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Review Article

Indirect and Direct Pulp Capping: Reactionary vs. Reparative Dentins

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Abstract

Pulp therapies aiming to keep alive the dental pulp use either indirect (IPT) or direct procedures (DPC). It is depend of the stage and depth of the carious lesion, of the exposure time, and the degree of bacterial invasion, associated or not with the pulp degradation. Our aim was to clarify the formation of reactionary or reparative dentin.

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INDIRECT AND DIRECT PULP CAPPING: INTRODUCTION AND GENERALITIES

Indirect pulp treatment

The most appropriate treatment of the carious teeth implicates primarily to make a good diagnosis of the pulpal status. Spontaneous severe pain is a crucial factor. Finger pressures, radiographs, unrestorable tooth after pulp therapy, and teeth close to exfoliation are limiting factors to indirect pulp capping.

The stepwise excavation approach intends to change the carious environment and not to remove the carious tissue close to the pulp because there is a risk of pulp exposure. The aims of this technique is

- To verify the arrest and have a clinical control of the tooth reaction,
- To remove the slowly progressing slightly infected demineralized dentin before filling the cavity with a final restoration [1].

The rationale for this treatment option implies to encourage the formation of a reactionary layer of dentin with preservation of pulpal health and vitality. It implicates also the removal of the deep carious lesion and restoration of the crown after the placement of an appropriate material (first lining the deepest part of the lesion and secondly, restoring the cavity with an appropriate biomaterial). About 90% clinical success was observed after 3 years follow up. This procedure is recommended for permanent teeth but not for primary molars.

Indirect pulp capping implicates the preservation of a layer of soft carious dentin. Removal step-by step with hand instruments (excavators) of the carious dentin layers implicate to keep some demineralized dentin in the deep part of the deteriorated tissue. It is mandatory to avoid drilling with rotating burrs. Elimination of the carious dentin, associated with substantial changes in preventive measures, hygiene conduct, and limitations in carbohydrates intake, favor remineralization. There is an 86% rate of success over 10 years.

Beneath a dense calcio-traumatic line, tubular or a tubular reactionary dentin (or tertiary dentin) is formed. This tertiary dentin is developed in reaction to trans dentinal stimulation of the odontoblasts, bacterial toxins or adverse components released by restorative materials. Reactionary dentine may be considered as an extension of physiological dentin genesis. However, since it is a pathological response to injury, it should be regarded as distinct from the primary and secondary dentin genesis.

Removal of the soft carious dentin, covered by a temporary material containing a calcium hydroxide base, is beneficial for the evolution of active caries into an arrested lesion. Zinc oxide-eugenol cement is laid down, and after 2-3 weeks, the arrested carious dentin (sclerotic or sound) is actually removed, and a “permanent” filling is inserted. The risk of pulp exposure

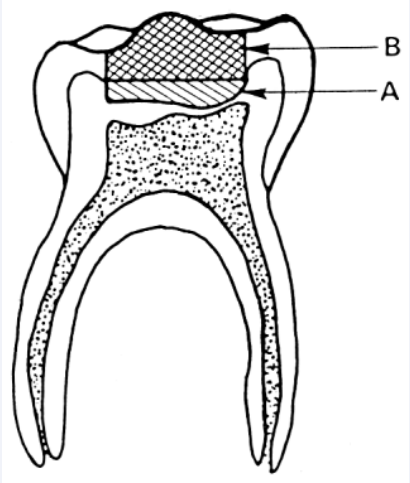

Figure 1 Indirect pulp capping technique [9].

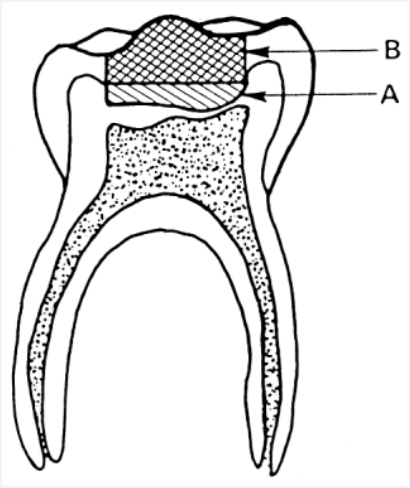

Figure 2 Direct pulp-capping technique [9]. The pulp exposure is covered by the capping material (A), the protective base of ZnO-eugenol cement (B), and C: restorative material Amalgam or GIC.

increased with complete excavation of caries compared with stepwise excavation and/or indirect pulp capping [2].

The biologic validity of the various vital pulp treatments involves indirect pulp treatment. It is an acceptable procedure for primary teeth with reversible pulp inflammation. Indirect Pulp Treatment (IPT) was a success in 95%. Calcium hydroxide liners increased the success rate of IPT. Direct pulp capping (DPC) and calcium hydroxide has been widely used with high success rates in young permanent teeth, but the results in primary teeth are less satisfactory [3,4]. The rationale for using calcium hydroxide should be reserved for iatrogenic exposures in asymptomatic teeth expected to exfoliate within a short period of time.

Indirect pulp treatment is recommended for teeth that have deep carious lesions approximating the dental pulp, but no signs or symptoms of degeneration. Indirect pulp treatment, using calcium hydroxide as liner, gives after 2 years 83% of success. In this procedure, the deepest layer of the remaining carious dentine is covered by a biocompatible material to prevent pulp exposure. Three materials are most commonly used in indirect pulp treatment: the calcium hydroxide (CH), zinc oxide-eugenol paste (ZOE) and glass ionomer cements. There is high probability that this solubilizing effect of cavity conditioners results in the release of TGFβ from the tissue, diffusing through the dentinal tubules, promoting a reactionary dentin genic response stimulated by the underlying odontoblasts.

The ultimate objective of this treatment is to maintain pulp vitality, while arresting the carious process, promoting dentine sclerosis (reducing permeability), stimulating the formation of tertiary dentine, and remineralization of the carious dentine.

Direct pulp capping

Pulp healing is influenced by the prevention of bacterial leakage. Operative debris, inflammatory and pulp cell activity, absence of dentin bridge formation, tunnel defects in dentin bridges emphasized the failures of direct capping.

Pulp exposure after stepwise implies the removal of the bulk carious tissue and application of calcium hydroxide. This therapy was compared with direct complete excavation of deep carious lesion in young posterior permanent teeth. After a period of 8-24 weeks, all the carious dentin was removed, following sealing of the cavity with ZOE and a restorative material [5].

The control of pulp bleeding after the exposure has a direct effect on pulp cap success. Saline, sodium hypochlorite (at concentrations ranging from 0.12% to 5.25%), hydrogen peroxide, ferric sulfate and chlorhexidine have been shown to be useful. The chances for tooth survival are excellent if the tooth is asymptomatic and well-sealed, even if residual caries remains [6]. MTA demonstrates comparable results to calcium hydroxide. MTA demonstrates successes as a direct pulp cap agent in short-term data.

When a healthy pulp is inadvertently exposed during an operative procedure, a calcium hydroxide [$Ca(OH)_2$] is placed over the exposure and dentine formation is stimulated. Direct pulp capping by calcium hydroxide is associated with dentin bridge formation. Tunnel defects are present in the area of operative debris, together with the pulp inflammatory activity. Direct pulp capping is one of the treatments of an exposed vital pulp, and/or pulpotomy. It is used to stimulate the maintenance of a vital pulp. It is however mandatory to develop new biologically-based therapeutics that reduce pulp inflammation, promote the continued formation of a renewed dentin-pulp complex, and restore vitality by stimulating the regrowth of pulpal tissue. The odontoblasts-like cells secrete tertiary dentin (reparative dentin) either when irritated by the chemicals diffusing through the dentin, or when toxic bacterial metabolites diffuse through dentinal tubules.

The capping materials were associated with varying levels of pulp healing defects, including tunnel defects, operative debris, pulp inflammatory cell activity and bacterial leakage [7]. TGFβ and Bone Morphogenetic Proteins may also induce reparative dentin genesis in a direct pulp capping situation. The ideal dressing material for the radicular pulp should be bactericidal, harmless to the pulp and surrounding structures, promote healing of the radicular pulp, and not interfere with the physiologic process of root resorption. Recent clinical studies have reported promising results using ferric sulphate (FS), a hemostatic agent, in pulpotomized human primary teeth. Better results were obtained with Mineral Trioxide Aggregate (MTA), and statistically significant differences were reported when compared with ferric sulphate. Success was defined as lack of complaints from the patient, positive reaction to cold testing, and no sensitivity to percussion [8].

The aim of vital pulp therapy is to maintain pulp viability by eliminating bacteria from the dentin-pulp complex and to establish an environment in which apex genesis can occur. A complicating factor in treating immature teeth is the difficulty predicting the degree of pulpal damage. Currently, the best method appears to be the ability to control pulpal hemorrhage by using sodium hypochlorite. Mineral trioxide aggregate (MTA) currently is the optimum material to use in vital pulp therapy. Compared with the traditional material of calcium hydroxide, it has superior long-term sealing ability and stimulates a higher

quality and greater amount of reparative dentin. The control of pulpal hemorrhage with NaOCl seems to be the best method of treatment, MTA being a good substitute for $Ca(OH)_2$ in vital pulp procedures.

The successes of direct pulp capping are less, decreasing to 37% after 5 years, and 13% after 10 years. Direct capping is effective when it is carried out on a pulp exposure, revealing an initial opening of a pulp horn, and accompanied with bacterial invasion. The exposed coronal pulp leads to treatment of the pulp by direct capping, using calcium hydroxide or other bioactive drug. The formations of reparative dentin, occluding the pulp exposure produce a bone-like structure, made of collagen and non-collagenous proteins (namely osteocalcin and osteopontin). This bonny structure is called osteodentin.

Reparative dentin genesis represents a more complex sequence of biological processes. Migration and differentiation of pulpal progenitor cells must take place, followed by a generation of odontoblasts-like cells, and prior to matrix secretion. A series of stereotypic wound healing reactions occur in the pulpal connective tissue that includes vascular and cellular inflammatory reactions. In vitro and in vivo experiments on reparative odont genesis demonstrate that the pulp constitutes an appropriate environment where competent pulp cells that are potential pre-odontoblasts differentiate into new odontoblasts-like cells, forming reparative dentine occluding the pulp exposure.

TREATMENT OF PRIMARY TEETH

The remaining radicular pulp can be rendered inert by using form cresol. It fixes or denatures the vital pulp, so there is no longer a pulp that is alive. The radicular pulp might be preserved through minimal inflammatory insult by using a hemostatic agent such as ferric sulfate to preserve the deeper remaining pulp tissue. Pulpotomy mechanism encourages the radicular pulp to heal and form a dentin bridge by using calcium hydroxide or mineral trioxide aggregate [4].

Practitioners should not try to have access to the sclerotic carious layers, isolating the pulp from the advancing front of the lesion. There is a risk to incite a pulp exposure that would leads to a direct pulp capping and/or more destructive pulpotomy or pulpectomy therapies. This is why in addition to indirect pulp capping; the two stages procedure or stepwise excavation has been introduced in the everyday practice [1]. For deep caries approaching the pulp, the choice of Indirect Pulp Treatment (IPT) or pulpotomy is up to the treating dentist. IPT has been shown to have a lower cost, higher long-term success, better exfoliation pattern treating reversible pulpitis instead of pulpotomy.

Calcium hydroxide ($Ca(OH)_2$ or CH)

Since more than fifty years, calcium hydroxide has been used in a number of applications such as root resorption, intra canal medicament, perforation management, and root canal sealers. $Ca(OH)_2$ is a strong base that dissociate when in contact with aqueous fluids into calcium hydroxide and hydroxyl ions [10]. After an initial bactericidal effect, it promotes healing and repair. In a 4-9 days/period, coagulation necrosis (pH 12.5, in the 1.5-2mm superficial portion of the pulp) occurs together with the formation of osteodentin. Under the odontoblastic layer, a normal pulp is found. Direct and indirect pulp capping is subjected to evidence-based recommendations to guide clinicians in their decision-making process [6].

Antibacterial activity of $Ca(OH)_2$ was combined with chlorhexidine or sodium hypochlorite against Gram positive and Gram negative bacteria. $Ca(OH)_2$ and NaOCl had effects on all the tested bacteria while 2%CHX was less effective [11]. The antibacterial effect is due to the destruction of the bacterial cytoplasmic membrane, followed by protein lysis and bacterial DNA damage. Osteodentin formation is uncompleted and results in the formation of tunnel defects, allowing the possibility of reinfection [12].

The effects of calcium hydroxide are caused by several sequential mechanisms:

a) A chemical action, inducing damage to the microbial cytoplasmic membrane.

b) Physically, filling the space within the canal and preventing the ingress of bacteria into the root canal system.

c) The biologic properties include biocompatibility, healing of hard tissue around the infected canals, and inhibition of root resorption.

Over the years, calcium hydroxide has been the most commonly employed wound dressing. It creates conditions conducive to healing of the pulp tissue. The outcome of MTA and calcium hydroxide treatment, with or without pulpal exposure, depends largely on how extensively the pulp is infected at the time of treatment. The outcome also depends on the age of the patient, the treatment approach (indirect or direct pulp capping) and the choice of material applied to the exposed pulp tissue. The capacity of the restorative material to prevent leakage of bacteria is another important factor [2].

The initial effect of calcium hydroxide applied to exposed pulp is the development of a superficial necrosis. Necrosis causes slight irritation and stimulates the pulp to repair. Direct pulp capping is occluding the pulp exposure by reparative dentin formation. Multiple tunnel defects were shown and cell inclusions in bridges following pulp capping with $Ca(OH)_2$. Eighty nine per cent of dentin bridges formed by calcium hydroxide cement contained tunnel defects. This may lead later to bacterial penetration into the pulp tissue. The tunnels are not caused by the CH itself but are rather are a consequence of the severity of the trauma to the pulp and the number of vessels injured by the mechanical exposure. Inside the tunnels there are blood vessels, which maintain the calcium source to the necrotic tissue (coagulation necrosis). The calcium ions in the necrotic layer are responsible for partial dystrophic calcification. Cells in contact with $Ca(OH)_2$ are killed, due to its alkaline pH, forming a necrotic layer of variable thickness. The success rates of direct pulp-capping with calcium hydroxide decrease with time. Rates are more than 90% after 1 to 2 years and drop from 82% to 37% after 2 to 5 years.

The subjacent pulp tissue is responsible for the healing associated with hard tissue barrier formation. The multiple tunnel defects present a morphological disruption of the dentin bridge barrier. They fail to provide a long-term biological seal against bacterial infection. Multiple defects in the bridge allow fluid and

bacteria to penetrate into the pulp, which in turn can lead to internal resorption, and ultimately to tooth loss. Consequently, the tunnels permit oral contaminants, such as bacteria and their toxic factors, to eventually gain access to the pulp tissue through the marginal gap formed at the tooth / restoration interface. The presence of bacteria and their products that penetrate via micro leakage is the main factor responsible for pulp inflammation and necrosis.

Calcium hydroxide is still a « gold standard » for direct pulp capping materials among other materials a number have been used with more or less success, all of them allowing preserving pulp vitality.

Ferric sulphate has gained some popularity as a replacement for form cresol and calcium hydroxide in pulpotomies. It is claimed to have low toxicity and no systemic side effects.

MINERAL TRIOXIDE AGGREGATE (MTA)

MTA was used as direct pulp capping in young permanent teeth [13]. At 24 months the clinical and radiographic success rate was 93%, with some evidence of continued root growth.

Mineral trioxide aggregate (MTA) cement has a composition similar to that of 75% Portland cement (PC). In addition, MTA contains 20% bismuth oxide, which provides radiopacity. The major component is a mixture of dicalcium silicate, tricalcium silicate, tricalcium aluminate, gypsum, and tetra calcium aluminoferrite. MTA is a powder that contains trioxides and hydrophilic particles. It set in the presence of moisture. MTA cements exhibit calcified tissue-conductive activity and facilitate the differentiation of human orofacial mesenchymal stem cells and the mineralization process in human dental pulp cells. They also have the potential to be used as pulp-capping materials. MTA materials have been shown to have a biocompatible nature and have excellent potential when used in endodontic treatment. Thus, MTA can be described as a calcium-hydroxide releasing material and, therefore, is expected to present various properties similar to those described above for calcium hydroxide. The advantages of MTA are believed to be its sealing ability, biocompatibility, bioactivity and capacity to promote mineralized tissue formation.

In vitro bacterial leakage studies of MTA materials were found to exhibit similar root-end bacterial leakage resistance using a Streptococcus salivarius model with both materials having significantly less bacterial leakage than a ZOE preparation. Biocompatibility studies assess the compatibility by monitoring the expression of Interleukin [IL-1α, IL-6, IL-8, IL-11] and macrophage colony stimulating factor (M-CSF). In vivo studies were shown to induce little or no inflammation. Pulp capping carried out on animals models or human studies have shown physical properties, sealing ability, biocompatibility, and clinical performance of MTA materials [14,15].

MTA is more effective and better than calcium hydroxide materials, as it has an enhanced interaction with dental pulp tissue. The pulp tissue necrosis is limited, facilitated the proliferation/ differentiation of human dental pulp cells, and exhibited calcified tissue-conductive activity with the ability to stimulate faster complete dentine bridge formation and preventing infection.

BIO DENTINE™

Bio dentine™ contains mainly tricalcium and dicalcium silicate. Zirconium dioxide serves as contrast medium. The liquid consists of calcium chloride in aqueous solution mixed to polycarboxylate. Once mixed, Bio dentine™ sets in approximately in 12 minutes. Calcium hydroxide is formed during the setting of the cement. Its stimulate tertiary dentin formation. Calcium chloride accelerates the hydration reaction, and polycarboxylate reduces the amount of water required for mixing by providing proper consistency. Calcium carbonate in the powder is expected to act as a nucleation site. Bio dentine™ was shown to be biocompatible, in that it does not damage pulpal cells in vitro or in vivo, and is capable of stimulating tertiary dentin formation. Used for pulp capping, the material offers certain advantages over calcium hydroxide [16].

The bioactive material Bio dentine is stimulating apexo genesis, dentin replacement and pulp protection A continued apical closure was detected on radiography. Direct pulp capping with MTA after pulp exposure maintain pulp vitality in permanent teeth [8].

TheraCal is a novel light- curable MTA-like material for pulp capping [17]. It is composed of resin and calcium silicate. TheraCal released significantly more calcium than ProRoot MTA and Dycal. The surrounding fluid was able to alkalinize. Initially the pH varies around 10-11, between 3 h and 3 days. Then the pH was decreased (8-8,5) between 7 to 14 days. $Ca(OH)_2$-based and CaO-based materials were used for direct or indirect capping. They release hydroxyl and Ca ions. They are soluble and raise local pH with the formation of a necrotic layer at the material-pulp interface. This capping material has been designed for direct and indirect pulp-capping.

Calcium is a radiopaque water-based calcium hydroxide, containing urethane dimethacrylate resin, calcium dihydroxide, dimethylaminoethyl- methacrylate, and triethyleneglycol dimethacrylate (TEGDMA). Calcium (Voco) presented cytocompatibility values significantly lower than Biodentine (Septodont). Biodentine is an alternative to $Ca(OH)_2$ *versus* MTA used for direct pulp capping [18]. Our aim was to evaluate and compare the antimicrobial activity of different pulp-capping materials.

Antibacterial activity of $Ca(OH)_2$ was combined with chlorhexidine or sodium hypochlorite against Gram positive and Gram negative bacteria. $Ca(OH)_2$ and NaOCl had effects on all the tested bacteria while 2% CHX was less effective [11].

MTA-based products show lower cytotoxicity and valuable antibacterial activity. However, the conclusion that MTA-based pulp-capping material does not show cytotoxic effects in vitro should be taken with caution because the experimental design in vitro has some inevitable limitations with respect to the in vivo situation.

Although physical properties of resin composites are being improved constantly, in vivo studies have shown that the use of resins as restorative materials is occasionally associated with irritation and necrosis of the pulp. Most components of the adhesive systems and resin composites have been shown to have

definite cytotoxicity when in direct contact with mammalian fibroblasts. Adhesive resin systems are used to enhance retention, reduce micro leakage, and decrease postoperative sensitivity of composite resin restorations. Complete polymerization of adhesive resins might be unachievable during direct pulp capping procedures. In addition, it has been shown that the oxygen prevents complete polymerization of adhesive resin monomers. Consequently, unpolymerized monomers released from the resin-based material can diffuse directly into the pulp at the exposure site, as well as diffuse through the dentinal tubules to cause cytotoxic effects to the pulp cells. While unpolymerized and partially polymerized adhesive resin induced apoptosis were internalized rapidly in macrophages, undifferentiated pulp cells (OD-21) and mouse odontoblasts-like cells (MDPC-23) in corpate polymerized adhesive resin and induced significant apoptosis only in macrophages. Bonding agents have been found to release a photo initiator and photosensitizer widely used to generate free radicals including reactive oxygen species.

Unfavorable effects of dentin bonding systems, pathological changes of pulpal tissues, such as dilatation and congestion of blood vessels, inflammatory responses and production of irregular dentin as well as odontoblastic displacement or tooth sensitivity occur after placement of composite restorations. The monomers in contact with oxygen are not converted into polymers. The persistent inflammatory reaction and hyaline alteration of extracellular matrix inhibit completely pulp repair or dentin bridging.

FUTURE DIRECTIONS

Bioactive pulp capping agents such as Calcium hydroxide, bone sialoprotein (BSP), bone morphogenetic protein (BMP-7 - also termed OP-1) was used successfully [19]. BMP belong to the superfamily of the Transforming Growth Factors. TGF β) ισ α ποτεντ μοδυλατορ 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. Insulin-like growth factor-1 contributes to form a dentin bridge equal to Dycal after 28 days. Among Growth Factors, only the TGF-β1 enhance reparative dentin formation. Enzymes such as Heme-Oxygenase-1, simvastatin, stem cells, Emdogain and ODAM have been used with variable success. Many of these molecules may constitute suitable replacement for calcium hydroxide.

Pulp healing include tunnel defects, operative debris, pulpal inflammatory cell activity and bacterial leakage. This is influenced by the nature and composition of the capping materials [20,21].

It has been concluded that:

- Calcium hydroxide products are the best choice for conservative treatment of the pulp.
- Monomers present in resin composites and adhesive systems have cytotoxic effects as a consequence of direct contact with fibroblasts.
- In human pulps, direct pulp capping with adhesive systems produces different degrees of pulp inflammation, even without the presence of bacteria, and absence of dentin bridge formation, as well as pulp repair.
- RMGICs are more cytotoxic to the pulp cells than conventional GICs due to the presence of unpolymerized monomers, and they should not be applied directly to the pulp tissue.

A calcium phosphate material equipped with poly (lactic-co-glycolic acid) (PLGA) microspheres was effective for pulp capping. The composition with 400 ng TGF-beta-1 was able to trigger the resident stem cells to differentiate into odontoblasts-like cells and induce the formation of tertiary dentin, suggesting that this material might be a good candidate for vital pulp therapy.

The application of anti-inflammatory factor(s) to caries-exposed pulp limits the inflammation, accelerates tissue regeneration, and lead to the deposition of mineralized dentin. The advantage of this approach is that the increased risk of pulpal necrosis or excessive calcification resulting from calcium hydroxide-induced tissue irritation is avoided.

To conclude, the ability of the dental pulp to regenerate should be kept in mind by clinicians that should avoid total pulpectomy. Indirect Pulp Capping or Treatment (IPT) may be used in presence of deep carious lesion without pulp exposure (orthodentin or osteodentin). Beneath a calciotraumatic line, a layer of secondary tubular or atubular dentin is formed (DPC). Direct pulp capping may be used after pulp exposure, and a plug of osteodentin occludes the pulp perforation (calcospherites; diffuse pulp mineralization and/or pulp stones). Indirect or direct capping associate in therapeutic strategy three key elements, the same that are involved in tissue engineering. The association of (1) stem cells, (2) morphogens or growth factors, and (3) a scaffold of biomimetic extracellular matrix, might help the direct differentiation of dental stem cells and the subsequent regeneration of a functional dentin-pulp complex [21]. Apexogenesis and/or apexification are the two targets of pulp capping therapies.

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