

A Comparative Clinical, Histological, and Radiographic Evaluation of Different Pulp Capping Materials on Permanent Teeth: Current Prospective and Future Direction

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Abstract

Pulp capping is a vital procedure in preserving the vitality of dental pulp in cases of pulp exposure due to caries or trauma. This study aimed to compare the clinical, histological, and radiographic outcomes of different pulp capping materials used on permanent teeth and explore current perspectives and future directions in this field.

A comprehensive literature review was conducted to identify relevant studies published in peer-reviewed journals. Studies comparing the effects of various pulp capping materials, such as mineral trioxide aggregate (MTA), calcium hydroxide, and biodentine, on permanent teeth were included. Clinical parameters, such as success rates and postoperative symptoms, were evaluated. Histological assessments focused on pulp tissue response and dentin bridge formation. Radiographic evaluations assessed the extent of pulp healing and periapical changes.

Results from the reviewed studies showed that MTA and biodentine were more effective in promoting pulp tissue healing and dentin bridge formation compared to calcium hydroxide. Furthermore, these materials exhibited higher success rates and lower rates of postoperative complications. However, further long-term studies are needed to confirm these findings and evaluate the durability of these materials.

In conclusion, MTA and biodentine are promising materials for pulp capping in permanent teeth, showing superior clinical, histological, and radiographic outcomes compared to calcium hydroxide. Future research should focus on standardizing study protocols, conducting randomized controlled trials, and exploring novel materials to improve the success and longevity of pulp capping procedures.

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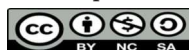
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INTRODUCTION

Pulp capping can be best described as capping of the exposed pulp and is indicated for irreversible pulp injury after physical or mechanical trauma. The success of vital pulp treatment of traumatic exposure is considered predictable; however, much



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controversy exists regarding capping cariously exposed pulp. The essential difference between the two clinical presentations is that in a traumatic exposure, the level of pulp inflammation is uniform and can be accurately predicted.

Studies have shown that a tooth is more likely to survive direct pulp capping if the initial exposure is due to mechanical reasons rather than caries. Caries penetration into the pulp will result in bacterial invasion of the pulp, resulting in pulpal inflammation. This leaves the pulp less able to respond and heal, compared to a mechanical injury in which pre-existing inflammation is not present. The control of infection and biocompatibility of the pulp capping material are important factors determining the treatment outcome. Ultimately, the goal of treating the exposed pulp with an appropriate pulp capping material is to promote the dentinogenic potential of the pulpal cells. Preservation and maintenance of pulp vitality is the primary objective in endodontics. Direct pulp exposures can be a challenging problem, and such pulp exposure presents a treatment dilemma. Direct pulp capping is the coverage of exposed pulp by a biocompatible material after traumatic or carious exposure. The purpose of this procedure is to seal it against bacterial leakage, stimulate dentinal barrier formation, and maintain the vitality of the pulp.

Historically, pulp capping was first performed in 1765 by Philip Pfaf, using gold foil. In 1923, Davis suggested using a complex of zinc sulphate and calcium sulphate with zinc oxide for direct pulp capping. Harman (1930) used calcium hydroxide $[Ca(OH)_2]$ as pulp capping for the first time, and from the early 1940s till now, it is considered as the "gold standard" for pulp capping. Several other materials such as Zinc Oxide Eugenol, Polyacrylates, Glass ionomer cement, Resin adhesive systems, Ferric sulphate, Form cresol, Calcium Hydroxide, Bioactive glass, and Mineral trioxide aggregate have been used for direct pulp capping. Interestingly, no one material seems to enjoy a significant preference. Calcium hydroxide has been indicated to promote healing in many clinical situations. They provide an option for reparative dentin formation, but long-term studies have shown results to be variable and somewhat unpredictable. The spectrum of success rates for calcium hydroxide ranges from 14% to 97%.

Mineral trioxide aggregate (MTA) was introduced by Torabinejad in 1995 for sealing all the existing pathways between the root canal system and the outer surface of the tooth. This material became known as an appropriate material

for pulp capping because of its several good features such as high sealing effect and high pH, biocompatibility, long-term stability, prevention of bacterial leakage, and stimulation of cementum, bone, and dentin formation. MTA has a pH of 12.5, which is comparable with the pH range achieved by $Ca(OH)_2$ preparations after application on the exposure area. In spite of this, there appears to be differences in pulpal tissue reaction to MTA compared with $Ca(OH)_2$ in direct pulp caps. Dentin bridge formation with MTA seems to be more homogenous but it is a technique sensitive material that can be difficult to place and it takes about four hours to set when in contact with moisture. Vital pulp therapy is a treatment devised to conserve protect and maintain a healthy pulp. The prime objective of the treatment strategy is to aid in the formation of a reparative hard tissue barrier following pulpal injury. It includes direct and indirect pulp capping partial and complete pulpotomy. These the rapies prevent further pulp injury by protecting the pulp from the various chemical assaults, bacterial insults, mechanical and thermal toxic effects.

Mineral Trioxide Aggregate (MTA) is a bioactive tricalcium silicate cement with success as a pulp capping agent as shown by several studies. The seems to be successful because of its small particle size, good sealing ability slow calcium on release and alkaline pH when set. It is non absorbable, sets in the presence of moisture has a relatively higher compressive strength and sustained high alkaline pH.

MTA has shown to induce proliferation of the pulp cells release of cytokines and an interface with dentin is synthesised that resembles hydroxyapatite composition. However the main drawbacks of MTA include a potential for discolouration presence of toxic elements in the material composition like arsenic difficult handling characteristics long setting time, high material cost higher toxicity in its freshly mixed state no effective solvent that would aid in its retrieval and its removal after hardening is difficult. A material which overcomes all these short comings and provides properties ideal for a pulp capping agent is still in the search. Recently platelet concentrates are being tried in various fields of dentistry including pulp identin complex regeneration.^{3,4}

PRF is the second generation platelet concentrate introduced in 2001. The development of PRF focused on simplified preparation without biochemical blood handling. Compared to PRP, the preparation protocol of PRF is relatively simple, involving

one centrifuge cycle and excluding the use of anticoagulant and clotting factors. Centrifuging should be commenced as soon as the blood is obtained from the patient because the blood will clot immediately in the tube. The recommended protocol is a spin cycle at 2700 rpm (400-g force) for 12 min. After centrifuge, the blood will separate into three layers: erythrocytes at the bottom, platelet-poor plasma on the top and a PRF clot with entrapment of platelets and leukocytes in the middle. The PRF is capable of slow release of growth factors for more than seven days. After removal with tweezers the PRF can be cut into pieces or further pressed into a membrane by driving out the serum. Because of the slow and natural fibrin polymerization mode, PRF forms a three-dimensional (3D) fibrin matrix with a physiologic architecture which is particularly favorable for cytokine entrapment and cellular migration. The PRF incorporates the three critical parameters for tissue engineering: cells (platelets and leukocytes) that promote tissue healing and regeneration, continuous release of growth factors and a fibrin scaffold. Recent *in vitro* studies showed that PRF improved the migration, proliferation and differentiation of stem cells from the apical papilla (SCAPs). Therefore, PRF has been perceived as a better alternative to blood clot or PRP for REPs. Clinical studies showed that the use of PRF achieved favourable outcomes in the resolution of periapical lesion, root lengthening, dentin wall thickening and the restoration of tooth vitality.^{5,6}

L-PRP and L-PRF contain higher concentrations of leukocytes compared to PRP and PRF; these cells play a prominent role in the anti-infectious action and immune regulation of the wound healing process. Leukocytes in L-PRP and L-PRF produce large amounts of angiogenic stimulators such as vascular endothelial growth factor (VEGF). In recent years, L-PRF has been used as a biomaterial scaffold in REPs in an immature permanent tooth in association with apical surgery or in autologous DPSCs therapy for a mature permanent tooth with symptomatic irreversible pulpitis. A multicenter controlled clinical trial was recently reported to evaluate the effect of L-PRF on REPs of immature permanent teeth. Twenty-nine patients between 6 and 25 years with an inflamed or necrotic immature permanent tooth were included and divided into the test group (REPs with L-PRF) and control group (REPs without L-PRF). After 3, 6, 12, 24 and 36 months the patients were recalled and the teeth were clinically and radiographically examined at each recall session. Twenty-three teeth (9 test, 14 control) were analyzed, and the results showed that complete periapical bone healing was obtained

qualitatively (91.3%) and quantitatively (87%) in most of the cases based on periapical radiograph evaluation with no significant difference between the groups with respect to the baseline. No significant difference was found between the control and the test group regarding further root development based on peri-apical radiograph evaluation. Despite the limitations of this study, L-PRF seems to be a viable biomaterial scaffold in REPs to obtain peri-apical bone healing and aid further root development of necrotic immature permanent teeth. It is worth noting that flare-ups appeared only in three teeth of the test group in the first-year post REPs. The pro-inflammatory cytokines in L-PRF might lead to flare-up when applied in REPs.

The implanted decellularized scaffold promoted the recruitment of apical stem cells to form pulp-like tissue with the expression of odontoblastic marker. In a more recent study, bovine pulp was successfully decellularized and processed to create a 3D macro-porous injectable scaffold which favoured the viability, proliferation, attachment and morphology of human bone marrow mesenchymal stem cells. Xenogenous dental pulp has the adverse potential of inducing antigenic response or disease transmission. An ideal tissue decellularization protocol involves meticulous removal of all antigenic cellular components without adversely altering ECM composition, morphology and stem cell scaffold functions. As such, the protocols for preparing xenogenous pulp tissues need to be improved and optimized. A study compared the effect of seven different decellularization protocols on the decellularization of bovine dental pulp tissues. The remnant cellular and nuclear contents, collagen and glycosaminoglycan composition, as well as the immune compatibility of the pulp ECM were evaluated. Among the seven decellularization protocols, the 12E-0S-1T protocol had the best performance for REPs.^{7,8}

Scaffolds fabricated by conventional techniques may fail to recapitulate the complex physiological microstructure of dental pulp tissue with heterogeneous, porous, and permeable properties. Moreover, an ideal scaffold should mimic the microenvironment in the dentin-pulp complex and facilitate the temporal and spatial regulation of cell distribution and cell proliferation. The emerging 3D bioprinting technologies may serve as a promising alternative to address challenges and provide possibilities in the manufacturing of customized constructs with three-dimensional patient-tailored shapes and compositions. A recently published

study showed that compared with Alginate/gelatin hydrogel scaffold, 3D printed Alginate/gelatin hydrogel scaffold is more suitable for the growth and adhesion of hDPSCs. The aqueous extract of the 3D-printed scaffold contained more calcium and phosphorus ions and can better promote cell proliferation and differentiation.^{9,10}

Concentrated Growth Factor (CGF) is an advanced second generation platelet concentrate. The alternated and controlled speed mode of centrifugation provides a higher chance to collide with the glass wall and results in platelet rupture, improving the release of growth factors. This results in a fibrin matrix that is much larger denser and richer in growth factors. However, there are only a few in vitro studies assessing the effect of CGF on dental pulp cells and no animal studies in vivo studies or case reports to substantiate the effect of CGF in direct pulp capping.¹¹

Both of the morphologic assays, namely scanning electron microscopic visualization and immunofluorescence staining expectedly support the aforementioned findings. The lower cytocompatibility exhibited by ThLC translates into the following observable indicators of cellular death: the presence of cell debris, the lack of cellular adhesion and the absence of functionally oriented cells whereas the opposite was observed in the ThPT- and BD-treated hDPSCs. The morphologic differences between the ThLC- and ThPT treated hDPSCs observed in the present study confirm those reported in a previous study performed by our research group. Altogether the results from the cytocompatibility assays disfavored the inclusion of ThLC in the cell plasticity assay because of its negative influence on hDPSC viability proliferation, adhesion and morphology. The decision to exclude ThLC from this assay was further supported by previous studies in the field in which it was also excluded from a cell plasticity assay it was associated with significantly lower rates of stem cells from human exfoliated deciduous teeth viability the ThLC-treated hDPSCs exhibited a significantly lower ALP activity than BD and MTA and it adversely affected the osteogenic differentiation of hDPSCs.¹²

With better understanding of biological mechanisms and advent of new materials a new treatment paradigm in endodontics oriented toward preservation and tissue regeneration has evolved. Mature permanent teeth with irreversible pulpitis have traditionally been managed with complete pulpectomy. However this procedure significantly reduces the survival time of the tooth with a hazardous

ratio of 7.4:1. Acknowledging the inherent healing potential of an infection free pulp attempts have been made to use pulpotomy as a treatment modality in permanent teeth with complete root development exhibiting symptoms of irreversible pulpitis, where radicular pulp is still healthy.

An alternative gold standard mineral trioxide aggregate (MTA), is available as a direct pulp-capping material. However MTA is difficult to use because of its long setting time, poor handling properties cost and the potential discoloration of teeth and soft tissue. To overcome some of these limitations, other bioactive tricalcium silicate cements have been recently introduced on the market. One material is Biodentine. It consists of a powder and liquid. The powder primarily contains tricalcium silicate ($3\text{CaO} \cdot \text{SiO}_2$) and dicalcium silicate ($2\text{CaO} \cdot \text{SiO}_2$) and calcium carbonate (CaCO_3). Zirconium dioxide (ZrO_2) is a contrast medium. The liquid consists of calcium chloride ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$), which is used as a setting accelerator and water-reducing agent in aqueous solution with an admixture of polycarboxylate (i.e. a superplasting agent). Mixing is achieved by using an amalgamator for 30s at 4000–4200rpm.^{13,14}

Recently, the fetal derived mesenchymal stem cells (MSC) from the placenta or other gestational tissues like the amniotic fluid umbilical cord are novel materials with rich stem cell reserves. The matrix of Human Amniotic Membrane (HAM) contains abundant growth factors like keratinocyte growth factor (KGF), basic fibroblast growth factor (b-FGF) transforming growth factor-beta ($\text{TGF-}\beta$) nidogen growth factor (NGF) and epidermal derived growth factor (EDGF) which promote tissue regeneration. These growth factors provide a natural healing environment and mimic the stem cell niche for ex vivo growth.^{15,16}

Amniotic Membrane (AM) has a proven rate of success in the field of dentistry as guided tissue regeneration root conditioning haemostatic and wound dressing agent. It has inherent properties like low immune response and toxicity ability to promote cellular growth and attachment. Hence, the present study was aimed at comparing the success of pulpotomy outcomes using amniotic membrane and formocresol by evaluating them both clinically as well as radiographically.

To prepare the water soluble form of AM extracts, the AM (e.g. Am stroma stroma-removed AM, placenta, chorion) is transferred to a sterile 50ml centrifuge tube and centrifuged at 4°C for 5 min at 5000 xg to remove the excess fluid. The AM is weighed transferred to a 100mm or 150 mm

sterile Petr dish, and frozen in the air phase of a liquid nitrogen container for 20 min to facilitate the subsequent homogenization. The frozen Am is then sliced into small pieces with a disposable scalpel or ground to fine particles using a Bio Pulverizer (Biospec Products, Inc. Bartlesville, OK) or other suitable device, and homogenized with Tissue Tearor (Biospec Products Inc. Dremel W or other suitable device in phosphate buffered saline (PBS) or DMEM without phenol red (Invitrogen, Carlsbad, CA) at neutral pH. For biochemical characterization and purification the above solutions are supplemented with the following proteinase inhibitors: 1mg/ml aprotinin, 1mg/ml leupeptin, 1mg/ml pepstatin A and 1m MPMSF. However if the extract is to be directly added to cell culture no protease inhibitor is added.

Amniotic membrane matrix contains plenteous growth factors (GFs) including basic fibroblast growth factor (b-FGF), nidogen growth factor (NGF), keratinocyte growth factor (KGF) epidermal derived growth factor (EDGF), and transforming GF-beta growth factor (TGF- β) which promote tissue regeneration.¹⁴ These GFs mimic the stem cell niche for ex vivo growth and provide a natural healing environment. It acts as a structural scaffold supporting proliferation differentiation and regeneration due to presence of fibronectin, laminins proteoglycans collagen types I, III, IV, V and VI elastin, nidogen, and hyaluronic acid in its stromal layer, and act as an excellent candidature for a native scaffold in tissue engineering.¹⁷⁻¹⁸

Conclusions and Scope for further work

The control of infection and biocompatibility of the pulp capping material are factors determining the treatment outcome. Ultimately the goal of the exposed pulp with an appropriate pulp capping material is to promote the dentinogenic potential of the pulpal cells.

Clinicians have used many materials and techniques for direct pulp capping including calcium hydroxide hydrophilic resins, resin-modified glass ionomer cements among others. Mineral trioxide aggregate has generated considerable interest as a direct pulp capping agent in recent years. MTA is bioactive silicate cement that has been shown to be an effective pulp-capping material in canine models and in non human primates. The material is successful because of its small particle size, sealing ability, and slow release of calcium ions. MTA is non absorbable sets in the presence of moisture, has a relatively high compressive strength and has a sustained alkaline pH. The results of previous

studies using MTA and Biodentine are encouraging. With the advent of newer biomaterials there is further scope is present in this field to preserve the vitality of tooth.

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