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Recent advances in pulp capping agents

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ABSTRACT
The notion of biomimetics in dentistry has a lot of importance, and many studies have been conducted, either to modify the existing material or to develop new material. It is more likely to be successful, have a better prognosis, and have superior biocompatibility if the lost dental tissue is replaced rather than mild replacement with dental materials. Dentin, enamel, cementum, and pulp that have been lost could be successfully replaced through biomimetic dentistry, opening a new era of dentistry. The last few decades have seen tremendous growth in the field of dentistry. But each procedure has its own drawbacks and limitation due to the complex natural tooth structure. Therefore, the utilization of such biomimetic materials that could successfully restore the destroyed enamel, dentine, dentino-enamel junction, cementum, and even the pulp tissue will be required in the future of dentistry. The development of a substitute that restores or mimics the natural dental tissue is in progress.

Keywords:
Direct pulp capping, Indirect pulp capping, Proroot MTA, MTA Angelus, Retromta, Biodentine, Theracal LC, Melatonin, Vital pulp therapy

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I. INTRODUCTION

Preservation of pulp vitality is a critical factor in long-term tooth survival. The vitality of the dental pulp can be compromised by the presence of a deep carious lesion and by its subsequent management; therefore, treatment options aimed at preserving pulp vitality are recommended. Traditionally, such lesions are treated with complete (non-selective) caries removal, but emerging evidence suggests that risk of pulp exposure associated with complete caries removal could be avoided by adopting more conservative, partial (selective) caries removal approaches.[1] Despite advances in the understanding of the effects of selective caries removal in managing deep carious lesions, non-selective caries removal techniques remain common. There are several treatment options available for carious exposure, varying from conservative minimally invasive vital pulp treatments (VPT), including direct pulp capping (DPC), partial and complete pulpotomy to the more invasive pulpectomy and root canal treatment. Although root canal treatment is the traditional treatment of choice for the cariously exposed pulps, it is destructive and a technically demanding procedure. DPC is a more conservative treatment strategy, based on the premise that a biologically active material placed in direct contact with the pulp wound can determine the pulpal response and result in the development of a reparative hard tissue bridge to preserve pulp vitality.

The requirement for new kinds of bioinspired material leads to introducing biomimetic bond composition as an essential clinical and scientific task. One of the most commonly used dental materials as filler and bond is calcium hydroxide having higher efficiency due to similar physicochemical properties with the inorganic constituents to dental hard tissues and bone. Hydroxyapatite-based materials have regenerated and replaced tissue to modify cement bonding. Biomimetically restored tooth results in deformation and stress concentrations, eliminating sensitivity and postoperative pain and preserving vitality, as bacteria cannot invade and kill the pulp.

MATERIALS USED :-
CALCIUM HYDROXIDE

Calcium hydroxide is a widely used pulp capping material that has been in use for many years. It is a white, odourless, and alkaline substance that is prepared by combining calcium oxide (quicklime) with water. In dentistry, calcium hydroxide is used as a direct pulp capping material due to its excellent biocompatibility and antimicrobial properties. When applied to an exposed pulp, it can stimulate the formation of a dentin bridge, helping to protect the pulp and promote healing. It has several beneficial properties, antimicrobial activity, alkalinity, and the ability to stimulate reparative dentin formation. It is typically used in cases of small pulp exposures, caries lesions, and traumatic injuries.[2]

For many years, conventional or resin-modified calcium hydroxide/oxide–based materials like Dycal (1962), Life (1979) and Calxyl (1988) have been used in clinical practice. Other biomaterials such as Lime-Lite have been proposed as pulp capping agents due to their ability to release Ca and OH ions.

MINERAL TRIOXIDE AGGREGATE (MTA)

Calcium silicate-based materials have gained significant popularity in recent years due to their similarities to mineral trioxide aggregate (MTA) and their wide range of applications in dentistry. One commercially available calcium silicate material is "Biodentine (2009)" as a dentin replacement material. Conventional Mineral Trioxide Aggregate (MTA) has good biocompatible and physical properties like longer setting time, presence of a cytotoxic component, i.e., tricalcium aluminate (TCA), moderate compressive strength, and moderate antimicrobial activity.

MTA ANGELUS

Portland cements, commonly named mineral trioxide aggregate (MTA Angelus) cement is therapeutic, endodontic repair calcium silicate materials introduced at first as a grey cement. It promotes the proliferation/differentiation of human dental pulp cells and show calcified tissue-conductive activity with the ability to encourage new hard tissue formation in terms of dentine bridge development over the exposed pulp.

MTA PLUS

Bismuth oxide (Bi_2O_3), a radiopacifying agent contained in most MTA-based cements such as MTA Plus, plays a crucial role in the hydration processes of calcium silicates as well as in potential tooth discoloration, especially when in contact with sodium hypochlorite. MTA Plus had high values of open porosity and solubility. MTA PLUS contains a fine powder of tricalcium silicate (alite), dicalcium silicate (belite), calcium sulphate (anhydrite).

NEO MTA PLUS

Recent bioceramic material has been introduced to dental market, namely, Neo MTA Plus, which is regarded as a possible substitute to MTA for pulp capping procedure. NMP consists of fine powder of calcium silicate and gel mixed to form putty-like consistency to improve the handling characteristics. The calcium ions released from NMP react with the phosphate ions of the surrounding tissue fluids, resulting in the deposition of a calcium phosphate layer able to seal the open voids. NMP used as pulp capping agents induced complete dentin bridge formation with no pulpal inflammation.[3]

ProRoot MTA

ProRoot MTA showed dye absorbance values comparable to the other materials. The excellent and unique property of MTA is its ability to promote regeneration of cementum, thus facilitating the regeneration of the periodontal apparatus. It was found that the presence of moisture in perforations during the placement of MTA increases its adaptation to perforation walls.

RetroMTA

A novel RetroMTA (Korea) material was recently introduced, which is a mixture of hydrophilic powders that are not derived from Portland cement. It consists of calcium carbonate, silicon dioxide, aluminum oxide, hydraulic calcium zirconia, and it has an initial setting time of only 150s. RetroMTA is a hydraulic bioceramic material newly formulated for application in perforation repair and vital pulp therapy. It is claimed to have comparatively shorter setting time than ProRoot MTA, good handling properties, no cell toxicity, setting reaction initiated by moisture, no heavy metals, and greater washout resistance than ProRoot MTA.

BIODENTINE

As a response to the disadvantages of MTA, a new tricalcium silicate-based cement Biodentine (France, 2011). BD is available in the form of a capsule containing powder composed of tricalcium silicate, dicalcium silicate, zirconium oxide, calcium carbonate, calcium oxide and iron oxide. A single capsule containing 0.7 g of powder is mixed for 30 s in a mixing device at a speed of 4000–4200 rpm. Based on the calcium (Ca^{2+}) and hydroxide (OH^{-}) ion release from material, it may be concluded that tricalcium silicate materials such as BD may be preferable for IPC.[4]

PREMIXED BIOCERAMICS

In the past 50 years, bioceramics have been extensively used in medical sciences for the replacement of joints, bone tissues, heart valves, and cochlear replacement. In dentistry, these materials were introduced for their odontogenic/osteogenic properties. Bioceramics are chemically stable, inorganic, biocompatible materials. Premixed bioceramics are hydrophilic in nature and necessitate moisture from the adjacent tissues to set.

THERACAL LC

TheraCal LC (USA, 2011) to overcome poor bonding of CSMs to resins in final restorations. It's a light-cured calcium silicate-based material designed as both a direct and indirect pulp capping material that facilitates the immediate placement of final restoration. It was found that TheraCal LC produced the least favorable pulpal responses compared to both ProRoot MTA and RetroMTA. Although sufficient bioactivity, superior handling properties and superior quality of bonding with the final overlaying restoration could justify the use of TheraCal LC as the IPC agent.

ENDOCEM-Zr

Various materials have been used for pulp capping over the ages. Among these, MTA has proven to be a dependable pulp capping material. However, its disadvantages include long setting time, low washout resistance, and tooth discolouration. To counter these, ENDOCEM-Zr (Korea), a pozzolan cement derived from MTA. ENDOCEM was introduced as retrograde filling and repair material, but few studies were done to assess the mineralization and biocompatibility of the cement which gave an insight into whether it can be used for pulp capping. As a direct pulp capping agent, ENDOCEM has shown no significant difference as compared to MTA.

MELATONIN

Melatonin plays an essential role in the regulation of bone growth. The pulp response to melatonin used for direct pulp capping to evaluate the antioxidant effect of melatonin administered orally and its influence on dental pulp. Melatonin not only promotes bone regeneration, but also seems to prevent bone resorption through various mechanisms that include osteoblast differentiation and an increase in osteoblastic activity, as well as a reduction in osteoclast differentiation and activity, together with an increase in osteoprotegerin expression and the neutralization of free radicals responsible for bone resorption. The proven anti-inflammatory action of melatonin encouraged its employment as a pulp-capping agent.

PROCEDURE

A. INDIRECT PULP CAPPING: TWO-STAGE APPROACH

When used appropriately, both direct and indirect pulp capping procedures have the potential to preserve pulp health, function, and vitality. In the case of indirect pulp capping, where the cavity preparation is in close proximity to the pulp but with no visible exposure, various one- and two-stage protocols have been advocated. With two-stage or stepwise caries removal techniques all carious dentin typically is removed from the walls and dentino-enamel junction of the cavity preparation. A layer of deep carious dentin, which is usually discoloured but firm, may be left on the floor of the preparation if its removal might cause a pulp exposure. Typically, a liner such as calcium hydroxide [$Ca(OH)_2$] is then placed and overlaid by a provisional restoration such as zinc oxide and eugenol or glass ionomer. A recent clinical study restoring deep carious lesions using a two-stage indirect pulp capping protocol that used a resin-modified glass ionomer (RMGI) provisional with and without first placing a calcium hydroxide liner found no clinical benefit to using said liner. After several months, and assuming all goes well during the provisional trial period (ie, no signs or symptoms of pain or pathology), the patient returns for the second step of the two-stage indirect pulp capping procedure. While there are variations in materials and technique, the provisional is typically removed, remaining caries is removed to hard tissue, and a final restoration is placed.[5]

Indirect Pulp Capping: One-Step Approach

With one-stage indirect pulp capping techniques typically all or most of the caries is removed at the initial appointment, some type of indirect pulp capping material is placed in close approximation to but not in direct contact with the pulp, and the final restoration is placed, all in the same appointment. One common technique is to remove only the "infected dentin" (dentin that is demineralized with denatured collagen, infiltrated with bacteria, and irreparably damaged) while leaving the "affected dentin" in place (dentin that is also demineralized but with the collagen structure still largely intact, is bacteria free, and still has the potential for remineralization). Many dentists prefer to place some type of base or liner in deep cavity preparations prior to the use of an adhesive system and placement of the final restoration.[6]

B. DIRECT PULP CAPPING

Direct pulp capping is used when the pulp is visibly exposed (vital pulp exposure) due to caries, trauma, or iatrogenic insult such as accidental exposure during tooth preparation or caries removal. The procedure typically involves arresting any pulpal haemorrhage followed by covering and sealing exposed pulp tissue in some fashion to preserve its health, function, and viability. Calcium hydroxide has traditionally been considered the "gold standard" and is the most commonly used material in this regard. This is partly because of its ability to dissociate into calcium and hydroxyl ions, its high pH, antibacterial properties, and apparent ability to stimulate odontoblasts and other pulp cells in various ways to form reparative dentin. Studies have also shown that the high pH of calcium hydroxide causes superficial coagulation necrosis where it contacts the pulp. This provides a degree of haemostasis and stimulates mineralized tissue and dentin bridge formation.[7]

DENTIN REGENERATION

Regenerative endodontics aims to restore normal pulp function in necrotic and infected teeth, restoring protective functions, such as innate pulp immunity, pulp repair through mineralization, and pulp sensibility. In regenerative dentistry, DPC is a treatment procedure that utilizes the regenerative abilities of human dental pulp cells that has been described previously. Pulp capping aims to facilitate the healing of injured pulp by using bioactive materials to ensure the formation of mineralized tissue or dentin bridge. The use of this method may be a more conservative alternative to root-canal treatment in cases where the pulp has been exposed due to reversible injury or does not exhibit symptoms of inflammation. Numerous studies were conducted to assess the effectiveness of the DPC materials with the following outcomes: pulp vitality, dentin-bridge formation, inflammation, and presence of bacteria. Recently, calcium silicate–based cement has been considered as the most suitable material for pulp capping as a surface-active hard-tissue substitute because of its excellent bioactivity and biocompatibility. They are widely utilized for conservative treatment, such as direct/indirect pulp capping, apexification, apexogenesis, and the repair of furcation, due to their biocompatibility, chemical bonding with tooth structure, easy handling characteristics, and good sealing ability.[8]

REHARDENING OF DEMINERALIZED DENTIN

In recent years, the concept of minimal intervention (MI) to save as much sound dentin as possible and minimize invasion has become widespread in the treatment of dental caries. In such cases, atraumatic indirect pulp capping（AIPC）is recommended, in which pulp extraction is avoided but instead preservation of the pulp is attempted by intentionally leaving the infected dentin adjacent to the pulp to paste a calcium hydroxide formulation or polycarboxylate cement combined with tannin-fluoride preparation, and promoting the sterilization and remineralization of the infected dentin that was left as well as the formation of tertiary dentin（reparative dentin).

EFFICACY OF NOVEL BIOMIMETIC REMINERALISING TECHNOLOGIES

Dental caries is one of the most prevalent chronic diseases and affects individuals of all ages. It is initiated by the demineralisation of tooth mineral by organic acids produced by fermentation of dietary sugars by dental plaque bacteria. Fluoride is regarded as an important strategy in managing caries and erosion. The latest advances in remineralisation technologies involve the biomimetics of various elements of the natural mineralisation systems in saliva and enamel formation. These elements are the calcium-stabilising salivary protein-like ion delivery vehicles, and the hydroxyapatite, hydroxyapatite-like or enamel protein-like nucleation templates. Examples of the biomimetic technologies related to these elements are casein phosphopeptide-stabilised amorphous calcium phosphate nanocomplexes (CPP–ACP) based on the salivary protein Statherin; bioactive glass BioMin F as a hydroxyapatite-like nucleation site and ion-releasing template and the self-assembling template peptide P11-4 as a biomimetic of amelogenin. For the CPP–ACP biomimetic technology, CPP contains the sequence which stabilises supersaturated solutions of calcium, phosphate and fluoride ions to produce electroneutral casein phosphopeptide-amorphous calcium fluoride phosphate nanocomplexes (CPP–ACFP). The CPP are biomimetics of the salivary protein Statherin which contains the sequence Asp-Ser(P)-Ser(P)-Glu-Glu-; however, due to the greater content of Ser(P), CPP is claimed to be superior to Statherin in is ability to stabilise and deliver calcium, phosphate and fluoride ions to remineralise ESLs. The BioMin bioglass biomimetic mineralisation template technology is based on fluoro calcium phosphosilicate which is claimed to diffuse into the ESLs, to release ions and provide a hydroxyapatite-like nucleation site for the formation of fluorhydroxyapatite. Finally, the amelogenin-biomimetic technology P11-4 peptide (Curodont Repair) has also been claimed to diffuse into ESLs and act as a self-assembling template for remineralisation. The self-assembling peptide P11-4 has the amino acid sequence: Ace-Gln-Gln-Arg-Phe-Glu-Trp-Glu-Phe-Glu-Gln-Gln-NH_2 which exhibits similar physicochemical properties to amelogenin-derived peptides that act as templates for the mineralisation of enamel. BioMin F and Curodont Repair are new oral care products and there is insufficient independent evidence to assess their true clinical potential. [6]

CALCIUM PHOSPHATE NANOCOMPOSITE ON
IN-VITRO REMINERALIZATION OF HUMAN DENTIN LESIONS

Advances in resin compositions, filler particles and the resin–filler interface have improved the composite properties. However, the lifetime of composite restorations is limited by inferior properties such as polymerization shrinkage/stress formation, fracture, abrasion and wear resistance, and marginal leakage. Marginal leakage can result in the formation of secondary caries, the main reason for composite restoration failures.

A promising approach to combat caries is to use composites containing calcium phosphate (CaP) particles. These composites have been shown to release calcium (Ca) and phosphate (P) ions and remineralize tooth lesions *in vitro*, *in situ* in the oral environment, and *in vivo* in human volunteers. Indeed, enamel subsurface lesions were remineralized by a CPP-ACP solution. In this approach, CPP-ACP was included in a sugar-free chewing gum to control dental caries *via* active remineralization and salivary stimulation. A drawback with previous CaP composites for dental restorations was that these composites used traditional CaP particles and had low mechanical properties, which were inadequate for bulk restoratives.

In demineralized dentin, unlike enamel, there are fewer residual mineral seed crystals present, which may make it more difficult to remineralize dentin compared to enamel. Clinically, treatment of carious dentin lesions is dependent on the depth of the lesion. In shallow to moderate lesions, the carious material can be completely removed and restored with composite, amalgam or glass ionomer. In asymptomatic deep lesions, where there is a risk of pulp exposure but restoration of tooth function is possible, partial removal of the carious dentin may be considered the clinically conservative approach. The treatment can involve an attempt to remineralize the demineralized dentin by either indirect pulp treatment or stepwise caries removal. In indirect pulp treatment, most of the carious lesion is removed and the finished cavity preparation is lined with a remineralizing material (calcium hydroxide, resin-modified glass ionomer, *etc*.) and the final restoration is placed to provide a good seal. Stepwise caries removal is a 2-step process, requiring removal of less carious dentin, followed by an interim placement of glass ionomer cement to aid in remineralization. After several months, remineralization is assessed and, if successful, a permanent restoration is placed. While CaP nanocomposites were shown to release more Ca and P ions and possess much better mechanical properties than traditional CaP composites, the remineralization of dentin caries *via* nanocomposite containing NACP has yet to be reported.[7]

II. CONCLUSION

Development of minimally invasive biologically based therapies aimed at preservation of the pulp vitality remains the key theme within contemporary clinical endodontics. The present findings confirm that both MTA and Biodentine are reliable materials in the matter of inducing dentin bridge formation while keeping a vital pulp in both direct and indirect pulp capping procedures. Antibacterial-enhanced MTAs showed reduced cytotoxic properties when compared to conventional MTA. Biodentine was associated with the highest cell viability at all time periods. Enhancing the properties of such bioactive cements can be hugely beneficial and will lead to clinically superior results.[3]

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