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Review Article

Dentistry Section

Recent Advances in Pulp Capping Materials: An Overview

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ABSTRACT

Emphasis has shifted from the "doomed" organ concept of an exposed pulp to one of hope and recovery. The era of vital-pulp therapy has been greatly enhanced with the introduction of various pulp capping materials. The aim of this article is to summarize and discuss about the various and newer pulp capping materials used for protection of the dentin-pulp complex.

Keywords: Biocompatible, Dentin bridge, Pulp capping, Pulp capping agent, Reparative dentin

INTRODUCTION

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

- Stimulate reparative dentin formation
- Maintain pulpal vitality
- Release fluoride to prevent secondary caries
- Bactericidal or bacteriostatic
- Adhere to dentin
- Adhere to restorative material
- Resist forces during restoration placement and during the life of restoration.
- Sterile
- Radiopaque
- Provide bacterial seal [1].

Calcium Hyroxide

Calcium hydroxide ($Ca(OH)_2$) was introduced to the dental profession in 1921 by Hermann and has been considered the "gold standard" of direct pulp capping materials for several decades, against which new materials should be, tested [2-4].

Zinc Oxide Eugenol (ZOE) Cement

Tronstad and Mjör stated that ZOE cement is more beneficial for inflamed and exposed pulp. However in the literature Glass and Zander, Hembree and Andrews, Watts, Holland et al., found that ZOE, in direct contact with the pulp tissue, produced chronic inflammation, lack of calcific barrier, and end result is necrosis [5].

Corticosteroids and Antibiotics

Corticosteroids like hydrocortisone, Cleocin, cortisone, Ledermix (calcium hydroxide plus prednisolone), penicillin, neomycin and Keflin (cephalothin sodium) along with calcium hydroxide was used for pulp capping with the thought of reducing or preventing pulp inflammation.

Gardner, et al., found that vancomycin, in combination with calcium hydroxide was somewhat more effective than calcium hydroxide used alone and stimulated a more regular reparative dentin bridge. Watts and Paterson cautioned that anti-inflammatory compounds should not be used in patients at risk from bacteremia [6,7].

Polycarboxylate Cement

McWalter, G et al., found that it lacks an antibacterial effect and calcific bridge formation [8].

Inert Materials

Bhaskar SH et al., and Heys DR et al., investigated isobutyl cyanoacrylate and tricalcium phosphate ceramic as direct pulp capping materials. Although pulpal response in the form of reduced inflammation and unpredictable dentin bridging were found, but none of these materials have been promoted to the dental profession as a viable technique [9,10].

Collagen

Dick HM and Carmichael DJ reported that collagen fibers are less irritating than $Ca(OH)_2$ and promotes mineralisation but does not help in thick dentin bridge formation [11].

Bonding Agents

According to Miyakoshi et al., 4-META-MMA-TBB adhesives and hybridizing dentin bonding agents provide superior adhesion to peripheral hard tissues and effective seal against micro leakage. But they have poor outcome due to its cytotoxic effect and absence of calcific bridge formation [12].

Calcium Phosphate

Calcium phosphate cement was suggested as viable alternative because of its good biocompatibility, superior compressive strength and its transformation into hydroxyapatite over time. Yoshimine et al., demonstrated that in contrast to calcium hydroxide, tetracalcium phosphate cement induced bridge formation with no superficial tissue necrosis and significant absence of pulp inflammation [13].

Hydroxyapatite

It is the most thermo dynamically stable of the synthetic calcium phosphate ceramics. It has good biocompatibility with neutral pH -7.0. It can be used as scaffolding for the newly formed mineralized tissue [14].

Lasers

Melcer et al., suggested between the years 1985 and 1987 that the carbon dioxide (CO_2) (1W) laser used for direct pulp capping [15-17].

Yasuda Y, et al., did a study to examine the effect of CO_2 laser irradiation on mineralization in dental pulp cells in rats and the results suggested that CO_2 laser irradiation stimulated mineralization in dental pulp cells [18].

Neodymium-doped yttrium-aluminium-garnet laser emits an infrared beam at a wavelength of 1064nm can be of therapeutic benefit for direct pulp capping and pulpotomy in clinical practice [19].

Glass Ionomer/Resin Modified Glass Ionomer

Glass ionomer also provides an excellent bacterial seal and good biocompatibility when used in close approximation but not in direct contact with the pulp.

RMGIC as direct pulp capping agent exhibited chronic inflammation and lack of dentin bridge formation; whereas the calcium hydroxide control groups showed significantly better pulpal healing [20].

Mineral Trioxide Aggregate (MTA)

MTA was introduced by Torabinejad in early 1900s. Several studies reported that MTA induced less pulpal inflammation and more predictable hard tissue barrier formation in comparison to hard setting calcium hydroxide [21].

MTYA1-Ca

Atsuko Niinuma developed resinous direct pulp capping agent containing calcium hydroxide. The powder composed of 89.0% microfiller, 10.0% calcium hydroxide and 1.0% benzoyl peroxide and was mixed with liquid (67.5% triethyleneglycol dimethacrylate, 30.0% glyceryl methacrylate, 1.0% o-methacryloyl tyrosine amide, 1.0% dimethylaminoethylmethacrylate and 0.5% camphorquinone).

MTYA1-Ca developed dentine bridge formation without formation of a necrotic layer, revealed to have good physical properties, and was not inferior to Dycal histopathologically. Therefore, it is suggested that the newly developed material, MTYA1-Ca promises to be a good direct pulp capping material [22].

Growth Factors

Growth factors regulate growth and development and induce wound healing and tissue regeneration.

Bone Morphogenic Protein (BMP)

BMP belongs to super family transforming growth factor beta (TGF-β). TGF β is a potent modulator of tissue repair in different situations. BMP-2, 4, and 7 plays a role in the differentiation of adult pulp cells into odontoblasts during pulpal healing.

Lianjia et al., found that BMPs are responsible for dentinogenesis, inducing non differentiated mesenchymal cells from the pulp to form odontoblast-like cells, obtaining osteodentin and tubular dentin deposition, when used as direct protectors [23].

Recombinant Insulin Like Growth Factor-I

Lovschall H, et al., evaluated recombinant insulin like growth factor-I (rhIGF-I) in rat molars and concluded that dentin bridge formation was equal to dycal after 28 days [24].

Other Growth Factors

Hu et al., evaluated the various growth factors like epidermal growth factor, basic fibroblast growth factor, insulin-like growth factor II, platelet-derived growth factor-BB, TGF-β 1in rat molars and concluded that only TGF-β 1-enhances reparative dentin formation [25].

Bonesialoprotein

According to Goldberg M et al., Bone sialoprotein (BSP) was the most efficient bioactive molecule, which induced homogeneous and well mineralized reparative dentin. Both BSP and BMP-7 were superior to calcium hydroxide in their mineralization inducing properties [26].

Biodentin

Biodentine is new bioactive cement with dentin like mechanical properties and can be used as dentin substitute. It has a positive effect on vital pulp cells and stimulates tertiary dentin formation [27].

Enzymes

Heme-Oxygenase-1

Heme oxygenase-1(HO) is the rate limiting enzyme in heme catabolism. Odontoblasts and oxidatively stressed dental pulp cells express HO-1, indicates that the pulp might respond to oxidative stress at the molecular level.

HO-1 induction protects against hypoxic stress and nitric oxide-mediated cytotoxicity. It has been reported that HO-1 might play a cytoprotective role against pro inflammatory cytokines and nitric oxide in human pulp cells. In addition, bismuth oxide containing Portland cement (BPC) induced HO-1 expression in dental pulp cells plays a protective role against the cytotoxic effects of BPC [28].

Simvastatin

It is a 3-hydroxy-3-methylglutaryl coenzyme, a reductase inhibitor and first line drug for hyperlipidemia. Statin improves the osteoblast function via the BMP-2 pathway and suppresses osteoclast function, resulting in enhanced bone formation. Therefore, statin might improve the function of odontoblasts, thus leading to improved dentin formation.

Statin is known to induce angiogenesis and increase neuronal cells, indicating the possible effectiveness of statin in pulp regeneration along with dentin regeneration. It has an anti-inflammatory effect in various tissues, so it is considered as an ideal active ingredient in pulp capping material to accelerate reparative dentin formation [29].

Stem Cells

Dental pulp stem cells (DPSCs) and Stem cells from Human Exfoliated Deciduous Teeth (SHED) have been identified as a novel population of stem cells that have the capacity of self-renewel and multi lineage differentiation.

Nakamura S et al., used mesenchymal stem cells for clinical application in tissue engineering and regenerative medicine. In this study, they compared the proliferation and stem cell marker of SHED, DSPCs and Bone Marrow Derived Mesenchymal Stem Cells (BMMSCs). In addition, gene expression profile of DSPCs and SHED were analyzed by using DNA microarray. They concluded that SHED has got significantly higher proliferation rate than that of DSPCs and BMMSCs and this could be a desirable option as a cell source for therapeutic applications [30].

Propolis (Russian penicillin)

It contains flavonoids, phenolics, iron, zinc and other various aromatic compounds [31].

Parolia A, et al., compared propolis, MTA and Dycal histologically in human dental pulp and concluded that Propolis and MTA showed similar bridge formation when compared to Dycal [32].

Novel Endodontic Cement (NEC)

NEC consists of calcium oxide, calcium phosphate, calcium carbonate, calcium silicate, calcium sulfate, and calcium chloride.

Mohammad Hassan Zarrabi evaluated MTA and NEC histologically in human dental pulp and concluded that NEC induced a thicker dentinal bridge with less pulp inflammation [33].

Emdogain (EMD)

EMD is enamel matrix derivative secreted from Hertwig's epithelial root sheath during porcine tooth development. It is an important regulator of enamel mineralization and plays an important role during periodontal tissue formation. It stimulates the regeneration of acellular cementum, periodontal ligaments, and alveolar bone.

EMD contains BMP like molecules and BMP expressing cells. BMP like molecules in EMD promote odontoblast differentiation and reparative dentin formation. Recently,it was reported that EMD suppresses the inflammatory cytokine production by immunocytes and contains TGF-β like molecules. It might create a favourable environment for promoting wound healing in the injured pulp tissues [34].

Nakamura Y et al., concluded that amount of hard tissue formed in EMD treated teeth was more than twice that of the calcium hydroxide treated control teeth [35].

Al-Hezaimi K evaluated Calcium hydroxide, ProRoot White MTA and white Portland cement after EMD application on the exposed pulp. MTA produced a better quality reparative hard tissue response with the adjunctive use of EMD compared with calcium hydroxide [36].

Odontogenic Ameloblast Associated Protein (ODAM)

ODAM is expressed in ameloblasts, odontoblasts, and pulpal cells. ODAM involved in ameloblast maturation and enamel mineralization.

Yang IS et al., stated that rODAM accelerates reactionary dentin formation close to the pulp exposure area, thereby preserving normal odontoblasts in the remaining pulp [37].

Endo Sequence Root Repair Material

It consists of Calcium silicates, monobasic calcium phosphate, zirconium oxide, tantalum oxide, proprietary fillers and thickening agents [38].

Hirschman et al., compared Cytotoxicity of MTA-Angelus, Brasseler Endosequence Root Repair Putty (ERRP), Dycal and Ultra-blend Plus (UBP)-(light curable $Ca(OH)_2$) and concluded that ERRP and UBP are less cytotoxic [39].

Castor Oil Bean (COB) Cement

The COB consists of 81-96% triglyceride of ricinoleic acid, and is considered a natural polyol containing three hydroxyl radicals. COB or RCP (Ricinus Communis Polyurethane) was originally developed as a biomaterial for bone repair and regeneration after local bone damage. Due to these positive characteristics, the material is considered to be an excellent candidate for use in pulp capping [40].

Theracal

TheraCal LC is a light cured, resin modified calcium silicate filled liner designed for use in direct and indirect pulp capping, as a protective base/liner under composites, amalgams, cements, and other base materials. TheraCal LC performs as an insulator/barrier and protectant of the dental pulpal complex.

The proprietary formulation of TheraCal LC consists of tricalcium silicate particles in a hydrophilic monomer that provides significant calcium release making it a uniquely stable and durable material as a liner or base. Calcium release stimulates hydroxy apatite and secondary dentin bridge formation. TheraCal LC may be placed directly on pulpal exposures after hemostasis is obtained. It is indicated for any pulpal exposures, including carious exposures, mechanical exposures or exposures due to trauma. [Table/Fig-1] shows the physical properties of Theracal LC.

Gandolfi et al., compared chemico physical properties of TheraCal, ProRoot MTA and Dycal and concluded that TheraCal displayed higher calcium releasing ability and lower solubility than either ProRoot MTA or Dycal. The capability of TheraCal to be cured to a depth of 1.7 mm may avoid the risk of untimely dissolution. These properties offer major advantages in direct pulp capping treatments [41]. [Table/Fig-2] shows the summary of advantages and disadvantages of various pulp capping agents.

Physical Properties				
	Shear bond strength(Mpa)	Water solubility (µg/mm2)	Radiopacity (mm Al)	Calcium release
Theracal LC	4.35 (2.93)	0	2.63	188 (µg/cm2)
Prisma VLC Dycal	0.94 (0.92)	110 (17)	0.79	NA

[Table/Fig-1]: Shows physical properties of Theracal LC

Pulp capping agent	Advantages	Disadvantages
Ca (OH)2 (1960's)	• Gold standard of direct pulp capping material • Excellent antibacterial properties • Induction of mineralization • Low cytotoxicity	• Highly soluble in oral fluids • Subject to dissolution over time • Extensive dentin formation obliterating the pulp chamber • Lack of adhesion • Degradation after acid etching • Presence of tunnels in reparative dentin
Zinc oxide eugenol cement (1960-70's)	• Reduces inflammation	• Lack of calcific bridge formation • Releases eugenol in high concentration which is cytotoxic • Demonstrate interfacial leakage
Corticosteroids and antibiotics (1970's)	• Reduces pulp inflammation • Vanocmycin + Ca(OH)2 stimulated a more regular reparative dentin bridge.	• Should not be used in patients at risk from bacteremia.
Polycarboxylate cement (1970's)	• Chemically bond to the tooth structure	• Lack of antibacterial effect • Fail to stimulate calcific bridge formation
Inert materials (1970's) (Isobutyl cyanoacrylate and Tri calcium phosphate ceramic)	• Reduces pulp inflammation • Stimulate dentin bridge formation	• None of these materials havebeen promoted to the dental profession as a viabletechnique
Collagen (1980)	• Less irritating than • Ca $(OH)_2$ and promotes mineralisation	• Does not help in thick dentin bridge formation
Bonding agents (1995) 4-META-MMA-TBB adhesives and hybridizing dentin bonding agents	• Superior adhesion to hard tissues • Effective seal against microleakage.	• Have cytotoxic effect • Absence of calcific bridge formation • *In vivo* studies have demonstrated that the application of an adhesive resin directly onto a site of pulp exposure, or to a thin layer of dentin (less than 0.5 mm), causes dilatation and congestion of blood vessels as well as chronic inflammatory pulpal response

Calcium phosphate (1900's)	• Helps in bridge formation with no superficial tissue necrosis • significant absence of pulp inflammation compared to Ca(OH)2 • Good physical properties	• Clinical trials are necessary to evaluate this material
Hydroxyapatite (1995)	• Biocompatible • Act as scaffold for the newly formed mineralized tissue	• Mild inflammation with superficial necrosis of pulp
Lasers (1995-2010) CO2 Nd: YAG	• Formation of secondary dentin • sterilization of targeted tissue • Bactericidal effects	• Technique sensitive • Causes thermal damage to pulp in high doses • Technique sensitive • Causes thermal damage to pulp in high doses
Glass ionomer/ Resin modified glass ionomer (1995)	• Excellent bacterial seal • Fluoride release, coefficient of thermal expansion and modulus of elasticity similar to dentin • Bond to both enamel and dentin • Good biocompatibility •	• Causes chronic inflammation • Lack of dentin bridge formation • Cytotoxic when in direct cell contact • Poor physical properties, high solubility and slow setting rate • RMGIC is more cytotoxic than conventional GIC, so it should not be applied directly to the pulp tissue
Mineral trioxide aggregate (1996-2008)	• Good biocompatibility • Less pulpal inflammation • More predictable hard tissue barrier formation in comparison to calcium hydroxide • Antibacterial property • Radiopacity • Releases bioactive dentin matrix proteins	• More expensive • Poor handling characterstics • Long setting time • Grey MTA causes tooth discoloration • Two step procedure • High solubility
MTYA1-Ca (1999)	• Helps in dentine bridge formation without formation of a necrotic layer • Shear bond strength is higher than conventional GIC and similar to RMGIC • Dentin bridge formation without reduction of pulp space in MTYA1-Ca, but there is reduction of pulp space is seen in dycal. • Better adhesion to dentine	• Presence of 10% $Ca(OH)_2$ interferes with complete curing of material, residual monomers causes cytotoxicity
Growthfactors (1900-2007) Bone Morphogenic Protein (BMP 2,4,7) Recombinant insulin like growth factor-I Other growth factors (1998) Epidermal growth factor Fibroblast growth factor Insulin like growth factor II Platelet-derived growth factor-BB TGF-β 1	• Formation of osteodentin and tubular dentin • Formation of more homogeneous reparative dentin • Superior to Ca(OH)2 in the mineralization inducing properties • Dentin bridge formation was equal to dycal after 28 days • Only TGF-β1 induced reparative dentin formation	• Possibility of unexpected side effects and the production • cost can be obstacles for their clinical application • Fail to stimulate reparative dentin in inflamed pulp • Half life is less • High concentration is required • Delivery vechicles used for the molecules show potent effects at the pictogram level and appropriate carriers will be required to facilitate their handling in the clinical situation • Appropriate dose response is required to avoid uncontrolled obliteration of pulp chamber • Possibility of immunological problems due to repeated implantation of active molecules • Other factors does not induced reparative dentin formation
Bonesialoprotein (2000)	• Induced homogeneous and well mineralized reparative dentin • Superior to Ca(OH)2 in the mineralization inducing properties	• Further clinical studies are needed
Biodentin (2000)	• Biocompatible • Good antimicrobial activity. • Stimulate tertiary dentin formation • Stronger mechanically, less soluble and produces tighter seals compared to Ca(OH)2 • Less setting time, good handling characteristics than MTA	• More long-term • clinical studies are needed for a definitive evaluation of Biodentine
ENZYMES Heme-Oxygenase-1 (2008) Simvastatin (2009)	• Play a cytoprotective role against pro inflammatory cytokines and nitric oxide in human pulp cells • Prevent H_2O_2 induced cytotoxicity and oxidative stress in human dental pulp cells. • Anti inflammatory action • Induction of angiogenesis • Improve the function of odontoblasts, thus leading to improved dentin formation	• Further in vitro and in vivo studies are required • In high concentration causes pulp tissue damage. • Careful evaluation is required before clinical application to determine the suitable concentration when applied indirectly to a cavity or directly to pulp tissue.
STEM CELLS (2009) Dental pulp stem cells (DPSCs) Stem cells from human exfoliated deciduous teeth (SHED)	• Regeneration of dentin-pulp complex • SHED is superior to DPSCs	• Less economic • Technique sensitive
Propolis (2005-2010)	• Antioxidant, antibacterial, antifungal, antiviral and anti-inflammatory properties • • Superior bridge formation compared to Dycal, similar results to MTA • • Forms dental pulp collagen, reduces both pulp inflammation and degeneration. • • Stimulate reparative dentin formation	• • Showed mild / moderate inflammation after 2,4 weeks with partial dentinal bridge formation.
Novel endodontic cement (2010)	• Biocompatible • Shorter setting time • Do not cause tooth staining • Good handling characteristics compared to MTA • Induced a thicker dentinal bridge with less pulp inflammation than MTA	• Further assessment is required for evaluation of pulp response to this material in inflamed pulp.
Emdogain (2001-2011)	• Promote odontoblast differentiation and reparative dentin formation • Suppresses the inflammatory cytokine production and create a favourable environment for promoting wound healing in the injured pulp tissues • Amount of hard tissue formed in EMD treated teeth was twice that of the calcium hydroxide • Post operative symptoms were less • MTA produced a better quality reparative hard tissue response with the adjunctive use of Emdogain compared with calcium hydroxide	• EMD gel (EMD dissolved in propylene glycol alginate gel) when applied on exposed pulps without the adjunctive use of a pulp-capping material was proven to be ineffective in producing a hard tissue barrier because of its poor sealing qualities. • • Clinical advantages of using EMD are unproven

Odontogenic ameloblast associated protein (2010)	• Biocompatible • Accelerates reactionary dentin formation • Normal pulp tissue appearance withoutexcessive tertiary dentin formation and obliteration of the pulp cavity compared to MTA	• Till now only in vitro study was conducted. • Further studies containing • a larger number of samples and longer follow-up assessments with various studies with higher primates should be followed
Endo sequence root repair material (2010-11)	• Antibacterial property • Less cytotoxic than MTA, Dycal and light cure Ca(OH)2	• Bioactivity of the cells as well as ALP activity were decreased gradually when exposed to ERRM
Castor oil bean cement (2010-11)	• Good antibacterial property • Less cytotoxic • It showed less inflammatory response in subcutaneous tissue of rats when compared with calcium hydroxide cement. • Facilitates tissue healing • Better sealing ability than MTA & GIC • Good mechanical properties • Low cost	• Bio inert rather than bioactive • Further clinical trials are required
Theracal (2012)	• Act as protectant of the dental pulpal complex • Bond to deep moist dentin • Used as a replacement for Ca(OH)2, glass ionomer, RMGI, IRM/ZOE and other restorative materials • Have strong physical properties,no solubility, high radiopacity • TheraCal displayed higher calcium releasing ability and lower solubility than either ProRoot MTA or Dycal	• It is opaque and "whitish" in color, it should be kept thin so as not to show through composite materials that are very translucent affecting final restoration shading

[Table/Fig-2]: Shows the summary of advantages and disadvantages of various pulp capping agents

CONCLUSION

Clarity on the biology of caries, comprehension of technological advances and conviction about improved restorative materials has initiated a pulp preservation that indeed is a boon to the clinician and the patient.

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