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Bioactive pulp capping Materials - A Review

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Abstract

The purpose of the article is to evaluate available research by comparing the properties of bioactive pulp capping materials. The properties and clinical implications of each calcium-silicate cements (ProRoot MTA, MTA Angelus, RetroMTA and Biodentine), a light-cured calcium silicate-based material (TheraCal LC) and a resin-modified glass-ionomer (ACTIVA BioACTIVE) is discussed exclusively . Though Mineral Trioxide Aggregate remains the most accepted and preferred materials as validated through both clinical and laborator based studies .Rest superior materials like Biodentine have fared well on in-vitro studies but remain elusive on its clinical performance lacking substantial supportive in-vivo studies . Therefore, despite all the research studies resin based materials like TheraCal LC and ACTIVA BioActive still is not recommended as pulp capping agents due to limited evidence of its usage.

Keywords: Direct Pulp Capping, Indirect Pulp Capping, Proroot MTA, MTA Angelus, retroMTA, biodentine; theraCal LC, ACTIVA BioACTIVE

Introduction

The paradigm shift in operative dentistry is now towards bioactive materials and procedures to achieve the ultimate goal of pulp vitality preservation and protection with longterm predictable outcomes. This fundamental change in the management of deep caries utilizes selective caries removal avoiding pulp exposure and invasive treatment like root canal treatment of teeth. Traditional deep caries management have become obsolete due to its limited scientific evidence and aggressive treatment nature [1]. The surge of vital pulp treatment (VPT) techniques such as pulp capping, partial and complete pulpotomy are pretty evident treating cariously exposed pulp more biologically and in an anatomic driven manner[2].The current trend of minimal invasive and biomimetic dentistry thus targets towards oral care and well being of basically the adult population which comprises the major bulk of world [3,4]. Retention of natural dentition is the sole goal of modern dentistry. Bioactive materials have been the new so-called tools to achieve this same purpose [5, 6]. On gross summary, bioactivity results from

biointeractivity of the restorartive materials which helps to exert its biological effects. This majorly induces specific and eventual mineral attachment to the dentine substrate [7]. In terms of restorative dentistry, bioactive material is defined as “one that forms a surface layer of an appetite-like material in the presence of an inorganic phosphate solution”. So, the remineralization of demineralized dentine lays the process of restoring minerals through the formation of inorganic mineral-like matter [8, 9].

A total of Six different bioactive materials have been compared and analyzed: four calcium-silicate cements—ProRoot MTA (Dentsply Sirona, York, PA, USA), MTA Angelus (Angelus, Londrina, Brazil), RetroMTA (BioMTA, Seoul, Korea) and Biodentine (Septodont, Saint-Maur-des-Fossés, France); a light-cured calcium silicate-based material TheraCal LC (Bisco, Schaumburg, IL, USA); and a resin-modified glass-ionomer (RMGIC) with improved physical properties—ACTIVA BioACTIVE (Pulpdent Corporation,Watertown, MA, USA) [10].

The article reviews the properties of bioactive materials applied for pulp capping and compare their clinical performances.

Vital Pulp Therapy (VPT) in Deep Caries Management

The pulp capping procedure is generally used in deep cavity, with or without carious dentine left behind in close proximity to the pulp but showing no visible signs of pulp exposure [11, 12]. According to the latest European Society of Endodontology (ESE)-approved criteria for deep caries management pulp capping due to removal of both soft and firm carious dentine until hard dentine is reached, is nowadays considered aggressive, and in many cases becomes redundant [13].

One-step selective carious-tissue removal includes the application of a bioactive material on a dentine barrier after either firm or soft dentine is left only on the pulpal base of the cavity, while the peripheral carious dentine is removed till hard dentine and permanent restoration placed. On the other side, stepwise procedure propose re-entry after 6–12 months after application of a bioactive material in a two-stage, selective carious-tissue removal technique. The first stage involves selective carious removal to soft infected dentine, to an extent that facilitates proper placement of a temporary restoration, and the second stage includes removal upto firm dentine. Eventually, final permanent restoration is performed. Tooth disinfection and isolation is carried out irrespective of the pup exposure status [13–18].

According to the latest (2019) position statement of the ESE, deep caries management should avoid pulp exposure by selective one-stage carious-tissue removal or stepwise excavation treatment, rather than the conventional indirect pulp capping procedure [13].

Use of Direct pulp capping (DPC) treatment is substantiated vital pulp with no symptoms is visibly exposed (pin-point) due to caries or trauma, or due to an iatrogenic mishap during tooth preparation or caries removal [7].

The procedure involves application of a bioactive material directly on the exposed pulp, followed by immediate sealing and placement of a permanent restoration. A diligent protocol should be employed with magnification, an irrigant for disinfection and calcium trisilicate cement, as the evidence based protocol suggest its usage in Vital pulp therapy.

Apart from pulp capping, partial pulpotomy also preserves the vitality but not regenerate pulpal tissues. Removal of 2-3 mm of exposed inflamed pulp filled by bioactive material restoration is the usual accepted protocol. The choice of proper treatment relying on just visual analysis to distinguish between inflamed and non-inflamed pulp

tissue is sufficiently accurate [19]. The factor of hemostasis of pulp within 5 minutes indicate the deemed status of pulp for partial pulpotomy or the failure to control bleeding demand a further invasive full pulpotomy procedure respectively.

Materials Used in Direct and Indirect Pulp Capping

Calcium hydroxide (Ca(OH)2) has been the time tested material and considered the gold standard. The initial reports of successful Ca(OH)2 pulpal healing were reported between 1934 and 1941 and thus serving innumerable clinical observations later on regarding its usage and performance [20]. Still several drawbacks like insufficient adherence to dentinal walls, multiple tunnel defects in the induced dentin bridges [21], poor sealing ability, dissolution over time [22] and lack of antibacterial properties were inherent. Most of the long follow up clinical studies showed success rates of calcium hydroxide pulp capping to be variable, highly unpredictable and often unsuccessful [23]. Thus, calcium hydroxide is the least preferred material of choice nowadays [24]. Due to its high alkalinity, calcium hydroxide on direct contact with the pulpal tissue locally destroys a layer of pulp , and eventually creates an uncontrollable necrotic zone. This necrotic zone inducts an inflammatory response which extends with time, or leads to formation of intra-pulpal calcifications [25]. However, the Ca(OH)2 highly dissociative capacity in oral fluids is the major drawback of its intended use as a pulp capping agent. The solubility of the material within one and half to two years after application and the formation of tunnel defects in reparative dentin underneath the capping material are responsible for its disappointing performanc against bacterial infection due to poor sealing ability.

Currently, with the advent of new generation materials like calcium silicate materials (CSMs) and RMGIC the clinical outcomes are more predictable [26,27]. The superiority of CSMs is subjected to its high biocompatibility, intrinsic osteoconductive activity and ability to induce regenerative responses in the human body tissues; namely, dentin bridges of improved quality and enhanced sealing of the pulp capped surface.Wide variety of application Of calcium trisilicate materials includes broadly into restorations and as endodontic sealers. Differences between compositions of each material are presented in Table 1.

Mineral Trioxide Aggregate

Mineral trioxide aggregate (MTA) was introduced by Torabinejad et al. in the early 1990s as an endodontic repair and root-end filling material [28] with favourable physical properties [29]. The wide variety of application of MTA includes direct [14,15,30,31] and indirect pulp capping, perforation repairs in roots or in furcation's [32] and the apexification procedure [33–35]. The powder of MTA is a mixture of a purified Portland cement and bismuth oxide to provide radiopacity. The main constituents of cement are tricalcium and dicalcium silicate and tricalcium aluminate [36,37]. ProRoot MTA, having been available on the market for almost two decades, which has been extensively studied and proven to be biocompatible. However, due to the long setting time and also high cost the development of new types of MTA-based materials surfaced to overcome these drawbacks (Table 1). The newer materials must be more accessible, more cost effective and set in a shorter time. The new formulation like MTA Angelus was developed, offering the advantage of reduced final setting time of 24–83 min. [37,40]. Another fast-setting calcium silicate cements is Retro MTA, with a final setting time of about 12 min [39]. Althoug studies evaluating biocompatibility of each of these products with that of Pro Root MTA are limited and inconclusive. Characteristics of those materials were collected and presented in Tables 1.

The biocompatibility and sealing ability of MTA result from the predominant calcium ion released from the material which reacts with phosphates in tissue fluid, inducing hydroxyapatite formation (Table 1) [59]. Formation of this layer is a key characteristic responsible for the chemical seal between MTA and the dentinal walls, and is not a conventional bonding process [60]. The first formulation of MTA was grey, but due to the reported discoloration of teeth [61], an altered chemical composition of white MTA was presented to the market (Table 1). The chemical component of iron is absent in white MTA, although discoloration is still observed and remains one of the major drawbacks of the material [62,63].

Despite the high clinical advantages of MTA cement, the limitation of long setting time and difficult handling prevented clinicians from incorporating it into the daily armamentarium. The aforementioned properties of MTA are listed in Tables 1. In a randomized clinical trial, the probability of failure at 24 months was 31.5% for Ca(OH)2 and 19.7% for MTA. A review of the few clinical assessments in 9–10-year observation revealed 92.5–97.96% success for the teeth pulp-capped with MTA [31,57,58]. Clinical success rates for compared materials are presented in Table 1. In addition, MTA is less toxic, easier to use in pulp capping procedures and causes less pulpal inflammation than Ca(OH)2 [67]. A histological study confirmed that the application of MTA has a direct effect upon regeneration potential of the dental pulp and is associated with increase in TGF-1 secretion from pulp cells (Table 1) [68]. The factor directs the progenitor cells migration to the material-pulp interface and stimulates their differentiation to odontoblastic cells secreting reparative dentin; which affects the quality of the induced hard barrier. Other histological study confirmed that the formation of calcified hard tissue after pulp capping with fast-setting MTA (RetroMTA) was not particularly the product of genuine odontoblast differentiation and lacks characteristics of “regular dentine” [69]. These results suggest that the formation of calcified tissues may be more appropriately regarded as a reparative process more than a genuine regeneration response. So thus due to the limited bioactive potential of pulp-capping material (RetroMTA), its use is discouraged in regenerative dentistry. Moreover, in contrast to calcium hydroxide, mineral trioxide aggregate (WhiteProRoot®MTA, Dentsply Sirona, York, PA, USA) and Biodentine show favorable metabolic activity and promote desired cellular response, resulting in higher clinical success rate and also overcoming the tunnel defects [70]. Thus data indicates that both MTA and Biodentine induced hard tissue barriers and that MTA induced dentin with superior characteristics (Table 1) [71]. Therefore, MTA remains the material of choice in direct pulp capping [70,72].

Other key factors for successful pulp capping procedures are the ability of the bioactive material to seal to the tooth structure, the bond strength between the pulp capping material and restorative properties (Table 1). Recent studies suggest that placement of composite used with a two-step etch and rinse adhesive (E&R) over white MTA performed significantly better than an all-in-one system in terms of bond strength [76]. Other studies concluded that the highest bond strength was obtained when the E&R adhesive was used after 24 h resulting in shear bond strength (SBS) of 7.3 _ 1.49 MPa [77,78].

Supplementary surface treatment protocols were investigated to reliably asses SBS after final composite restoration (Table 1). Additional silanization (Silane, Ultradent, South Jordan, UT, USA) was recommended after treating the surface of ProRootMTA with 9% hydrofluoric acid (HF) for 90 s before the application of

dentin bonding agent (DBA) for higher bond strength [82]. Further research also suggested air abrasion of MTA Angelus surface after 72 h with 50 _m Al2O3 particles to achieve higher bond strength to the resin composite compared to specimens treated with 37% phosphoric acid (16.98-4.24 MPa and 11.40-3.19 MPa, respectively) [54]. Although the manufacturers of ProRoot, MTA Angelus and Retro MTA claimed short setting times (165 min, 15 min and 1.5 min, respectively), studies showed adequate setting only after at least 7 days to acquire proper surface properties (Tables 1) [83,84]. Additionally, evidence exists thatMTA continues to mature up to 1 year beyond the setting time with impacts on its mechanical integrity and hence SBS values [85]. This research also puts forward the importance of leaving MTA to mature before the application of the overlying restoration to prevent bacterial infection.

Novel Mineral Trioxide Aggregate Restorative Cements

Alternation in material characteristics has recently led to development of new generation MTA-based cements; namely, Neo MTA Plus (Avalon Biomed Inc., Houston, TX, USA) and the iRoot (Innovative BioCeramix Inc., Vancouver, BC, Canada) products family. Both materials share the same clinical applications in vital pulp treatment, but only a few studies are available to assess their use in clinical practice [89–92]. Neo MTA Plus was developed to be used in pulpotomies without the risk of discoloration due to elimination of bismuth oxide. The radiopacifying agent was replaced by tantalum oxide, which provides a radiopacity value of 3.76 ± 0.13 mm Al and does not exert any effect on hydration [89,92]. What is important is that the final setting time of Neo MTA Plus was proven to be prolonged up to 315 ± 5 min [89]. Moreover, compared to MTA Angelus, NeoMTA Plus showed

better apatite formation, higher crystallinity and higher Ca/P, but a lower CO3/PO4 ratio, which might result in increased bioactivity [90]. Further studies are required to validate these findings.

Addressing the difficult handling of MTA, the iRoot products are available in different consistencies, offering an advantage of choosing suitable one for each clinical application. To name, iRoot BP (IBC, Burnaby, BC, USA) is deposited on preloaded syringes, while the iRoot BP Plus is available in jars and with a thicker consistency, and the iRoot FS was especially developed to set faster with final setting time of 57.0 ± 2.7 min [83]. A systematic review concluded that iRoot BP and iRoot BP Plus are biocompatible materials that enhance human dental pulp cells' proliferation, migration, mineralization and dentinal bridge formation in pulp capping procedures [93]. These findings were coincided with those obtained in another study, stating that iRoot BP Plus showed superiority over calcium hydroxide as a pulpotomy agent [94].

There are only a few studies on novel CSMs, as the scientific evidence is in general focused on materials that have been available for a longer time, such as ProRoot MTA and the Biodentine. To determine their clinical efficacy, more studies are deemed necessary.

Biodentine

As a response to the disadvantages of MTA, a novel tricalcium silicate-based cement Biodentine (Septodont, France) was introduced in 2011. This comparatively new bioactive material claimed to possess properties similar to MTA and is currently explored for application in vital pulp therapy procedures. Biodentine was designed as a permanent, biocompatible [95] dentin substitute meant for single clinical sitting usage for final adhesive restoration with the sandwich technique or as an interim restoration for an observation period before the final restoration. The manufacturer recommends the setting time to be between 9 and 12 min [96]; however, it was proven to set finally after 45 min (Table 1) [43].

Biodentine is available in the form of a capsule containing powder composed of tricalcium silicate, dicalcium silicate, zirconium oxide, calcium carbonate, calcium oxide and iron oxide. A single capsule containing 0.7 g of powder is mixed for 30 s in a mixing device at a speed of 4000–4200 rpm with exactly five drops of liquid containing calcium chloride which act as an accelerator [97]; a hydrosoluble polymer functioning as a water reducing agent; and water (Table 1). The setting accelerator improves its handling properties and strength and mitigates the risk of partial material loss and alteration of the interface when compared to MTA [13,22,45]. Concerning drawbacks of the material, radiopacity is significantly lower than MTA Angelus (Table 1) despite the presence of zirconium oxide [98]. Radiopacity gradually decreases with time, which causes difficulties in long-term radiographic observations subsequently. The interactions of Biodentine with hard and soft tissues in both the direct and indirect capping procedure lead to a marginal sealing and provide protection to the underlying pulp by inducing tertiary dentin synthesis and remineralization. Based on the calcium (Ca^{2+}) and hydroxide (OH^-) ion release from material, it may be concluded that tricalcium silicate materials such as Biodentine suffice as a recommended IPC material (Table 1) [99].

Marginal sealing is provided by micromechanical retention due to penetration of Biodentine into the dentin tubules forming tag-like structures, and represents similar bond strength to dentine compared to MTA [49,100]. However, such findings are inconsistent with results of other studies regarding Biodentine in terms of sealing ability [101–103]. When compared to MTA, advancements in Biodentine properties, such as setting time, mechanical qualities and initial cohesiveness, led to widened range of applications, including endodontic repair and vital pulp therapy. Biodentine is mechanically stronger, less soluble and produces a tighter seal than the gold standard $Ca(OH)_2$ [100].

Biodentine and MTA have comparable success rates when used as direct pulp capping or pulpotomy material in permanent mature teeth with carious exposure (Table 1). A randomized clinical trial was conducted to investigate the outcome of the Direct pulp capping of permanent young teeth with Biodentine; it showed no failures after 12 months, while both calcium hydroxide and MTA had a 13.6% failure rate after the same time period [106]. Other studies also support claims of Biodentine's and MTA's superiority over calcium hydroxide in terms of success rate in pulp capping procedures [107,108]. Another study reported that the success rate of DPC with BD is 90.9% in patients younger than 40 and 73.8% in patients 40 or older [109].

Based on a numerous cell/tissue culture model, it can be concluded that materials used in pulp capping procedures directly affect the regeneration potential of the dental pulp by modulating the secretion of factors such as TGF-α1 [68,110]. Biodentine applied directly onto pulp, induces reparative dentine formation resulting in complete dentin bridge formation, absence of an inflammatory pulp response and layers of well-arranged odontoblasts and odontoblast-like cells observed after 6 weeks [108].

There is plethora of evidence for the positive effects of BD on vital pulp cells, for stimulating tertiary dentin formation and for early formation of reparative dentin [111]. Biodentine shows similar effect on dentin bridge formation to MTA (Table 1) [71,112,113]. In contrast to another study [46], a clinical trial in adults showed complete dentin bridge formation in 100% of Biodentine cases, compared to 11% and 56% in TheraCal®and ProRoot®MTA, respectively [114]. In terms of quality of induced dentin, MTA exceeds Biodentine, although concerning completion of the dentin bridge, Biodentine

showed better results. Therefore, according to reports the choice of reliable pulp capping material remains inconclusive. Nevertheless, in the later stages of differentiation and mineralization of Dentin Bridge, Biodentine had been observed to have a better performance which is majorly attributed to its rise in alkaline phosphatase expression and calcium nodule formation compared to the MTA characteristics [70]. The antibacterial properties of BD and MTA can refer to the high alkaline pH of these materials, which has an inhibitory effect on the growth of microorganism and causes disinfection of dentin (Table 1) [115]. Due to unsatisfactory aesthetics and physical properties of Biodentine, there is a need for an overlying material with final restoration, usually a dental composite. Yet, despite the possibility of immediate restoration placing after initial set, there is statistically significant increase in SBS when bonding with Biodentine after a 72-h maturation period [86]. Moreover, Biodentine presents a considerably lower SBS to composite than glassionomer cement (GI) even after a 2-week maturation period (Table 1).

Although Biodentine offers many advantages over MTA, it presented significantly lower SBS values than MTA to restorative materials, including composite (Filtek Z250, 3M, Saint Paul, MN, USA), compomer (Dyract XP®) and RMGI cement (Photac-Fil Quick Aplicap, 3M, Saint Paul, MN, USA) [116]. On the other hand, another study showed clinically acceptable scores and higher SBS of Biodentine compared to MTA when used with the methacrylate-based composite [53]. Inferior results obtained with Biodentine might be explained by the deficient intrinsic maturation, which can take over 2 weeks [87,88]. Most of the results thus, highlight the importance of leaving Biodentine and MTA to mature before the application of the overlying restoration for better clinical outcomes.

TheraCal LC

TheraCal LC (Bisco, Schaumburg, IL, USA) was introduced in the market to overcome poor bonding of CSMs to resins in final restorations. TheraCal LC is a light-cured calcium silicate-based material designed as both a direct and indirect pulp capping material that facilitates the immediate placement of final restoration.

A material's ability to remineralize tooth's structure is associated with the resin formula of TheraCal LC that possesses calcium and hydroxide ion release properties. The bioavailability of calcium ions released form TheraCal LC is proven to be in the concentration range for potential stimulatory activity for dental pulp and odontoblasts, although significantly lower than that of Biodentine [117–119]. The hydration process of Theracal LC was found to be incomplete due to the limited moisture diffusion within the material [118]. Thus, no calcium hydroxide is produced, and less calcium ion leaching is recorded, resulting in an inferior remineralization potential compared to Biodentine. The omission of calcium hydroxide in set TheraCal LC suggests that calcium ions released from this material are not in the usual hydroxide form. Hence, it can be concluded that the presence of a resin matrix modifies the setting mechanism and calcium ion kinetics of TheraCal LC, resulting in lower calcium-releasing ability (Table 1) [120]. In vitro study reported that the CSMs (Biodentine, ProRoot MTA) induced remineralization of artificially demineralized dentine at a definitely higher speed and intensity than TheraCal LC [121]. The material seals the pulp capping site despite contact with dentinal or pulpal fluids, as its solubility is lower than ProRoot MTA, MTA Angelus and Biodentine (Table 1) [26].

Additionally, dentinal fluids play a crucial role in the release of calcium and hydroxide ions supporting the sealing capacity of the induced apatite. TheraCal LC

exhibited superior sealing ability and comparable interfacial microleakage to MTA and Biodentine, showing better cumulative performance [122]. Lack of cytotoxicity and biocompatibility remain the significant factors of pulp capping agents which directly affect the clinical outcome. It was found that TheraCal LC produced the least favorable pulpal responses compared to both ProRoot MTA and RetroMTA. Overall, research reported that TheraCal specimens had lower quality calcific barrier formation, extensive inflammation and less favorable odontoblastic layer formation (Table 1).

Those findings were accounted to the presence of acrylic monomer Bis-GMA in the material. However, it was noted that Bis-GMA was not detected, despite being listed in the safety data sheet provided by the supplier [124]. Presence of resin in the pulp capping agent which may remain unpolymerized is often associated with adverse pulpal reactions that lead to pulp toxicity and inflammation. The study designed to investigate the consequences of adding resins to tricalcium silicates by comparative analysis showed that TheraCal is toxic to pulp fibroblasts and has a higher inflammatory effect and a lower bioactive potential than Biodentine [125]. Those findings coincide with another study which reported that the reparative capacity of TheraCal LC is inferior to Biodentine [126]. TheraCal LC results showed dentin bridge formation with mild chronic inflammation, reduced dentin bridge thickness and a higher inflammatory score, which may be attributed to the hydration properties of TheraCal LC (Table 1). Moreover, despite that the photopolymerization of TheraCal LC is associated with low heat generation, it could still potentially induce adverse pulpal effects when used in pulp capping procedures [127].

TheraCal LC exhibited higher bond strength values than Biodentine when layered with either composite or glassionomer cement [128,129].

Although sufficient bioactivity, superior handling properties and superior quality of bonding with the final overlaying restoration could justify the use of TheraCal LC as the IPC agent, further in vitro and in vivo studies on this front are required. Also, TheraCal cannot be recommended for DPC [125].

ACTIVA BioACTIVE

ACTIVA BioACTIVE-BASE/LINER (Pulpdent, USA) was launched in the market iin the year 2014 claiming the strength, aesthetics and physical properties of composites and increased release and recharge of calcium, phosphate and fluoride in comparison with glass ionomer (GI). On the other hand, studies proven that the fluoride ion release of ACTIVA is lower than that of the conventional GI (Keta Molar Quick Aplicap, 3M ESPE, Saint Paul, MN, USA) and also than that of RMGI cement (VitremerTM, 3M-ESPE, Saint Paul, MN, USA) [130,131]. The results indicate the ACTIVA BioACTIVE does uptake fluoride and re-release it, which could be beneficial by decreasing incidence of secondary caries. Despite claimed bioactivity, the manufacturer recommends the use of ACTIVA BioACTIVE products in cases without pulpal involvement and ACTIVA BioACTIVE-BASE/LINER only in cases of Indirect pulp capping.

In comparison to both MTA and Biodentine, ACTIVA BioACTIVE represents a favorable setting time with no delay in placing final restoration (Table 1). The material has three setting mecha-nisms; it cures with low intensity light for 20 s per layer and has both glass-ionomer (acid-base reaction) and composite self-cure setting reactions (Table 1). The anaerobic, self-cure setting-time is 3 min with self-cure for 15–20 s before light curing.

The bioactive properties of ACTIVA BioACTIVE products are based on a mechanism whereby

the material responds to pH cycles and plays an active role in releasing and recharging of significant amounts of calcium, phosphate and fluoride [131]. Some authors have suggested that ability to release biologically active ions is more accurately termed "biointeractivity" and is a prerequisite for a material to be bioactive [117]. These mineral components are responsible for stimulating the formation of mineralized hard tissue. As calcium ions play a key role in the material-induced proliferation and differentiation of human dental pulp cells, they also stimulate the formation of a connective apatite layer and seal at the material-tooth interface. ACTIVA exhibited the potential to stimulate biomineralization similar as MTA, Biodentine and TheraCal LC on the basis of releasing the same amount of Ca and OH ions (under ionic supplemented conditions) [133].

Despite the fact that ACTIVA BioACTIVE products are RMGICs, the laboratory and clinical findings indicate that the self-adhesive ability of the material is still not clear [52]. The so called hypothesis was confirmed in a 1-year clinical follow-up of posterior restorations made with ACTIVA BioACTIVE Restorative, indicating a very high initial failure rate [134]. Studies have reported overall higher microleakage of cavities restored with ACTIVA BioACTIVE if no previous etching was performed nor an adhesive applied, compared to cavities restored with resin composite [135,136].But contrarily the manufacturer does not recommend any pretreatment on surfaces. Similar observations were presented in the study where bond strength measurement of ACTIVA BioACTIVE Restorative after 28 days was not possible due to loss of restorations if no pretreatment was performed or if dentine was etched [52]. So in view of this study, the self-adhesive property of ACTIVA BioACTIVE products seem nonexistent and counterproductive as vital pulp therapy agent (Table 1).

Considering the material's characteristics and handling, the application of ACTIVA BioACTIVE for pulp capping is justified. The resin in pulp capping materials such as ACTIVA BioACTIVE BASE/LINER exaggerate inflammation-regeneration balance skewed to the latter. As with respect to the other light-cured tricalcium silicate, incomplete resin photopolymerization leads to free monomers' release and increase the cytotoxicity which is detrimental to the pulp [137]. Further in vitro and in vivo studies are necessary to assess and evaluate the use of ACTIVA BioACTIVE for Vital pulp therapy. On the contrary, calcium silicate materials such as Biodentine and MTA shift the balance towards regeneration, resulting in successful clinical outcomes [138].According to a recent in vivo study concluded that ACTIVA BioACTIVE BASE/LINER exhibited excellent biocompatibility and healing for rat subcutaneous tissues in comparison with CSMs (MTA-HP and iRoot BP Plus) [139]. But, this claims need to be validated for better clinical outcomes.

Conclusions

So Biological driven dentistry with primary aim of preservation and protection of the pulp vitality remains the fundamental of the modern endodontics. So the present studies and its key findings confirms Calcium trisilicates (MTA and Biodentine) are reliably induce dentin bridge formation consistently and qualitatively while keeping a vital pulp in pulp capping procedures [71,104,108,112,140].

Also this review emphasize superiority of Biodentine in relatively better manipulation, cost effective and favourable setting time in comparison to MTA. Although long-term clinical studies are needed for a definitive evaluation of Biodentine as a pulp capping agent.

New generation of light-cured resin-modified calcium silicates; namely, TheraCal LC and ACTIVA BioACTIVE BASE/LINER should be evaluated more on clinical research study basis to delineate its indications and usage. Nevertheless, all potential materials should categorically pass the litmus test of cytotoxicity, quality of induced dentin bridge and protocols for higher bond strength to tooth structure and final restoration for predictable and long term successful outcomes.

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Legend Table

Table 1: Properties of Bioactive Materials

Property	Material			
	MTA	Biodentine	Theracal LC	Activa Bio Active (Base/Liner)
Marginal Seal	Chemical and mechanical adhesion Penetration in dentinal tubules		Low SBS due topolymerization shrinkage Poor chemical ormicromechanical adhesion	Poor chemical or micromechanical adhesion due to lack of self-adhesive propertiesGood seal after DBA application
pH	10.48-9.45	11.98-11.16	10.66-9.85	8.00
Calcium release (ppm)	11.7-55.1	18.0-95.3	12.6-34.2	-NA-
Surface treatment in dentin/pulp	Rinse with 2.5-5.0% NaOcl	Hemostasis	Hemostasis	Lightly dry,DBA for higher SBS
Pulp response	Non-inflammatory reaction,Increase in TGF-β1,Non toxic topulpcells,Favourable odontoblast layer formation	Non-inflammatory reaction,Increase in TGF-β1,Non toxic to pulp cells,Wellarranged odontoblasts	Mild chronic inflammation, Increase in TGF-β1,Toxic to pulp fibroblast, Less favourable	Biointeractive, Toxic to pulp cells due to resin content

			odontoblasts layer formation	
Quality of hard tissue barrier	Regular Homogenous Uniform thickness Lacks characteristic of natural dentine	Complete Dentin bridge formation Regular Uniform thickness	Low quality calcific barrier Inferior dentin bridgeformation Reduced dentin bridgethickness	-NA-
Surface treatment before composite	9%HF(90s), Silane	2 SE DBA	E and R DBA(higherSBS)	-NA-
Maturation period	≥ 7 weels	72 h	-	-NA-
NA-Not available;ER-Etch and rinse;2 SE- Two step Self etch;DBA-dentin Bonding agents;SBS-Shear bond strength.				