Meil on rõõm jagada üht hiljuti avaldatud kirjanduse ülevaadet Biodentine'i kohta, mille on kirjutanud prof. Imad About.

Teema: "**Biodentine: biokeemilistest ja bioaktiivsetest omadustest kliiniliste kasutusvaldkondadeni**"
Link: https://dx.doi.org/10.1016/j.gien.2016.09.002
Autorist:

Prof. Imad About on suubioloogia professor hambaravi teaduskonnas Aix-Marseille Ülikoolis Prantsusmaal. Ta on Rahvusvahelise Hambaraviuuringute Assotsiatsiooni (IADR) pulbi bioloogia ja regeneratsiooni rühma asepresident ning Mandri-Euroopa divisjoni juhatuse liige. Ta on rahvusvaheliselt tunnustatud pulbi tüvirakkude ja kudede regeneratsiooni ekspert, kes on avaldanud rohkem kui 190 revideeritud artiklit, kokkuvõtet ja raamatupeatükki.

Tegemist on kirjanduse ülevaatega, milles on viidatud 50-le Biodentine'i artiklile erinevate materjaliomaduste aspektist, mis viitasid ilmselgelt kõigile Biodentine'i suurepärastele ja unikaalsetele omadustele, ning tsiteeriti peaaegu kõiki Biodentine'i puudutavaid olulisi kliinilisi uuringuid, histoloogilisi uuringuid ja juhtumiaruandeid.

Mõned olulisemad punktid:

1. Biodentine'i kasutusalade alla kuuluvad:
a) Restauratiivne hambaravi
b) Laste hambaravi
c) Endodontiline hambaravi

2. Biodentine'i kliiniliste kasutusalade positsioneerimine:
a) Permanentne dentiini aseaine
b) Ajutine emaili aseaine
c) Võimalik kasutada puuduva/kahjustunud dentiini mahu taastamiseks
d) Võimalik kasutada pulpotoomias Formocresoli alternatiivina

3. Milline on Biodentine võrreldes teiste laialdaselt kasutatavate ja tavapäraste pulbi katmismaterjalidega?

Biodentine võrreldes kaltsiumhüdroksiidiga
a) Mehaaniliselt tugevam tänu selle koostisele ja madalale poorsusele
b) Vähem lahustuv
c) Tihedam täitmine

Biodentine võrreldes MTA-ga
d) Lihtsam käsitseda
e) Mehaaniliselt tugevam ja lühem kõvastumisaeg
f) Võimalik kasutada ajutise emaili aseainena kuni 6 kuud
g) Ei vaja pinna ettevalmistust
h) Ei tekita hammaste värvusemuutust (röntgenkontrastaine tsirkooniumoksiid) võrreldes MTA-ga (röntgenkontrastaine vismutoksiid)

4. Uus avastus Biodentine kohta: selle kasutamine dentiinil/pulbil vähendab põletikku ja selle tulemusena operatsioonijärgset valu ja ülitundlikkust.

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LITERATURE REVIEW/ REVISIONE DELLA LETTERATURA

Biodentine: from biochemical and bioactive properties to clinical applications

Biodentine: dalle proprietà biochimiche e bioattive alle applicazioni cliniche

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KEYWORDS
Biodentine;
Tricalcium silicate-based material;
Dentin substitute;
Bioactivity;
Clinical applications.

Abstract Biodentine is a tricalcium silicate-based material designed as a permanent dentin substitute. It is biocompatible and bioactive material. Its interactions with both hard and soft tissues lead to a marginal sealing preventing marginal leakage and provide protection to the underlying pulp by inducing tertiary dentin synthesis. Unlike other dentin substitutes, Biodentine application does not require any conditioning of the dentin surface and the restoration sealing is provided by micromechanical retention as Biodentine penetrates into the dentin tubules forming tag-like structures. After setting, Biodentine can be cut and reshaped like natural dentin. It can also be bonded with different types of adhesives before finishing the final restoration with composite resin. Published clinical trials, histology of human teeth and clinical cases show that Biodentine has a wide spectrum of clinical applications as a permanent bulk dentin substitute in endodontics, in restorative dentistry, and pediatric dentistry as a possible replacement material of formecresol. This review brings a comprehensive understanding of Biodentine composition, preparation properties and the mechanism of interactions with hard and soft tissues. It explains the scientific mechanisms of the induction of these specific functions and illustrates the scientific basis beyond their clinical successful use. The article provides an overview of Biodentine clinical applications summarizing published clinical trials and reporting published clinical cases with this material in restorative and pediatric dentistry as well as in endodontics.

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PAROLE CHIAVE
Biodentine;
Cementi a base di trisilicato di calcio;
Sostituti della dentina;
Ricerca;
Applicazioni cliniche.

Riassunto Biodentine è un materiale a base di silicato tricalcico progettato come sostituto permanente della dentina. Si tratta di un materiale biocompatibile e bioattivo. Le sue interazioni con entrambi i tessuti duri e molli portano ad una sigillatura marginale in grado di prevenire l'infiltrazione marginale e forniscono una protezione alla polpa sottostante inducendo sintesi dentina terziaria. A differenza di altri sostituti della dentina, l'applicazione di Biodentine non richiede alcun condizionamento della superficie dentinale e la tenuta della restaurazione è fornito dalla ritenzione micromeccanica in quanto Biodentine penetra nei tubuli dentinali formando strutture di simili ai resin-tag. Dopo l'indurimento, il Biodentine può essere tagliato e rimodellato come dentina naturale. Può anche essere trattato con diversi tipi di adesivi prima di terminare il restauro definitivo. Studi clinici pubblicati, istologia di denti umani estratti e casi clinici dimostrano che Biodentine ha un ampio spettro di applicazioni cliniche, come sostituto permanente della dentina in endodonzia, in odontoiatria restaurativa e odontoiatria pediatrica. Questa review si propone di descrivere in maniera completa la composizione di Biodentine, le proprietà di preparazione e il meccanismo di interazione con i tessuti duri e molli. Essa spiega i meccanismi scientifici che caratterizzano queste funzioni specifiche e illustra la base scientifica del suo successo nell'utilizzo clinico. L'articolo fornisce inoltre una panoramica delle applicazioni cliniche di Biodentine riassumendo gli studi clinici e riportando i casi clinici pubblicati con questo materiale in odontoiatria restaurativa e pediatrica, così come in endodonzia.

Introduction

Over the past decades, search on restorative materials focused on replacing amalgams in small anterior restorations and on posterior restorations of moderate size by direct composite restorations. Opposed to amalgams, a micro-mechanical retention of resin composites can be achieved with these materials by applying different adhesives. However, some drawbacks have been reported with resin-based materials such as wear resistance under high stress, shrinkage upon polymerization leading to microleakage and toxic monomers release.[1,2] In order to protect the pulp from resin-based materials toxic components, Calcium hydroxide-based materials have been widely used in direct pulp capping procedures. In spite of a highly alkaline pH of this material, a dentin bridge can form within 3 months providing a protection to the underlying pulp with mild or moderate inflammation. However, several studies demonstrated a partial dissolution and that this bridge has tunnel defects.[3,4] The recent focus on biocompatible materials such as Portland led to the development of Mineral trioxide aggregate (MTA) as a root-end filling material and direct pulp capping. This material is mainly composed of tricalcium and dicalcium silicates.[5] When applied for pulp capping, it induces reparative dentin production leading to a regular tubular dentin bridge formation within 2 months with no signs of inflammation.[4] However, some shortcomings have been reported with this material. These are related to its long setting time of 2 h 45 min, weak mechanical properties and difficult handling properties.[6] Additionally, tooth discoloration has been reported when this material is used for revascularization.[7,8] Biodentine is a recently released tricalcium silicate-based material developed as a permanent dentin substitute to replace the damaged dentin.[9]

In this review, the material composition, preparation method and application, mechanical and physical properties will be described, its interactions with the soft and hard dental tissues will be explained and finally, Biodentine clinical applications based on published works will be reported.

Biodentine composition

Biodentine is a two components material. The powder is mainly composed of Tricalcium silicates. It also contains Di-Calcium Silicate as a second core material and Calcium Carbonate and Oxide as filler. The powder contains Zirconium oxide as a radio-opacifier. The liquid contains Calcium Chloride as a setting accelerator and a water reducing agent (Table 1). The presence of a setting accelerator allows the material setting in 12 min and the presence of a water reducing agent avoids the formation of cracks within the material. Such cracks are usually observed after setting of cements containing high percentage of water.[9] The material is prepared by adding 5 drops of liquid to the powder present in the capsule. These components are then triturated with an amalgamator for 30 s at 4000 rpm leading to the formation of a paste of creamy consistency. The preparation method and proportions between powder and liquid should

Table 1 Biodentine composition: two components: liquid and powder to be mixed with an amalgamator for 30 s at 4000 rpm.[9]

Powder	Role
Tri-calcium silicate (C_3S)	Main core material
Di-calcium silicate (C_2S)	Second core material
Calcium carbonate and oxide	Filler
Iron oxyde	Shade
Zirconium oxyde	Radio-opacifier
Liquid	
Calcium chloride	Setting accelerator
Hydrosoluble polymer	Water reducing agent

be respected and applied according to the manufacturer's instructions as these proportions greatly influence the material's setting and mechanical properties. This is of particular significance mainly for applications under mechanical loads such as applications in Class II cavities.

The setting reaction is a hydration reaction

When Biodentine powder and liquid are mixed with an amalgamator, the setting of the material is a hydration reaction. While Calcium silicates partially dissolve by adding the liquid, a hydrogel of hydrated silicate is produced. This will precipitate on the remaining Silicate particles' surface and in the spaces between the particles leading to a significant decrease in the material's porosity and an increase in its compressive strength over time.[9]

Biocompatibility

Like any other restorative material, Biodentine Biocompatibility was investigated to ensure its safety when applied onto the cells. Evaluation of its genotoxicity on bacteria strains by the Ames test and its effects on the formation of micronuclei by human lymphocytes demonstrated the absence of any mutagenic effect of the material. Similarly, when tested on target human pulp cells, no DNA breaks or damage was observed with the Comet assay. These results demonstrated no genotoxic effects of Biodentine in vitro. The biocompatibility of the material was also investigated through its direct application to human pulp cells simulating the direct pulp condition and indirectly through a dentin slice to simulate its indirect pulp capping in vivo. Under both conditions Biodentine was not found to affect target cell viability under in vivo application conditions.[9] Additionally, when Biodentine was applied onto human pulp cells to investigate its effects on their specific functions by studying expression of odontoblast specific functions such as expression of Nestin (a human odontoblast specific marker) and Dentin Sialoprotein, Biodentine was not found to inhibit the expression of these proteins but rather induce their expression and the cells mineralization capacity.[9–11] Further investigations demonstrated the absence of toxicity of Biodentine to human MG63 human osteoblast cells with the MTT assay with properties comparable to that of MTA.[12]

Interactions with hard tissues: no surface preparation is needed to apply Biodentine™

Clinical application of Biodentine in restorative dentistry implies an intimate interaction with hard and soft tissues as well as with other restorative materials. This should lead to a marginal sealing in vivo which provides pulp protection and marginal sealing. Thus investigating these properties in ex vivo is of prime importance.

An experimental work using third molar teeth was used to investigate the marginal sealing of Biodentine alone or in combination of other resin-based materials using the silver nitrate penetration method in Class II cavities. No marginal leakage was observed at the Biodentin/dentin interface or at the enamel/Biodentine interface when the whole cavity was filled with Biodentine alone as a bulk restorative material replacing dentin and enamel without any conditioning treatment. No leakage was observed when Biodentine surface was prepared with the total etch technique and resin composite application. The results of this investigation demonstrated that the results obtained with Biodentine were similar to those obtained with resin-modified glass ionomer cement (Fuji II LC) considered as a reference material in this type of indications.[13] An interesting study compared the shear bond strengths of different adhesive systems to Biodentine. Adhesive systems such as Prime & Bond NT: etch-and-rinse adhesive system, Clearfil SE Bond: 2-step self-etch adhesive system and Clearfil S3 Bond: 1-step self-etch adhesive system were applied onto Biodentine discs for 12 min and 24 h then a Composite (Clearfil Majesty) was applied. Data showed that the shear bond strengths were the same for different adhesive systems to Biodentine.[14] This confirms that the marginal sealing of Biodentine is equivalent to that of RMGIC (Fuji II LC) and that Biodentine can be etched and treated like natural dentin. Different restorative materials can be successfully applied on top of Biodentine. Whatever the surface treatment used on Biodentine, this material can be used in combination with composite resins.[13,14]

Biodentine interacts with hard tissues by micromechanical retention

Interactions of Biodentine with the dentin provided cues to understanding how this material provides a marginal sealing without any dentin surface preparation: no etching and no bonding. In an experimental work performed ex vivo, dentin slices were prepared and Biodentine was prepared and mixed with a fluorescent dye before its application onto the dentin surface. Confocal laser scanning electron microscopy and scanning electron microscopy were used to study the interface between Biodentine and dentin. Confocal laser scanning electron microscopy revealed that Biodentine penetrated into the dentin tubules forming tag-like structures into the dentin tubules. Scanning electron microscopy revealed that the dentin tubules appeared with plugs of mineralization crystals just beneath the interface obliterating the dentin tubules. These results explain the micromechanical retention of the material on the one side and the marginal sealing on the other side.[15]

Bioactive properties in vitro

An entire human tooth culture model was used to investigate both the material hydration when placed for pulp capping and its effects on the pulp response. The tooth culture model provides a useful tool to investigate the initial steps of dentin-pulp regeneration and the consequence of applying pulp capping materials. Since the teeth used are immature impacted third molars, they also have the advantage of a high regeneration potential and not to be in contact with the oral flora. Biodentine was applied into pulp cavities then an adhesive resin was applied onto Biodentine and overlayed with a composite resin. Hydration was allowed to proceed under conditions similar to those in vivo by incubating teeth in culture medium. After 14 days, back-scatter scanning electron micrographs revealed that the material was homogenous and appeared completely hydrated at all areas

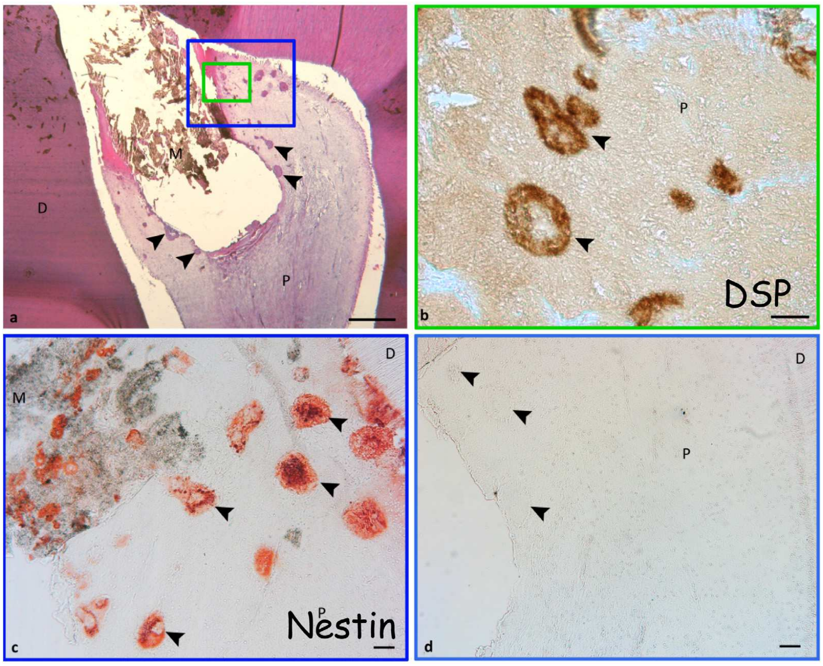

Figure 1 Biodentine direct application onto human pulp in human entire tooth culture for 4 weeks. Biodentine induced odontoblastic differentiation and reparative dentin secretion. Mineralization foci containing sequestered cells are observed in the dental pulp beneath Biodentine. The sequestered cells express odontoblast markers such as Dentin Sialoprotein (DSP) and nestin.[10]

examined: within the material, at the Biodentine/dentin interface, at Biodentine/composite resin interface and at the Biodentine/pulp interface. The hydration of this type of materials leads to the release of Calcium ions which are necessary for the mineralization. X-ray diffraction analysis of the material after setting demonstrated a significant peak of Calcium hydroxide formation which has long been used for pulp capping with a well demonstrated ability to induce dentin bridge formation.[16]

This culture model provided valuable information on the response to Biodentine application directly onto the pulp.

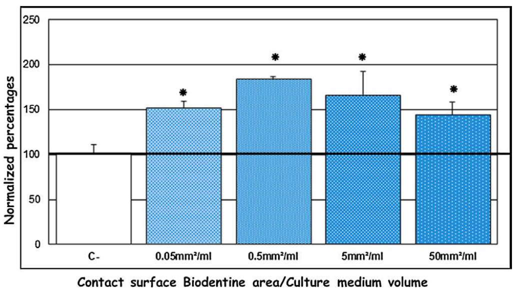

Figure 2 Effect of Biodentine on TGF-b1 release from human pulp cells. Biodentine induces release of TGF-b1 from human pulp cells. *Significant as compared to the control.[10]

Indeed, after application of Biodentine and culture for 14 days, mineralized structures appeared in the form of foci in close vicinity of the material. This mineralization seemed to be directly linked to Biodentine as some cement particles were seen within the mineralized structures but not in the neighboring pulp tissue. This mineralized tissue corresponds to an early form of reparative dentin as cells sequestered within these mineralizations express odontoblastic markers such as nestin and dentin sialoprotein (Fig. 1).

This mineralization seems to be due to the release of a growth factor, namely Transforming factor beta 1 (TGF-b1) from pulp cells incubated with Biodentine (Fig. 2). This factor has been shown to be involved in odontoblastic differentiation and recent investigations revealed that this factor is involved in the recruitment of pulp stem cells to TGF-b1 production site[17] which is related to Biodentine application. Interestingly, increase in TGF-b1 was significant whatever the ratio between the Biodentine surface area and cell culture volume.[10] This has a clinical significance as it indicates that this cement can be applied onto the pulp whatever the injured pulp surface area (Fig. 2).

Biodentine interactions with soft tissues induce tertiary dentin synthesis

When Biodentine was used for vital pulp therapy in vivo, investigations carrier out on different animal models showed that this material can be applied for both pulp capping and pulpotomy. Indeed, Biodentine induced tertiary dentin synthesis when applied as direct or indirect pulp capping material in rat teeth.[18,19] After direct pulp capping, the dentin bridge observed after 4 weeks in rat teeth was tubular and its porosity was similar to that of MTA.[19] Similar results demonstrated in miniature swine teeth. Indeed, after pulp capping with Biodentine, no pulp inflammation was observed while a thick dentin bridge formed after 3 and 8 weeks.[20] Similar results were reported in primary pig teeth after 4 weeks and 90 days. Application of Biodentine in pulpotomy was also investigated in primary pig teeth and compared to formecresol and white MTA (WMTA). The results with Biodentine showed no inflammation and a thick dentin bridge formed in 90%of the cases.[21] These data were comparable to the results obtained with WMTA and indicate the biocompatibility of these materials and their suitability for pulp capping and pulpotomy.

Clinical applications

Although Biodentine is a recently developed material as it has been released by the end of the year 2010 in Europe, different clinical applications have been so far published with this material. These include applications in restorative dentistry, pediatric dentistry and endodontics. Although it can be used as a temporary enamel substitute for upto 6 months, Biodentine is mainly used as a permanent dentin substitute. It can be used to replace the missing/damaged bulk dentin volume. It can also be used as an alternative to Formecresol in pulpotomy. The major clinical trials and histological studies in human teeth are detailed below and reported (Table 2) while the clinical case reports are only listed in the same table.

Table 2 Biodentine clinical applications and type of clinical works published on each application. Biodentine can be used in restorative dentistry, pediatric dentistry and endodontics as a permanent dentin substitute. It can be used to replace the missing/damaged whole dentin volume. It can also be used as an alternative to formecresol in pulpotomy.

Application	Type of investigations/ references
Crown	
Temporary enamel restoration	Clinical trials[22]
Permanent dentin substitute in	
Deep/large carious lesions	Clinical trials[22]
Deep cervical/radicular lesions	Case reports[36–38]
Indirect pulp capping	Clinical trials[22,23]
Direct pulp capping	Clinical and histological studies[25,26]
Pulpotomy	Clinical trials[27,39]
Root	
Root canal/furcation perforations	Case reports[40]
External resorption	Case reports[41]
Internal resorption	Case reports[42]
Regenerative endodontics	Case reports[43]
Apexogenesis after traumatic exposure	Case reports[33,44]
Apexification	Case reports[45–48]
Retrograde root canal obturation	Case reports[49,50]

Indirect pulp capping

Arandomized clinical study was performed in the restoration of posterior teeth with Biodentine. 397 cases were included with a three years follow-up. Biodentine was applied as a bulk restorative material in deep dentin cavities in replacement of both dentin and enamel. The scoring scales included consistency, working time, adhesion to instruments, ease of handling, anatomic form, marginal adaption, quality of proximal contact, marginal discoloration, surface roughness, secondary caries and post-operative pain. The results of this trial reported that Biodentine was easy to handle, showed, a, excellent anatomic form, marginal adaptation and very good interproximal contact. During the follow-up, the restoration with Biodentine™ in comparison to the composite resin Z100 was well tolerated in all cases with no post-operative pain. The anatomic form, marginal adaptation and interproximal contact started to deteriorate only after 6 months. Due to the deterioration, a complementary treatment was performed. Biodentine was kept as dentin substitute as the pulp vitality test was positive. Biodentine presented a good resistance to burring and the composite Z100 was applied onto Biodentine surface and evaluated for up to 3 years. The conclusions of this study is that Biodentine can be used as a posterior restoration material for up to 6 months as a temporary enamel substitute. When covered with Z100[1] , it is a well-tolerated permanent dentin substitute. Additionally, Biodentine can be cut and shaped like the natural dentin.[22] In another clinical study, the efficacy of Biodentine as an indirect pulp capping material was evaluated and compared to a glass ionomer cement (Fuji IX) in irreversible pulpitis. 36 restorations with Biodentine and 36 Fuji IX were placed randomly in 53 patients. The clinical efficacy at 12 months revealed no statistically significant differences in clinical efficacy between Biodentine and Fuji IX.[23]

The reported absence of post-operative pain and post-operative sensitivity in the clinical trial[22] may be due at least to 2 factors:

1) The infiltration of Biodentine into the dentin tubules[15] due to the precipitation of crystals within the tubules decreases the dentin tubule permeability and fluid movement which may decrease post-operative sensitivity.
2) The reduction odontoblast pain receptor expression and function and the reduction of the secretion of pro-inflammatory cytokines. Indeed, odontoblasts express pain receptors of the transient receptor potential family of ion channels (TRP) namely TRPA1. These receptors play a significant role in nociception and neurogenic inflammation. When extracts of Biodentine were applied on odontoblast-like cells, expression of these receptors decreased together with their functional activity as measured by an intracellular calcium level increase. Additionally, Application of Biodentine decreased the pro-inflammatory tumor necrosis factor secretion (TNF-a) from odontoblast like cells[24] as measured by Enzyme-linked immunosorbent assay (ELISA).

Direct pulp capping

Pulps of 28 non-carious molars scheduled for orthodontic treatment were exposed mechanically and pulps capped directly with Biodentine or MTA in class I cavities. 7 patients complained from mild pain on the day of surgery. 4 of these patients were treated with Biodentine and 3 with MTA. No symptoms were reported in the other patients. Teeth were tested before extraction for cold and electro-sensitivity and all confirmed the pulp vitality. The absence of periapical pathology was confirmed radiographically before the treatment and just before the tooth extraction. The histological examination of the pulp state and response after direct pulp capping with Biodentine as compared to MTA in human teeth revealed an absence of pulp inflammation and the formation of a complete dentin bridge beneath both materials after 6 weeks.[25] Tomographic data evaluating the density and volume of reparative dentin revealed that these values were higher for Biodentine.[26] These results indicate that Biodentine can be safely applied directly onto the human vital pulp.

Pulpotomy

Clinical application of Biodentine in pulpotomy has been investigated in few clinical studies as a pulpotomy medicament. A randomized clinical study was performed in children of 4–9 years of age. 84 pulpotomies were performed and attributed to MTA or Biodentine. All teeth were restored with stainless steel crowns. Clinical and radiographic evaluations were performed after 6 and 12 months. Data showed that one molar of the MTA group had an internal resorption while 1 molar of Biodentine treated group had internal resorption and another showed a radiographic radiolucency. Over all, both materials had a very high clinical success rate[27] and the overall clinical success after 12 months is reported (Table 3). Another study evaluated Biodentine and compared it to MTA in a short term clinical study. Biodentine was applied in pulpotomy in 20 teeth followed by restoration with stainless steel crowns. At 3 and 6 months, patients were recalled and Biodentine was shown as equally efficient as MTA with similar radiographic success.[28] A similar study was performed comparing Biodentine to MTA and Propolis as pulpotomy medicaments. After 9 months, Biodentine and MTA showed comparable results with a high radiographic success rate and more favorable than Propolis.[29] Finally, a confirmation of all these data reported no significant differences between MTA and Biodentine used as pulpotomy medicaments even after 18 months with clinical success higher than 95% for both materials.[30] Taken together, although longer term clinical evaluations are required, these data indicate that Biodentine has the potential to be used as a substitute for formocresol in primary molar pulpotomies.

Table 3 Evaluation of Biodentine as compared to MTA in pulpotomy after 12 months. Clinical success rates are reported in number of cases and percentage showing a high clinical success rate of both MTA and Biodentine in pulpotomy after 12 months.[27]

	Success/total number of cases	Success (%)
MTA	36/39	92
Biodentine	38/39	97

Case reports on the other clinical applications

In addition to the above detailed indications, many case reports have been published with Biodentine in different clinical indications. These include deep cervical/radicular lesions, root canal/furcation perforations, external/internal resorption, regenerative endodontics, apexogenesis after traumatic exposure, apexification and retrograde root canal obturation. These applications are listed and corresponding case report references are provided (Table 2).

Discussion

Although Biodentine is among the most recently developed tricalcium silicate-based materials, a significant and increasing number of investigations have been published on this material. While many studies reported its biocompatibility and Bioactivity in vitro and in vivo, preclinical investigations shed the light on the mechanisms of its interaction with the dental hard tissue. Indeed, many investigations performed both in vitro and in vivo demonstrated that the interactions of Biodentine with both hard and soft tissues provide a hermetic seal protecting the dental pulp by preventing bacterial infiltration. These studies demonstrated that, through its interactions with the hard tissues, Biodentine provides a micro-mechanical retention by infiltrating the dentin tubules. On the other hand it induces the target tissue specific functions by inducing tertiary dentin synthesis which provides further protection to the pulp. These two combined effects might be responsible, at least in part, for the absence of post-operative pain and hypersensitivity. Another important investigation reported that the application of Biodentine reduces both TRPA1 pain receptor expression and function. More importantly, when applied on odontoblast-like cells Biodentine decreases pro-inflammatory TNF-a secretion. This indicates that, in addition to the abovementioned roles of Biodentine, its application onto the dentin/pulp reduces the inflammation and consequently the post-operative pain.

How does Biodentine compare to other widely used and common pulp capping materials

When compared to Calcium Hydroxide, Biodentine is stronger mechanically due to its composition and low porosity. It is less soluble and the produced dentin bridge shows no tunnel defects as compared to that under Calcium hydroxide thus it has a better sealing ability than Calcium hydroxide.[19,31] When Compared to MTA, Biodentine is easier to handle,[22] stronger mechanically and has a shorter setting time.[6] It can be used as a temporary enamel substitute up to 6 months and in different applications as a permanent dentin substitute without any surface treatment. Additionally, while discoloration with MTA[32] and its derivatives have been reported in regenerative endodontics and seem to be mainly due to the presence of Bismuth oxide as a radio-opacifier,[7] no discoloration of tooth crown has been reported after 48 months with Biodentine which does not contain Bismuth oxide but Zirconium oxide as a radio-opacifier.[33–35]

Conclusions

Taken together, through in vitro, in vivo, clinical trials/reports, this review shows that Biodentine is biocompatible, has strong mechanical properties and can safely be applied in restorative dentistry, in pediatric dentistry (as a possible alternative to formecresol) and in endodontics. It is important to know that Biodentine does not require any surface conditioning treatment. It can be cut and reshaped like natural dentin. It can be used as a bulk permanent dentin substitute to replace the whole damaged/lost dentin and not only as a pulp capping material. Biodentine surface can be bonded like the natural dentin with different adhesives before final composite resins application.

Conflict of interest

The author's original works on Biodentine were partially supported by Septodont.

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References

1. Mitchell RJ, Osborne PB, Haubenreich JE. Dental amalgam restorations: daily mercury dose and biocompatibility. J Long Term Eff Med Implants 2005;15(6):709–21.
2. Lutz F, Phillips RW, Roulet JF, Setcos JC. In vivo and in vitro wear of potential posterior composites. J Dent Res 1984;63: 914–20.
3. Niinuma A. A newly developed resinous direct pulp capping agent containing calcium hydroxide. Int Endod J 1999;32:475–83.
4. Aienehchi M, Eslami B, Ghanbariha M, Saffar AS. Mineral trioxide aggregate and calcium hydroxide as pulp capping agent in human teeth: a preliminary report. Int Endod J 2002;36:225–31.
5. Camilleri J, Montesin FE, Brady K, Sweeney R, Curtis RV, Pitt Ford TR. The constitution of mineral trioxide aggregate. Dent Mater 2005;21:297–303.
6. Torabinejad M, Rastegar AF, Kettering JD, Pitt Ford DR. Bacterial leakage of mineral trioxide aggregate as root-end filling material. J Endod 1995;21:109–12.
7. Vallés M, Mercadé M, Duran-Sindreu F, Bourdelande JL, Roig M. Influence of light and oxygen on the color stability of five calcium silicate-based materials. J Endod 2013;39(4):525–8.
8. Camilleri J. Color stability of white mineral trioxide aggregate in contact with hypochlorite solution. J Endod 2014;40(3):436–40.
9. Laurent P, Camps J, De Méo M, Déjou J, About I. Induction of specific cell responses to a Ca(3)SiO(5)-based posterior restorative material. Dent Mater 2008;24(11):1486–94.
10. Laurent P, Camps J, About I. Biodentine(TM) induces TGF-b1 release from human pulp cells and early dental pulp mineralization. Int Endod J 2012;45(5):439–48.
11. Zanini M, Sautier JM, Berdal A, Simon S. Biodentine induces immortalized murine pulp cell differentiation into odontoblast-like cells and stimulates biomineralization. J Endod 2012;38:1220–6.
12. Attik GN, Villat C, Hallay F, Pradelle-Plasse N, Bonnet H, Moreau K, et al. In vitro biocompatibility of a dentine substitute cement on human MG63 osteoblasts cells: Biodentine™ versus MTA(1). Int Endod J 2014;47(12):1133–41.
13. Raskin A, Eschrich G, Dejou J, About I. In vitro microleakage of Biodentine as a dentin substitute compared to Fuji II LC in cervical lining restorations. J Adhes Dent 2012;14(6):535–42.
14. Odabaş ME, Bani M, Tirali RE. Shear bond strengths of different adhesive systems to Biodentine. Sci World J 2013;10:626103. http://dx.doi.org/http://dx.doi.org/10.1155/2013/626103.
15. Atmeh AR, Chong EZ, Richard G, Festy F, Watson TF. Dentin-cement interfacial interaction: calcium silicates and polyalkenoates. J Dent Res 2012;91(5):454–9.
16. Camilleri J, Laurent P, About I. Hydration of Biodentine, Theracal LC, and a prototype tricalcium silicate-based dentin replacement material after pulp capping in entire tooth cultures. J Endod 2014;40(11):1846–54.
17. Mathieu S, Jeanneau C, Sheibat-Othman N, Kalaji N, Fessi H, About I. Usefulness of controlled release of growth factors in investigating the early events of dentin-pulp regeneration. J Endod 2013;39(2):228–35.
18. Goldberg M, Pradelle-Plasse N, Tran XV, Colon P, Laurent P, Aubut V, et al. Emerging trends in (bio)material research. In: Goldberg M, editor. Biocompatibility or cytotoxic effects of dental composites. 1st ed. Oxford, UK: Coxmoor Publishing Company; 2009. p. 181–203.
19. Tran XV, Gorin C, Willig C, Baroukh B, Pellat B, Decup F, et al. Effect of a calcium-silicate based restorative cement on pulp repair. J Dent Res 2012;91:1166–71.
20. Tziafa C, Koliniotou-Koumpia E, Papadimitriou S, Tziafas D. Dentinogenic responses after direct pulp capping of miniature swine teeth with Biodentine. J Endod 2014;40(12):1967–71.
21. Shayegan A, Jurysta C, Atash R, Petein M, Abbeele AV. Biodentine used as a pulp-capping agent in primary pig teeth. Pediatr Dent 2012;34(7):e202–8.
22. Koubi G, Colon P, Franquin JC, Hartmann A, Richard G, Faure MO, et al. Clinical evaluation of the performance and safety of a new dentine substitute, Biodentine, in the restoration of posterior teeth — a prospective study. Clin Oral Investig 2013;17(1): 243–9.
23. Hashem D, Mannocci F, Patel S, Manoharan A, Brown JE, Watson TF, Banerjee A. Clinical and radiographic assessment of the efficacy of calcium silicate indirect pulp capping: a randomized controlled clinical trial. J Dent Res 2015;94(4):562–8.
24. El Karim IA, McCrudden MT, McGahon MK, Curtis TM, Jeanneau C, Giraud T, et al. Biodentine reduces tumor necrosis factor alpha-induced TRPA1 expression in odontoblastlike cells. J Endod 2016;42(4):589–95.
25. Nowicka A, Lipski M, Parafiniuk M, Sporniak-Tutak K, Lichota D, Kosierkiewicz A, et al. Response of human dental pulp capped with Biodentine and mineral trioxide aggregate. J Endod 2013;39(6):743–7.
26. Nowicka A, Wilk G, Lipski M, Kołecki J, Buczkowska-Radlińska J. Tomographic evaluation of reparative dentin formation after direct pulp capping with Ca(OH)2, MTA, Biodentine, and dentin bonding system in human teeth. J Endod 2015; 41:1234–40.
27. Cuadros-Fernández C, Lorente Rodríguez AI, Sáez-Martínez S, García-Binimelis J, About I, Mercadé M. Short-term treatment outcome of pulpotomies in primary molars using mineral trioxide aggregate and Biodentine: a randomized clinical trial. Clin Oral Investig 2015 [Epub ahead of print] November 18.
28. Niranjani K, Prasad MG, Vasa AA, Divya G, Thakur MS, Saujanya K. Clinical evaluation of success of primary teeth pulpotomy using mineral trioxide aggregate(1), laser and Biodentine(TM) —an in vivo study. J Clin Diagn Res 2015;9(4):ZC35–7.

29. Kusum B, Rakesh K, Richa K. Clinical and radiographical evaluation of mineral trioxide aggregate, Biodentine and propolis as pulpotomy medicaments in primary teeth. Restor Dent Endod 2015;40(4):276–85.
30. Rajasekharan S, Martens L, Vandenbulcke J, Jacquet W, Bottenberg P, Cauwels R. Efficacy of three different pulpotomy agents in primary molars —a randomised control trial. Int Endod J 2016;11. http://dx.doi.org/http://dx.doi.org/10.1111/iej.12619.
31. Cox CF, Sübay RK, Ostro E, Suzuki S, Suzuki SH. Tunnel defects in dentin bridges: their formation following direct pulp capping. Oper Dent 1996;21(1):4–11.
32. Parirokh M, Torabinejad M. Mineral trioxide aggregate: a comprehensive literature review—Part III: Clinical applications, drawbacks, and mechanism of action. J Endod 2010;36(3): 400–13.
33. Martens L, Rajasekharan S, Cauwels R. Pulp management after traumatic injuries with a tricalcium silicate-based cement (Biodentine™): a report of two cases, up to 48 months follow-up. Eur Arch Paediatr Dent 2015;16(6):491–6.
34. Vallés M, Roig M, Duran-Sindreu F, Martínez S, Mercadé M. Color stability of teeth restored with Biodentine: a 6-month in vitro study. J Endod 2015;41(7):1157–60.
35. Marconyak Jr LJ, Kirkpatrick TC, Roberts HW, Roberts MD, Aparicio A, Himel VT, et al. A comparison of coronal tooth discoloration elicited by various endodontic reparative materials. J Endod 2016;42(3):470–3.
36. Karypidou A, Chatzinikolaou ID, Kouros P, Koulaouzidou E, Economides N. Management of bilateral invasive cervical resorption lesions in maxillary incisors using a novel calcium silicate-based cement: a case report. Quintessence Int 2016;23. http://dx.doi.org/http://dx.doi.org/10.3290/j.qi.a36385.
37. Baranwal AK. Management of external invasive cervical resorption of tooth with Biodentine: a case report. J Conserv Dent 2016;19(3):296–9.
38. Salzano S, Tirone F. Conservative nonsurgical treatment of class 4 invasive cervical resorption: a case series. J Endod 2015;41(11): 1907–12.
39. El Meligy OA, Allazzam S, Alamoudi NM. Comparison between Biodentine and formocresol for pulpotomy of primary teeth: a randomized clinical trial. Quintessence Int 2016;47(7):571–80.
40. Sinkar RC, Patil SS, Jogad NP, Gade VJ. Comparison of sealing ability of ProRoot MTA, RetroMTA, and Biodentine as furcation repair materials: an ultraviolet spectrophotometric analysis. J Conserv Dent 2015;18(6):445–8.
41. Pruthi PJ, Dharmani U, Roongta R, Talwar S. Management of external perforating root resorption by intentional replantation followed by Biodentine restoration. Dent Res J 2015;12(5): 488–93.
42. Umashetty G, Hoshing U, Patil S, Ajgaonkar N. Management of inflammatory internal root resorption with Biodentine and thermoplasticised Gutta-Percha. Case Rep Dent 2015;2015: 452609.
43. Khoshkhounejad M, Shokouhinejad N, Pirmoazen S. Regenerative endodontic treatment: report of two cases with different clinical management and outcomes. J Dent 2015;12(6):460–8.
44. Martens L, Rajasekharan S, Cauwels R. Endodontic treatment of trauma-induced necrotic immature teeth using a tricalcium silicate-based bioactive cement. A report of 3 cases with 24-month follow-up. Eur J Paediatr Dent 2016;17(1):24–8.
45. Nayak G, Hasan MF. Biodentine —a novel dentinal substitute for single visit apexification. Restor Dent Endod 2014;39(2):120–5.
46. Evren OK, Altunsoy M, Tanriver M, Capar ID, Kalkan A, Gok T. Fracture resistance of simulated immature teeth after apexification with calcium silicate-based materials. Eur J Dent 2016;10(2):188–92.
47. Vidal K, Martin G, Lozano O, Salas M, Trigueros J, Aguilar G. Apical closure in apexification: a review and case report of apexification treatment of an immature permanent tooth with Biodentine. J Endod 2016;42(5):730–4.
48. Bajwa NK, Jingarwar MM, Pathak A. Single visit apexification procedure of a traumatically injured tooth with a novel bioinductive material (Biodentine). Int J Clin Pediatr Dent 2015;8(1):58–61.
49. Caron G, Azérad J, Faure MO, Machtou P, Boucher Y. Use of a new retrograde filling material (Biodentine) for endodontic surgery: two case reports. Int J Oral Sci 2014;6(4):250–3.
50. Gupta PK, Garg G, Kalita C, Saikia A, Srinivasa TS, Satish G. Evaluation of sealing ability of Biodentine as retrograde filling material by using two different manipulation methods: an in vitro study. J Int Oral Health 2015;7(7):111–4.