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Vital Pulp Therapy: an attempt to a minimally invasive Endodontics - a review

Universidade Fernando Pessoa

Porto, 2021

I. RESUMO

A Terapia Pupar Vital compreende uma série de procedimentos que pretendem manter o tecido pupar vital e controlar a progressão da doença periapical após o avanço da cárie para a zona da câmara pulpar. O objetivo do presente estudo foi avaliar as evidências científicas da Terapia Pupar Vital em pacientes adultos com pulpite irreversível em dentes molares. A pesquisa estruturada resultou em 538 resumos, dos quais 33 estudos foram selecionados para leitura de texto completo, sendo que 3 estudos forma eleitos para discussão. Após um correto diagnóstico, sob o uso de isolamento absoluto, de desinfeção da superfície dentária e controlo da hemostasia com solução de hipoclorito de sódio, a pulpotomia seguida de aplicação direta de Agregado Trioxido Mineral ou de Biodentine™ são procedimentos alternativos ao tratamento de dentes molares permanentes com pulpite irreversível, com elevada probabilidade de sucesso, para além da enorme vantagem de manutenção da polpa radicular.

Palavras-chaves: capeamento pulpar; pulpotomia; cárie; terapia vital pulpar; endodontia regenerativa

II. ABSTRACT

Vital Pulp Therapy comprises a range of procedures that aim to maintain the pulp vitality and to control the progression of periapical disease after caries progression to the pulp chamber. The aim of present study was to evaluate the scientific evidence of the Vital Pulp Therapy in adult patients with irreversible pulpitis in molar teeth. The structured search resulted in 538 abstracts, of which 33 studies were selected for full-text reading, and 3 studies were chosen for discussion. After an adequate diagnostic, using absolute isolation, disinfection of tooth surface and hemostasis control with sodium hyploclorite solution, pulpotomy followed by direct application of Mineral Trioxide Aggregate or Biodentine™ are alternative procedures to tooth treatment in permanent molars with irreversible pulpitis, with a high probability of success and an enormous advantage of maintaining the radicular pulp, as well.

Keywords: pulp capping; pulpotomy; caries; vital pulp therapy; regenerative endodontics

III. ACKNOWLEDGMENTS

I would like to manifest my acknowledgments for the Fernando Pessoa University; the Magnificent Dean, Prof. Dr. Salvato Trigo; the Coordination of Integrated Master in Dentistry, Prof. Dr. Patrícia Manarte Monteiro and Prof. Dr. Ana Moura Teles.

It was a grateful honor to the opportunity of being supervised by Prof. Ana Moura Teles, who conducted the supervision of the present dissertation and have highlighted to the importance of a conservative (minimally invasive) approach in the management of the Endodontics treatment.

I would like to mention and to thank the constant support and encouragements from my parents, Regina and Flavio, and from my brother, Rafael, to keep my academic career path in the Dentistry Sciences in Portugal.

I would like to express my gratitude for the hospitality from the Portuguese nationals who made possible my stay in Portugal.

As well, I would like to mention my best regards and respect for the Portuguese Scientific Community.

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V. ABBREVIATION INDEX

AAE – American Association of Endodontics

ADA – American Dental Association

$Ca(OH)_2$ / CH – Calcium Hydroxide

ESE – European Society of Endodontics

DNA – Deoxyribonucleic Acid

DSPP - Dentin Sialophosphoprotein (DSPP)

LCRMGI - Light-Cured Resin-Modified Glass Ionomer Cement

M- Man

Micro-CT – Micro-Computed-Tomography

MMP-3 – Matrix Metalloproteinase-3

MTA – Mineral Trioxide Aggregate

NaOCl – Sodium Hypochlorite

PAI – Periapical Index

RCT – Root Canal Treatment

RNA – Ribonucleic Acid

RUNX2 - Runt-related Transcription Factor-2

VPT – Vital Pulp Therapy

W - Woman

YO – Years Old

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1. INTRODUCTION

Vital Pulp Therapies (VPT) aim to preserve tooth pulp vitality (Edwards *et al.*, 2021) and is a strategy aimed at maintaining the health of all or part of the pulp, in which is comprised a range of procedures such as pulp capping partial pulpotomy and full pulpotomy (Duncan *et al.*, 2019).

According to the current Glossary of Endodontic Terms of the American Association of Endodontics (AAE, 2019), pulp cap is defined as a treatment of an exposed vital pulp by sealing pulpal wound with dental materials such as calcium hydroxide or mineral trioxide aggregate (MTA) to induce reparative dentin formation, being the direct pulp cap the act of placing the dental material directly on the resultant wound of a mechanical or traumatic pulp exposure. Nevertheless, VPT also encompasses procedures such as apexogenesis, which is a procedure to encourage continued physiological development and formation of the root end, in cases of immature apex.

Hydraulic calcium disilicate cement is a potential bioactive endodontic biomaterial which may become VPT procedures more predictable (Edwards *et al.*, 2020; Edwards *et al*., 2021). As well, MTA is also an applicable endodontic cement that endows satisfactory success rate in VPT procedures (Parirokh *et al*., 2018; Torabinejad *et al.*, 2018; Eghbal *et al*., 2020).

Surveillance to the pulpal inflammatory state, aseptic management, application of suitable VPT materials and reasonable follow-up time (1 year) after VPT are key recommendations proposed in the statement of the European Society of Endodontology (ESE) for management of the exposed pulp (Duncan *et al*., 2019).

Most of the success of VPT lies in the assumption of the potential of pulp healing and the control of the inflammation and potential bacterial contamination of the exposed pulp, after the insult removal. The prediction of the inflammation state of the pulp is a hallmark to case selection and diagnostic, even though it is impossible to presume the histological condition of the pulp. Thereby, control hemorrhage and aspect of pulp are features to presume the inflammatory state and are the main driver to case selection and to predict outcomes (Edwards *et al.*, 2021).

According to the glossary of Endodontic Terms of the American Association of Endodontics (AEE, 2019), pulpotomy (pulp amputation) is the removal of the coronal portion of a vital pulp with radicular portion' remaining, which may be performed as an

emergency procedure for temporary relief of symptoms or therapeutic measure, as in the instance of a Cvek´s pulpotomy (trauma). *In continuum*, Cvek´s pulpotomy consists of the partial pulpotomy (or shallow pulpotomy) that is defined as the removal of a small portion of the vital coronal pulp to preserve radicular pulp tissues and the remaining coronal.

Based on the European Society of Endodontics (ESE) statement to the management of deep caries and the exposed pulp, extremely deep caries is defined as penetrating caries to the entire thickness of the dentine, and pulp exposure is unavoidable during operative treatment (Duncan *et al.*, 2019).

According to the current ESE statement (Duncan *et al.*, 2019), direct pulp capping is followed by the preservation of an aseptic working field and, application of a biomaterial directly onto the exposed pulp, prior to immediate placement of a permanent restoration (Figure 1) and, is indicated in two situations: pulp exposure after traumatic injury of the tooth or an iatrogenic exposure (Class I); pulp exposure instead of preoperative presence of a deep or extremely deep carious lesion with inflamed underlying pulp tissue and bacterial contamination (Class II). In Class II situation, enhanced protocol is recommended as aseptic procedure using magnification, disinfectant, and application of a hydraulic calcium silicate cement. The partial pulpotomy is defined as the removal of a small portion of coronal pulp tissue after exposure and, the full pulpotomy comprises the complete removal of the coronal pulp at the level of root canal orifice(s). In both situations, the application of a biomaterial is inserted directly onto the remaining pulp tissue or at the level of the root canal orifice(s), prior to the placement of a permanent restoration.

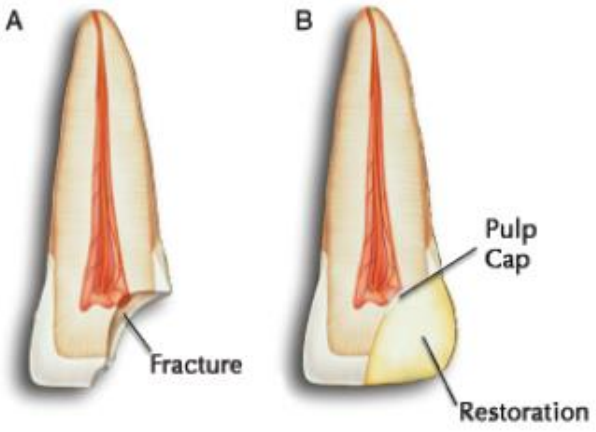

Figure 1. Illustration of the pulp cap procedure after a fracture, according to Swift *et al.* (2003)

Meanwhile, the terms “pulp cap” as reported according to AEE (2019) and “pulp capping” as stated by ESE (Duncan *et al.,* 2019) are terms that are applicable as similar along with the present manuscript and are expressed as cited by authors´ references.

This is a dissertation which has been submitted in partial fulfillment of the requirements for the Master´s Degree of Dental Medicine in the Integrated Master in Dentistry of the Fernando Pessoa University (Oporto, Portugal). The scope of present study is in the Endodontics, whereas VPT procedures has become a prospective approach to maintain pulp vitality after irreversible pulpitis in permanent teeth. Indeed, the dissertation was proposed in the Endodontics scope due to the previous background of the master’s degree candidate (Gabriel Fukunaga Kato), who was an Endodontics specialist in São Paulo (Brazil).

The aim of the present work attempts to summarize the main principles and clinical protocols around the scope of VPT for permanent teeth affected by irreversible pulpitis trough a structured comprehensive review, to establish the outcomes and driven concepts to a clinical practice based in scientific evidence.

A. Materials and Methods

The search aimed to obtain scientific evidence around VPT concept in teeth with diagnostic of irreversible pulpitis or pulp exposure during caries removal. VPT procedures were limited to direct pulp cap and pulpotomy being the filling procedure with bioactive biomaterials analyzed. Publication year was limited to the last 20 years (2001 to March 2021).

Articles submitted to the qualitative synthesis were selected to be pointed on the clinical features related to VTP, such as selection criteria, underlying complaints, hemostasis control, pulp capping material (“bioactive filling biomaterial”), type of restoration performed after VPT, reported outcome and time of follow-up.

Diagnostic procedures to determine the irreversible pulpitis diagnostic had to be clearly stated for the study to be selected. Only prospective studies which aimed to establish any outcome related to the survival outcome or another prognosis measurement were selected. Studies without explicit criteria around mature state of root formation or age selection were not included.

The screening procedure was based on the abstracts and full-text analysis of the selected papers. To avoid duplicate data, in the situation of serial publications from the same researcher group with similar methodologies, distinguished features around their methodologies were assessed to be included in present synthesis.

Experimental materials for pulp cap and scaffolds for regenerative purposes were not included.

The population of interest was adult patients with permanent teeth, complete root formation, and diagnostic of irreversible pulpitis. The intervention of interest was the insertion of a bioactive filling biomaterial after pulpotomy or in cases of direct pulp cap. The outcome of interest was the success rate (clinical and radiographic status) according to the proposed methodology.

Data were collected related to the operative procedures which descriptions must meet criteria according to the Glossary of Endodontics Terms (AEE, 2019) or based on the ESE position statement to the management of deep caries and the exposed pulp (Duncan *et al.*, 2019).

A structured search was performed with Pubmed (National Library of Medicine, Bathesda, USA), Web of Science (Clarivate, Boston, USA), Scopus (Elsevier B.V, New York, USA) database and B-on search (FCCN, Lisboa, Portugal) provided by EBSCO Host (EBSCO Industries, Inc., Birmingham, USA). Search strategy was performed with combinations of controlled terms and Boolean search commands according to the advanced search tool form each database engine.

Medline, EBSCO Host and Web of Science: (((("VITAL PULP THERAPY" OR "VITAL PULP TREATMENT" OR "PULPOTOMY" OR "PULP CAP*") AND ("PULPITIS")) AND ("HUMAN*")) NOT ("REVIEW")

Scopus: ((((("VITAL PULP THERAPY" OR "VITAL PULP TREATMENT" OR "PULPOTOMY" OR "PULP CAP*")) AND ("PULPITIS") AND ("HUMAN*") AND NOT ("REVIEW")))

The chosen engine to MEDLINE database was Pubmed. Thus, to reduce duplication findings in the EBCO Host engine, MEDLINE was not included as database supplier to the EBSCO search strategy. Database files obtained from the database were exported to Mendeley Desktop Version 1.19.8 (Mendeley Ltd., New York, USA) and references were compiled, being removed duplicated abstracts.

A total of 538 abstracts were retrieved through the engine database, being 117 abstracts from Web of Science, 109 abstracts from Scopus, 163 abstracts from Pubmed, 149 abstracts from EBSCO Host. Out of 538 retrieved abstracts, 449 abstracts were submitted to the screening selection after duplication removal.

Out of 449 abstracts analyzed after duplication removal, a total of 33 abstracts were selected to full-text analysis, whereas 3 studies were excluded as case reports (Witherspoon *et al.,* 2006; Eghbal *et al.,* 2009; Tahira et al., 2018). 4 studies were not selected due to consist of retrospective studies (Dammascke *et al.,* 2010; Mente *et al.,* 2010; Asgary e*t al.,* 2017; Linas *et al.,* 2020). 1 study was not included due to consist of an *in vitro* study (Wenjing *et al.,* 2021). 12 studies were not included due to the inclusion of teeth with reversible pulpitis diagnosis (McDougal *et al.,* 2004; Barrieshi-Nusair and Qudeimat, 2006; Simon *et al.,* 2013; Alqaderi *et al.,* 2014; Song *et al.,* 2015; Brizuela *et al.,* 2017; Kundzina *et al.,* 2017; Taha *et al.,* 2017; Parinyaprom *et al*., 2018; Suhag *et al.,* 2019; Tan *et al.,* 2020; Vishanth *et al*., 2020). 1 study (Vural *et al.,* 2017) was not included as it investigated the management of caries with indirect pulp capping. 4 studies (Nyerere *et al.,* 2006; Asgary and Eghbal, 2010; Eren *et al.,* 2018; Bagheri *et al.,* 2019) were not included as outcome measurement was pain control and dexamethasone administration were compared (Bagheri *et al.,* 2019). Despite the relevance of these 2 studies (Mente *et al.,* 2016; Sharma et al., 2020), those studies were not included as the aim was to establish matrix metalloproteinase 3 (MMP-3) concentration in pulpal blood as potential prognostic biomarker related to pulpitis. 3 studies were excluded because of age criteria that also included teenagers with permanent teeth (Asgary and Eghbal, 2010; Asgary *et al.,* 2010; Asgary and Eghbal, 2013).

Therefore, 3 studies (Taha and Khazali, 2017; Taha and Abdelkhader, 2018; Koli *et al*., 2021) met criteria and their qualitative synthesis was resumed in the Supplement File - Table 1.

2. DEVELOPMENT

Briefly, in the 3 selected studies (Taha and Khazali, 2017; Taha and Abdelkhader, 2018; Koli *et al*., 2021), Periapical Index (PAI) according to Ørstavik *et al.* (1986) was adopted as radiographic criteria to establish success outcome or as inclusion criteria related to the

pulpitis severity. Casuistic was mainly composed by permanent molar teeth of thirties adult patients.

As clinical protocol, all studies proposed cleaning teeth surface with sodium hypochlorite (NaOCl) solution before caries excavation. Pulp tissue was amputated with high-speed hand piece, in the level of the orifices (Taha and Abdelkhader, 2018; Koli *et al.*, 2021) or in the depth of 2-3mm (Taha and Khazali, 2017).

Hemostasis was proposed to be achieved with cotton-pellet moistened with 2.5% NaOCl and was pressured initially for 2 minutes. Additive pressure was proposed, ranging among 2 minutes or 3 minutes (Taha and Khazali, 2017; Taha and Abdelkhader, 2018) to 6 minutes (Koli *et al.*, 2021) and cavity was dried with dry cotton pellet before pulp capping material application. Provisional restoration and luting material were performed with light-cured resin modified glass ionomer.

The outcome results are resumed in the Supplement File - Table 2.

Koli *et al.* (2021) reported significant statistical difference of pain relief rate after 48 hours of VPT (86.7%) with ProRoot MTA® (Denstply, USA), when compared with RCT (53.7%). Taha and Abdelkhader (2018) reported pain relief on 93.8% with Biodentine™ (Septodont, France).

The highest observed success rate was observed in Taka and Abdelkhader (2018) cohort study, which Biodentine™ -VPT promoted 98% success rate and the two-reported failures had undergone to RCT and one-case had been extracted after coronal fracture.

The only selected study with 2-years of follow-up (Taha and Khazali, 2017) reported 80% of success rate with MTA-VPT. As well, Koli *et al.* (2021) reported significant statistical difference among MTA/VPT success rate (93.3%) when compared to RCT (90%), which failure occurred due to progression of the apical rarefaction (PAI >5).

3. DISCUSSION

Part of decision-tree related to differ “reversible” to “irreversible” diagnostic of pulpitis was based on clinical evidence related to the patients ‘pain complaints, such as spontaneous pain or related to response to hot and cold stimuli. The nuance among “reversible” to “irreversible” pulpitis diagnostic determinates the indication of a clinical

procedure ranging from a conservative approach such as a caries excavation to a pulp extirpation followed both to proper coronal restoration.

VPT concept assumes that, biologically, the pulp has the capacity to regenerate and repair if the insult is removed, and the inflammation is successfully managed whereas the inflammatory status of the pulp is possible to be evaluated only histologically (Edwards *et al.*, 2021).

In fact, symptoms and clinical appearance do not reflect the state of inflammation of the pulp tissue (Edwards *et al.*, 2021; Koli *et al.*, 2021). Inflammation is mainly an immunological response and a vascular response, therefore, the capacity to achieve mechanically hemostasia could be a valuable feature to presume the inflammatory state of the pulp.

Time to hemostasia control between 6 minutes (Taha and Khazali, 2017; Taha and Abdelkhader, 2018) and 8 minutes (Koli *et al*., 2021) was proposed as inclusion criteria, whereas Taha and Abdelkhader (2018) reported the exclusion of 8 teeth due to not achieved hemostasia in 6 minutes. The indication of VPT procedure do not impede further indication of RCT in case of failure, as happened in the reported studies (Taha and Khazali, 2017; Taha and Abdelkhader, 2018; Koli *et al*., 2021).

The application of NaOCl solution prior the caries excavation and during hemostasia acts a sanitizing, reducing the bacteria activity in the coronal portion of the tooth. Therefore, MTA and hydraulic silicate are bioactive materials (Careddu and Duncan, 2018) which can favor bridge dentin formation and to seal the pulp wound.

Asgary and Parhizkar (2021) stated VPT is at the core management in the conservation of healthy pulpal tissue in extremely deep caries and carious pulp exposures, whereas achievement of hemostasis is referred to as a constituent in reaching successful outcome of VTP and time needed for hemostasis has been considered as an essential indicator. However, “time to stop bleeding” may not be an important factor in distinguishing irreversible from reversible pulpitis. On the contrary, high blood flow could be regarded as a sign indicating immense pulpal blood supply and may be a requirement to the pulp vitality and repair/regeneration. Thus, Asgary and Parhizkar (2021) pondered duration/intensity of bleeding, application of different biomaterials/other hemostatic agents as factors which should be investigated further in well-designed randomized clinical trials with an adequate casuistic and long-term follow-up time.

A successful VPT procedure lies on an accurate diagnosis and a premature treatment that interrupts caries progression. In case of VPT success, the teeth remain vital, with normal pulpal response and biological activity (immune and proliferative) (Edwards *et al.*, 2021; Koli *et al.,* 2021).

As a convenience criterion, literature review was established within the temporal period of 20 years. To the best of our knowledge, the term VPT was first reported by Swift *et al.* (2003), in which direct pulp capping, partial pulpotomy, and full pulpotomy were comprised in this VPT "umbrella term".

Ørstavik *et al.* (1986) established a periapical index (PAI) which is ranged from 1 (healthy) to 5 (severe periodontitis with exacerbating features). Taha and Abdelkhader (2018) and Koli *et al.* (2021) admitted as success outcome PAI between 1 or 2, whereas Taha and Abdekhader (2018) also accepted as success outcome the lesion reduction. Taha and Khazali (2017) admitted as success outcome PAI values lower than 3.

PAI Index (Ørstavik *et al.*, 1986) is a radiographical assessment criteria whereas prognosis and outcomes related to the non-surgical endodontic treatment is also established with radiographic and clinical evaluation, as the Strindberg criteria (Strindberg, 1956) which comprised both radiographic and success clinical outcome. Recently, the position paper from ESE related to the outcome measures and effectiveness of endodontic treatment (Duncan *et al.*, 2021) stated as a classic outcome to VPT and pulpectomy the prevention of apical periodontitis (by lack of emerging radiolucency on periapical radiograph) after at least one year, whereas patient-related outcomes measures such as absence of pain, medication, swelling could be completed at shorter follow-up periods of one to two weeks. Cushley *et al.* (2021) established a systematic review and meta-analysis around the efficacy of direct pulp capping for the management of carious exposed pulps in permanent teeth in which success was defined as the absence of signs and symptoms of irreversible pulpitis, apical periodontitis, or loss of pulp vitality. Hence, direct pulp capping with MTA and Biodentine™ (Septodont, France) described success rate and higher long-term outcomes than calcium hydroxide (Cushley *et al.*, 2021).

In continuum, most of the minimally invasive operative procedure to pulpotomy was concepted as described initially by Cvek (1978). Pulp capping had been proposed and had been discussed as an attempt to promote recalcification of dentine and to protect the pulp since 1878 (Barrett, 1878). Historically, cauterization of underlying tissue with irritating materials such as creosote or carbolic acid (Barrett, 1878; Beebee, 1885) had been also

proposed as a pulp capping procedure due to cessation of temperature conduction into the pulp (Bebee, 1884). (Figure 2)

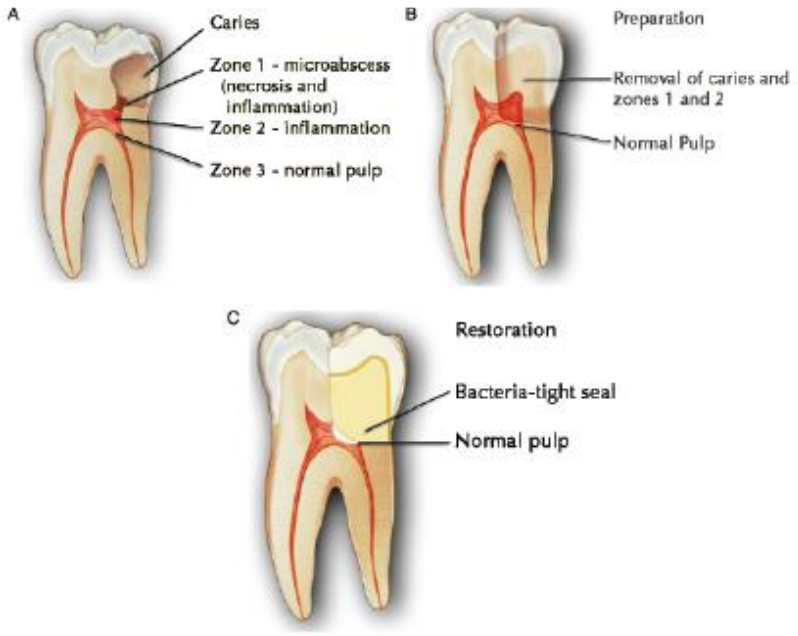

Figure 2. Diagram of carious pulpal exposure and pulp cap procedure. Extracted from Swift *et al.* (2003). (A) Diagram of carious pulpal exposure. The pulp contains a microabscess (necrosis and infection) and a zone of inflammation overlying normal tissue. (B) Preparation involves the removal of the abscessed and inflamed pulpal tissue. (C) The pulp is capped.

Likewise, formocresol was widely applicable for pulpotomies in primary teeth, which a zone of fixed tissue could be evident if formocresol would be applicable in direct contact to the underlying pulp tissue (Chandrashekhar and Shashidhar, 2014). The major concern about formocresol is the exposure to formaldehyde, which is an extremely reactive chemical that interacts with protein, deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) that has the potential to carcinogenic activity (Athanassiadis *et al.,* 2015).

Formocresol is reported with strong a recommendation and moderate-quality evidence according to a panel of experts from the American Dental Association (ADA) as a direct pulp cap material in primary teeth with deep caries lesion as VPT procedure, as well, the MTA material (Dhar *et al.*, 2017) basing on the meta-analysis of Coll *et al.* (2017) that reported higher success rate to MTA and formocresol as direct pulp cap material in primary teeth. Formocresol is an inexpensive, quick, and effective dental material for the acute pain management; however, it is potentially harmful to the patient during the

pulpotomy procedure. Therefore, MTA is strongly recommended as a first-choice material to the direct pulp cap (Bloks, 2009).

Borgen and Ricucci (2020) reported a 20-years of follow-up on a MTA apexification in a traumatized maxillary left central incisior (#21) of a seven-year-old male with swelling and suppuration that, periapical healing and normal tooth function was evident after 20-year review.

In fact, recently, new agents such as MTA and tri-calcium silicate encompass the regenerative endodontics approaches to the pulp regeneration (Bloks, 2009; Simon and Smith, 2014; Kim *et al.*, 2016; Careddu and Duncan, 2018; Elmsmari *et al,* 2019; Li *et al.*, 2019; Cushley *et al.,* 2021). MTA and Biodentine™ (Septodont, France) were described as bioactive dental cements which were capable to induce reparative dentin formation as observed with micro-Computed-Tomography (micro-CT) in histological sections with hematoxylin-eosin (HE) staining of extracted rat molar teeth (Kim *et al.*, 2016).

A systematic review proposed by Pedano *et al.* (2020) pointed the excellent biocompatibility *in vitro* and *in vivo* when tested on human cells and teeth. Comparatively, the quality synthesis of *in vitro* studies suggested resin-free hydraulic calcium-silicate cements, such as Biodentine™ (Septodont, France), described better results related to cell viability and bioactivity towards human dental pulp cells when compared with resin-based calcium silicate cements, such as Theracal® (Bisco, USA).

Resin-modified calcium silicate, such as Theracal PT® (Bisco, USA), is a new dual-cured dental cement indicated to the pulpotomy treatment aiming at pulp vitality. Primary cell culture with human dental pulp stem cells from third molars presented *in vitro* cytocompatibility and bioactive proprieties, due to the upregulation of Dentin Sialophosphoprotein (DSPP) and Runt-related Transcription Factor-2 (RUNX2) gene expression assay and mineralized nodule formation (Rodríguez-Lozano *et al.,* 2021).

The restorability of pulp capping teeth after pulpotomy is a concern for the adhesive proprieties of the pulp capping materials, that the development of new resin-modified calcium silicate cement may favor the possibility of direct restauration immediately to the pulp capping procedure with adequate adhesive properties. Taha and Khazali (2017) reported definitive restauration with amalgam or composite after 1 week of MTA application, followed by the substitution of zinc oxide paste (IRM®; Dentsply, USA) to

light-cured resin modified glass imonomer (LCRMGI; Vitremer®, 3M,. USA) as a liner and further restauration with amalgam or composite. On the other hand, Taha and Abdelkhader (2018) reported direct filling with LCRMGI (Vitremer®, 3M,. USA) onto the layer of Biodentine™ (Septodont, France) followed by composite or amalgam as definitive restoration. Meanwhile, Biodentine™ (Septodont, France) described better adhesive performance on shear bond strength assay when compared with MTA materials (Palma *et al.*, 2018).

Calcium hydroxide ($Ca(OH)_2$) is a pioneer regenerative material which stimulates tissue repair after pulp exposure and was used for several years before (Zander, 1939; Swift *et al.*, 2003; Taha and Khazali, 2017; Li *et al.*, 2019; Cushley *et al.*, 2021) as the recommendation mentioned just above.

For instance, as described by Zander (1939), after the extraction of primary teeth, histological sections reveled dentin bridge formation near to the pulp tissue whom observed, during 2 years, pulpotomies in primary teeth which were performed with bleeding control by the application of sterile cotton pellets soaked in a saturated solution of $Ca(OH)_2$, followed by the application of $Ca(OH)_2$ paste to cover the ends of the root pulps, and a thin coat of paraffin covering the cement.

Therefore, Cushley *et al.* (2021) reported a success rate of MTA ranging, from 91% (6-months follow-up) to 86% (1 year follow-up), 84% (2 years or 3 years follow-up) and 81% (4 years or 5 years follow-up), whereas to the Biodentine™ it was assessed a success rate from 96% (6 months follow-up) to 86% at 1 year, 2 years, or 3 years of follow-up. Calcium hydroxide success rate was 74% at 6-months, 65% at 1 year, 59% at 2 years or 3 years, 56% at 4 years or 5 years of follow up. The meta-analysis established as random effects established MTA had better success than calcium hydroxide at 1-year (OR=2.66, 95% CI 1.46-4.84, $p< 0.01$) and 2- to 3-year follow-up (OR=2.21, 95% CI 1.42–3.44, $p<0.001$), whereas it was not observed statistical difference between MTA and Biodentine™ around the success rate.

Wolters *et al.* (2017) positioned less invasive alternative strategies to treat pulpitis could increase the success of Endodontic procedures, whereas new insights in pulp biology have been gained and would provide options for the development of new biologically driven treatment protocols. Therefore, pulp tissue should be preserved, and physiological and defensive functions would be maintained, whereas biological immune response from the

preserved pulp would control the infection onto the apical area. Moreover, while less hard tissue would be removed, tooth weakening would be minimized.

Swift *et al*. (2003) proposed pulpotomy and direct pulp capping after caries excavation as a VTP procedures in mature permanent teeth with simple restorative needs and without signs of inflamed pulp, as with carious pulp exposure. Direct pulp capping referred to the placement of a material such as calcium hydroxide or a resin adhesive directly onto an exposed pulp, which would be indicated after traumatic exposures or mechanical non-carious exposures during cavity preparation within 24 hours. *In continuum*, partial pulpotomy (or Cvek´s pulpotomy) would be defined as the removal of inflamed pulp tissue to the level of health coronal pulp with a sterile diamond rotating at high speed under copious water spray to surgically excise inflamed pulp tissue. Partial pulpotomy would be indicated as an alternative to direct pulp capping, instead of an extended pulpal inflammation is expected. In the other hand, full pulpotomy involves removal of the entire coronal pulp to the level of the root canal orifice(s). Theoretically, if the inflamed tissue is removed, the biological insult to the pulp tissue is removed and, the underlying tissue is more likely to remain healthy and to seal the exposure with hard tissue bridging of the exposure site.

Swift *et al.* (2003) had also described the removal of excess blood by rising with sterile saline or anesthetic solution and dry with a sterile cotton pellet, as well, sodium hypochlorite or chlorhexidine can be used to facilitate hemostasis. The formation of a blood clot should be avoided and may compromise prognosis. If the pulp wound is large enough as 1-2mm loss of tissue through necrosis, calcium hydroxide liner should be accommodated in the wound cavity.

According to the current Glossary of Endodontic Terms of the American Association of Endodontics (AAE, 2019), pulp cap is defined as a treatment of an exposed vital pulp by sealing pulpal wound with dental materials such as calcium hydroxide or mineral trioxide aggregate to induce reparative dentin formation, being the direct pulp cap the act of placing the dental material directly on the resultant wound of a mechanical or traumatic pulp exposure (AAE, 2019).

Methodologically, pulp capping is a MeSH term indexed since 1965 and is defined as "application of a protective agent to an exposed pulp (direct capping) or the remaining thin layer of dentin over a nearly exposed pulp (indirect capping) to allow the pulp to recover and maintain its normal vitality and function" ("Dental Pulp Capping" MeSH

Descriptor Data 2021). Despite the fact “pulp capping” would be not adequate to define the application of the bioactive biomaterials after pulpotomy, the present structured search included the “pulp capping” term as strategy to retrieve related studies to VPT concept.

Briefly, VPT aim at preserving and maintaining pulp tissue that has been compromised by trauma, caries, or restorative procedure in a healthy state (AEE, 2019). These therapies may be an alternative for root canal treatment (RCT) to attempt a conservative approach in permanent teeth after pulp exposure.

Whereas the main goal on RCT is to control the apical lesion progression and to achieve periapical healing with normal periodontal ligament space around the root (Duncan *et al.*, 2021), conceptually, VPT aim to maintain pulp vitality (Duncan *et al.,* 2019; Cushley *et al.*, 2021; Duncan *et al.,* 2021), as well, its capacity to immune response to caries (Hahn and Liwehr, 2007) and repair (Ricucci *et al.,* 2014).

Meta-regression of Elmsmari *et al.* (2019) established the preoperative status as prognostic factor, which the presumptive diagnostic of irreversible pulpitis resulted in worse results. Included studies was related to partial pulpotomies followed by calcium hydroxide or MTA application in which a success rate of 92% (CI: 0.83-0.97) for cariously exposed pulp of permanent teeth was estimated after 2-years of follow-up.

Recently, Li *et al.* (2019) assessed in a meta-analysis the effectiveness of pulpotomy materials such as MTA or calcium hydroxide in permanent teeth with carious pulp exposures; their results favored an interpretation of a better overall success at 24 months for the MTA option.

In summary, VPT is a suitable clinical approach to the management of irreversible pulpitis, whether local infection had not progressed to the periapex. A reasonable diagnostic procedure is necessary to indicate VPT, with evaluation of the absence of sinus tract, swelling, positive pulpal response to cold stimuli and without apical rarefaction detected in periapical radiographies. Absolute isolation with rubber dam is mandatory, as well, disinfection of caries cavity with NaOCl solution previously to the caries excavation. After pulpal exposure and pulpotomy, application of 2.5% NaOCl solution with a cotton pellet or flushing is indicated to hemostasis control. MTA or hydraulic calcium disilicate (Biodentine™, Septodont, France) are suitable bioactive filling materials to the pulp capping. Restoration with light-cured resin modified glass ionomer

(LCRMGI) as liner and further restored with resin or amalgam (definitive restoration) was preconized. Surveillance and clinical follow-up are mandatory and must be established during 1-year (Duncan *et al.,* 2019). A success rate was observed ranging from 85% with MTA after 2-years of follow-up (Taha and Khazali, 2017) to 98% of success rate with Biodentine™ (Septodont, France) as reported by Taha and Abdelkhader (2018) after 1-year of follow-up, whereas Koli *et al.* (2021) reported a success rate of 93.3%with MTA after 1-year of follow-up.

4. CONCLUSIONS

In conclusion, VPT is a reasonable protocol to the management of deep caries with diagnostic of irreversible pulpitis as was proposed. A success rate between 85% with MTA to 98% with Biodentine™ was reported.

Moreover, this is a minimally invasive approach which permits a biological-driven response to the pulp repair and to maintain pulp vitality, immunological and proliferative response.

Controlling contamination with sodium hypochlorite solution, as well, flushing or pressuring a cotton pellet to the bleeding control (hemostasis control) followed to the application of MTA or hydraulic calcium disilicate onto the pulpal chamber are suitable procedures to the VPT approach.

Adequate coronal restoration, both interim and definitively, is mandatory, as well, 1-year clinical surveillance. Meanwhile, root canal treatment could be indicated in case of unsuccess with periapical rarefaction progression and septic manifestation, as well.

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VI. Supplements:

Table 1: Qualitative synthesis of selected studies

	Koli *et al.* (2021)	Taha and Abdelkhader (2018)	Taha and Khazali (2017)
Type of study	Prospective study	Prospective study	Prospective study, randomized clinical trials
Casuistic	60 mandibular molar teeth. Age ranging 18-35YO	64 molar teeth 52 patients Average age 32.2YO	50 patients (27W, 23M) 50 molar teeth (15 first upper molar, 35 lower molar teeth) Mean age = 30.3±9.6YO
Inclusion criteria	Irreversible pulpitis Positive pulpal response without the use of antibiotic (past 1 month) or analgesic (past 3 days). Hemostasis within 8 min	Irreversible pulpitis, without swelling, sinus tract or apical rarefaction. Hemostasis achieved within 6 min	Irreversible pulpitis, positive pulpal response to cold test. >20YO with complete root formation. Hemostasis achieved within 6 min
Therapeutics	30 teeth: RCT 30 teeth: MTA	64 teeth: Biodentine™ (Septodont, France)	23 teeth: MTA 27 teeth: CH
Protocol of the full pulpotomy	Rubber dam. 2.5% NaClO (before caries excavation) High-speed diamond burr in the level of the orifices	Pain level assessed previously Rubber dam 5% NaClO before carie excavation. High speed sterile round bur, pulp tissue amputated to the level of canal orifices	Rubber dam 5% NaClO before caries excavation. High speed sterile round bur to pulp tissue amputation in depth 2-3mm
Hemostasis	Application of cotton pellet moistened with 2.5% NaClO pressured for 2 min + 6 min, followed by dry cotton pellet soaking	Pulp wound flushed 2.5% NaClO, cotton pallet soaked during 2 or 3 min, plus 2 or 3 min	Pulp wound flushed 2.5% NaClO, cotton pallet soaked during 2 or 3 min, plus 2 or 3 min
Restoration	LCRMGI Fuji II LC (GC Corp)	LCRMGI Vitremer® (3M) as liner, followed by composite or amalgam	CH group: LCRMGI Vitremer® (3M) directly MTA group: Zinc oxide paste IRM ®(Dentsply); after 1 week, substituted by Vitremer® (3M) Definitive restoration with resin or amalgam, after 1 week
Follow-up	Call (24h, 48h, 72h). Clinical/radiological evaluation after 6 months, 1 year and 2 years	Post-treatment pain assessed after 2 days Clinical/radiological evaluation after 6 months and 1 year	6 months, 1 year, 2 year Positive response to cold test, no pain or discomfort on chewing or eating, no tenderness to percussion or palpation, soft tissue around the tooth with normal aspect, no swelling or sinus tract
Success outcome	PAI < 2	PAI between 1 or 2, or reduction	First days of post-operatory without pain PAI < 3

Footnotes: CH - Calcium Hydroxide; LCRMGI: Light-Cured Resin Modified Glass Ionomer; M – man; MTA – Mineral Trioxide Aggregate; PAI - Periapical Index, according to Ørstavik *et al* (1986); RCT – Root Canal Treatment, W – woman; YO - Years-Old.

VI. SUPPLEMENTS

Table 2: Outcome results

	Koli et al (2021)	Taha and Abdelkhader (2018)	Taha and Khazali (2017)
Pain relief	48h: VPT 86.7% RCT 53.7% (p<.05) 72h: VPT 100% 90% RCT (p >.05)	48h: 93.8%	Rate not established. 4 patients reported pain after 3 months (RCT indicated) and was excluded
Final restoration	VPT: LCRMGI (Fuji II LC; GC Dental) RCT: Composite Tetric E-Ceram Bulk Fill (Ivoclar-Vivadent)	Composite Z250 (3M, ESPE) or amalgam 43 teeth with amalgam, 23 teeth with composite. Two- and three-wall restorations were advised to indirect restoration with cusp coverage	Amalgam in 22 teeth Composite in 27 teeth
Excluded cases and follow-up	100% recall rate	4 patients lost to follow-up 16 excluded teeth: 3 teeth without pulp bleeding; 4 necrotic pulp; 9 teeth without hemostasis after 6 min	3 patients lost to follow-up 4 patients reported pain after 3 months (RCT indication) 4 teeth with negative pulpal vitality and periapical rarefaction 1-year follow-up: 32 out 37 patients recalled 2-year follow-up: 36 out 36 patients recalled
Reported outcomes	Asymptomatic 5 non-healed teeth: 3 RCT, 2 VPT PAI >5, periapical radiolucency, and loss of coronal restoration	50 out 64 teeth (78%): Hemostasis within 4 min 9 cases with preoperative periapical rarefaction: 7 healed,1 lost of follow-up, 1 unchanged, 1 RCT	2-year follow-up: 4 failed cases related to CH group; 3 patients with history of severe pain (RCT initiated), 1 patient with fractured tooth (extracted) Not observed obvious discoloration of the crowns
Success rate	VPT: 28/30 (93.3%) RCT: 27/30 (90%) (p >.05) 1-year follow-up	98% success rate 2 failures: 1 submitted to RCT, 1 extracted due to fracture 1-year follow-up	2-year of follow-up: MTA: 85% success rate (22 out 26 teeth) CH: 43% (10 out 23 teeth)

Footnotes: CH – (calcium Hidroxide); LCRMGI - Light-Cured-Resin-Modified-Glass-Ionomer-Cement; MTA - Mineral Trioxide Aggregate); RCT - Root Canal Treatment; VPT - Vital Pulp Therapy.