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DIRECT PULP CAPPING IN PRIMARY MOLARS USING A NEW MTA-RESEMBLING MATERIAL. A PROSPECTIVE CLINICAL TRIAL.

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Επιβλέπων Καθηγητής για την εκπόνηση της Μεταπτυχιακής Διπλωματικής Εργασίας: Βαδιάκας Γεώργιος

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INTRODUCTION

INTRODUCTION

1. BIOLOGY OF THE DENTINE - PULP SYSTEM

A. Elements of pulp embryology and anatomy

The dental pulp is a differentiated connective tissue surrounded by a differentiated mesenchymatogenic calcified tissue, dentine. The pulp and the dentine form a single structure based on their embryonic origin and structural correlation and therefore it is considered as a complex (Baume 1980; Avery 1994; Goldberg and Lasfargues 1995; Olgart and Bergenhotlz, 2010). The pulp is embryologically derived from the oral ectomesechyme. It contains cells, which belong to different functional groups and provide dentinogenic, defensive and other functions (dentinoblasts, fibroblasts, undifferentiated progenitor cells), extracellular material (mainly collagen fibers and ground substance), and very well organized vascular and nervous system. Generally the dental pulp anatomical structure is not uniform, but it is organized into two different regions, the periphery of the pulp which is in direct contact with the dentine and the main pulpal parenchyme at the center of coronal and radicular pulp (Olgart and Bergenholtz, 2010).

- **Periphery of the pulp**

This region has specific organization that is more characteristic in coronal pulp and in the coronal part of the root canals. This organization serves the principal role of the pulp during the embryonic tooth period (dentine production) and the basic defensive and sensory functions of

the tooth during the post-embryonic period. Three anatomical zones characterize the periphery of the pulp (Avery 1994; Olgart and Bergenholtz, 2010):

1. Odontoblastic layer. The odontoblasts are high cylindrical cells with a very high differentiation degree and inability for further mitotic activity. The functional role of odontoblasts is related to the production of primary dentine from the beginning of dentinogenic procedure to the end of the formation of radicular part of the tooth, the production of the secondary dentine throughout the functional tooth period and the localized production of tertiary reactive dentine as defense against external stimuli. Histologically, odontoblasts are characterized by their large cellular length, with a round core placed at the base of their cellular body, with a great gulp that springs from the top of the cell, which is the area where the odontoblasts are associated with dentine and with excellent cellular organization in the intermediate cytoplasmic region.

2. Cellfree zone of Weil. Itis a 40μm subodontoblastic acellular area that contains multiple branched cytoplasmic processes of adjacent cells, a rich organization of coronal pulp capillaries and a network of sensory and autonomic nerve fibers.

3. Cell rich zone. This region includes spindle bipolar cells (fibroblasts and undifferentiated cells) having as their primary mission the dynamic function of pre-odontoblasts, meaning the replacement of odontoblasts in cases of their destruction following an external stimulus and the production of the tertiary restorative dentine. There are no clear limits to transition of the multicellular zone into the pulp parenchyme (Pashley et al, 2002).

- **Parenchyme of the pulp**

The central pulp contains two basic cell lines, fibroblasts and undifferentiated cells, extracellular material, large vessels and central nervous fibers. The pulp tissue is rich in collagen fibers type III at 30-45%, while collagen type I, which is the main dentine collagen also coexists. These fibers are incorporated into the ground substance in gel-like form with essential carbohydrate polymeric components (chondroitin sulfate, hyaluronic acid, dermatan sulfate), proteoglycans and glycoproteins, which have a characteristic function of hydration and exchange of matter in the peculiar anatomical conditions of the pulp(Linde,1989).

- **Vessels and nerves of the pulp**

The pulp vessels and the multiple nerves enter the pulp from the smallest diameter of the entire pulp space, the apical foramen. This fact creates unique conditions in the development of the inflammatory process after the influence of external stimuli on the pulp (Heyeraas, 1990; Oligart and Bergenholtz, 2010). Small diameter arteries and ultra thin wall arterioles run along the radicular pulp and give a network of central vessels in the coronal pulp resulting in the extensive capillary network in the subodontoblastic acellular area (subodontoblastic vascular network). On spiral path and around from central arteries, there are veins and larger venous vessels. The most of the efferent's communication with afferent vessels takes place through the rich capillary subodontoblastic network, but a smaller part of the vascular delivery can occur through the arteriovenous anastomoses, which is triggered in exceptional hyperaemic conditions. In close contact with the vascular stems, myelinated and unmyelinated nerve fibers enter through the apical foramen. The myelinated nerve fibers are branched into a peripheral nervous network, most of which are in the subodontoblastic region and the odontoblastic layer

(Byers, 1990). Limited number of myelinated aesthetic fibers, losing the myelin sheath, enter inside some dentinal tubules for the first 60-100 μm (Akai and Wakiska, 1990). The number of nerved dentinal tubules varies in different dental walls of the coronal pulp and becomes extremely small in the radicular pulp(Narhi,2010).

B. Embryonic origin of the dentine-pulp system

During the early development of the fetal head a group of neural crest cells migrate to the region of the developing jaws and form together with the mesenchymal cells of the region of the first branchial arch, the oral ectomesenchyme. In connection with the development of oral epithelium resulting in the organized structure of the enamel epithelium, the structure of the dental lamina is formed, which is a set of ectomesenchymal cells enclosed within the structure of the enamel organ. The dental papilla interacting with the inner part of the enamel epithelium creates the biological conditions of the odontoblastic layer formation through the odontoblastic differentiation mechanism (Thesleff and Vaahtokari, 1992; Ruch et al, 1993; Lesot et al, 1994). In summary, this mechanism includes the following: When the growth of the enamel epithelium reaches the bell stage, cells of the periphery of the dental papilla multiplied by more intense mitotic activity are oriented along the basement membrane, the acellular structure separating the epithelium from the ectomesenchymal structure. The oriented spindle-shaped ectomesenchymal cells in contact with the basement membrane are driven by the epigenetic effects of differentiated internal enamel epithelium cells (ameloblasts) on the gradual expression of their specific odontogenic potential (pre-odontoblasts). Pre-odontoblasts are

then differentiated into odontoblasts, cell forms capable of producing collagen type I and a dentine-specific set of non-collagenous proteins in a large amount and in perfectly oriented form (predentine). In fact, differentiation includes highly specialized intracellular changes (Veis, 1985; Linde, 1989; Butler and Ritchie, 1995). The connection of odontoblasts with the basement membrane is maintained despite the deposition of predentine at the top of the cellular bodies, leading to the formation of cellular odontoblastic process and giving the characteristic tubular structure of dentine (Goldberg and Smith, 2004). The gradual mineralization of predentine leads to the formation of dentine, which is not merely the mineralized form of predentine, since the biochemical profile of the two substances is not quite similar (Ten Cate, 1985). The differentiation of odontoblasts and the onset of predentine production signs the conversion of dental papilla into dental pulp. Thus, some of the cells of the periphery of the dental papilla that have received the epigenetic effects of the enamel epithelium remain in the multicellular zone or in the pulp parenchyme region with preodontoblastic properties (Lesot et al, 1994). These cells, as well as the multipotent stem cells of the pulp remain after the dentinogenesis onset as cellular reserves for the healing of dentine - pulp complex injury. It is under research the assumption that only dental pulp cells have the ability to differentiate into odontoblasts. In any case, however, it is generally recognized that biological signals originating from the differentiated cells of the enamel epithelium are implicated in the basic mechanism of primary dentinogenesis initiation. These signals are also the basis of regenerative therapeutic dentine - pulp complex techniques (Thesleff and Vaahtokari, 1992; Ruch et al, 1993; Rutherford, 1999; Tziafas et al, 2000; Smith, 2003).

C. Elements of anatomy and biochemistry of dentine

Morphologically, the dentine is characterized by its unique tubular structure, the presence of parallelly spaced tubules extending from the enamel - dentine junction to the pulp. The dentinal tubules contain tissue fluid and crystals inside them, while small number of collagen fibers are also found. During dentine formation, odontoblastic processes are found in the dentinal tubules, through which the deposition of some of the non-collagenous proteins that play a role in the mineralization of predentine to dentine is completed (Olgart and Bergenholtz, 2010). In fully developed teeth, the processes are found only in the pulpal third of the dentinaltubules, while at the pulpal end ofthe dentine the unmyelinated ends of the myelinated aesthetic nerve fibers are found (Avery, 1994). The wall of dentinal tubules forms the peritubular dentine, while the dentinal substrate between the dentinal tubules is the intertubular dentine. The first layer of dentine produced during the odontoblast differentiation completion phase is called mantle dentine, which, unlike the rest of the dentine mass (peripulpal dentine), has a lower degree of calcification associated with its non-typical biochemical structure due to incomplete differentiation of odontoblasts. The biochemical structure of dentine includes collagenous proteins, glycoproteins, phosphoproteins, growth factors, lipids, serum proteins, etc (Linde and Goldberg 1993; Veis, 1993).

1. The **collagenous dentine proteins** consist largely (> 95%) of collagen type I, as is the case with bone. Collagen type V and smaller amounts of VI are usually found, while small amount of collagen types I trimer and III have been reported but not fully confirmed (Butleretal,2003).

2. The group of **glycoproteins** contains osteonectin, osteopontin, bone sialoprotein and specialized dentinal sialoprotein secreted by the cells producing the primary and reparative dentine (Bronckers et al, 1989; Ritchie et al, 1995; D'Souza et al, 1995).

3. **Phosphoproteins** are the largest and most characteristic group of non collagenous dentine proteins and include two high grade, one moderate grade and one low grade phosphorylated molecules, and a serine-rich phosphoprotein called dentine substrate protein, characterizing the uniqueness of the biochemical structure of dentine (Georgeet al,1993).

4. In the group of **growth factors** that have drown the interest of the researchers over the past two decades, mainly family members of Transforming Growth Factors beta (TGF-b), Insulin-like Growth Factors (IGF) and Bone Morphogenetic Proteins (BMPs) are included (Smith et al, 2012). The particular interest of these polypeptidesis related to the fact that under normal conditions these molecules are found to be associated with the dentine parenchyme collagen and their biological activity is covered by the presence of dentine crystals. However, in conditions of dentine decalcification and enzymatic hydrolysis of collagen, they are released in the area of the dentine - pulp complex and mediate the activation of the biosynthetic activity of the odontoblasts, or the differentiation of the progenitor pulp cells into new odontoblasts (Sloan and Smith, 2007).

As already mentioned in relation to the odontoblastic biosynthetic activity, three types of dentine are distinguished (Avery, 1994; Smith et al,1995;Tziafas,1995):

1. The **primary dentine**, which is the skeleton of the dentaltissues oftooth crown and root, is formed during the period of high degree of biosynthetic activity of odontoblasts from the beginning of their differentiation to the completion of tooth development.

2. The **secondary dentine** is the product of the life-long low rate of production activity of odontoblasts. There are no significant biochemical or morphological differences between primary and secondary dentine.

3. The production of **tertiary reactive dentine** is associated with a specialized defensive function of the pulp in case of injury to the dentine - pulp system. The reactive dentine is deposited on the pulp periphery, by primary dentinoblasts, which after the influence of external stimuli, are reactivated in increased biosynthetic activity. The histological structure of reactive dentine varies according to its production rate (Avery, 1994). Its slow production leads to the formation of a similar reactive dentine structure. Conversely, the rapid formation of reactive dentine leads to the production of non-tubular dentine or even dentine of low degree of calcification(Baume,1980).

Furthermore, the production of **reparative dentine** implies the differentiation of progenitor cells of the multicellular layer or pulpal parenchyme into new odontoblasts or odontoblast-like cells (Rutherford, 1999). The cellular and molecular mechanisms of differentiation of new odontoblasts and production of reparative dentine have many common features with the mechanisms of primary dentinogenesis initiation (Goldberg and Smith, 2004). On a morphological level, the reparative dentine is characterized by the production of a tubular

structure of calcified tissue in a polarized form of predentine-like production from high cylindrical cells with a characteristic presence of their nuclei at the base of the cellular body.

2. ELEMENTS OF PATHOLOGY OF THE DENTINE –PULP SYSTEM

The pathology of the dentine-pulp system is a set of defensive processes of cells and vascular and neural network of the dental pulp, which manifest when microbial, traumatic and iatrogenic nature stimuli affect the dental tissues. The structural organization and specialized physiopathological mechanisms of the dentine - pulp system affect the function of specific defense processes and hence the outcome of therapeutic treatment methods (Olgart and Bergenholtz, 2010). The major pathological and physiopathological mechanisms that affect the conservative treatment of dental pulp are presented below:

i. The integrity of anatomical structure of the odontoblastic layer is the first defense zone of the dentine-pulp system:

The layer of odontoblasts joined together by closed intercellular connections, allows the function of a filter with selective transfer of liquids, ions and molecules (Koling and Rask-Andersen, 1984; Bishop 1985). The disruption of the integrity of anatomical structure of the odontoblastic layer causes partial elimination of the selective function of the filter and thus the extent of inflammatory responses of the pulp (Turner et al, 1989).

ii. The basic pathophysiological difference between dental pulp and other types of connective tissue is the limited space of the dental pulp:

The hyperaemic reactions, which are the first physiopathological change in inflammation, lead to extensive vasodilation and increased vascular permeability, which, when manifested in the closed pulp space, dramatically increase the intrapulpal pressure (Van Hassel, 1971). Feedback mechanisms have been described that can regulate increases in hydrostatic pressure across the pulp space (similar to those found in other connective tissues) and prevent edema, when the development of inflammatory reactions concerns only part of the pulp space (Heyeraas, 1990). Whereas, however, the mechanisms of pulp reaction in vasoconstriction are similar for all connective tissues, the defense against stimuli inducing vasodilation alterations, such as pulp reactions to carious or iatrogenic attack, are significantly different. In pulp, the reaction to a sudden increase in vascular delivery, is followed by dramatic vasoconstriction, with consequences on the progression of the inflammatory reaction and on the defensive function (Kim, 1990). The particular physiopathological mechanisms have the consequence that the sequence of inflammatory reactions is more dependent on exogenous factors, the type and intensity of the stimulus than on other tissues. This assumption explains the fact that the growth of pulpal inflammation often leads to pulpal necrosis (Olgart and Bergenholtz, 2010).

iii. The activation of sensory nerve fibers resulting from external iatrogenic, or microbial and traumatic stimuli causes in addition to manifestation of sensitivity, significant vascular changes:

Under the influence of low intensity stimuli, the existence of this type of defense mechanisms has a beneficial effect by limiting the consequences of inflammation (Akai and Wakiska, 1990; Olgart 1990). It has also been reported that the stimulation of periodontal nerves may increase vascular delivery to the pulp (Olgart, 1992). The role of regulating the function of arterio-venous anastomoses through the stimulation of sensory nerve fibers is mandatory, resulting in bypassing the larger part of the pulpal vascular network blood drainage in hyperaemic conditions of pulpal inflammation (Kim 1985; Heyeraas and Kvinnsland, 1992).

iv. The structural integrity of the dental pulp periphery is essential for the long - term preservation of the pulp vitality:

When the effect of external stimuli causes destruction of part of the pulp periphery and more specifically pulp exposure without the dentinal wall mediation, endogenous healing mechanisms are initiated, which include as part of the repair process the differentiation of new odontoblasts from the multicellular layer and the parenchyma of the pulp and the production of hard tissue bridge (Baume, 1980; Yamamura, 1985; Lesot et al, 1993; Smith et al, 2001; Tziafas, 2004). The occurrence of this process, and especially the quality of the product produced, meaning the effective protection provided by the dentine bridge, depends on the interaction of many factors. It is generally accepted that the two basic conditions, which create a favorable environment for the healing of pulpal inflammation with full reconstitution of the typical structure of the pulp periphery, are the absence of chronic pulpal inflammation and the noninvolvement of microorganisms in the reparative process (Bergenholtz, 1977; 1981; 2001).

v. Chronic mild exogenous effects motivate homeostasis mechanisms of the pulp - dentine system:

The development of destructive chronic damage to the pulp-dentine system (caries, erosion, attrition, abrasion) creates molecular changes in the dentinal tubules (Trowbridge, 1981; Larmas, 1986). Recent research studies show that release of biologically active molecular dentine components occurs, such as non collagenous dentine proteins (Sloan and Smith, 2007). The release of these factors and their transport through the dentinal tubules to the odontoblasts induces mechanisms for stimulating the biosynthetic activity of odontoblasts by dentine production or for differentiation of new odontoblasts and production of reparative dentine (Tziafas et al, 2000; Magloire et al, 2001; Smith, 2003; Goldberg et al, 2006). These homeostatic defensive mechanisms of dentine - pulp system alter dentine permeability through the production of peritubular and peripulpal dentine (Rutherford et al, 1993; Smith et al, 2001; Kalyva et al, 2010). The reduced permeability reduces these defensive mechanisms and therefore leaves the pulp - dentine system exposed to chronic stimuli (Olgart and Bergenholtz, 2010). The presence of microorganisms in the above process alters the conditions of expression and performance of the above defense processes (Murray et al, 2008; Tziafas et al, 2014).

vi. Acute iatrogenic and traumatic stimuli in the dentine - pulp system cause significant vascular changes in the pulp and unfavorable environment for manifestation of the defensive pulp mechanisms:

The physiomechanical damaging irritation of odontoblast processes during dental tissue cutting, dentine drainage and application of toxic dental materials leads to the destruction of the odontoblast process cell wall, the discharging of hydrolytic enzymes at the pulp periphery and the local damage establishment, which is irrespective of the primary stimulus a secondary cause of pulpal reactions (Ten Cate, 1985; Stanley, 1993). The further motivation of vascular responses, due to stimulation of sensory nerve fibers,and the limited function of the protective role as an odontoblastic layer filter, create conditions for the initial lesion extention (Ohshima, 1990; Avery and Chiego, 1990). It should be noted here that the intrinsic defensive mechanisms of the pulp activate the basic tissue reactions of the early stage of inflammation, which, through blood coagulation factors, control the transfer of toxic effects from the oral environment to the pulp tissue, lead to the regeneration of intracellular connections between odontoblasts surviving after the stimulus effect and increase in their activity to produce hard tissue that will limit the continuation of the injurious effect or the involvement of other harmful factors(Brannstromet al,1979;Avery,1994).

vii. Dental pulp cells have the intrinsic ability to differentiate during the reparative process of pulp in various forms of productive hard tissue deposition cells:

Differentiated (primary) odontoblasts react to exogenous effects at a different rate of reactive dentine deposition (Smith et al, 1995). The quality of this hard tissue and hence the performance of this defense mechanism depends on its deposition rate (Murray et al, 2008). Under controlled conditions, the reactive dentine has a tubular structure similar to the primary

dentine, although its first zone is non-tubular hard tissue. The deposition of reactive dentine at a fast pace can lead to the formation of hard tissue with imperfections in its structure (Lesot et al, 1994; Smith et al, 2001). The production of reparative dentine provides for the differentiation of new odontoblasts. The type of hard tissue produced depends on the degree of differentiation of the new odontoblasts, which is a gradual and progressive maturation process concerning the biochemical profile of the hard tissue bridge (Mc Dougal, 1992; Couble et al, 2000; Tziafas et al, 2000; About et al, 2005). Low degree of differentiation leads to the formation of osteo - typical structure (osteo - dentine), hard tissue that does not provide protection from exogenous chemical and microbial stimuli (Smith, 2002; Tziafas, 2004; Nakashima, 2005). The high degree of differentiation of pulp cells leads to high cylindrical cells with a nucleus located at the base of the cell and polarized production of tubular hard tissue structure with a biochemical profile similar to dentine (reparative dentine) (D 'Souza et al, 1995; Tziafas et al, 2000). The reparative dentine is the ideal hard tissue that can replace the damaged structure of the pulp periphery (Smith, 2003). The protection that the reparative dentine bridge can provide is completely dependent on its anatomical structure, meaning its full and continuous presence on the surface of the injured pulp. The endogenous ability of the dentine - pulp system to produce hard tissue as part of the defense and reparative process involves gradual maturation of differentiated odontoblasts (Smith, 2003). Thus, hard tissue production starts with low differentiation cells and osteo - dentine production and is completed by final differentiation of new odontoblasts and production of reparative dentine (Stanley 1989; Mjor et al, 1991; Smith, 2003). Appropriate pulp environment, which includes the control

of the inflammatory effects and the activation of the reparative processes, is required for the completion of this gradual maturation of odontoblasts(Rutherford, 1999;Smith,2003).

3. CONSERVATIVE PULP TREATMENT IN PRIMARY TEETH

The conservative pulp therapy (vital pulp therapy), is defined as a set of therapeutic techniques of the traumatized dentine - pulp complex in order to directly minimize the inflammatory response, induce the healing process of pulp damage by reconstituting the continuity of the physiological structure of the pulp periphery and enable the protection of the treated pulp from toxic effects of bacterial, chemical, physico-mechanical factors and the long-term preservation of pulp vitality (Stanley, 1989; Smith, 2002). Pathological stimuli that can cause pulpal reactions include dental caries, physical injuries, mechanical injuries such as abrasion and erosion, iatrogenic physico-mechanical damaging effects such as dental tissue cutting and dehydration, and iatrogenic chemical harmful effects on the application of dental materials. A prerequisite for applying conservative therapeutic pulp techniques is the estimation of the ability of the pulp to reduce the effects of the inflammatory reaction and lead to a wound healing process. It has been widely accepted that the development of the inflammatory reaction in the peculiar pulp conditions is distinguished in two different phases (Horsted-Bindslev and Bergenholtz, 2010):

- the reversible phase (reversible pulpitis or pulp hyperaemia) which, under appropriate treatment, can lead to healing and preserving the vitality of the pulp and

- the irreversible phase (irreversible pulpitis or pulpitis) that irrespective of treatment leads to generalized inflammation and pulp necrosis.

The clear distinction between these two pulp conditions can only be achieved through the histological study of the pulp. Under current clinical circumstances, this particular differential diagnosis between reversible and irreversible pulpitis is not always possible (Narhi 2010; Olgart and Bergenholtz, 2010). For this reason there have been set two specific criteria for clinical differential diagnosis:

a. The clinical presence of pulpal pain, meaning the existence of a history of automatic or concomitant pain.

b. The presence of contaminated pulp exposure, such as the exposure that occurs when removing the carious dentine, or the delayed treatment of exposure of traumatic or mechanical-iatrogenic aetiology.

Factors that are also related to the ability of the pulp to heal trauma of the dentine - pulp system are:

- Age of the patient
- Type of trauma
- Location of trauma
- Extent of trauma
- Treatment method, which includes among others the properties of the materials used for the conservative pulp treatment (Horsted-Bindslev and Bergenholtz, 2010).

The review of the literature suggests that the prognosis of conservative pulp treatment in primary teeth remains problematic and indeterminate. A key factor underlying the failure of treatment is microbial transfection in the first phase of wound healing or later through marginal microleakage and incomplete structure of damage repair (Bergenholtz, 2001). It is therefore clear that the healing process of the damage and the factors involved, affect the integrity of its repair structure and hence the long-term success of the treatment (Murray et al, 2008). The selection of appropriate capping material is one of the most important factors determining the healing process of the damage and consequently the success of the treatment (Murray and Smith, 2002). Conservative pulp treatment should be applied only if the pulp is healthy or has developed reversible pulpal inflammation (Horsted-Bindslev and Bergenholtz,2010). The greatest potential of the pulp for a successful treatment outcome is the direct treatment of the iatrogenic exposures arising from the cutting of healthy dentine (Murray and Smith 2002; Horsted-Bindslev and Bergenholtz, 2010). In these cases the pulp is healthy and the probability of bacterial contamination is small. The incidence of teeth with traumatic aetiology exposures even after a limited time exposure to the oral environment show high potency if control of pre-operative and post-operative transfection is ensured. Young teeth possessing a larger number of cells, better organized vascular network and larger pulp space have much greater chance of successful outcome with complete healing and dentine bridge formation (Murray et al, 2002). The effect of the exposure location on the prognosis of the treatment has been investigated with relevant research. Previous studies haveconcluded that the exposures of incisal or occlusal surfaces have good prognosis. The remaining surfaces may cause healing disturbance due to blood contamination of more coronal pulp sites. However, more recent evidence suggests that

avoiding the propagation of the capping material can effectively prevent the above issues. The pulp exposure size does not appear to be a contraindication to the application of conservative pulp treatment, but the choice of the appropriate technique depends on the exposure size in relation to the other factors and especially the available pulp tissue at the site of exposure (Horsted-Bindslev and Bergenholtz, 2010). The clinical factors associated with the conservative pulp treatment technique are important prognostic factors (Stanley, 1981; Mjor, 1983; Tziafas et al, 2000; Smith 2002; Murray et al, 2008):

- Mild handling prevents extensive injury to the underlying pulp affecting the healing process and especially the quality of the hard tissue bridge produced.

- The placement of the capping material without pressure ensures that the material is not inserted in the pulp, which increases the chances of healing.

- Effective control of bleeding at the exposure site and the avoidance of thrombus formation are important predictors of the successful outcome of therapy with good quality of dentine bridge. According to the instructions provided by the official scientific organizations, the failure to control bleeding is a contraindication to the choice of conservative pulp therapy. The retention of further thrombus in the site of capping material placement increases in short term the possibilities of incomplete healing, and in long term the contamination conditions given that the blood clots are the ideal microbial growth substrate.

-The use of effective materials for coronal restoration to ensure avoidance of microbial penetration is, according to all researchers, a very important factor in the completion of the

healing process in the first few weeks after the treatment and the long-term survival of the treated pulp (Bergenholtz 2001; Horsted-Bindslev and Bergenholtz, 2010).

Currently, there are three vital pulp therapy options for treatment of deep dental caries approximating the pulp in primary teeth (A) Indirect Pulp Treatment (IPT), also known as indirect pulp capping; (B)Pulpotomy and (C) Direct Pulp Capping (DPC)(Fuks et al, 2013; American Academy of Pediatric Dentistry ReferenceManual,2016).

A. Indirect pulp capping

The Indirect pulp treatment is a procedure performed in a tooth with a deep carious lesion approximating the pulp but without signs or symptoms of pulp degeneration (Fuks, 2013). The caries surrounding the pulp is left in place to avoid pulp exposure and is covered with a bio-compatible material (Büyükgüral et al, 2008). A radiopaque liner such as a dentine bonding agent, resin modified glass ionomer, calcium hydroxide, zinc oxide/eugenol or glass ionomer cement is placed over the remaining carious dentine to stimulate healing and repair (Falster et al, 2002; de Souza et al, 2003; Al-Zayer et al, 2003; Pinto et al, 2006; Marchi et al, 2006; Menezes et al, 2006; Lo et al, 2007; Davidovich et al, 2007). If calcium hydroxide is used, a glass ionomer or reinforced zinc oxide/eugenol material should be placed over it to provide a seal against microleakage since calcium hydroxide has a high solubility, poor seal, and low compressive strength (Tam et al, 1989). The use of glass ionomer cements or reinforced zinc oxide/eugenol restorative materials has the additional advantage of inhibitory activity against cariogenic bacteria (Duque et al, 2005). The tooth then is restored with a material that seals the

tooth from microleakage. Interim therapeutic restorations (ITR) with glass ionomers may be used for caries control in teeth with carious lesions that exhibit signs of reversible pulpitis. The ITR can be removed once the pulp's vitality is determined and, if the pulp is vital, an indirect pulp cap can be performed. Current literature indicates that there is no conclusive evidence that it is necessary to reenter the tooth to remove the residual caries. As long as the tooth remains sealed from bacterial contamination, the prognosis is good for caries to arrest and reparative dentine to form to protect the pulp (Coll et al, 2008; Thompson et al, 2008; Schwendicke et al, 2013). Indirect pulp capping has been shown to have a higher success rate than pulpotomy in long term studies. It also allows for a normal exfoliation time (Farooq et al, 2000; Falster et al 2002; de Sooza et al, 2003; Al-Zayer et al, 2003; Vij et al, 2004; Pinto et al, 2006; Marchi et al, 2006; Menexes et al, 2006; Davidovich et al, 2007; Coll et al, 2008). Therefore, indirect pulp treatment is preferable to a pulpotomy when the pulp is normal or has a diagnosis of reversible pulpitis.

B. Pulpotomy

A pulpotomy is performed in a primary tooth with extensive caries but without evidence of radicular pathology when caries removal results in a carious or mechanical pulp exposure. The coronal pulp is amputated, and the remaining vital radicular pulp tissue surface is treated with an appropriate medicament (Smith et al, 2000; Burnett and Walker, 2002; Ibricevic and Al-Jame, 2003; Loh et al, 2004; Markovic et al, 2005; Vargas and Packham, 2005; Huth et al, 2005). Several studies have utilized sodium hypochlorite with comparable results to formocresol and

ferric sulfite (Vostatek et al, 2011; Ruby et al, 2012; Shabbzendedar et al, 2013). Calcium hydroxide has been used, but with less long term success (Zurn et al, 2008). MTA is a more recent material used for pulpotomies with a high rate of success. Clinical trials show that MTA performs equal to or better than formocresol (Coll 2017). Electrosurgery has also demonstrated success. After the coronal pulp chamber is filled with zinc/oxide eugenol or other suitable base, the tooth is restored with a restoration that seals the tooth from microleakage. The most effective long-term restoration has been shown to be a stainless steel crown. However, if there is sufficient supporting enamel remaining, composite resin can provide a functional alternative when the primary tooth has a life span of two years or less. Published studies concerning pulpotomy have been reported since the early 1900's, and currently pulpotomy is the most frequently used VPT technique for deep dental caries in primary teeth.

C. Direct Pulp Capping (DPC)

- **Definition & Objectives of DPC**

Direct pulp capping involves the application of a bioactive dental material on the exposed pulp. The principle goal of DPC is to maintain pulpal vitality by stimulating reparative dentine formation. Reparative dentine provides a natural source of pulpal protection from bacteria and dental materials (Holland et al, 1979; Bodem et al, 2004). Pulp capping materials are therefore evaluated heavily on their ability to regenerate a hard tissue barrier. A successful direct pulp cap can eliminate the need for root canal treatment, thus avoiding a more invasive, expensive, and time consuming intervention. Vital teeth show higher rates of long-term survivability than

endodontically treated teeth, particularly for molars. Therefore, preservation of vital tooth structure is favorable and, when indicated, direct pulp capping can help attain this goal (Caplan et al,2005).

- **Prognosis of DPC**

Direct pulp cappings are deemed successful when there is formation of a hard tissue bridge with minimal communication between the capping material and the pulp (Schroder, 1985). Case selection is key, as direct pulp capping is not indicated for all pulp exposures. Direct pulp capping is usually indicated in a primary tooth with healthy pulp exposed during cavity preparation over 1 mm or less. Rather, the decision to place a direct pulp capping should be based on the pulpal and periradicular diagnosis and the conditions under which the exposure occurred (Lim and Kirk, 1987).The state of pulpal health and degree of inflammation at the time of exposure dictates the ability for healing to occur and the direct pulp cap to be successful (Lim and Kirk, 1987; Pashley et al, 2002). Proper assessement of the pulp condition is essential, whenever there is evidence or suspicion of caries approximating the pulp. Direct pulp caps can be considered for teeth with viable and healthy or reversibly inflamed pulp status and are contraindicated in teeth with evidence of irreversible pulpitis or pulpal necrosis (Fouad et al, 2008). Determining whether a pulp is reversibly vs. irreversibly inflamed using vitality tests and patient reported symptoms can be difficult and inaccurate (Seltzer et al, 1963; Chen and Abbott, 2009; Gopikrishna et al, 2009). The ability to control pulpal hemorrhage at the time of exposure may be a more reliable indicator of inflammatory status (Matsuo et al, 1996). If uncontrollable bleeding exists in a primary tooth, irreversible pulpitis is the likely diagnosis, and pulpectomy is the appropriate treatment. The presence of bacteria in the pulp is the greatest

cause of direct pulp capping failures (Ghoddusi et al, 2014). This is best judged clinically by whether the exposure occurred during caries removal (carious exposure) vs. cavity preparation on non carious tooth structure (mechanical exposure). The “Position statement on Vital Pulp Therapy” published by the American Association of Endodontists indicates that Vital pulp therapy (VPT) techniques are means of preserving the vitality and function of the dental pulp after injury resulting from trauma, caries, or restorative procedures. (American Association of Endodontists, 2021). A systematic review showed that direct pulp capping placed on carious exposures to have high long-term success rates ranging from 87.5% to 95.4% (Aguilar and Linsuwanont, 2011)This is comparable to the 70-98% success rates seen with non carious mechanical exposures (Dammaschke et al, 2010). Other important factors to consider are degree of isolation at the time of exposure and the ability to provide a well-sealed definitive restoration in a timely manner. Bacterial contamination from saliva during cavity preparation or as a result of microleakage beneath the restoration will reduce success rates of pulp cap considerably (Milosevic, 1991; Bergenholtz, 2000). For this reason it is imperative that a rubber dam be used during any restorative procedure wherein pulp exposure is a suspected outcome, and care should be taken to optimize the marginal seal of the final restoration (Lin et al, 2014). Dental materials used for pulp capping and restorative procedures have been shown to elicit cytotoxic and immunosuppressive effects on the pulp (Modena et al, 2009). The closer the material is to the pulp, the greater the effect (Sidhu and Schmalz, 2001). Therefore, choosing materials that limit damage and promote healing are optimal for situations where direct contact between pulp and dental material is unavoidable.

- **Success rates of DPC versus IPC and pulpotomy**

Many studies have been conducted to determine the efficacy of IPT, DPC, and pulpotomy. Investigations vary in design, techniques, materials used, and diagnostics for determining and reporting outcomes, all of which affect the quality of the evidence produced. Therefore, standardization of methodology has been critical to analyzing VPT studies; in recent years, as the number of randomized controlled clinical trials (RCTs) conducted and published has increased, reporting quality has improved. VPT is so frequently used in the management and maintenance of the primary dentition that an analysis of the existing literature is imperative. Previous systematic reviews and meta-analyses have compared one or more types of vital pulp therapy; however, only one has included all the three vital pulp therapy options (IPT, DPC, and pulpotomy) or compared medicaments for these treatment options. According to the meta-analysis of Coll et al (2017), the 24-month overall success rate of DPC irrespective of the capping agent was 88.8 percent (95% CI: 73.3, 95.8), and the meta-analysis showed the capping agent had no effect on success (RR 1.05 95% CI: 0.89, 1.25) (P=0.56). However, the quality of the evidence for whether DPC agent affected success at 24 months was assessed as very low because of the high degree of heterogeneity in the studies (I2= 83%) and small sample size (Coll et al,2017). According to the same meta-analysis, the 24-month overall success rate of IPC irrespective of the liner was 94.4% (95% CI: 84.9, 98.0 percent). The meta-analysis showed the liner had no effect on IPC success (P=0.88) (RR 1.00 95% CI: 0.98, 1.03). At 48 months, the overall success rate of IPC decreased to 83.4% (95% CI: 72.9 percent, 90.4 percent). The quality of the evidence for liners was best at 24 months, and was assessed as moderate because of small sample size issues. At 48-months the quality of evidence was assessed as low due to the

very small sample size issues. Concerning pulpotomy, the 24-month combined success rate for all pulpotomies was 82,6 percent (Colletal,2017).

- **Direct pulp capping materials**

It is generally accepted that the most important factor for the successful outcome of exposed pulp treatment is the case selection and the absolute indication of application (Stanley, 1989). Under these conditions, the properties of the capping material for the treatment of exposed pulp are:

- The anti-inflammatory effects on the injured pulp
- The absence of immediate cytotoxic effects
- The biological properties for reparative dentine induction in order to form hard tissue bridge that provides effective protection of the exposed pulp from exogenous iatrogenic or microbial damaging effects (Murray et al, 2008; Horsted-Bindslev and Bergenholtz,2010).
- The maintenance of pulpal vitality
- The adherence to dentine and other restorative materials
- The resistance to forces during placement of the final restoration and masticatory forces (Samer Nagui Hanna et al 2020)

A large number of experimental and clinical studies have been collected so far with the application of a plurality of capping materials on different experimental models and evaluated with different histological and clinical criteria. This has greatly complicated the

export of clinically useful conclusions for the evaluation of these materials, but the superiority of some of them has been demonstrated, in the clinical guidelines published by scientific organizations (International Association of Pediatric Dentistry, American Association of Endodontics, European Society of Endodontics, American Academy of Paediatric Dentistry). Materials that have been distinguished in the research over the past decade for their beneficial behavior in direct pulp capping cases are calcium hydroxide and calcium silicate formulations. The application of adhesive and glass-ionomer cement based materials directly to the exposed pulp has in recent years subsided despite the fact that there are conflicting findings from in vitro and clinical studies. The earlier practice of using formulations based on fixative materials, especially in primary teeth, is still under discussion despite the fact that the objections to the safety of this application have been documented (WHO, 2006, Milnes, 2008). However, recent research has shown some effective alternatives such as calcium enriched mixture cement, tricalcium phosphate, statins, enamel matrix derivative, bioactive glasses, nanocrystalline hydroxyapatite, but more clinical trials have to be conducted.

1. Calcium hydroxideformulations

Numerous studies over the past 60 years have provide strong indications for calcium hydroxide formulations (Bergenholtz et al, 2005). Today Ca(OH)2 is considered the gold standard among pulp capping materials. The number of samples with pulpal inflammation and necrosis has been shown to be limited after direct pulp capping with calcium hydroxide

formulations (Cvek et al, 1987; Cox et al, 1996). The ability of calcium hydroxide to cause reparative dentine formation has been confirmed, with percentage up to 80% (Holland et al, 1979; Heys et al, 1981; Cox et al, 1982; Mjor et al, 1991; PittFord et al, 1996; Olson et al, 2006). Despite the general agreement on the dentinogenic effect of calcium hydroxide preparations, little evidence exists in the literature on the molecular mechanisms involved in tertiary dentinogenesis (Tziafas et al, 2000; Bergenholtz, 2005). CH main activity comes from the dissociation of calcium (Ca2+) and hydroxyl (OH-) ions, when CH is in contact with aqueous fluids. Further experimental research has shown that the production of reparative dentine is not a specific biological effect of calcium hydroxide but part of the healing process of the pulp (Murray and Garcia-Godoi, 2006). This assumption suggests that as a result of the multifactorial healing process, the production of reparative dentine is unpredictable, both in terms of its morphology and its structure. It has been repeatedly proven that the dentine bridge is often discontinuous with porous structure (Cox et al, 1996; Nair et al, 2008), while the predominant reparative dentinogenesis mechanism involves intermediate production of permeable osteodentine (Schroeder, 1985; Stanley, 1989; Mjor et al, 1991). These elements have a significant effect on the effectiveness of the formed dentine bridge to isolate the pulp from exogenous stimuli, and thereby to the success of the treatment. The pH values of most current CH-based cements range from 10-12. The alkalinity stimulates reparative dentine formation and is bactericidal, but is also extremely toxic to pulp cells. When in direct contact with the pulp, CH produces a superficial layer of coagulative necrosis up to 2mm in depth as well as inflammatory changes in deeper tissue. Reparative dentine formation is a result of the pulp's defense

mechanisms against CH's irritating effects. The exact mechanism of induced hard tissue formation is poorly understood. Not only does the dentine barrier serve to protect the pulp from future injury, but is also a sign of biological recovery. Several in vitro and animal studies have detected tunnel defects in dentine bridges that form in response to CH. Such disruptions in the dentine barrier could compromise its protective benefits by serving as conduits for microleakage. However, Hilton reported in a 2009 review that tunnel defects related to CH were a less common finding in human studies. Another advantage of CH is its ability to inhibit bacterial growth. This effect is produced by the hydroxyl ions released from CH in an aqueous environment. Hydroxyl ions are highly oxidant free radicals, with extreme reactivity capable of causing bacterial cell death. Despite its advantages, CH is highly soluble and lacks inherent sealing capabilities. These properties can create opportunities for bacterial contamination. Therefore, CH pulp caps require placement of an overlying hard setting liner such as a glass ionomer (GI) or composite-based cement to provide an adequate seal and reduce microleakage. Studies have identified two undesirable consequences of CH pulp caps. First, CH can produce a persistent stimulating effect on dentine formation, leading to pulpal obliteration. If root canal treatment is needed in the future, the hypercalcification can make this procedure difficult if not impossible. Another potential adverse effect of direct pulp caps with CH is chronic inflammation, which can eventually lead to internal resorption (Cochrane Review, 2014).

2. Calcium silicate formulations

Two categories of calcium silicate based materials have been tested for their physicochemical and biological properties to date: The first material is based on Portland cement and has been introduced into clinical practice two decades ago, called Mineralized Trioxide Aggregate (MTA). It was originally developed as a root end filling material and is now a popular choice among clinicians for direct pulp capping as well. MTA is a refined Portland cement with bismuth oxide added for radiopacity. Portland cement is the main ingredient in mortar and concrete. It contains calcium silicate, tricalcium silicate, tricalcium aluminate, gypsum, and tetracalciumaluminoferrite. MTA exists as a powder that is mixed with water in a 3:1 powder/liquid ratio to form a silicate hydrate gel that hardens as it sets. Calcium hydroxide is also formed during this hydration reaction, resulting in the high alkalinity of MTA. Its pH increases from 10.2 during manipulation to 12.5 after setting. Although the exact mechanism of action of this material has not been fully elucidated MTA is proposed as the material of choice for direct pulp capping and pulpotomy. Experimental findings show that MTA has a high degree of histocompatibility (Koh et al, 1998; Koulaouzidou et al, 2005; 2008; Zarrabi et al, 2011) and satisfactory physicochemical properties (Dong et al, 2011; Raskin et al, 2012; Camilleri και et al, 2014). In fact, its cytotoxicity has been likened to that of titanium alloy, which is chemically inert. It induces limited tissue necrosis and inflammation in vivo and is also capable of inducing hard tissue formation at a faster rate and of greater thickness and quality than CH-based materials (PittFord et al, 1996; Tziafas et al, 2002; Nair et al, 2008).MTA is also able to form an excellent seal with tooth structure that protects against bacterial leakage (Oudeimat et al,

2007; Tuna and Olmez, 2008). This is a major advantage over CH-based materials, as bacterial contamination is the greatest threat to the pulp's healing capacity. Finally, MTA has an antibacterial effect, although it is less robust than that of CH. Despite its many advantages, MTA has some important drawbacks that may limit its effectiveness. Perhaps its greatest drawback is a prolonged setting time of up to 4 hours. For this reason, it is ideal to place a moist cotton pellet and temporary restoration over the unset MTA to allow for complete setting and avoided disturbance before the definitive restoration is placed, usually at a consecutive visit. To avoid the need for an additional visit, another acceptable approach is to place a hard-set lining material over the unset MTA, followed immediately by the definitive restoration (Hilton, 2009). Another shortcoming of MTA is its porosity, which may limit its ability to shield the pulp from bacteria and other irritants (Gandolfi et al, 2014). The porosity increases with the amount of water added, incorporation of air bubbles when mixing, and the acidity of the local environment (Parirokh and Torabinejad, 2010). Like CH, MTA's mechanism of action lacks detailed understanding. Many investigators believe that because CH is formed during the setting reaction, their mechanisms are similar or identical (Camilleri and Pitt Ford, 2006). However, MTA's enhanced biologic properties suggest activity that is unique to MTA. While only a few studies have investigated the specific quality of MTA that provides its favorable biocompatibility, there is strong evidence that it is due to its ability to form hydroxyapatite in physiologic solutions. MTA has also demonstrated bioinductive capabilities, promoting the formation of morphogenetic proteins and growth factors such as BMP-2 and TGF-β1 (Guven etal,2007). A modified calcium silicate formulation, introduced over the last years, is the commercial preparation

called Biodentine (Biodentine; Septodont, Saint Maur des Fosses, France). The material consists of powder and liquid. In the powder, the main ingredient of Portland cement (tricalcium silicate and dicalcium silicate) has been enriched with calcium carbonate and zirconium oxide, while the liquid consists of an aqueous solution of calcium chloride and a polycarboxylicplasticiser component. The most important advantage of this material is the much improved manipulation and clotting properties (Raskin et al, 2012, Natale et al, 2015; Kim, et al, 2015). In vitro studies have shown that this material also has improved physicochemical properties and very good biocompatibility (Laurent et al, 2008; 2012;Peng et al, 2011; Leiendecker et al, 2012; Zanini et al, 2012), in relation to the low strength mechanical properties of MTA and Dycal formulations. Histological investigations on human teeth (Nowicka et al, 2013) and mouse teeth (Tran et al, 2012) have shown the ability of the material to cause a hard tissue bridge production. The mechanism of action of the specific material has not been elucidated, as well as the ability of the material to cause specialized processes of biological stimulation of dentinogenic mechanisms in the pulp is under investigation. Another material used in various clinical studies is Portland Cement (PC), which differs from MTA by the absence of bismuth ions and the presence of potassium ions. Both materials have comparable antibacterial activity and almost identical properties macroscopically, microscopically and by X-ray diffraction analysis. It has also been shown that PC and MTA have similar effect on pulpal cells when used for direct pulp capping in rat teeth. Holland, et al. studied the rat subcutaneous connective tissue response to implanted dentine tubes filled with MTA, PC and calcium hydroxide and found very similar mechanisms of action. In addition, both MTA and PC allowed for dentine bridge formation

after pulpotomy was performed in dogs. Finally, it is observed that PC allowed the expression of mRNAs of a dentine - specific protein and a non collagenous protein involved in mineralization in cultured human pulp cells. Taking into account the low cost and apparently similar properties of PC in comparison to MTA, it is reasonable to consider PC as a possible substitute for MTA in endodontic applications (Contiet al, 2009).

A resin-modified Portland cement-based material called TheraCal has been introduced for endodontic treatments such as DPC. After being set by light – curing devices, Theracal releases calcium ions which leads to environment alkalization and exerts bioactive properties (i.e. apatite formation followed by new dentine production), cell growth, and proliferation. TheraCal has shown greater calcium ion release, and lower solubility and water absorption compared to ProRoot MTA or selfsetting calcium hydroxide, which can make TheraCal advantageous in DPC (Erfanparast et al, 2018).

- **Alternative direct pulp capping materials**

Calcium enriched mixture (CEM) cement, a recently introduced biomaterial, has good biocompatibility, ability to induce hard tissue formation, including hydroxyapatite, and it can resist microbial re-entrance. CEM cement has appropriate sealing ability. Sets in aqueous environments, remarkable antibacterial activity and quick setting time (<1 hour) (Ghajari et al 2010; 2013).

Tricalcium phosphate (TPC) is a porous bioceramic material whose biological properties include non-reactivity and resorbability. It can serve as scaffolding for bone ingrowths, as it

progressively degrades and is replaced by bone. Because of its osteoconductivity and bone replacement capability, TPC is highly promising for use in numerous dental and craniofacial procedures, while it is also proving useful in endodontics. Theoretically, the biocompatibility of TCP combined with calcium release may allow TCP to stimulate odontoblasts, thus promoting the formation of dentinebridges(Shayegan et al,2009).

Dentine adhesive resin systems (DAR) are among materials which have been proposed as substitutes to CH. DAR have lower pH and cause less aggravations to the pulp. Additionally, it has been shown that selfetching resins have antimicrobial activities and alleviated gap formation and microleakage. The most important fact in application of DAR is their proper sealing ability in dentinal margins (Akhavan et al, 2017). In recent years, the use of bonding systems, which form a hybrid layer that intimately unites resin with dentine, has gained increasing interest as a pulp-capping procedure. The rationale behind adhesive pulp capping is to hermetically re-seal the pulpal wound in order to protect it against bacterial leakage and the ingress of toxins, which may be more critical for healing than the material used for capping. Some authors have observed pulp tissue repair when bonding systems were tested in animal models. Conversely, results of human studies showed impairment of dental pulp repair with varying degrees to necrosis when different adhesive systems were used as capping agents in primary teeth. Others have investigated the interactions of dentine bonding agents with vascular tissue in vitro, as placement of some resin-based materials on pulp exposures may promote hemorrhage, which in turn seriously impairs the healing process. Thus, employment of a hemostatic material or technique that may prevent the exposed pulp from further bleeding could be a critical factor in determining the success of

adhesive pulp capping in primary teeth. Based on the results of animal studies, sodium hypochlorite (NaOCl) seems to be one such solution that has been claimed to provide effective hemostasis over the mechanically exposed pulp, besides exerting a digestive effect on diseased tissues and a limited effect on normal, healthy tissues (Demiretal,2007).

Statins are structural analogs of HMG-CoA (3-hydroxy-3-mthylglutaryl-coenzyme A). These drugs are the first-line for hyperlipidemia and it has been recognized to be a safe and low-priced drug as a result of its worldwide longtime usage. Moreover, statin has multiple functions including anti-inflammation, induction of angiogenesis and improvement of the vascular endothelial cell function. Another interesting and important function of statin is its effect on bone formation. It has been reported that several statins such as simvastatin and lovastatin have anabolic effects on bone metabolism at in vitro and in vivo studies. They promote mineralization in non - mineralizing osteoblasts through induction of BMP-2 and osteocalcin. Furthermore, in vitro studies showed that statins promote osteoblastic differentiation in mouse osteoblastic cells (Aminabadi et al, 2013).Since statins are known to induce angiogenesis and to regulate the survival and increase neurogenesis of neuronal cells, that indicates the possible effectiveness of statins in pulp along with dentin regeneration (Mahendran K et al, 2019)

Enamel Matrix Derivative (EMD) is a biomaterial derivated from the extracellular enamel matrix that is rich in amelogenin and amelin. These proteins have been related to important biological functions in tooth development. As a dressing in pulpotomies of primary teeth, it has proven to have successful clinical and histological results. As a DPC material, EMD has been used on animal teeth and human premolars with promising results. It has been

demonstrated that EMD stimulates the production of a large amount of new, dentin-like tissue when applied as a DPC material onto the exposed pulp of permanent molars in adult miniature swine. Its regenerative process consists of differentiation of odontoblasts and subsequent dentine formation and pulpal wound healing without affecting the normal function of the remaining pulp in a behavior similar to normal dentinogenesis. However, its effects in pulp capping on primary teeth has not yet been elucidated (Garrocho-Rangel et al,2009).

Bioactive glasses (BAGs) are relatively new materials in the field of dentistry. They have been studied for more than 30 years as bone substitutes. They react with aqueous solutions and produce a carbonated apatite layer. BAG is biocompatible and can bind to the bone, but also based on present documents, BAG is able to stimulate hard tissue formation and mineralization. BAG can be the material of choice for pulp capping and periapical bone healing because it is biocompatible and has antibacterial properties. However, results of studies remain controversial (Haghgoo et al,2007).

Recently, a fully synthetic **nanocrystalline hydroxyapatite (NHA)** paste containing approximately 65% water and 35% nanostructured apatite particles was introduced for augmentation procedures in cases of osseous defects. Compared to bulk materials, the advantages of such a nanostructured material are its close contact with surrounding tissue, its rapid resorption capacities, and the high number of molecules on its surface. The NHA paste is attracting increasing interest in medicine and dentistry and has already been used in orthopedic surgery and for jaw cysts and periimplantitis lesions. Theoretically, the biocompatibility of NHA, combined with its structural similarity to teeth, may allow NHA to

stimulate odontoblasts, thus promoting the formation of dentine bridges. The existing literature on its use as a direct pulp capping material in primary teeth is limited and the results are still under discussion (Shayegan et al, 2010).

Aloe vera is a medicinal plant commonly grown in tropical climate. Acemannan, abacetylatedpolymannose extracted from Aloe vera gel, shows cytocompatibility with various cell types. It is also showed that acemannan stimulates the proliferation, differentiation and mineralization of human dental pulp cells in permanent teeth. Moreover, when used as a DPC agent, acemannan enhanced reparative dentine formation in an animal model. However, the clinical effects of acemannan as a DPC material on primary teeth have not yet been elucidated (Songsiripradubboon et al, 2015).

- **Composite RestorativeMaterials and Pulp**

The key to the long-term success with direct pulp capping is a well-sealed restoration (Hilton, 2009). Resin-based composites are a popular choice of restorative material due to their esthetic properties and ability to chemically bond to tooth structure. They consist of a resinmatrix usually containing bis-GMA in addition to inorganic glass fillers and silane coupling agents (Zimmerli et al, 2010). A major disadvantage to the use of composite materials is their toxicity to the pulp. Several studies have confirmed the cytoxicities of various composite restorative materials (Huang and Chang, 2002; Furey et al, 2010). The mechanism appears to involve the impairment of mitochondrial function, producing irreversible effects on cellular metabolism (Huang and Chang, 2002). In vivo studies have

shown composite restorations to be associated with pulpal irritation and necrosis. The organic monomers contained in the resin phase of composite materials such as bisphenol A-glycidyl methacrylate (Bis-GMA), urethane dimethacrylate (UDMA), triethylene glycol dimethacrylate (TEGDMA), and 2-hydroxyethyl methacrylate (HEMA) are thought to be largely responsible for these toxic effects. These monomers are leached from composites that have not reached complete conversion and can diffuse through dentin tubules as well as porous or poorly sealed pulp caps to reach the pulp (Modenaet al, 2009).Thetoxicityof composite materials may interfere with the regenerative goals of direct pulp capping. Studies point to the ability of composites to prevent reparative dentin formation following pulp exposure by inhibiting odontoblast differentiation (About et al, 2002). Lack of a hard tissue barrier greatly reduces the pulp's ability to combat bacterial and chemical irritants and over the long-term will almost certainly result in vitality loss. Therefore, placing composite materials in close proximity to pulp may negatively influence outcomes of vital pulp therapy. In spite of this, composite materials are commonly used for deep restorations including those that require a direct pulp cap. If the definitive restoration is to be placed immediately after an MTA pulp cap, a hard setting composite-based liner is often used to protect the unset MTA from disturbance during the restorative process. Composite liners are also recommended for placement over CH pulp caps for the purpose of providing an adequate seal, which CH-based cements inherently lack. A composite restoration is often placed on top of the lining material.

D. Clinical studies for direct pulp capping in primary teeth

In recent years it is supported that mechanically exposed pulps, should be considered for DPC and that successful outcomes are possible under defined conditions (symptom-free tooth, disinfection of pulp exposures, Class-I cavity) and appropriate sealing of the cavity with an effective dentine seal (AAPD Guidelines, 2017; Boutsiouki et al, 2018). However, from reviewing the existing literature, it was found that clinical studies on direct pulp capping in primary teeth arelimited(Table1).

CLINICAL STUDIES	SAMPLE SIZE	DPC MATERIAL	FOLLOW-UP (months)
Nakashima et al, 1989	124	Ca(OH)2	24
Caicedo et al, 2006	10	**MTA**	6
Demir &Cehreli, 2007	100	Ca(OH)2; Acetone-based	24
Tuna &Olmez, 2008	50	Ca(OH); **MTA**	24
Garrocho-Rangel et al, 2009	90	EMD; Ca(OH)2	12
Ghajari et al, 2010	42	**CEM; MTA**	6
Aminabadi et al, 2010	120	FC; Ca(OH)2	24
Ghajari et al, 2013	42	**CEM; MTA**	20
Kotsanos et al, 2014	60	Ca(OH)2	21
Ulosoy et al, 2014	40	Ca(OH)2; Calcium Sulfate Hemihydrate	12
Aminabadi et al, 2015	160	Simvastatin; 3Mix; 3Mixtatin; **MTA**	12
Songsiripradubboon et al, 2015	42	Acemannan; Ca(OH)2	6
Luczaj-Cepowicz et al, 2017	30	**MTA**	24
Erfanparast et al, 2018	92	**Theracal; MTA**	12
MohamadrezaShahamfar et al, 2020	90	**MTA; protooth**	6

Table 1: Clinical studies for direct pulp capping in primary teeth.

One trial appeared to favour formocresol over calcium hydroxide (Aminabadi et al, 2010) however, there are safety concerns about formocresol.

In a systematic review and meta analysis(Coll et al 2017), it was found that the 24- month overall success rate of DPC irrespective of the capping agent was 88.8 percent (95% CI: 73.3, 95.8), and the meta-analysis showed that the capping agent had no effect on success (RR 1.05 95% CI: 0.89, 1.25) (P=0.56). However, the quality of the evidence for whether DPC capping agent affected success at 24 months was assessed as very low because of the high degree of heterogeneity in the studies (I2= 83%) and small sample size (Collet al, 2017).

In the systematic review of Dhar et al (2017), the panel made weak recommendations regarding choice of medicament in direct pulp capping and the quality of evidence was very low after 24 months. Success of the treatment was independent of type of medicament used.

In the most recent Cochrane Database systematic Review (2018), the clinical and radiographic failure (at 6, 12 and 24 months) was compared between different medicaments for direct pulp capping. It was concluded that there is insufficient evidence to conclude that 1 medicament is superior to the other (Cochrane Database Systematic Review, 2018). Moreover, the quality of the evidence was assessed as low or very low for all comparisons. The authors reported that the small number of studies and low quality of the evidence limited interpretation of the results (Cochrane Database systematic Review,2018).

Longer follow-up periods, more clinical studies, comparable conditions, and clear definitions of evaluation criteria are needed to confirm the results of direct pulp capping in primary teeth (Boutsioukiet al, 2018).

AIM

The aim of the present clinical study was to investigate the clinical outcome of direct pulp capping in carious primary molars with pulp exposure, following caries removal, after 12 months of follow-up, using a new MTA-resembling material (neoMTA) as a pulp capping agent.

MATERIALS & METHODS

MATERIALS & METHODS

1. STUDY DESIGN

This is a prospective clinical trial, which includes: a) a complete medical and dental history and written consent from the parents, b) initial clinical and radiographic examination and assessment of the primary molars that are candidates for the study, based on the selection criteria, c) caries removal, direct capping of the exposed pulp and final restoration of the primary molars, d) clinical and radiographic evaluation at 3, 6 and 12 months and e) statistical analysis of the results.

2. STUDY SAMPLE SELECTION

The study sample consisted of healthy patients aged 4-11 years old, that presented in the Postgraduate Clinic of Paediatric Dentistry at the National and Kapodistrian University of Athens, seeking for dental treatment.

3. MEDICAL-DENTAL HISTORY-WRITTEN CONSENT

Prior to the examination, a detailed medical and dental history of the child and a written consent regarding the treatment was taken from the parents (Ethics committee, Dental School, National and Kapodistrian University of Athens (417-26/5/2019)

4. INCLUSION CRITERIA

The patients were included in the study if they met the following eligibility criteria:

- Had an uneventful medical history

• Presence of first or second deciduous molars with deep active caries lesions, resulting to pulp exposure after caries removal.

• All participating teeth had a negative history of pain and were free of signs and symptoms indicative of irreversible pulp inflammation.

- All teeth had to bewere restorable with composite resin.

The specific clinical and radiographic criteria that had to be fulfilled, for participation into the study sample, are presented in tables 2 and 3.

Table2: History and clinical inclusion criteria for the participation into the study sample.

• **No history of pain**
• **Healthy periodontal tissues in the absence of fistula/ swelling**
• **Lack of mobility and percussion sensitivity**
• **Pulp exposure < 1-2mm**
• **Spontaneous Hemostasis (without hemostatic agents) within 2-3min**
• **Teeth restorable with composite resin**

Table 3: Radiographic inclusion criteria for the participation into the study sample.

• **No pathological sign in the permanent successor**
• **No periapical or furcal radiolucency and no internal or external resorption and calcification**
• **Continuous and intact lamina dura**
• **Remaining root length at least half of the original**

5. STUDY GROUP

Primary molars, that were candidates for inclusion in the study were examined clinically and radiographically by a paediatric dentist, to determine whether they met all the inclusion clinical and radiographic criteria mentioned above. The initial radiographic examination included a periapical radiograph. All teeth were treated with neoMTA as pulp capping material.

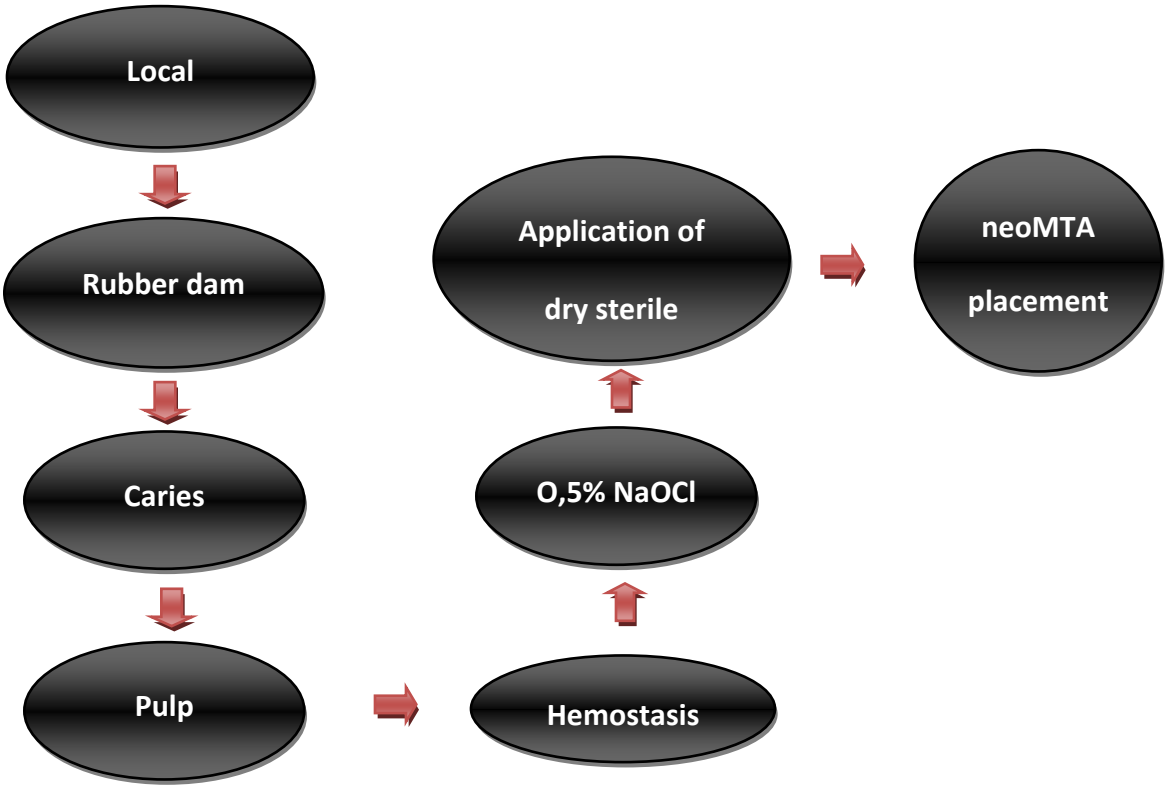
6. PROCEDURE

All direct pulp capping procedures were performed by the same paediatric dentist. The teeth were anaesthetized locally with articaine 4% with epinephrine 1/200.000 and isolated with rubber dam. All enamel and dentine caries was removed. Teeth with an exposure less than 2 mm, surrounded by sound dentine were candidates for direct pulp capping. If the size of pulp exposure was greater than 2 mm, or if the bleeding was not controlled with a sterile cotton pellet within 2-3 minutes, the tooth was excluded from the study and a pulpotomy was performed. Hemostasis was achieved spontaneously and then gently rinse the cavity

preparation using a NaOCl (3.0-6.0%)were performed for disinfection, followed by application of dry sterile cotton pellets (Figure 1). NeoMTA was placed on the exposed pulp. After its mixture according to the manufacturer's instructions, the material was left to set(Initial Setting Time at 37°C: ~15 min when thickly mixed with Gel), a light-cured glass ionomer cement was placed on top of the pulp capping material and the tooth was restored with composite resin. A periapical radiograph was taken immediately post-treatment.

In figures 2& 3, two clinical cases of direct pulp capping in primary molars, using neoMTA are presented.

Figure 1: Clinical procedure followed for direct pulp capping in primary molars



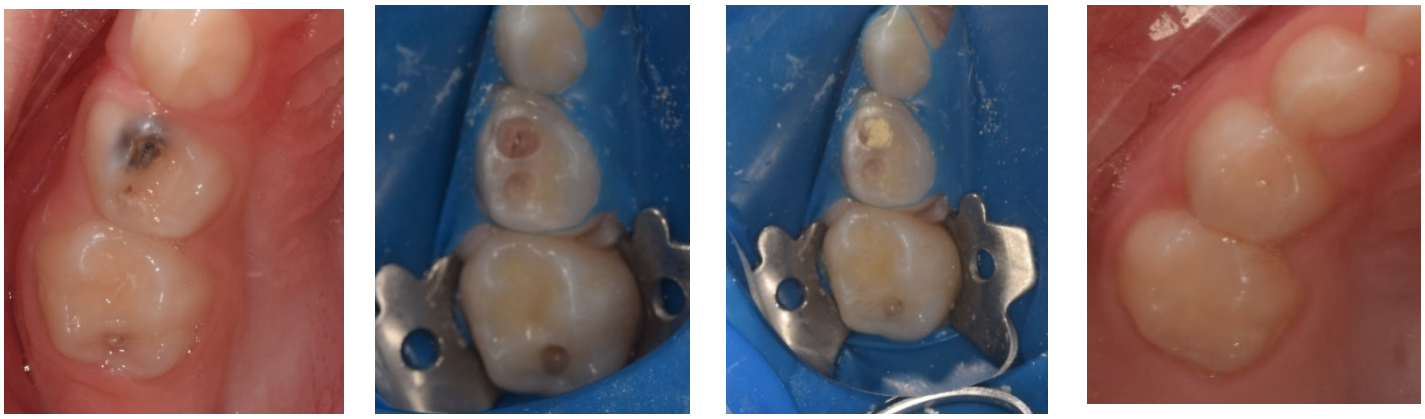


Figure 2: Case of an upper 1st primary molar. After caries removal and pulp exposure, neoMTA was placed at the exposure site , followed by application of a light cured glass ionomer cement. The tooth was restored with composite resin.

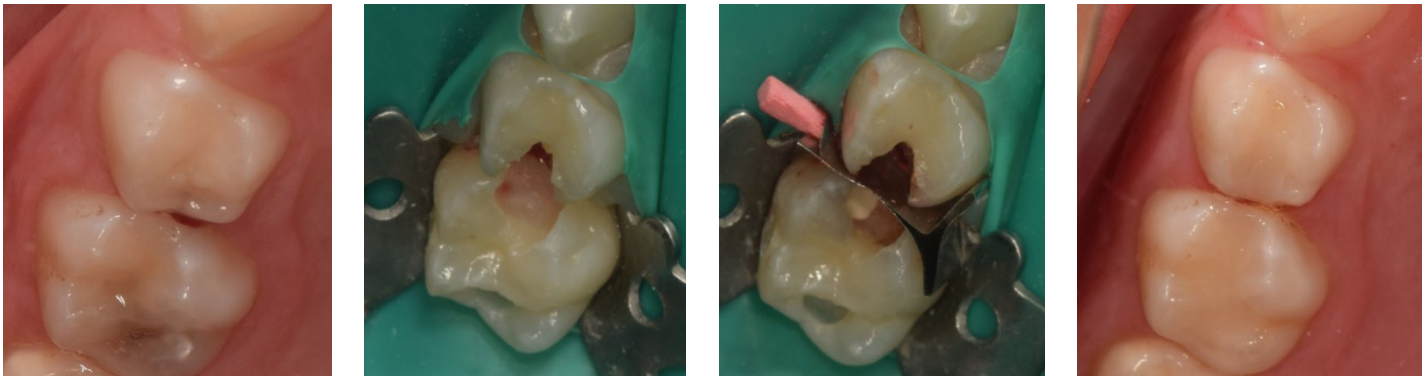


Figure 3: Case of an upper 2ndprimary molar. After caries removal and pulp exposure, the exposure site was capped with neoMTA, a light cured glass ionomer cement was placed and the tooth was restored with composite resin.

7. FOLLOW UP

Follow up

Patients were re-examined at 3, 6 and 12 months after treatment. The recall examination included clinical and radiographic evaluation of the diagnostic criteria used by two other blinded and previously trained and calibrated pediatric dentists (inter-examiner reproducibility kappa = 0.96). All teeth were assessed for presence of signs or symptoms of pain, sensitivity to percussion or palpation, fistula, swelling, internal or external resorption, periapical or furcal radiolucency, which are indicative of pulp necrosis(Table 4).

Table 4: Clinical and radiographic diagnostic criteria of failure/success

CLINICAL	RADIOGRAPHIC
Symptoms of pain	Internal / External resorption
Sensitivity to percussion or palpation	Periapical / Furcal radiolucency
Mobility	
Fistula / Swelling	

8. STATISTICAL ANALYSIS

Descriptive statistics with cross tabulations were performed.

RESULTS

RESULTS

A total of 41 patients, 21 girls (mean age 7, SD: 1.69) and 20 boys (mean age 7.1, SD: 1.46) with a mean age of 7.5 years(SD 1.68),ranging from 4 to 11 years, participated in the study.

The total number of primary molars included in the study was 47. Of them 19 were first primary molars, 28 were second, 27 lower and 20 upper, 29 right and 18 left. Class II composite resin restorations were placed in 39 teeth, while only 8 teeth were restored with a Class I restoration.

From the initial 47 teeth included in the study, 8 patients with 8 teeth (3 first primary molars, 5 second primary molars, 4 upper, 4 lower, 2 right and 6 left) treated with DPC failed to attend the follow-up visits and were considered as drop outs.

Available for examination were 39 teeth, at 3 and 6 months and 35 teeth at 12 months .

The total number of molars treated with DPC and diagnosed as failed were 4, bringing the overall failure for direct pulp capping up to 10.3%.(Figure 2)

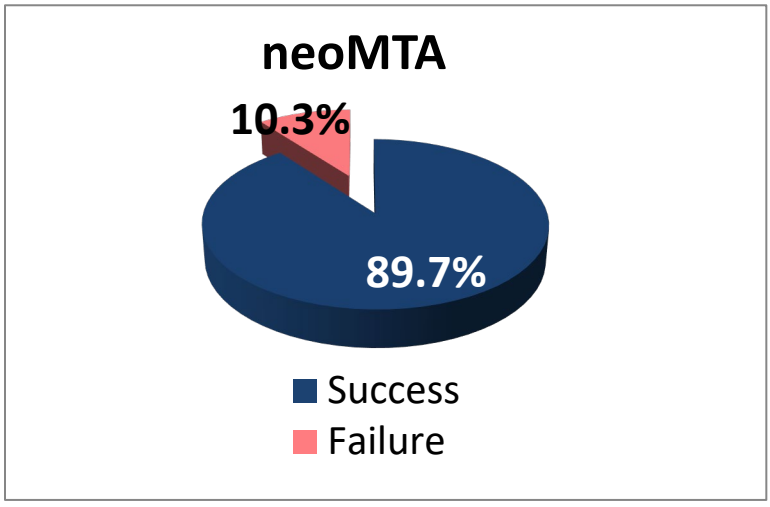


Figure 2. Success rate after 12 months of follow-up

With regard to the type of failure, of the 4 teeth failed, 3 appeared with swelling and 1 with a furcal radiolucency. (Table 5)

It is worth mentioning that the event of failure, for all failed teeth, occurred within the first 6 months, post-treatment.

The distribution of the failures during the follow-up time period is presented in table 5.

Table 5:Distribution of failures during the follow-up time period

Follow-up Teeth	3m	6m	12m
Examined	39	39	35
Swelling and Subsequent extraction	0	3	0
Furcal Radiolucency	0	1	0
Drop-outs	8	0	0

DISCUSSION

DISCUSSION

In the present study, we attempted to assess the efficacy of direct pulp capping in primary molars, using neo MTA as a direct pulp capping material. This is a new MTA-resembling material, fairly recently marketed, that demonstrates improved characteristics over classic MTA. Neo MTA has excellent biocompatibility, similar to MTA sealing ability and long term seal. It offers dentin bridge formation and hard tissue induction. Compared to MTA, it has better mixing and handling properties, shorter setting time and causes less coronal discoloration. A major shortcoming is the high cost, although lower than MTA (Abuelniel et al. 2020, Haikal et al 2020). So far neoMTA has not yet been tested for Direct pulp capping in primary teeth.

According to the literature on direct pulp capping in primary teeth (Table 1), Ca(OH)2 and MTA are the most commonly studied DPC materials, while neoMTA has not yet been tested for DPC in primary teeth. Therefore, to the best of our knowledge this is the first clinical study using neoMTA as a DPC material in primary molars.

The dental pulp is a highly vascular and innervated connective tissue that is capable of healing by forming hard-tissue barriers or dentin bridges after direct pulp capping. Innovative therapies have been used in an attempt to apply biologic modulators that have been identified during tooth and bone embryogenesis and cloned experimentally; these agents are intended to improve treatment modalities and induce tissue regeneration. Direct pulp capping has almost disappeared from the wide repertory of pulp treatments in primary teeth, because previous studies demonstrated that direct pulp capping may have poor prognosis. Compared to permanent teeth, it is considered to be a compromising and risky procedure owing to its likelihood of producing internal dentin resorption and, with less frequency, pulp calcification,

necrosis, and damage to the surrounding alveolar bone (Ghajari et al, 2010). Higher cell concentration of the primary pulp tissue could be the cause of these abnormalities; it is supposed that the mesenchymal cells become differentiated to odontoclastic cells in response to the capping material, thereby causing internal root resorption (Fuks, 2013). DPC has been limited to those cases where exfoliation of affected primary teeth is expected within 1 or 2 years (Garrocho Rangel et al, 2009).

DPC has the advantage of being a conservative vital pulp therapy reducing the need for more invasive treatments. Therefore, targeting the mechanisms that protect, control and regulate abnormal root resorption may help in preserving a primary tooth for its expected lifetime (Ghajari et al, 2010). Nevertheless, an ideal material for DPC of primary teeth has not been completely accepted; Nor has there been a standardized DCP technique for primary teeth, such as those developed or suggested by experienced clinicians, that considerably improves the prognosis of treatment (Garrocho Rangel et al, 2009).

It is already known that the primary tooth pulp maintains structures necessary for its healing and repair until advanced stages of root resorption. Its histological similarity with the permanent tooth pulp suggests comparable healing capacity to withstand inflammation and means that the management of the compromised primary tooth pulp needs to be reappraised. Restorative procedures with hermetic adhesion of dental materials to the sound peripheral dental tissues are now more feasible than in the past, further aided with new materials (Kotsanos et al, 2014). According to the literature, several materials have been used as final restoration, such as amalgam, composite material, stainless steel crowns etc. Following any vital pulp treatment, the objective is that ‘the restorative material should seal completely the

involved dentin from the oral environment'. In the present study, all primary molars were restored using glassionomer cement as a base and composite resin as the final restorative material.

Comparing our results with those from the literature, we found that in our study the overall success rate of DPC in primary teeth was 89.7% after 12 months of follow-up, while in the literature after the same follow-up period the overall success rate ranges from 64 to 100%, revealing the high degree of heterogeneity between studies. If we focus on the studies with MTA and MTA-like materials the success rates are higher and range from 80% to 100%.

As far as the type of failure is concerned, in the present study, of the 4 teeth failed, 3 appeared with swelling and pain and 1 with only radiographic findings. The event of failure, for all the 4 failed teeth, occurred within the first 6 months, post-treatment. Therefore, these results imply that the clinical evaluation of the therapeutic outcome is not sufficient for determining the success rate in pulp therapy of primary teeth, and that concomitant radiographic evaluation is necessary. The reason 4 cases failed is not known. It is possible that misdiagnosis of the initial pulp condition has led to inclusion of teeth with pulp inflammation that could not be reversed. Teeth with an extensive, non reversible pulp inflammation are not candidates for DPC and should not be treated with DPC.

In the literature, the clinical studies on DPC in primary teeth are limited (Table 1), with the sample sizes ranging from 10 to 160 primary teeth. Our sample size consisted of 47 primary molars, which was considered small for detection of any significant differences (Table 1). Regarding the follow-up time periods, in our study the follow-up time was 12 months and in the

literature the range is from 6 to 24 months, indicating the need for studies with longer follow-up periods (Table 1).Therefore, considering rigid criteria for case selection and meticulous procedure as prerequisite for successful treatment, we also acknowledge the need for further large-scale randomized clinical trials including bigger sample size and adequate follow-up duration to test the outcomes.

CONCLUSIONS

CONCLUSIONS

The conclusions of the present master thesis can be summarized in the following:

- Direct pulp capping in asymptomatic primary molars with a cariously exposed pulp, using neoMTA as a pulp capping material, exhibited an overall success rate of 89.7% based on clinical and/or radiographic diagnostic criteria, after a follow-up period of 12 months.

- The event of a failed pulp treatment was diagnosed within the first 6 months, post-treatment.

- Longer follow-up periods are needed to further assess the long-term clinical and radiographic effectiveness of direct pulp capping after application of the material studied.

SUMMARY

Introduction: Direct Pulp Capping (DPC) described as the application of a material to an exposed pulp to maintain its vitality and induce the formation of reparative dentine, is an alternative pulp treatment method for vital primary teeth. The ideal direct pulp capping material should biologically stimulate odontoblasts or pulp cells and induce the formation of new hard dental tissue around the exposed pulp. The fast setting Ca(OH)2 has been traditionally the material of choice for DPC in permanent teeth. Nevertheless, it exhibits a number of shortcomings that question its use in clinical praxis. MTA was introduced to overcome several of calcium hydroxide's limitations. Over the last few years, a new set of MTA-resembling materials have been manufactured and demonstrate improved characteristics when compared to MTA. Neo MTA is a new material that has excellent biocompatibility, similar to MTA sealing ability and long term seal. It offers dentin bridge formation and hard tissue induction. In addition, it has better mixing and handling properties, shorter setting time and less coronal discoloration, compared to MTA.

Aim: The aim of the present clinical study was to investigate the clinical outcome of direct pulp capping in carious primary molars with pulp exposure, following caries removal, after 12 months of follow-up. A new MTA-resembling material (neoMTA) was used as a pulp capping agent.

Materials and Methods: This is a clinical trial, which includes: a) a complete medical and dental history and written consent from the parents, b) initial clinical and radiographic examination and assessment of the primary molars that are candidates for the study, based on the selection criteria, c) caries removal, direct capping of the exposed pulp and final restoration of the

primary molars, d) clinical and radiographic evaluation at 3, 6 and 12 months and e) statistical analysis of the results. Prior to the examination, a detailed medical and dental history of the child and a written consent regarding the treatment was taken from the parents (Ethics committee, Dental School, National and Kapodistrian University of Athens). The study sample consisted of healthy patients aged 4-11 years old that presented in the Postgraduate clinic of Paediatric Dentistry of National and Kapodistrian University of Athens, seeking for dental treatment. All participating children received a full preventive treatment and restoration of all carious teeth. Teeth were included in the study if they met the following eligibility criteria: first and second primary molars with deep caries lesions, leading to pulp exposure after caries removal, negative history of pain and free of signs and symptoms indicative of irreversible pulp inflammation, while the teeth had to be restorable with composite resin. More specifically, all included teeth presented with lack of mobility and percussion sensitivity and healthy periodontal tissues, in the absence of fistula or swelling. Radiographically, the presence of periapical or furcal radiolucency, internal or external resorption, calcification and pathological sign in the permanent successor were all findings for exclusion. The lamina dura should be continuous and intact and the remaining root length at least half of the original. Caries should extent to the inner half of the dentine approaching the pulp. Pulp exposure as a result of caries removal should not exceed 1-2 mm, while bleeding should be controlled by using a dry cotton pellet under light pressure, within 2-3 min. If haemorrhage control was unsuccessful, the tooth was excluded from the study and followed a different treatment approach. Primary molars, that were candidates for the participation into the study were examined clinically and radiographically by a paediatric dentist, to determine whether they met all the inclusion clinical

and radiographic criteria mentioned above. The initial radiographic examination included a periapical radiograph. neoMTA was used as pulp capping material. All direct pulp capping procedures were performed by the same paediatric dentist. Following clinical and radiographic examination (periapical radiograph), the teeth were anaesthetized locally with articaine 4% with epinephrine 1/200.000 and isolated by rubber dam. Enamel and dentine caries were removed. Teeth with an exposure less than 2 mm, surrounded by sound dentine were candidates of direct pulp capping. The cavity was washed with 0.5% NaOCl for disinfection followed by application of dry sterile cotton pellets to achieve hemostasis and remove the excess moisture. neoMTA was placed on the exposed pulp. After its mixture according to the manufacturer's instructions, the material was left to set, a light-cured glass ionomer cement was placed on top of the pulp capping material and the tooth was restored with composite resin. A periapical radiograph was taken immediately post-treatment. Patients were re-examined at 3, 6 and 12 months after treatment. The recall examination comprised a clinical and radiographic examination of the treated teeth, to assess pulp vitality. The clinical parameters used for assessment included the presence/absence of pain symptoms as reported by the child and the parent, sensitivity to percussion and palpation, fistula, swelling and mobility (not related to natural exfoliation). All radiographs were assessed for findings indicative of pulp necrosis, including the presence of pathological internal and external resorption, furcal or periapical radiolucency and disruption of lamina dura. Statistical analysis: Descriptive statistics with cross tabulations were performed.

Results: A total of 41 patients, 21 girls and 20 boys with a mean age of 7,5 years , mean age 7.1 years for girls and 7.1 years for boys and range from 4 to 11 years old participated in the study.

The total number of primary molars included in the study and treated with DPC was 47. Of them 19 were first primary molars, 28 were second, 27 lower and 20 upper, 29 right and 18 left. Class II composite resin restorations were placed in 39 teeth, while only 8 teeth were restored with a Class I restoration. Available for examination at 3,6 and 12 months were 39 teeth, since 8 patients with 8 teeth (3 first primary molars, 5 second primary molars, 4 upper, 4 lower, 2 right and 6 left)treated with DPC failed to attend the follow-up visits. The overall failure for direct pulp capping was 10.3%. With regard to the type of failure, of the 4 teeth failed, 3 appeared with swelling and 1 with a furcal radiolucency. The event of failure, for all the failed teeth, occurred within the first 6 months, post-treatment.

- **Conclusions**: Direct pulp capping in asymptomatic primary molars with a cariously exposed pulp, using neoMTA as a pulp capping material, exhibited an overall success rate of 89.7% based on clinical and/or radiographic diagnostic criteria, after a follow-up period of 12 months. The event of a failed pulp treatment was diagnosed within the first 6 months, post-treatment. Longer follow-up periods are needed to further assess the long-term clinical and radiographic effectiveness of direct pulp capping after application of the material studied.

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