulp capping with CO<sub>2</sub> lasers.<sup>48</sup> It was reported that low-intensity laser applications regulate the inflammatory response in injured tissues without causing side effects.<sup>49</sup> As a result of a clinical study in which direct pulp capping with CO $_{\textrm{\tiny{2}}}$  laser + CaOH $_{\textrm{\tiny{2}}}$  and only CaOH $_{\textrm{\tiny{2}}}$ were followed up for an extended period, vitality was reported as 93% in the laser treated group and 68% in the CaOH $_{\textrm{\tiny{2}}}$  group only. Researchers reported that laser applications in direct pulp capping can be recommended to increase success.<sup>48</sup>

Bleeding may begin again after the pulp capping material is placed in the exposed area. This can both cause microleakages by affecting the polymerization of adhesive systems and disrupt the sealing of pulp capping materials, leading to the presence of bacteria and bacterial invasion in the exposed area. Therefore, the use of lasers in pulp capping has come to the fore.<sup>6</sup>

### **High Frequency Radio Waves**

The clinical success of direct pulp capping is closely related to achieving hemostasis in the pulp. When the pulp is exposed, providing hemostasis with a fast and reliable method as possible, this will increase clinical success. For this reason, high-frequency radio waves have found use in direct pulp capping. High frequency radio waves (HRW) creates coagulation in the soft tissue using 4 MHz radio signals.<sup>11</sup>

In the results of direct capping applications using HRW in mice, dentin bridge density increased as the intensity of the HRW application increased, but the dentin bridge formed in the most intense HRW group was more irregular and tunnel defected compared to the other 2 groups. As a result of this study, researchers reported that ensuring hemostasis reduces pulpal inflammation and triggers the formation of a better quality dentin bridge.<sup>50</sup>

#### **CONCLUSION**

According to the results of this literature review, it may be concluded that calcium phosphate can form a more regular, faster and thicker dentin bridge compared to calcium hydroxide. MTA, Biodentine, CEM and NEC may also be used safely in pulp capping in order to maintain pulp vitality and healing.

Future and long-term *in vivo* studies for pulp capping are necessary to investigate the clinical use of the promising materials and techniques, such as growth factors and proteins, propolis, laser applications and high frequency radio waves.

# **MAIN POINTS**

• Pulp capping is a technique used in dental restorations to prevent the dental pulp from necrosis, after being exposed, or nearly exposed during a cavity preparation, from a traumatic injury, or by

a deep cavity which reaches the center of the tooth causing pulp necrosis.

- Biodentine; a tricalcium silicate-based material, reported to be the best pulp capping material is discussed in this review.
- Light Cured Tricalcium Silicate Cement; TheraCal LC which provides a better bonding with dentin than Biodentine may be an alternative for pulp capping.
- Calcium-Rich Mixture (CEM) is considered as an alternative to MTA for pulp capping, as it hardens in a shorter time, is more fluid, has less film thickness, can be easily shaped and does not cause tooth discoloration.
- Today, MTA has taken its place in clinical studies as the gold standard compared to calcium hydroxide.

#### **ETHICS**

#### **Authorship Contributions**

Concept: Ş.A., N.U., Design: Ş.A., N.U., Data Collection and/or Processing: Ş.A., N.U., Analysis and/or Interpretation: Ş.A., N.U., Literature Search: Ş.A., N.U., Writing: Ş.A., N.U.

#### **DISCLOSURES**

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