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A Holistic Approach to Vital Pulp Treatment Using Bioactive Materials: Review of Literature

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Abstract

Pulpal inflammation resulting from untreated dental caries remains one of the most common conditions worldwide, affecting adults and children alike. Different modalities have been used to diagnose and treat the inflamed vital dental pulp. However, dental professionals have long faced challenges in accurately diagnosing the degree of pulpal affection and of providing a definitive treatment that keeps the pulp vital. The purpose of this literature review is to shed light on recent modalities in diagnosis, challenges of vital pulp treatment and outcome measurement of treating pulpitis. Patient-oriented factors as well as operator-oriented factors should guide researchers in defining a core outcome measurement set for endodontic procedures, and should guide clinicians along with cost and time factors in treating pulpitis.

Keywords: Reversible pulpitis, irreversible pulpitis, pulpotomy, bioceramic, biological, patient-centered

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1. Introduction

Oral diseases are the most widespread conditions worldwide. They have remained the most dominant among conditions and diseases affecting humanity since 1990, when the first data on oral disease was published in the Global Burden of Disease dataset [1]. Among the oral diseases, dental caries affects more than one third of the world's population and remains the most widespread noncommunicable disease and a major disease burden for populations and governments.

2. The Challenge of Diagnosis

Untreated dental decay can affect the pulp in varying degrees and dentists have long found diagnosing and treating pulpal conditions challenging. There are several diagnostic aids available to allow for a differential diagnosis of pulpal disease due to caries [2]. However, systematic reviews have pointed to critical gaps in knowledge concerning the effect of diagnostic tests commonly used to determine the pulpal condition [3]. Preoperative as well as intraoperative

diagnostic criteria remain unable to give a definitive prognosis of different pulp therapy treatments [4-5]. Although the history of presence or absence of pain may not be reliable in the differential diagnosis of the condition of the pulp, the history of pain should be the first consideration in selection of teeth for vital pulp therapy [6-7]. Pain coinciding with or immediately after a meal may not indicate extensive pulp inflammation but can rather be due to food accumulation within a carious lesion, pressure or chemical irritation to a vital pulp protected by a thin layer of intact dentin.

A severe toothache at night is usually a sign of extensive pulp degeneration and calls for more than conservative pulp therapy [8]. The American Association of Endodontists (AAE)'s classical distinction of pulpitis as "reversible" where pain symptoms are transient and do not linger, or "irreversible" where they are persistent or spontaneous is a useful aid and is widely used clinically [6]. The AAPD further categorizes teeth with reversible pulp inflammation as candidates for vital pulp treatment (VPT) [9]. However, this clinical distinction does not always match the histological status of the pulp or its ability to maintain vitality after treatment [10]. Few authors have suggested the need to reconsider how pulpitis is classified clinically, considering our improved understanding of the pulp biology and the importance of preserving the vital pulp [4,11]. Wolters et al., proposed a classification of "mild pulpitis", with a heightened and lengthened response to cold testing but no spontaneous symptoms, "moderate pulpitis" with prolonged and occasionally spontaneous symptoms, and "severe pulpitis" where there is clear spontaneous pain and prolonged pain to warm and cold, with possible pain to percussion and lying down [11]. They also expanded the classification of pulpitis and included patient symptoms in addition to possible histologic picture and related them to different VPT modalities. A gingival abscess or draining fistula associated with a tooth with a deep carious lesion is a clinical sign of an irreversibly diseased pulp and infection which can only be resolved by eradication of infection through successful extensive pulp therapy or tooth extraction. Abnormal tooth mobility is another clinical sign of a severely diseased pulp. During assessment of mobility of a mobile tooth, minimal or complete absence of pain during manipulation of the tooth denotes a more advanced and chronic degenerative condition of the pulp. In primary teeth, this pathologic mobility is to be distinguished from physiological mobility near exfoliation [8]. Sensitivity to percussion or pressure and pain on palpation of the vestibule near a deep carious lesion are clinical symptoms suggestive of a more acute inflammatory stage during the degenerative process of the pulp, i.e. degenerative pulp disease with inflammatory involvement of the periodontal ligament [8]. Radiographic examination with a periapical film is unable to accurately determine the proximity of a carious lesion to the pulp [12]. Nevertheless, preoperative radiographic assessment can aid in evaluation of the restorability of the tooth by assessing remaining tooth structure, bone level and root resorption [13]. Evidence of periradicular or periapical radiolucency or widening of the periodontal ligament space precludes VPT [8-9].

3. Diagnosis Towards Accurate Determination of Pulp Condition

A more accurate determination of pulpal inflammation is said to be possible through specific pulpal biomarkers, which objectively measure the level of inflammation in the pulp, whilst preserving pulp vitality, maintaining the integrity of the tooth and directing treatment choice. As with any inflammatory process in the body, molecular mediators are involved in the suppression and progression of the inflammatory response of the dental pulp. These mediators are found to be secreted via dentinal tubules into the gingival crevicular fluid (GCF) [5]. Studies have reported the availability of different biomarkers in the GCF including cytokines, proteases, elastase, neuropeptides, and growth factors [14-15]. These molecular mediators derived from the pulp in various stages of disease can be useful to establish an accurate pulp diagnosis in clinical situations. The difference in expression of biomarkers such as interleukin-8, matrix metalloproteinase 9, tumor necrosis factor-α, and receptor for advanced glycation end products expression may help distinguishing between reversible and irreversible pulpitis. Proactive identification of pulpal disease and the measurement of the ability of the pulp to recover from inflammation, could aid in treatment decisions prior to performing invasive procedures of pulpally affected teeth. These chairside measures of inflammation have been also shown to have the potential to predict the outcome of VPT [5].

4. The Challenge of Treatment

As with diagnosis, the treatment of a deep carious lesion remains a challenge for clinicians with different techniques and procedures being suggested and extensively researched. The most recent trend is to treat caries affected teeth in the most conservative way. This concept is not limited to initial non-cavitated carious lesions but extends to cover all the spectrum of managing a carious tooth from incipient caries up to deep caries, pulpal affection, and even pulpal necrosis. VPT options are collectively strategies aimed at maintaining the health of all or part of the pulp [6]. Stepwise caries removal, selective caries removal, indirect pulp capping are conservative approaches to deal with a deep carious lesion approximating the pulp in an attempt to delay or avoid pulp exposure in the restorative cycle of the tooth [16]. However, if a carious exposure occurs during caries excavation or the patient reports history of pain of the affected tooth, capping of the exposed pulp directly has not provided good results consistently [8]. Therefore, a vital carious pulp exposure in a tooth usually requires a more exploratory pulpotomy procedure in an attempt to assess the pulpal condition before restoration of the tooth [17]. Pulpotomy entails the removal of coronal pulp tissue and maintenance of radicular pulp, as a more conservative alternative to complete pulp tissue removal or extracting the tooth. This treatment option is accepted in treating both primary and permanent teeth with carious pulp exposure. [3,18]. The justification of the procedure is that the coronal pulp tissue adjacent to the carious exposure usually contains microorganisms and shows evidence of inflammation and degenerative changes. Removal of this abnormal tissue allows healing to occur at the entrance of the radicular canal in an area of normal pulp [3]. This makes proper tooth selection and assessment of the condition of the pulp critical in the success of a vital pulpotomy procedure. The size of the carious exposure, appearance of the pulp, and amount of bleeding are of primordial importance in diagnosing the condition of the pulp. A true carious exposure – as opposed to a traumatic

exposure - will be accompanied by pulpal inflammation, the degree of which is usually directly related to the size of the pulp exposure. Histological evidence of fragments of necrotic dentin introduced into the pulp during caries excavation illicit an inflammatory response in pulpal tissue [19]. Assessment of the health of the exposed dental pulp is difficult to determine and there is a consensus that pulpal hemorrhage can be used as an indicator of the extent of pulpal disease [4].

Advanced pulp degeneration is often associated with a watery exudate, necrotic tissue, or pus at the exposure site and calls for nonvital pulp therapy or extraction. The presence of pulpal bleeding at the exposure site, however, is not a definitive indication of a vital pulp [20]. Furthermore, excessive hemorrhage at the exposure site or oozing of blood from a canal after complete coronal pulp amputation is an indication of pulpal hyperemia and a generalized pulpal inflammation extending into the radicular portion of the pulp, traditionally necessitating a pulpectomy procedure or extraction [9]. Another indication of pulpal hyperemia and inflammation is pain during caries removal and instrumentation despite correct anesthetic technique [21]. Additionally, pulpotomy has been proposed to treat curiously exposed pulps in teeth with symptoms suggestive of irreversible pulpitis. This conservative approach to managing irreversible pulpitis with the removal of part or all the coronal pulp tissue is said to eliminate the inflamed and potentially necrotizing tissue, and by using a calcium silicate-based cement is likely to induce a predictable hard tissue barrier by utilizing the innate reparative mechanisms of the pulp itself [2,24]. If long-term results remain the same, pulpotomy can be proposed as an alternative treatment modality for curiously exposed pulp tissue presenting with signs of symptomatic irreversible pulpitis even in mature teeth [3,25].

5. Treatment Towards MID and Regenerative Procedures

Invasive VPT techniques include direct pulp capping, partial pulpotomy, coronal pulpotomy or root canal treatment. These involve the amputation of inflamed pulp tissue, control of bleeding and placement of a capping material over the remaining pulp, or removing the pulp tissue entirely and filling the canals rendering the tooth pulp-less. This is usually completed during a single visit under local anesthesia and proper isolation of the tooth. Ideally, rubber dam isolation is indicated to keep the area clean and minimize bacterial contamination of the pulp tissue on exposure. Additionally, all peripheral carious tissue should be removed before excavation is begun on the portion of the carious dentin most likely to result in pulp exposure. This will ensure that most of the bacterially infected tissue is removed before actual pulp exposure occurs [8]. The prognosis after any type of pulp therapy usually improves in the absence of microbial contamination. Thus, biocompatible neutralization of any existing pulpal contamination and prevention of future contamination through microleakage are important goals in VPT. This is because vital pulp tissue can recover spontaneously from various insults when a favorable environment is provided. Even more desirable are treatment materials in direct contact with the pulp that inherently promote, stimulate, or accelerate a true tissue healing response [8].

6. Pulp capping materials towards biological approaches

Recently, trends for biological tissue regeneration have been rising. Regenerative endodontic procedures have been described as a paradigm shift in the treatment of pulpally involved teeth, owing to their ability to allow pulpal healing, root maturation with subsequent enhancement of the tooth's fracture resistance in addition to the potential for regeneration of vital tissues [26]. Concomitantly, minimally invasive dentistry is another rising concept with the main concern of preservation of tooth structure. Stemming from their potential to preserve the original tooth structure in optimal function, both regenerative and minimally invasive endodontics could be considered as two revolutionary sciences with one common goal [26]. Achieving this goal would entail the medical and dental professionals to use bioactive, biomimetic materials, and not merely biocompatible materials, to regenerate biological tissues for optimal function of the human body. Hence, the purpose of using biomimetic concepts and protocols is to conserve tooth structure and vitality in all treatment stages, increase the longevity of restorative dental treatments, and eliminate future retreatment cycles [16,27]. Materials exhibiting bioactive and regenerative potential are being studied for the purpose of preserving vitality of the radicular pulp with promising results. These include bio-ceramics, osteogenic protein, bone morphogenic protein, freeze-dried bone, bioactive glass, platelet rich plasma, enamel matrix derivative gel, nanohydroxyapatite paste and collagen particles impregnated in antibiotics [27,28]. Biomimetic dental materials are inherently biocompatible materials with excellent physico-chemical properties. This applies to calcium silicate-based materials, the bioceramics, which are suitable for biomedical and dental use [27]. Calcium silicate-based materials used in pulp therapy are classified by Kombayashi et al., into hydraulic cements, MTA and its derivatives, and resin modified MTA cement, TheraCal LC [29]. With both antimicrobial and sealing properties, bioceramic materials are one of the few dental materials available that contribute to both the disinfection and filling phases critical for success of pulp therapy and endodontic treatment [30]. MTA, and its derivatives Biodentine™ and other novel bioceramic materials have been used to promote pulp regeneration, root end closure and dentin bridge formation with promising results [31]. Investigations of the interaction between human inflammatory monocytes with human regenerative fibroblasts after exposure to different calcium silicate-based materials showed that calcium silicate-based materials modulate the monocyte inflammatory response, which subsequently induce differential effects on the recipient fibroblasts promoting hard tissue formation [32]. Over the years, clinical experience has revealed some disadvantages of MTA including discoloration potential, presence of toxic elements in the material composition, difficult handling characteristics, long setting time, high material cost, an absence of a known solvent for the material, and the difficulty of its removal after setting [33-36]. To overcome some of MTA's limitations, manufacturers attempted modifying the original Portland cement by addition of setting accelerators, removal of agents responsible for discoloration, and improving handling properties while preserving the known advantages [37]. Modified MTAs and MTA-like materials (Bioaggregate, Biodentine™, EndoSequence® BC RRM™, Totalfill® BC RRM™) as well as resin modified MTA (Theracal LC and Theracal PT) were introduced. A light

curable resin-modified calcium silicate, TheraCal LC (BISCO Dental Products, USA), commonly referred to as "light curable MTA" was introduced [38].

However, since the setting reaction depends on polymerization of the resin component, this material is excluded from the classification of hygroscopic dental cements that encompasses MTA as well as cements based on bioceramics, calcium silicate, or calcium sulfate [39]. TheraCal LC's significant calcium release has been shown to create an alkaline sustained environment promoting dentin-pulp complex healing and regeneration [40]. It was advocated for use over primary pulp stumps due to its short setting time and easier handling compared to MTA, which are important considerations in the pediatric population [41]. Clinical, radiographic and histological investigations of Theracal LC's potential effectiveness as a pulpotomy dressing in primary teeth showed a short-term success rate similar to formocresol over a 6 months period as reported by Wassel et al. [41]. However, TheraCal LC was found to induce an extensive pulp inflammatory reaction which was attributed to the acrylic monomer Bis-GMA present in the material and hence authors advised against the use of resin-containing TheraCal LC in direct contact with the pulp [42]. Later TheraCal PT, a dual-cured version of its predecessor, was marketed to overcome the potential adverse effects of residual unpolymerized monomers. According to Wassel et al., indirect pulp capping, direct pulp capping and pulpotomy on primary molars using TheraCal PT demonstrated acceptable 1-year results, while partial pulpotomy was associated with poor treatment outcomes [43]. The authors attributed this to the importance of clinical predictors and case selection when using Theracal PT. Biodentine™, a resin-free tricalcium silicate cement released by Septodont, France in 2009, was designed as a dentin replacement material, that is highly biocompatible and bioactive, having endodontic indications similar to those of MTA in addition to restorative indications. It was extensively studied regarding its ability to overcome the major drawbacks of MTA and was shown to exhibit a short initial setting time of 12 minutes, superior flexural strength and good sealing ability [33]. However, since the mixing and handling characteristics of the powder/liquid systems, such as MTA and Biodentine™, are technique sensitive, produce considerable waste and are time consuming [44]. A solution was the introduction of the premixed bioceramics, available to endodontists since 2008 from Brasseler USA as EndoSequence® BC RRM™ series and, since 2013, by FKG Dentaire, Switzerland as TotalFill® BC RRM™ Paste, Putty and Fast Set Putty [30]. NeoPUTTY®, initially released by Avalon Biomed™ and acquired by NuSmile® in 2016, is another premixed bioceramic material available in the market [45]. Premixed bioceramics present hydrophilic properties, using pulpal moisture to complete the setting reaction and were shown to set contraction free [46]. It has been proposed that they form hydroxyapatite when in contact with moisture, and ultimately form a bond between dentin and the filling material creating an impervious seal allowing for tissue healing [30]. Contrary to MTA and Biodentine™, premixed bioceramics were shown to possess desirable clinical properties that exemplify the benefits of premixed bioceramics in terms of treatment efficiency, being its reproducible consistency, lack of waste and ease of manipulation [47]. It was reported also to have a short setting time that makes it resistant to washout and ideal for root repair and VPT procedures [30,48-49]. A recent RCT compared the outcome of complete pulpotomy using two calcium silicate-based materials and MTA in 146 symptomatic mature permanent teeth with carious pulp exposure. The authors found that the 1-year success rate did not differ significantly between Biodentine™ pulpotomy, TotalFill® BC RRM™ Fast Set Putty pulpotomy, and MTA pulpotomy in permanent teeth [22]. Another premixed bioceramic is Well-Root™ PT by Vericom Korea, a premixed bioceramic putty in a syringeable compule, that was reported to form a dentin bridge comparable to MTA in immature irreversibly inflamed permanent molars after 12 months follow-up [50]. Additionally, several studies suggested that newer bioceramics allow restorative procedures immediately after pulp capping biomaterial placement (3 or 12 min, depending on the bioactive cement), therefore requiring one single appointment to complete the procedure

7. Outcome Measurement towards Operator and Patient centered outcomes

Operators' choice of materials depends on their familiarity with the materials and techniques of using them. Other factors include handling properties of the materials, personal preferences, as well as availability and cost [36,52]. Ali et al., found the experience and knowledge of the practitioner to be associated with choosing novel calcium-silicate based materials, while cost is a secondary factor [53]. Different outcome measurement criteria have been used to determine success of VPT procedures including absence of clinical and radiographic signs and symptoms. Researchers have frequently relied on radiographic assessment of radiolucent lesion size to measure treatment success, more than on retaining a functional and asymptomatic tooth and on the patient's feeling of wellbeing, which are important patient-centered outcomes [54-56]. In clinical practice, it is important to weigh radiographic and clinical findings with the patient's self-report of tooth function as well as the increased cost and distress of additional retreatments. This is why a core outcome set (COS) in endodontics should encompass in addition to clinical and radiographic findings, outcomes on tooth survival, post-operative pain, patient satisfaction, and the need for further interventions. This would help achieve a more holistic approach to VPT that includes operator- and patient-centered outcomes, homogenizing research and aiding in evidence-based clinical decision making [6].

4. Conclusions

The success of VPT is a function of several material and technique related factors as well as operator and patient related factors. Conjointly, they could provide a comprehensive and holistic approach to dental treatment.

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