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Clinical effectiveness of Resin modified calcium silicate cements

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Abstract

A thorough and critical analysis of basic properties of resin modified calcium silicate cements has been made. The problems related to the cytotoxicity and mineralization potential of this group of materials have been tracked. An important question that remains in the dental literature is whether these materials are suitable for direct pulp capping. The aim is to examine the data in the literature regarding the long-term clinical effectiveness of resin modified calcium silicate cements in direct pulp capping. A literature search base was undertaken in three electronic databases: PubMed, EBSCOhost and Google Scholar for the period 2015–2026. Resin modified calcium silicate cements belong to the fourth generation. These are materials that harden by light polymerization and hydration reaction. Issues related mainly to their cytotoxicity, bioactivity and clinical effectiveness were considered. The available information in the dental literature mainly concerns TheraCal LC. There are comparative data on the cytotoxicity of TheraCal PT and conventional calcium silicate cements.
For most of the new forms of resin modified calcium silicate cements, main information is from the manufacturers. Further studies on their cytotoxicity and bioactivity need to be done. An important conclusion that emerges from the analysis of the literature data is the need for definitive studies on the long-term clinical effectiveness of these materials as a means for direct pulp capping.

Keywords:

resin modified calcium silicate cement; direct pulp capping; cytotoxicity; bioactivity; generation biomaterial; hard tissue dentine bridge.

Introduction

Bioactive calcium silicate cements (CSC) are widely used in different areas of endodontics, including regenerative endodontics [1].

The first biomaterial put into practice by the Torabinejad and Dr White team in 1993 was MTA Original Dentsply Tulsa Dental, Tulsa, OK, USA) This material refers to the first generation of calcium silicate. The chemical composition is a ratio of 4 parts Portland cement Type I and 1 part bismuth oxide as a radiopaque agent [2].

A number of disadvantages of this first introduced calcium silicate cement such as long hardening time, manipulation difficulties related to its use in clinical practice, change in the color of hard tooth tissues, low compressive strength, high price, etc. led to the rapid development, improvement and introduction into dental practice of new preparations and forms based on calcium silicates [3].

There are many brands' biomaterials with different physicochemical properties in the dental market.

Classification of calcium silicate cements

The first generation biomaterial is ProRoot (Dentsply Tulsa Dental, Tulsa).It is a hydraulic calcium-silicate cement with an inorganic bioactive compound such as a

type I ordinary Portland cement. This material is a combination of powder and liquid, the hardening reaction is hydration [4].

The second-generation calcium silicate cements include materials related to modifications of MTA from the first generation. This generation includes: MTA Angelus, MTA Branco, etc. The third generation includes bioactive materials resulting from the modification of Portland cement. The following materials are related in these genera- tion: Bioaggregate, Biodentine, Aureoseal, Ortho MTA, MTA Plus, etc. This generation also contains conven- tional calcium silicate cements,that are in powder and liq- uid form and have a hydration setting reaction [5]. This reaction can occur in wet conditions.

Resin-modified calcium silicate cements belong, to the fourth, last generation. These are materials representing a combination of calcium silicates and resin. They are mainly indicated as means intended for direct and indirect pulp capping etc [6]. These methods are biological conservative treatments, which aim to maintain the vitality and functions of dental pulp (DP) through dentin bridge formation. The main difference between conventional calcium silicate cements and resin modified materials is the presence of the resin component. The addition of monomers in their composition and the possible risk of the presence of residual unpolymerized monomers in contact with vital but inflamed dental pulp raise the question of their biocompatibility [7].On the other hand, the inclusion of monomers in their composition provides better physicochemical properties, easier work, and the possibility of completing the treatment in one visit. The presence of a hydrophilic resin matrix in the composition ensures chemical adhesion to the dentin, which is a condition for hermetic sealing of the dental pulp communication [8].

The success healing process after direct pulp capping depends on more critical factors such as the type and stage of inflammation of DP(reversible); aseptic work; control bleeding; selecting a appropriate pulp capping agent [9,10].

An important part of clinical effectiveness is the choice of pulp capping material. Dentists expect these to be bioactive materials with high clinical effectiveness and the potential to form a quality dentin bridge, but there is still no definitive data on these materials regarding their long-term clinical effectiveness

This review aims to provide critical analysis and useful overview on the main problems, connected with clinical use and effectiveness of resin modified cal- cium silicate cements.

Literature Search

A literature search base was undertaken in three electronic databases:PubMed, Ebscohost and Google Scholar for the period 2015-2026.The following key words have been used: resin modified calcium silicate cements, clinical effectiveness, cytotoxity, direct pulp capping, residual monomers. The articles included and cited in the reference were selected based on application inclusion\ exclusion criteria.

Inclusion criteria: Articles that match the chosen topics: Language- Fully accessible open access articles in English, timeframe 2015-2026-, Publication type- Peer-reviewed journal articles, patent: and book, type of treatment method- direct pulp capping, types of participants-adults.

Exclusion criteria: Articles not relevant to the chosen topic: Articles outside the publication period: Articles, written in a language, other than English., type of treatment method – vital extirpation, types of participants-children

Discussion

Resin modified calcium silicate cements (RMCSC) or hybrid - main representatives and chemical composition These are materials that harden by light polymerization and hydration reaction. The hydration reaction in this group of cements is slow, because moisture is needed for the process, and it is supplied by the conditions of the environment and depends on the rate of diffusion [11,12]. The first hybrid biomaterial was put into practice in 2008 and it is a combination of silica 8%, resin 42.5% mainly consisting of 20% BisGMA and 77.25% the patent resin, 2.4% initiator and 5% barium sulfate[13].

Resin modified calcium silicate cements	Chemical composition
TheraCal lC	45% Portland cement third type,, 10% X-ray contrast substance - barium zirconate, 45% resin represented by BisGMA, polyethylene glycol, photoinitiato
TheraCal PT,	synthetic Portland Cemen, ,1-5% barium zirconate , resin -10-30% polyethylene glycol dimethacrylate, 5-10% Bis-GMA
Bright MTA	30–50% calcium silicates, 10-30% barium sulfate,

	resin – 10-30% polyethylene glycol dimethacrylate, without containing Bis-GMA
-BioCalp Cup	Portland cement, 7-12% barium sulfate, 35 – 45 wt. % hydrophilic resin

Table:1 Composition of resin modified calcium silicate cements

The main representative belonging to this generation is TheraCal lC (Bisco Inc, Schamburg, IL, USA [14] a material introduced into dental practice in 2017. According to the manufacturers, its chemical composition is presented in table 1 [15 - 17]. The material is a one-component paste that hardens after light polymerization for 20 seconds for each increment and a layer thickness of 1 mm. The manufacturer recommends an intensity of curing units of 1200 mW/cm²[14].

Recently, Bisco introduced a new dual resin modified calcium silicate cement TheraCal PT, with basic indication pulpotomy in pediatric dentistry. It consists of synthetic Portland Cement and polyethylene glycol dimethacrylate (10-30%) and Bis-GMA (5-10%) resin matrix, barium zirconate (1-5%) initiator (<1%)(8). The material hardens after light polymerization in 10 seconds[14].

Another new representative of the 4th generation is the resin modified calcium silicate cement - Bright MTA (Genoss, Suwon, Korea), its content is presented in Table 1 [18,19].

A new BioCal Cap was introduced into clinical practice in 2019(fig.1). According to the manufacturer, the material is a combination of 35 – 45 wt. % hydrophilic resin, Portland cement (PC) and barium sulfate 7 – 12 %. The curing time by light polymerization is 40 seconds for each increment [20] .For both of these new materials, there is a lack of information in the literature regarding their properties-

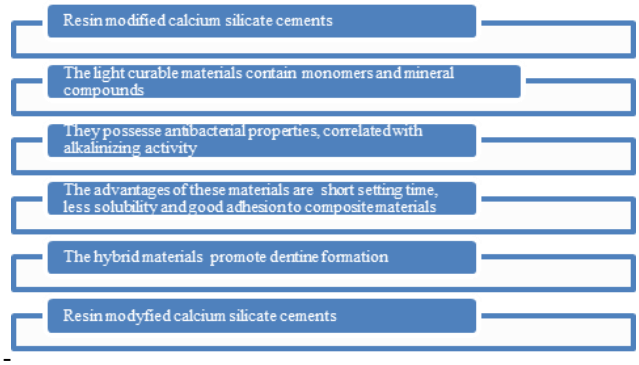

Fig.1 Basic properties of resin modyfed calcium silicate cements

Basic indications of these group materials are direct and indirect pulp capping. However, resin modified calcium silicate cements should have high mineralization potential and to provide formation of reparative dentin bridge [21]. A key factor for all materials intended for direct contact with the dental pulp in direct pulp capping is to be non-cytotoxic and biocompatible [21].

According to John C. Wataha [22] and A . Morsiya [23] a material is biocompatible when it elicits an appropriate biological response in a given application at the tissue level without causing systemic and local toxicity, allergic reactions, mutagenic effects, or carcinogenic effects [24]. Research on the biocompatibility of materials involves a variety of tests that are determined and depend on the location of application and the time of exposure [24,25]. The cytotoxicity of the material means capability of a substance to induce damage or living cell death either directly or through the release of leachable components, [26].

Tests for cytotoxicity study of the materials include freshly prepared and or hardened forms of the tested materials placed directly on tissue cells. Cytotoxicity tests are used to evaluate whether materials or their extracts promote cell death [27, 28].

The available information regarding the cytotoxicity of these hybrid CSCs in the literature is conflicting.

So e.g. A Buonavoglia et al [29] was not observed in Osteoblast-like cells treated with TheraCal lC and after 5 days, no cytotoxicity and the cells were organized to form.

In a comparative study of the cytotoxicity of different direct pulp capping materials on pulp stem cells, Manaspon C et al. found that Dycal and TheeraCal LC are cytotoxic to these cells [30].It was found that organic monomers from content of hybrid material have a negative effect on the migration and proliferation of pulp stem cells. [24].

Mehmet Adıgüzel et al. establish a significant reduction in the number of viable human pulp fibroblasts cells in the medium containing the Theracal LC samples from on human pulp fibroblasts[31]. Similar data were reported by other authors [32]. They found that TheraCal LC significantly decreased viable human monocyte cells and presented significant DNA damage in the comet assay. A Fathy SM et al establish a significant decrease in the number of viable mesenchymal stem cells- within time intervals of 24, 48, and 72 hours of contact with TheraCal LC[33].

It was found that TheraCalLC exhibits damaging effects in direct contact with human dental pulp stem cells [34, 35]. According to Zohre Moradia et al.[36]. TheraCal LC had higher cytotoxicity on the human dental pulp cells than Calcimol LC and Dycal, and lower cytotoxicity than ACTIVA BioACTIVE and Fuji II LC.

In a study of cytotoxity of various pulp capping agents on

the mouse fibroblast Balb/3T3 cell line was reported cell viability to be in 68,18% for Theracal LC at a 10% concentration [37]. TheraCal PT has been found to release significantly less Bisphenol A-glycidyl methacrylate and polyethylene glycol dimethacrylate than Theracal LC[38].

In a comparative study to assess the mineralization effect between MTA Angelus and resin-modified cements TheraCal PT, TheraCal LC on human dental pulp stem cells (hDPSCs) was found TheraCal LC showed the lowest cell viability, TheraCal PT demonstrated higher mineralization potential but less adhesion [39]. The authors believe that TheraCal PT contains more hydrophilic resin, which explains the improved interfacial interactions with the surrounding medium

There are no data on cytotoxicity studies conducted for the other available in the dental market forms RMCSC. So the question of the cytotoxicity of resin-modified CSCs still remains open?

This is due to the presence of organic components in the composition of hybrid CSCs can have a negative impact and lead to unsatisfactory clinical performance. It is believed that this is possibly due to the free unpolymerized monomers and their direct diffusion into the dental pulp [7,40]. The free unpolymerized monomers by diffusion to dental pulp tissue have a cytotoxicity and harmfull effect on pulp cell [41,42]. Collado-González et al found that 30% the total monomers in the content of RMCSC remain unpolymerized, but remain in the polymer matrix and only 9% of them may diffuse to the dental pulp [43]. Complex process including the degree of conversion after polymerization, the release of free monomers, and the degradation of the resin matrix cause various degrees of cytotoxicity [44].

According to Liu B et al. hydrophobic monomers such as Bis-GMA, UDMA had more cytotoxic effects than hydrophilic monomers such as HEMA and TEGDMA [45]. Similar conclusion was found from other authors [24, 45]. But the combination between them has a more toxic effect compared to the toxic effect alone. Similar data were found by Kraus et al. [46].

In our previous research through thermogravimetric analysis it was revealed that the new hybrid material BioCal-Cap was more resistant in comparison to TheraCal LC because no volatile compounds were found. The results after gas-chromatography of organic and inorganic and mass-spectrometry SIM mode analysis revealed that the extract of TheraCal LC contained nonreacted photoinitiators, while the same analysis for BioCal-Cap revealed no nonreacted monomers of HEMA [47].

And according to the results reported by Nilsen BW et al [48] hybrid TheraCal LC contains high levels of 2-(dimethylamino)ethyl methacrylate and camphorquinone, for which there is no adequate, relevant information from the manufacturer.

Evaluating the bioactivity of RMCSC

Bioactivity is mainly based on the amount of calcium ions released, ions that stimulate the dental pulp cells to dentinogenesis and the formation of an apatite layer in a biological environment. The bioactivity action is attributed to the capacity of calcium silicate cements to release Ca ions and start differentiation and proliferation of odontoblast-like cells at the level of pulp exposure place and formation of apatite crystals in contact with a suitable environment [48-54].

To evaluate the bioactivity of the hybrid CSCs, a methodology was used to determine the amount of calcium ions released. The released calcium ions have a key role in the differentiation of pulp cells into forming tissue cells [55]. According to Elbanna A, et al [56] the amount of calcium ions released from TheraCal LC samples significantly decreased over a period of 14 days and their release sharply decreased over a period of 28 days, these values being lower than the release of calcium ions over the same period from Biodentine .

In contrast, other authors Nagham A. et al [57] found that there were no statistically significant differences in the amount of calcium ions released from Biodentine and those from TheraCal LC over a 30-day period of comparison. According to Camilleri J. et al [58] the level of released calcium ions from TheraCal LC is significantly low and stops after the 4th day of its application as the reason for this is the presence of the resin modified matrix in the cured material. The amount of calcium ions released over 14 days by the newly introduced TheraCal PT was found to be significantly lower compared to that of TheraCal LC

And according to a comparative study by Gandolfi MG, et al [59] reported that TheraCal LC released a significantly higher amount of calcium ions compared to that of ProRoot MTA or Dycal for the same period of time. The same authors found a decrease in the release of hydroxyl ions from TheraCal LC at 7-14 days, which, according to the authors, is a condition for a favorable environment for the formation of new reparative dentin. Similar data are also reported by Ehab Mohamed Kamal et al [60]. They concluded that TheraCal LC has a low reparative capacity, the formed dentin bridge is of small thickness and accompanied by inflammatory reactions in the dental pulp .Similar data for low mineralization-inducing potentials of TheraCal compared to ProRoot was reported by Sohee Kang [61,62].

TheraCal LC contains resin ingredients, given proper curing, it seems to be a successful material for DPC.

The released calcium ions serve as bioactive signaling molecules for dentin bridge formation. A fully formed dentin bridge was found to be achieved within 28 days of application of TheraCal LC as a direct pulp capping agent [63]. Hard tissue bridge formation at 28 days was noticed by Cannon et al . in their study on TheraCal LC

[63]. Alkaline phosphatase is also a very important enzyme influencing the healing process and creating suitable conditions for tissue calcification [64].
In a comparative study of the effect of the use of TheraCal LC, Retro MTA, Biodentine and ProRoot MTA in dog partial pulpotomy on a fully formed quality dentin bridge was found after the use of TheraCal LC in only 33% of the samples, while the dentine bridge formed in 75% of the samples was of low quality [65]. Shehabeldin Saber et al [66] conducted a comparative study on the bioopotential of Biodentine, NeoPutty and TheraCal LC in inducing proliferation and adhesion of human periodontal ligament stem cells. The study revealed that TheraCal LC does not have the potential to be used as an endodontic repair material. In vivo study established that the application of TheraCal PT as a direct pulp capping agent resulted in significantly greater hard tissue formation than TheraCal LC[38]
In contrast, in a similar comparative study, but on the teeth of mice, it was found in all samples after using TheraCal LC that a quality dentine bridge was formed [67]. According to Singh S et al. TheraCal LC Histologically gives the characteristics of a complete dentin bridge formation, with maximum dentin thickness [68].
Similar data were established by other authors [69]. They found that all teeth treated with TheraCal LC in DPC formed a dentin bridge, and in 75% of all the dentin bridge was complete and qualitatively formed.
In a comparative histological study of direct pulp capping on upper and lower premolars treated with TheraCal LC, a bridge was found in all samples, and in 60% of the samples a dentin bridge with a thickness of more than 0.25 mm was registered in 60 % of samples [67].. Similar data were also reported by Kim et al. and Lee et al [70, 71].
In a comparative histological study, the effect between TheraCal LC and Biodentine was found that the samples treated with TheraCal LC had a complete and high-quality dentin bridge formed, with a maximum thickness compared to the samples treated with Biodentine [72].
Biomaterials used in pulp capping agents should have high mineralizing potential and capacity to formation the reparative tertiary hard tissue barrier over pulp exposure place [73].

Evaluating and comparing the clinical effectiveness of •RMCSC

RMCSC intended as a means for direct and indirect pulp capping. The goal is to preserve the vitality, structural and functional integrity of the dental pulp. The materials used for this purpose must be bioactive, stimulate the dental pulp to dentinogenesis, and have a strong antibacterial effect.[74].
For a successful outcome of direct pulp capping, it is very important to make a proper selection of the status of pulp inflammation. Success rates of direct pulp capping in permanent teeth have been shown to range 87.5–95.4% [75]. Data in the literature regarding the clinical effectiveness of RMCSC applied in direct pulp capping are conflicting. The reported curative effect of CSC on direct pulp capping according to literature data is between 85-100% [76]. According to the above authors, the clinical effectiveness for RMCSC is 43-92%.
It has been reported that TheraCal LC, used in DPC for permanent dentition showed a success rate of 93.3% for a period of 2 years [77]. According to Yan Wang et al TheraCal LC is clinically more effective pulp capping agent in deciduous teeth [77].
TheraCal LC exhibited comparable clinical and radiological outcomes to MTA in DPC of primary dentition after 12 months. The success rate in TheraCal groups was 91.9% [78, 79].
Meta-analyses were to evaluate the clinical and radiographic outcomes between Resin-modified and conventional calcium silicate materials as direct pulp capping agents. The analysis demonstrated TheraCal LC had short-term success compared to conventional materials[80].
There are authors who believe that the hybrid material TheraCal LC is not suitable to be applied in DPC, but as a means of indirect coverage only [15, 36, 81, 82].
Similar conclusions are also supported by other. Based on the histological findings,,resin-based materials are less suitable agent for pulp capping than conventional calcium silicate cement -MTA [83].
In a comparative clinical study and follow-up over a period of 6 months of the effect of the use of TheraCal LC, Biodentine and ProRoot MTA, no statistically significant differences in the quality of the formed dentin bridge were reported, but for a period of 12 months of observation more complications were reported with severe inflammation and poorly formed dentin bridge [16].
Similar data regarding good clinical effectiveness in a short period of 6 months after application of TheraCal LC were also established by other authors [81]. The reported clinical effectiveness of TheraCal LC, as a pulp capping agent in DPC for a period of 1 month, 6 months, 1 year, and 3 years, the overall success rate for TheraCal LC was found to be 96%, 83%, 73%, and 72% [84].
Similar data on good clinical success has been established by other authors [73]. They found clinical and radiographic data of success in DPC with MTA and TheraCal LC over the entire follow-up period of 24 weeks. Zhang et al reported good clinical results using TheraCal LC and iRoot BP Plus in DPC [75].
Long-term high clinical effectiveness of the application of TheraCal LC for a period of 2 and 4 years was reported by Gary A [15]. In a clinical study of the effect of treatment with TheraCal LC, a 93.3% success rate was reported over a period of 2 years [77].
The clinical effectiveness of RMCSC was evaluated

based on clinical indicators and radiographic data.

Clinical parameters such as spontaneous pain and objective examination data such as percussion, palpation, mobility, swelling and presence of fistula were used to assess clinical effectiveness. The radiographic assessment criteria used were continuity of the lamina dura, periapical lesion, furcation lesion and pathological root resorption. The presence of one or more of the clinical/radiographic findings was considered treatment failure. [85,86].

At the end of the 12-month follow-up period these authors reported 63.2% success rates of DPC after use TheraCal PTand 96.0% in the Biodentine [86]. In contrast, others C. Jeanneau, et al [40] and Bakhtiar, et al [7] concluded that TheraCal LC is not a suitable agent for direct pulp capping. Similar conclusions were established by Peskersoy C, et al [84].In a comparative clinical study of the effect between MTACerkamed, PO- LAND, Biodentine and TheraCaL LC, a success rate of 84.75%, 79.4% versus 72.1% for the hybrid cement was reported for an observation period of 36 months. A complete and well-constructed dentine bridge was reported in 86.7% of the cases in the MTA group, 85.7% for the group treated with Biodentine and 85.0% for TheraCal LC. The authors also report a relationship between the size of communication and clinical success. The success of the treatment for communication up to 0.5 mm is 79.1%, and for a size between 0.6 -1 mm, 63.5% success is reported. The quality of a hard tissue bridge at the ex- posture site has been recognized as an important factor for the clinical success of direct pulp capping [87,88].

A review of the literature shows a lack of consensus on the long-term clinical efficacy of using resin-modified CSCs as direct pulp capping.

The outcome success of DPC depends on several critical key factors, including the effective sealing properties of RMCSCs, adequate marginal adaptation to prevent microleakage and the formation of a hard tissue bridge[89,90,91,92, 93]. Based on the meta-analysis made by Silva et al ProRoot MTA promoted well organized hard tissue bridges with greater thickness com-pared to RMCSC [89]. In a clinical histological examination, it was found that TheraCal had higher complete dentin bridge formation, with maximum dentin thickness, compared to Biodentine[94].

A review of the literature shows a lack of consensus on the long-term clinical efficacy of using resin-modified CSCs as direct pulp capping. Based on the meta-analysis made by Cabrera-Fernández et al. reported comparable short-term success of Theracal LC to conventional CSC [91].

CONCLUSION

The review of the literature data clearly shows the need for further research on resin-modified calcium silicate cements. Research is needed to include the new materials available on the dental market. For most of them, the main information is from the manufacturers. Further studies on their cytotoxicity and mineralization potential need to be done. An important conclusion that emerges from the analysis of the literature data is the need for definitive studies on the long-term clinical effectiveness of these materials as a means for direct pulp capping. The question of the long-term clinical effectiveness and significance of resin-modified calcium silicate cements as a means suitable for direct pulp capping remains.

Abbreviations

- CSC- Calcium Silicate Cement
- MTA- Mineral Trioxide Aggregate
- DPC-Dental Pulp Capping
- RMCSC -Resin Modified Calcium Silicate Cements
- Hybrid CSCs-Other Name of Resin Modified Calcium Silicate Cements
- hDPSC- Human Dental Pulp Stem Cells
- BisGMA -Bisphenol A-glycidyl Methacrylate
- UDMA- Urethane-dimethacrylate
- TEGDMA, - Triethylene Glycol Dimethacry- late
- HEMA- 2-hydroxyethyl Methacrylate

Author Contributions

Conceptualization, methodology, formal analysis, Investigation, resources, data curation, writing—original draft preparation, writing—review and editing, visualization: I.D. The author has agreed and approved the published version of the manuscript

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Conflicts of Interest

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