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Endodontic Repair Filling Materials: A Review Article

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Review Article

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ABSTRACT

The emergence of Mineral Trioxide Aggregate (MTA) as endodontic repair filling material has generated a lot of interest due to its superior sealing ability and biocompatibility. Although MTA possesses superior sealing ability to traditional endodontic repair filling materials, such as calcium hydroxide, but it has poor handling characteristics. A novel endodontic repair filling materials with similar chemical composition, but improved handling characteristics, was recently developed. Recently, BioAggregate repair filling materials is claimed as biocompatible material and promotes cementogenesis and forms a hermetic seal inside the root canal. More recently, Biodentine and EndoSequence endodontic repair materials introduced to the market. Both materials have recommended for perforation repair, apical surgery, apical plug, and pulp capping. This article focused about physical properties of endodontic repair filling materials.

Keywords: Dentistry; endodontic repair filling materials; calcium hydroxide; mineral trioxide aggregate; biodentine; EndoSequence; BioAggregate.

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1. INTRODUCTION

An ideal endodontic repair material should provide an impervious seal, be dimensionally stable, radio-opaque, nonresorbable, nontoxic and well tolerated by the periradicular tissues. In addition, an ideal material should be bactericidal or bacteriostatic. Various materials have been used for root repair, including amalgam, Cavit, zinc oxide-eugenol, intermediate restorative material (IRM), composite resins carboxylate cements, zinc phosphate cements and glass ionomers. However, none of them are ideal for the special conditions and requirements of root repair. This review article will focus in calcium hydroxide, mineral trioxide aggregate, Biodentine, EndoSequence and BioAggregate.

For many decades calcium hydroxide has been the standard material for maintaining pulp vitality. Both clinically and histologically it has been found to produce satisfactory results in indirect and direct pulp capping, because it is capable of stimulating the formation of tertiary dentine by the pulp. In contact with vital pulp tissue it contributes to the formation of reparative dentine, a special variant of tertiary dentin, which seals exposures by newly formed hard tissue. Nevertheless, calcium hydroxide has some drawbacks. Poor bonding to dentine, material resorption and mechanical instability are among them. In addition, the high pH (12.5) of calcium hydroxide suspensions causes liquefaction necrosis at the surface of the pulp tissue [1].

Since the mid-1990s, Mineral Trioxide Aggregate (MTA) has been recognised as the reference material for the conservative pulp vitality treatments such as pulpotomy in temporary teeth and partial pulpotomy in permanent teeth [2,3]. Animal experiments have shown that MTA induces the formation of dentine “bridges” protecting pulp lesions markedly more effectively than that observed with calcium hydroxide [4,5].

New bioactive cement, Biodentine, was recently launched on the dental market as a dentine substitute. It shares both its indications and mode of action with calcium hydroxide, but does not have its drawbacks. This new calcium silicate-based material exhibits physical and chemical properties similar to those described for certain Portland cement derivatives [6]. This material has been recently developed to overcome some of shortcomings of white mineral trioxide aggregate, which are difficult handling, long setting time, and potential discoloration. Calcium silicate-based material, which called Biodentine, was declared by dental materials manufacturer Septodont in September of 2010, and made available in January of 2011. This material is new biologically active cement which has dentine-like mechanical properties. It also can be used as a dentine replacement in the tooth crown and root region.

EndoSequence root repair material putty and EndoSequence root repair material paste have been developed as ready-to-use, premixed bioceramic materials recommended for perforation repair, apical surgery, apical plug, and pulp capping [7]. The manufacturer stated that the moisture present in the dentinal tubules is adequate to allow the material to set. EndoSequence is stated by the manufacturer to bond to adjacent dentine, to have no shrinkage, and to be highly biocompatible, hydrophilic, radiopaque, and antibacterial due to a high pH during setting. The major advantages of this material are improved handling characteristics over traditional MTA and the delivery of a consistent product with each application.

BioAggregate root canal repair filling material has been successfully developed as new generation of a dental root canal filling material by Innovative BioCeramix Inc. (IBC), which is

a fine white hydraulic powder cement mixture for dental applications. It utilizes the advanced science of nano-technology to produce ceramic particles that, upon reaction with water produce biocompatible and aluminum-free ceramic biomaterials. Upon mixing, the hydrophilic BioAggregate Powder promotes cementogenesis and forms a hermetic seal inside the root canal. It is effective in clinically blocking the bacterial infection, its ease of manipulation and superior quality makes BioAggregate the most innovative and unique root canal repair material. It is indicated in: repair of root perforation, repair of root resorption, root end filling, apexification, and pulp capping [8].

2. CALCIUM HYDROXIDE

2.1 Introduction

Since the introduction to dentistry of calcium hydroxide by Hermann in 1930, this medicament has been indicated to promote healing in many clinical situations [9]. It has been used in a number of specific endodontic treatment procedures such as long term dressing in teeth with large periapical lesions or in traumatically injured immature teeth in order to obtain apical closure. Further uses of calcium hydroxide include treatment of persisting fluid exudation despite a thorough root canal preparation and used as a versatile medicament during root canal therapy [10].

Despite extensive researcher, the mode of action of calcium hydroxide is still not fully understood. A calcified barrier may be induced when calcium hydroxide is used as a pulp capping agent or placed in the root canal in contact with healthy pulpal or periodontal tissue [11,12].

The alkaline pH induced not only neutralizes lactic acid from the osteoclast, thus preventing dissolution of the mineral component of dentine, but could also activate alkaline phosphatase enzyme which is thought to play an important role in hard tissue formation [13,14]. Tronstad et al. [15] demonstrated that untreated teeth with pulpal necrosis had a pH of 6.0 to 7.4 in the pulp canal, dentine, and periodontal tissue whereas after calcium hydroxide has been placed in the canals, the teeth showed a pH range in the peripheral dentine of 7.4 to 9.6. They also suggested that calcium hydroxide may have other actions; these include for example, arresting inflammatory root resorption and stimulation of healing, it also had a bactericidal effect and will denature proteins found in the root canal, thereby making them less toxic. In a study made by Das [16] on the effect of certain dental materials on pulp, he found that calcium hydroxide was the material of choice for pulp capping in pulp exposure. He also demonstrated that calcium hydroxide was compatible with the pulp cells in tissue culture and the initial alkaline pH did not seem to have any lasting ill effect on later cellular proliferation.

Tziafas and Economides [17] indicated that various forms of crystals can be formed by reaction of calcium ions released from the calcium hydroxide containing materials with the free ions in the surrounding tissue fluids. These crystals played a role in the regulation of cell adhesion and initiation of polarized matrix deposition which is a critical step in hard tissue formation during pulpal or periodontal tissue wound healing. In addition, calcium hydroxide cement would provide a bactericidal effect on any remaining bacteria and encourage the formation of secondary dentine and a dentine bridge [18].

The promotion of bridging by hard-set bases used in pulp capping can be correlated with the pH they impart to the surrounding medium. The pH of calcium hydroxide containing dental materials that are used as bases or liners under restoration was shown to vary from 6.3 to 12.61 [19]. Behnia et al. [20] used a combined surgical and orthograde approach with a biocompatible restorative material (calcium hydroxide) and a clear, plastic light transmitting post to repair the iatrogenic perforation. Himel et al. [21] evaluated the repair of mechanical perforations of the pulp chamber floor using tricalcium phosphate or calcium hydroxide. Histologically they found that calcium hydroxide was more toxic and caused more destructive reaction than tricalcium phosphate and that the latter is more effective in inducing hard tissue apposition. Trope and Tronstad [22] suggested that repeated application of calcium hydroxide over a long period of time may result in hard tissue closure of root perforations. They also found that hard tissue barrier across the perforation defect took about 3 years to fully develop. Torneck et al. [23] demonstrated that the repair potential of periapex was enhanced by using calcium hydroxide paste as temporary filling. They showed higher incidence of apical closure with a paste fill [24]. Caliskan [25] documented that endodontic treatment with calcium hydroxide demonstrated a successful method in providing periradicular healing and apical root closure even in a mature tooth with a cyst like large periapical lesion. The presence of cyst does not preclude or prevent root end closure when treated with calcium hydroxide.

3. MINERAL TRIOXIDE AGGREGATE

3.1 Introduction

Mineral Trioxide Aggregate (MTA) was developed by Torabinejad and co-workers to fulfil the ideal criteria of a root perforation repair material [26].

MTA is a type of hydraulic cement that requires water to set. In simple terms, hydraulic cements are finely ground materials (powders) that when mixed with water gradually or instantly set and harden in air or in water; the reaction resulting in the formation of hydrated compounds whose strength increases with time. MTA consists of fine hydrophilic particles that on contact with water set to a hard composition through the creation of a colloidal gel [27,28].

3.2 Clinical Applications

MTA used increasingly in a wide range of clinical treatments. It was first developed and introduced in endodontics for the repair of root perforations [26]. Subsequently, it has been widely used as a root-end filling material [29,30]. It has also been used in vital pulp treatments, including direct pulp capping and pulpotomy of pulps in immature teeth as reported by Torabinejad and Chivian [31]. In addition, as hard tissue induction is one of its exceptional properties, it has been suggested as an apical barrier in treatment of teeth with open apices and necrotic pulps [32]. MTA also provides an effective seal against penetration of bacteria and their by-products [33] and thus has been recommended as a temporary filling material [34] and as a coronal plug after filling of the root canal system [33]. Moreover, it is recommended for the non-surgical repair of invasive cervical root resorption [35]. Yildirim and Gencoglu [36] reported new hard tissue formation in two horizontal root fracture lines after a 5-year follow-up and suggested the use of MTA in the treatment of such cases. In addition, Gomes-Filho et al. [37] reported that a sealer based on MTA stimulated mineralization and thus advocated its use as a root canal sealer. The use of MTA has also

been suggested in regenerative endodontics for treatment of immature permanent teeth with periapical disease [38-40].

3.3 Chemical Composition and Characteristics

MTA is a powder, which consists of fine hydrophilic particles of tricalcium silicate, tricalcium aluminate, tricalcium oxide, silicon oxide [41-43]. When MTA is mixed with water, it becomes a colloidal gel [35]. Setting time of MTA is approximately 3-4 hours. During the initial stages the pH is 10.2 and later when the material has set, it becomes 12.5 [44].

Camilleri et al. [42] showed through x-ray diffraction analysis, the components of MTA to be tricalcium silicates and aluminates with bismuth oxide. They also showed that the material was crystalline in structure. It was found that blood contamination affected the retention characteristics of MTA [45]. In a study conducted by Camilleri [46], it was seen that unreacted MTA was composed of impure tri-calcium and di-calcium silicate and bismuth oxide and traces of aluminate.

3.4 Biocompatibility and Cytotoxicity

Torabinejad et al. [47] compared bone tissue reaction to implanted MTA and Super EBA in guinea pigs and reported that MTA was considered as biocompatible materials. Torabinejad et al. [48] compared the periradicular tissue response in dogs to MTA and amalgam when used as a root-end filling material. Compared to amalgam, more fibrous capsule formation and less inflammatory response were reported adjacent to MTA. Favourable inflammatory reactions to implanted MTA in tibia and mandible of guinea pigs was also reported [49], suggesting the biocompatibility of MTA. The root-end induction capability of MTA in dogs was demonstrated by Shabahang et al. [50], suggesting its use as an apical plug in teeth with open apices and necrotic pulps. Dentine bridge formation follows pulpotomy by MTA and Portland cement was reported in dogs [51] confirming the tissue compatibility of MTA. The potential healing effect and formation of dentinal bridges following direct pulp capping with MTA in cats were also demonstrated by Hasheminia et al. [52]. They reported that treatment of exposed pulp tissue by lasers before direct pulp capping with MTA had no significant effect on the healing process or on the formation of dentine bridges. The superior healing process following direct pulp capping with MTA has also been reported in rats [53].Torabinejad et al. [48] compared the cytotoxicity of freshly mixed and set experimental materials including amalgam, Super EBA, IRM, and MTA on mouse L929 fibroblasts using the agar overlay and radiochromium methodologies. According to the results of the current study, the degree of cytotoxicity of fresh and set MTA was the least followed by amalgam, Super EBA and IRM. Osorio et al. [54] assessed the cytotoxic effects of original Mineral Trioxide Aggregate, amalgam, Ketac Silver, Gallium GF2 and Super-EBA. The results of their study revealed that among all tested materials MTA was not cytotoxic. In another study, using human periodontal ligament cell cultures, Keiser et al. [55] compared the cytotoxicity of freshly mixed amalgam, Super EBA and MTA. In addition, to evaluating the cytotoxicity of set materials, they incubated the experimental materials for 24 h at 37℃ and fully saturated humidity. The results indicated that the toxicity of freshly mixed MTA was lower than Super EBA and amalgam. Souza et al. [56] compared the cytotoxic effect of gutta-percha and set specimens of Super EBA, N-Rickert, amalgam, glass ionomer and MTA and concluded that all the materials were cytotoxic; however, MTA was ranked as the least cytotoxic. Koulaouzidou et al. [57] investigated the cytotoxicity of 2 brand of MTA and compared with

Super EBA and Vitrebond. They found that both MTA materials caused the least cytotoxic effect and could be regarded as biologically inert materials.

3.5 Bioactivity

MTA is considered as a bioactive material with possible osteoinductive properties [58]. Bonson et al. [59] exposed cell cultures of gingival and periodontal ligament fibroblasts to various root-end filling materials including MTA and indicated that only MTA was capable of modifying differentiation of both fibroblast populations, resulting in significantly increased levels of alkaline phosphatase activity. Activity of alkaline phosphatase is regarded as an indicator of bone formation. Moreover, the potential property of MTA to promote differentiation of dentinoblasts from clonogenic cells of the dental pulp has been demonstrated by Zhao et al. [60]. Recently, Orhan et al. [61] applied calcium hydroxide, mineral trioxide aggregate, platelet-rich plasma (PRP) and enamel matrix derivative (EMD) were applied as direct capping agents. They observed that reparative dentine formation, however were no significant difference among the groups.

3.6 Antibacterial Activity of MTA

Some of the major advantages of MTA, such as antibacterial activity and conduction of hard tissue, can be best rationalised as a result of its alkalinity [62]. In a laboratory study Torabinejad et al. [63] measured the pH value of the initial prototype of MTA and reported that its pH when freshly mixed MTA was 10.2, which rose to 12.5 after 3 h. Chng et al. [64] demonstrated that the pH value of tooth coloured MTA rose to 13.0 at 60 minutes after mixing, which was attributed to the continuous formation of calcium hydroxide during the hydration process [65]. The pH value of tooth coloured MTA was reported to be higher than grey MTA [64]. The pH of tooth coloured and ordinary Portland cement was shown to be more alkaline than their corresponding MTA and also reached the peak pH values more rapidly than corresponding MTA materials.

3.7 Sealing Ability

Nakata et al. [66] evaluated the ability of MTA and amalgam to seal furcal perforations in extracted human molars using an anaerobic bacterial leakage model. Fusobacterium nucleatum was used in this study and it was concluded that MTA was significantly better than amalgam at preventing leakage. Mangin et al. [67] tested the sealing ability of hydroxyapatite cement, MTA and super-EBA. It was concluded that there was no significant difference in the sealing ability of the three materials. Roy et al. [68] also observed that an acidic environment did not alter the sealing ability of MTA. Fogel and Peikoff [69] observed that MTA was better than amalgam, IRM, a dentine-bonded resin and super-EBA in preventing microleakage. All these studies prove that MTA is equivalent or superior in its sealing ability compared to contemporary root-end filling materials.

3.8 Properties of MTA

Sluyk et al. [70] evaluated the push-out force of MTA and showed that the bond strength of MTA increased gradually over time, suggesting that the placement of the permanent restoration over MTA should be delayed. Loxley et al. [71] evaluated the effect of various intracanal oxidizing agents on the push-out force of MTA, Super EBA and IRM and

demonstrated that MTA was significantly more resistant to displacement than Super EBA or IRM.

Torabinejad et al. [63] compared the compressive strength of the initial prototype of MTA, super-EBA and IRM at 24 h and 21 days after mixing and demonstrated that the compressive strength of all cements increased after 3 weeks. The strength of Super-EBA was significantly higher than that of IRM and MTA. In an attempt to decrease the setting time of MTA, Kogan et al. [72] evaluated the effect of various admixtures on the setting time of MTA and demonstrated that the addition of 5% calcium chloride decreased the setting time as well as its compressive strength. They concluded that the compressive strength of MTA could be affected by the nature of the liquid mixed with the powder.

4. ENDOSEQUENCE

4.1 Introduction

Endosequence root repair material (ERRM) has been developed as ready-to-use. This premixed bioceramic materials recommended for perforation repair, apical surgery, apical plug, and pulp capping. The manufacturer stated that the moisture present in the dentinal tubules is adequate to allow the material to set. ERRM is stated by the manufacturer to bond to adjacent dentine, to have no shrinkage, and to be highly biocompatible, hydrophilic, radiopaque, and antibacterial due to a high pH during setting. The major advantages of this material are improved handling characteristics over traditional MTA and the delivery of a consistent product with each application.

4.2 Chemical Composition and Characteristics

ERRM is composed of calcium silicates, monobasic calcium phosphate, zirconium oxide, tantalum oxide, proprietary fillers and thickening agents [73].The material has nanosphere particles with a maximum diameter of 1×10^{-3} μm that allow for the material to enter dentinal tubules, be moistened by dentine liquid, and create a mechanical bond upon setting [74]. This material has been manufactured to overcome some of the difficult handling characteristics of MTA.

4.3 Bioactivity

This material is bioactive due to its ability to form a hydroxyapatite [75,76] or apatite-like layer [77] on its surface when it comes in contact with phosphate-containing fluids. Hansen et al. [78] compared the diffusion of hydroxyl ions for ERRM and WMTA through root dentine. They found that although both materials showed diffusion of ions through dentine, the effect was less pronounced and of shorter duration for EndoSequence than WMTA.

4.4 Biocompatibility and Cytotoxicity

As stated the manufacturer, the ERRM is able to bond to adjacent dentine, to have no shrinkage, and to be highly biocompatible. AlAnezi et al. [73] used cultured mouse fibroblast cells to determine the cytotoxicity of ERRM as compared with gray and white MTA and found that both set and fresh samples showed no significant cell viability differences. Damas et al. [74] compared the cytotoxic effect of 2 brands of white MTA (ProRoot MTA and MTA-Angelus), ERRM by using human dermal fibroblasts. They concluded that the ERRM have

similar cytotoxicity levels to those of ProRoot MTA and MTA-Angelus. Ciasca et al. [79] concluded that ERRM and MTA showed similar cytotoxicity and cytokine expressions.

4.5 Sealing Ability

Hirschberg et al. [80] compared the sealing ability of MTA to the sealing ability of ERRM using a bacterial leakage model. They concluded that Samples in the ERRM group leaked significantly more than samples in the MTA group.

4.6 Antibacterial Activity

Lovato and Sedgley [81] investigated the antibacterial activity of ERRM against Enterococcus faecalis. They found that ERRM and white ProRoot MTA demonstrated similar antibacterial efficacy against clinical strains of E. faecalis. This research again validated earlier studies that found ERRM displayed similar in vitro biocompatiblity to MTA. Additionally, other study found that the ERRM had cell viability similar to Gray and White MTA in both set and fresh conditions [73].

5. BIODENTINE

5.1 Introduction

Calcium silicate-based material has been recently developed to overcome some of shortcomings of MTA, which are difficult handling, long setting time, and potential discoloration. Calcium silicate-based material, which called Biodentine, was declared by dental materials manufacturer Septodont in September of 2010, and made available in January of 2011. This material is new biologically active cement which has dentine-like mechanical properties. It also can be used as a dentine replacement in the tooth crown and root region.

Compared to MTA, Biodentine handles easily and needs much less time for setting. Unlike other Portland cement-based products, it is sufficiently stable so that it can be used both for pulp protection and temporary fillings [82]. This is why the manufacturer recommends to fill the entire cavity completely with Biodentine in a first step and to reduce it to a base/dentine substitute level in a second visit one week to 6 months later before definitive restoration. For successful capping it is, however, important to seal the cavity against bacterial invasion in a one-stage procedure [83,84]. While there is extensive evidence documenting that composite fillings are leak-proof, few pertinent data are available for Biodentine.

5.2 Clinical Applications

As stated by manufacture, Biodentine has many applications in Dentistry such as crown and root dentine repair treatment, repair of perforations or resorptions, apexification and root-end fillings. The material can also be used in class II fillings as a temporary enamel substitute and as permanent dentine substitute in large carious lesions. The manufacturer claimed about the biocompatibility and the bioactivity of the material, which is important when used as indirect and direct pulp capping and pulpotomy. Furthermore, it preserves pulp vitality and promotes its healing process.

Pérard et al. [85] assessed the biological effects of Biodentine for use in pulp-capping treatment, on pseudo-odontoblastic (MDPC-23) and pulp (Od-21) cells. Secondly, the same authors evaluated the effects of Biodentine and MTA on gene expression in cultured spheroids. They concluded that Biodentine and MTA may modify the proliferation of pulp cell lines. Their effects may fluctuate over time, depending on the cell line considered. The observed similarity between Biodentine and MTA validates the indication for direct pulp-capping claimed by the manufacturers. Likewise, Nowicka et al. [86] compared the response of the pulp-dentine complex in human teeth after direct capping Biodentine and MTA. They concluded that Biodentine had a similar efficacy in the clinical setting and may be considered an interesting alternative to MTA in pulp-capping treatment during vital pulp therapy.

5.3 Chemical Composition and Characteristics

According to the manufacturer, Biodentine consists of a powder in a capsule and liquid in a pipette. The powder mainly contains tricalcium and dicalcium silicate, the principal component of Portland cement, as well as calcium carbonate. Zirconium dioxide serves as contrast medium. The liquid consists of calcium chloride in aqueous solution with an admixture of polycarboxylate. Once mixed, Biodentine sets in approximately 12 minutes. The consistency of Biodentine is similar to that of phosphate cement [87].

Camilleri et al. [88] characterized and investigated the hydration of Biodentine and laboratory manufactured cement made with a mixture of tricalcium silicate and zirconium oxide and compared their properties to MTA Angelus. They reported that all the cement pastes tested were composed mainly of tricalcium silicate and a radiopacifier. The laboratory manufactured cement contained no other additives. Biodentine included calcium carbonate which together with the additives in the mixing liquid resulted in a material with enhanced chemical properties relative to TCS-20-Z prototype cement. On the other hand MTA Angelus displayed the presence of calcium, aluminum and silicon oxides in the un-hydrated powder. These phases are normally associated with the raw materials indicating that the clinker of MTA Angelus is incompletely sintered leading to a potential important variability in its mineralogy depending on the sintering conditions. As a consequence, the amount of tricalcium silicate is less than in the two other cements leading to a slower reaction rate and more porous microstructure.

Grech et al. [89] investigated the composition of materials and leachate of hydrated prototype cement composed of tricalcium silicate and radiopacifier and compared this to Biodentine and Bioaggregate to assess whether the additives in the proprietary brand cements affect the hydration of the materials. They found that Biodentine and Bioaggregate resulted in the formation of calcium silicate hydrate and calcium hydroxide, which was leached in solution. The hydrated materials were composed of a cementitous phase that was rich in calcium and silicon and a radiopacifying material. Biodentine included calcium carbonate, and Bioaggregate included silica and calcium phosphate in the powders. IRM was composed of zinc oxide interspersed in a matrix of organic material. Camilleri et al. [90] determined the elemental constitution and investigated the total and leachable arsenic, chromium and lead in Portland cement, pure tricalcium silicate, Biodentine, Bioaggregate and MTA. They concluded that dental materials based on tricalcium silicate cement and MTA release minimal quantities of trace elements when in contact with simulated body fluids. The results of acid extraction could be affected by nonspecific matrix effects by the cement.

5.4 Biocompatibility and Cytotoxicity

The manufacturer stated that Biodentine considered as biocompatible material. Biodentine was shown to be biocompatible, i.e. it does not damage pulpal cells in vitro or in vivo, and is capable of stimulating tertiary dentin formation. Hard tissue formation is seen both after indirect and direct capping with Biodentine.

Laurent et al. [91] compared the biocompatibility of Biodentine with that of MTA and a hardening calcium hydroxide. They reported that Biodentine is biocompatible. This new material has no adverse effect on cell differentiation or specific cell functions. Shayegan et al. [92] assessed and compared, in primary pig teeth, the pulp response after a pulpotomy using Biodentine, white MTA, or formocresol (FC) and repeat the same after direct pulp capping using Biodentine, white MTA, or calcium hydroxide. They concluded that Biodentine and white MTA are both suitable, biocompatible materials for pulp capping in primary teeth of pigs. Zhou et al. [93] examined the effect of a Biodentine on the viability of human gingival fibroblasts. They reported that Biodentine caused gingival fibroblast reaction similar to that by MTA. Both materials were less cytotoxic than glass ionomer cement.

5.5 Bioactivity

The manufacturer stated that Biodentine considered as bioactive material. Goldberg [94] described the bioactivity of this material, demonstrating the formation of apatite when immersed in phosphate solution. About et al. [95] investigated Biodentine bioactivity by studying its effects on pulp progenitor cells activation, differentiation and dentine regeneration in human tooth cultures. They concluded that Biodentine is stimulating dentine regeneration by inducing odontoblast differentiation from pulp progenitor cells. Laurent et al. [96] investigated the capacity of Biodentine to induce reparative dentin synthesis by modulating pulp cells to secrete transforming growth factor-beta 1 (TGF-ß1) and stimulate human dental pulp mineralization. Histologically, the bioactive tricalcium silicate demonstrated the ability to induce odontoblast differentiation from pulp progenitor cells. The resulting mineralized matrix had the molecular characteristics of dentine. Zhou et al. [93] reported that Biodentine maintain human gingival fibroblast viabililty on cell culture. Han and Okiji [97] compared white MTA, EndoSequence BC sealer and Biodentine with regard to their ability to produce apatites and cause Ca and Si incorporation in adjacent human root canal dentine after immersion in phosphate-buffered saline (PBS). They concluded that Biodentine and white MTA, BC sealer showed less Ca ion release and did not show Ca and Si incorporation as deeply in human root canal dentine when immersed in PBS for up to 90 days.

5.6 Sealing Ability and Success

Biodentine is stronger mechanically, less soluble and produces tighter seals. This qualifies it for avoiding three major drawbacks of calcium hydroxide, i.e. material resorption, mechanical instability and the resultant failure of preventing microleakages.

Pradelle-Plasse et al. [98] found that Biodentine causes alkaline corrosion on the hard tissue, which leads to a so-called “mineral interaction zone”. Due to remodelling processes, the sealing of the dentine by Biodentine improves in the course of time. They reported that Biodentine can deposit impermeably onto the cavity walls and prevents microleakage. About et al. [95] studied effect of Biodentine on pulp progenitor cells activation, differentiation and

dentine regeneration in human tooth cultures. Their study exhibited that Biodentine can stimulate dentine regeneration by inducing odontoblast differentiation from pulp progenitor cells. Han and Okiji [97] compared calcium and silicon uptake by adjacent root canal dentine in the presence of phosphate buffered saline using Biodentine and MTA. The results showed that both materials formed a tag-like structure composed of the material itself or calcium- or phosphate rich crystalline deposits. The thickness of the Ca- and Si-rich layers increased over time, and the thickness of the Ca- and Si-rich layer was significantly larger in Biodentine compared to MTA after 30 and 90 days, concluding that the dentine element uptake was greater for Biodentine than for MTA.

Camilleri [88] compared Biodentine to glass ionomer and resin modified cements in an "open sandwich" restoration. They reported that Biodentine demonstrated both structural and chemical changes when etched with 37% phosphoric acid. Biodentine exhibited lower calcium to silicon ratio and a reduction in the chloride peak height when etched. When used as a dentine replacement material in the sandwich technique overlayed with composite, significant leakage occurred at the dentine to material interface. On the other hand materials based on glass ionomer cement were etched successfully and no chemical and physical changes or micro-leakage were detected when the materials were used as bases under composite restorations. The micro-hardness of all the materials was unaffected by etching.

5.7 Antibacterial Properties

Firla [99] claimed that during the setting phase of Biodentine, calcium hydroxide ions are released from the cement. This results in a pH of about 12.5 and a basification of the surroundings. This high pH inhibits the growth of microorganisms and can disinfect the dentine.

5.8 Morphological and Chemical Characteristics of the Interface between Human Dentine and Biodentine

The morphological and chemical characteristics of the interface between human dentine and new calcium silicate based dental cement were investigated. The dentine Biodentine interface is dynamic and interactive; that is manifested by water movement between the two substrates, and hydrated cement diffusion into the dentine, accompanied by microstructural changes. Guneser et al. [100] evaluated the effect of various endodontic irrigants on the push-out bond strength of Biodentine in comparison with contemporary root perforation repair materials. They found that Biodentine showed considerable performance as a perforation repair material even after being exposed to various endodontic irrigants, whereas MTA had the lowest push-out bond strength to root dentine.

6. BIOAGGREGATE

6.1 Introduction

BioAggregate is new generation of a root canal repair filling material. The manufacturer claimed that BioAggregate is produced under controlled conditions to form contamination-free ceramic nano-particles. According to manufacturer, BioAggregate is developed as a result of utilizing the advanced science of nano-technology to produce ceramic particles that, upon reaction with water produce biocompatible and aluminum-free ceramic biomaterials.

BioAggregate has excellent handling characteristics after mixing with water, which aids in a repair process of the affected tooth. BioAggregate's radiopacity properties, convenient setting and hardening time and easy workability and handling properties make it an ideal root canal filling material. As stated by manufacturer, the working time of BioAggregate is at least 5 minutes. Upon mixing a thick paste-like mixture is formed. If additional working time is required, simply cover the mixture with a moist gauze sponge while unattended.

6.2 Chemical Composition and Characteristics

As stated by manufacturer, the composition of BioAggregate is tricalcium silicate, dicalcium silicate, tantalum pentoxide, and calcium phosphate monobasic. To provide radiopacity, tantalum pentoxide is used in BioAggregate rather than the bismuth oxide used in MTA. This was confirmed by Park et al. [101], when examined the chemical differences between white MTA and BioAggregate in both powder and set forms using X-ray diffraction. The results showed that MTA and BioAggregate have a similar chemical composition with some differences. BioAggregate contains a significant amount of tantalum oxide instead of bismuth oxide. In both groups, similar peaks were observed in the set and powder form, but sharper and stronger peaks were observed in the powder samples. Furthermore, Camilleri et al. [90] determined the elemental constitution and investigated the total and leachable arsenic, chromium and lead in Portland cement, pure tricalcium silicate, Biodentine, BioAggregate and MTA. They concluded that dental materials based on tricalcium silicate cement and MTA release minimal quantities of trace elements when in contact with simulated body fluids. The results of acid extraction could be affected by nonspecific matrix effects by the cement.

The BioAggregate powder promotes a complicated set of reactions upon mixing with BioA Liquid (deionized water), which leads to the formation of a nano-composite network of gel-like calcium silicate hydrate intimately mixed with hydroxyapatite bioceramic, and forms a hermetic seal when applied inside the root canal as prescribed by Manufacture. This is also supported by Grech et al. [89], who investigated the composition of materials and leachate of a hydrated prototype cement composed of tricalcium silicate and radiopacifier. They then compared this to other tricalcium silicate-based cements which are Biodentine and BioAggregate to assess whether the additives in the proprietary brand cements affect the hydration of the materials. They used IRM as a standard root-end filling material. They found that Biodentine and BioAggregate resulted in the formation of calcium silicate hydrate and calcium hydroxide, which was leached in solution. The hydrated materials were composed of a cementitous phase that was rich in calcium and silicon and a radiopacifying material. Biodentine included calcium carbonate; Whereas BioAggregate included silica and calcium phosphate in the powders. IRM was composed of zinc oxide interspersed in a matrix of organic material.

6.3 Clinical Applications

The manufacturer claimed that BioAggregate is a biocompatible pure white powder composed of ceramic particles. Upon mixing, the hydrophilic BioAggregate Powder promotes cementogenesis and forms a hermetic seal inside the root canal. It is effective in clinically blocking the bacterial infection, its ease of manipulation and superior quality makes BioAggregate the most innovative and unique root canal repair material. According to manufacturer, the BioAggregate is indicated for repair of root perforation, repair of root resorption, root end filling, apexification, and pulp capping.

6.4 Biocompatibility and Cytotoxicity

As stated by manufacturer, BioAggregate is more biocompatible than any other root end filling and repair materials. It does not produce any adverse side effects on microcirculation of the connective tissue. It also has excellent biocompatibility with the vital periradicular tissue.

Yan et al. [102] investigated the cytotoxicity of BioAggregate to human periodontal ligament (PDL) fibroblasts and its effect on differentiation of human PDL fibroblasts. Also the authors compared its performance to that of mineral trioxide aggregate. They reported that BioAggregate was nontoxic to human PDL fibroblasts and appeared to induce the differentiation of human PDL fibroblasts. Yuan et al. [103] investigated the cytotoxicity of BioAggregate and the effect of BioAggregate on mineral associated gene expression in osteoblast cells. BioAggregate appears to be a novel nontoxic root-end filling biomaterial and be able to induce mineralization-associated gene expression in osteoblast cells. De-Deus et al. [104] found that BioAggregate displayed similar biocompatibility to that seen for MTA when cultured with primary human mesenchymal cells. However, there have not yet been any reports on potential cytotoxicity of BioAggregate on osteoblast cells or BioAggregate's effects on mineralization associated gene expression in these cells. Mukhtar-Fayyad [105] evaluated and compared the cytotoxicity of BioAggregate and iRoot bioceramic repair filling materials on human fibroblast MRC-5 cells. They reported that Both BioAggregate and iRoot SP displayed an acceptable biocompatibility. Khalil and Eid [106] investigated and compared the systemic toxic effect of BioAggregate and MTA on the liver and kidney after 7 and 30 days. They concluded that MTA had adverse effects on the liver and kidney that were significantly more severe than BioAggregate but with no permanent damage.

Recently, the potential cytotoxicity of BioAggregate on osteoblast cells and BioAggregate's effects on mineralization associated gene expression in these cells was studied. Yuan et al. [103] investigated the cytotoxicity of BioAggregate and the effect of BioAggregate on mineral associated gene expression in osteoblast cells. They reported that BioAggregate appears to be a novel nontoxic root-end filling biomaterial and be able to induce mineralization-associated gene expression in osteoblast cells. Moreover, Batur et al. [107] evaluated and compared the cytotoxic effects of MTA and BioAggregate on subcutaneous rat tissue. Their results showed that BioAggregate significantly better than MTA. Therefore they concluded that BioAggregate is more biocompatible.

6.5 Bioactivity

Shokouhinejad et al. [108] evaluated the bioactivity of BioAggregate, ERRM, and MTA. They concluded that exposure of MTA, BioAggregate and ERRM to PBS resulted in precipitation of apatite crystalline structures that increased over time. This suggested that the tested materials are bioactive.

6.6 Sealing Ability and Success

Leal et al [109] compared the ability of Ceramicrete, BioAggregate and MTA to prevent glucose leakage through root-end fillings. They concluded that both endodontic bioceramic repair cements displayed similar leakage results to white MTA when used as root-end fillings materials. Ceramicrete had significantly lower glucose penetration. El Sayed and Saeed [110] evaluated and compared sealing ability of BioAggregate versus amalgam, IRM and

MTA. They reported that BioAggregate has high sealing ability. They authors considered that utilizing the BioAggregate as alternative to MTA. Aminov et al. [111] compared the recovery rate after treatment of root perforations in the interradicular area of the molars, using two different materials: MTA and ceramic nanoparticles mineral cement BioAggregate, by a clinical-radiological and statistical analysis over a period of up to 24 months. They reported that both MTA and BioAggregate are excellent materials for root perforation repair.

6.7 Properties of Bioaggregate

Tuna et al. [112] assessed the long-term fracture resistance of human immature permanent teeth filled with BioAggregate, MTA and calcium hydroxide. They suggested that BioAggregate-filled immature teeth demonstrate higher fracture resistance than other groups at 1year. Considering the long-term risk of cervical root fracture associated with immature teeth, the use of BioAggregate as a root canal filling material appears to be the most advantageous of the materials tested. Grech et al. [89] investigated the physical properties of prototype radiopacified tricalcium silicate cement, Bioaggregate and Biodentine. IRM was used as a control. They reported that the addition of admixtures to tricalcium silicate-based cements affects the physical properties of the materials.

Research suggests that the high pH and released calcium ions are required for a material to stimulate mineralization in the process of hard tissue healing [113]. It is known that the presence of specific agents in the composition of a dental material does not certainly imply their dissociation and release by the materials after curing, because the curing reaction and presence of another agent can inhibit the release of these ions [114]. Thus, evaluation of such properties in these most recent and experimental materials are essential.

Saghiri et al. [115] investigated the compressive strength of MTA, a nano-modification of white MTA and BioAggregate after its exposure to a range of environmental pH conditions during hydration. They authors concluded that the force needed for the displacement of the nano-modification of White MTA was significantly higher than for Angelus White MTA and BioAggregate. They stated that the more acidic the environmental pH, the lower was the compressive strength. Hashem et al. [116] compared the effect of acidic environment on the dislodgement resistance of MTA and Bioaggregate when used as perforation repair materials. They concluded that MTA is more influenced by acidic pH than BioAggregate. Storage for 30 days in PBS can reverse the affected bond of MTA by the acidic environment.

7. CONCLUSION

Recent progress in endodontic repair filling materials is reviewed for possible replacement the traditional endodontic repair filling materials. The existing literature review exhibited a solid base about new endodontic repair filling materials, namely; Biodentine, EndoSequence, BioAggregate, for possible replacement calcium hydroxide and MTA as an endodontic material.

Although there was major developed in endodontic repair filling materials that can improve physical properties for endodontic applications, further studies are needed to improve their properties. These developments in endodontic repair filling materials may improve the function and longer life span in their clinical uses.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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