

Biodentine as an Apical Plug Material in Immature Teeth: A Rapid Review

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Abstract

Nonvital immature teeth are newly erupted teeth with open apices and necrotic pulp that usually treated by apexification, a treatment that puts certain materials such as Ca (OH)₂ and MTA on the open apices. Biodentine™ then introduced as an alternative material for immature teeth. This study aimed to give an overview of Biodentine™ effectiveness as apical plug material in nonvital immature teeth apexification treatment. A rapid systematic review was conducted on PubMed, ScienceDirect, EBSCOhost, ClinicalKey databases using predefined search keywords, inclusion and exclusion criteria. Found the total of 138 articles which then filtered gradually according to PRISMA so the final results were 11 articles. Follow-up of 11 selected articles (7 case reports and 4 case series) showed satisfactory treatment outcomes. Clinical aspect of 8 articles reported variously, such as absence of swelling, pain, pus and sinus tract; revert of aesthetics and function; there is no teeth discoloration. Radiographic aspects of 11 articles reported varying results including: periapical lesions healing, periradicular tissues regeneration, continued root growth (increase in thickness and length of the apical, also formation of calcified apical barrier).

Based on its outcomes, Biodentine™ is effective to use as an alternative apical plug material for nonvital immature teeth apexification treatment.

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Introduction

Immature teeth are newly erupted teeth with open apices that can normally be closed after 3 years of teeth eruption.^{1,2} The thing that must be considered is when immature teeth are traumatized (the majority occurs under the age of 19 years to 25% of school-age children) or caries (occurs in 51.2 % of children aged 7-9 years) which is not treated properly so that it can lead to pulp disease, or even become necrotic. The prevalence of dental trauma causing necrotic pulp ranges from 17-100 % (depending on the severity of the trauma).^{1,3} Necrotic immature teeth can not continue the development process due to impaired blood supply so that dentin formation and root development will stop.^{1,4} This causes immature teeth have several characteristics such as wide root canal with open

apices, accompanied by thin and brittle dentin walls.¹ These situations will complicate clinicians to carry out conventional root canal treatment procedures.⁴⁻⁶

Treatment options for immature teeth based on their pulp vitality are divided into two, namely apexogenesis for vital teeth and apexification for non-vital teeth.^{2,7,8} Apexogenesis is a treatment carried out to maintain vital pulp tissue (radicular pulp) so that the physiological development and root apex formation can be continued to completion.^{8,9} Apexification is treatment that aim to induce the formation of calcified barrier at the root with open apices or continued development of apical root of immature teeth with necrotic pulp.¹⁰ The goal of apexification is to form apical barrier that can facilitate root canal obturation procedure easily and avoid the root canal filling material extrusion into periapical zone.^{9,11}

Calcium Hydroxide [Ca(OH)₂] becomes the first material that has been widely used for many years in apexification procedures.^{5,9} This material has the characteristics of a high pH, good antimicrobial activity, and has been proven to induce the formation of hard tissue barrier at

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the apical roots.^{9,12} Apexification treatment using this material has several drawbacks, including the need for multiple visits, a long period of time for overall treatment, recurrence of infection, and the risk of fracture.^{9,13-15}

Along with the development of biomaterials, Mineral Trioxide Aggregate (MTA) was discovered, a tricalcium silicate-based cement material that has excellent biocompatibility and sealing properties, also became the first material to support single visit apexification.^{2,16} The number of apexification visits using MTA could be shorter compared to Ca(OH)₂ related to its use as artificial barrier (apical plug). This artificial barrier can facilitate root canal obturation and strengthen the weak dentinal structures in the apical region, so it is not necessary for clinicians to wait for calcified apical barriers formation as in apexification procedure using Ca(OH)₂.¹ Ca(OH)₂, the material that was originally as the gold standard for apexification procedure for years, then MTA became another alternative material which has been proven successful.^{2,14,17} On the other hand, MTA with its various advantages still has several drawbacks, such as long setting time, potential for teeth discoloration, and poor handling characteristics, so researchers began to look for another alternative materials.¹⁸

In recent years, Biodentine™ (Septodont, St Maur des Fosses, France) has been discovered, a tricalcium silicate-based material same as MTA, but it can cover the lacks of MTA. The superiority of this material when compared to MTA is the better handling characteristic, better mechanical properties and biocompatibility, and shorter setting time.¹³ Biodentine™ has been widely used in dentistry clinical applications, including for indirect and direct pulp capping; affected dentin remineralization; direct restorative posterior filling; palatogingival treatment and palatoradicular groove; pulpotomy; retrograde restoration; invasive internal resorption and cervical resorption treatment; root and furcal perforation repair; vertical root fracture treatment; endodontic surgery; regenerative endodontic therapy; apexogenesis, and apexification.¹⁹⁻²²

Based on the preliminary literature search conducted by the authors on PubMed (www.ncbi.nlm.nih.gov) and ScienceDirect (www.sciencedirect.com) databases, it was found that there have been publications of several articles in the form of case reports, research

articles, and literature review which discusses the use of Biodentine™ in apexification procedures. However, there have been no published articles in the form of systematic reviews (study designs that are at the top of the evidence-based pyramid) that comprehensively review the characteristics of Biodentine™ related to its specific use in clinical applications of apexification treatment. Based on the stated background, the authors are interested in conducting a literature study that aims to provide an overview of the effectiveness of Biodentine™ as apical plug material for nonvital immature teeth apexification procedure using rapid review method, a simplified form of systematic review that allows it to be carried out in a relatively short time with limited sources.^{23,24}

Materials and methods

This study used rapid review method, which is a knowledge synthesis form that refers to a systematic review guideline, but with simplified processes or components to generate information in a timely manner. This simplification form includes limitation of research questions, interventions or results to be achieved, limitation of literature search by applying certain criteria (such as language, time, geographical area, and study design) adjusted to the available time. Rapid review can be carried out by at least 1 reviewer by utilizing 2 or more databases, with the time required ranging from 1 week - 6 months. Rapid review is usually used to answer research questions in a short time with limited resources.²³⁻²⁵ This rapid review was conducted in February – June 2021.

Search Strategy

The search was carried out on the PubMed, ScienceDirect, EBSCOhost, ClinicalKey databases using the boolean operators "AND" and "OR" with a combination of search keywords, namely *Biodentine*, *apexification*, *apical barrier*, *apical closure*, *apical plug*, *immature teeth*, *open apex*, and *open apices*.

Inclusion and Exclusion Criteria

The inclusion criteria used in this study were as follows: (1) English articles; (2) articles published in 2010 – 2020; (3) articles with observational and experimental study designs; (4) articles with research content discussing

Biodentine™ as an apical plug material in apexification treatment procedures, with sample characteristics: nonvital immature teeth (newly erupted teeth with open apex) with or without periapical lesions; (5) articles with research content mentioned about assessment parameters used in evaluating the use of Biodentine™ material in apexification treatments (these parameters can be in the form of a clinical/radiographic assessment after treatment). Exclusion criteria for this study include: (1) review articles; (2) animal research and laboratory study (in vitro).

Study Selection

The literature screening and selection procedure was done by following the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) protocol, that is a guide for conducting a systematic review with a systematic, gradual, and transparent approach. Screening is carried out in stages starting from duplicate articles, relevance of the titles and abstracts, as well as full-text assessments referring to the predefined inclusion criteria. The details of this procedure are carried out in the following steps (Figure 1).^{26,27}

Data Extraction and Presentation

Data taken from each article will be presented in tabular form, which includes author and publication, country, design of study, sample/participant(s), and treatment outcomes (this format can be seen in Table 1).

Data Analysis

The data analysis used thematic analysis, an analytical technique that identifies certain patterns or themes in the data. The goal is to use the theme or pattern that is important or interesting to answer a research question or discuss a problem. In addition to identifying and summarizing the data, a good thematic analysis will also interpret the data obtained.²⁸

Study Quality and Critical Appraisal Assessment

Articles that match the inclusion criteria will be graded on the level of evidence (with level 1,2, or 3) and strength of the recommendations (with categories A, B, or C) according to the SORT (Strength of Recommendation Taxonomy) guidelines from the American Family Physician

(2004).²⁹ In addition, a critical appraisal was carried out on each included article according to its study design following the critical appraisal tools developed by Joanne Briggs Institute (JBI). Critical appraisal is used to assess the methodological quality of a study and specify the extent of study can overcome the risk of bias in its design, conduct and analysis.³⁰⁻³³

Results

Search Results

Based on search results according to the keywords in four databases (PubMed, ScienceDirect, EBSCOhost, ClinicalKey), there were 138 total articles. From a total of 138 articles, 45 duplicate articles were removed, so that a number of 93 articles were screened according to the titles and abstracts relevance of the inclusion criteria. From 93 articles, only 12 articles were relevant (match the inclusion criteria). Last step is full content articles assessment so that the final results are 11 articles that meet the inclusion criteria. One article was excluded for not reporting the results of the post-treatment both clinically and radiographically. The flow of this article selection process can be seen in Figure 1.

Study Characteristics

Based on the final search results, 11 articles were found that met the inclusion criteria. From the total 11 articles, 7 articles are case reports, while 4 articles are case series. Details of the study characteristics based on the results of data extraction are presented in Table 1.

Critical Appraisal

Selected case report articles were critically appraised according to indicators from JBI (consisting of 8 indicators for case reports and 10 indicators for case series). The answer for each indicator is "Yes", "No", "Unclear, or "N/A (Not applicable)".^{30,31} The overall results assessment can be seen in Table 2 and Table 3. The assessment result of each article will be categorized into three: (a) Low risk of bias (meets > 75% of the overall assessment); (b) Moderate risk of bias (meets 50% - 74% of the overall assessment); (c) High risk of bias (meets < 49% of the overall assessment).³⁴

Discussion

Apexification is procedure that induces calcified barrier formation in root with open apex or continued development of apical immature teeth accompanied by necrotic pulp.¹⁰ According to the definition, apexification is indicated for nonvital immature teeth with an incomplete or open apex (blunderbuss canal).⁹ Open apex (immature) teeth can be closed by placing certain material such as calcium hydroxide to prevent the risk of apical pathosis in further years and to promote the apical closure by inducing hard tissue barrier formation.³⁵ Rao stated that apexification is a treatment that placing certain appropriate materials in order to facilitate the obturation process so it can support the formation of calcified apical barrier.⁸

Biodentine™ (Septodont, St Maur des Fosses, France) is a calcium silicate-based cement released in 2009.¹⁸ Biodentine™ has a modified composition that can improve its physical properties making it easier to manipulate.¹⁶ By its excellent viscosity characteristics, the shorter setting time than MTA (a material currently used in endodontic practices); good mechanical properties, biocompatibility, and color stability; low cytotoxicity and genotoxicity make Biodentine™ as an ideal material for use in endodontic practice including apexification.¹⁸

Based on review of 11 selected case reports, there were 7 case reports (Sinha et al., Khetarpal et al., Nayak & Hasan, Sharma et al.,³⁶ Niranjana et al., Vidal et al., Sharma et al.¹³) used Biodentine™ as an apical plug with a size of 4-5 mm, 1 case report from Songtrakul et al. with modified apexification using Biodentine™ as a plug with a size of 3 mm, and 3 other case reports (Elumalai et al., Martens et al., Pruthi et al.) did not mention how many mm in size of Biodentine was used.^{13,18,36-42} The range of Biodentine™ plug use measuring 3-5 mm is in the line with in vitro study conducted by Bani et al., the result of his research stated that Biodentine™ and MTA plug with a size of 3-4 mm were more resistant to apical leakage than 1-2 mm plug. The number of microleakages 3-4 mm plug group was significantly lower than 1-2 mm plug group.⁴³

A total of 10 articles (Sinha et al., Khetarpal et al., Nayak & Hasan, Sharma et al.,³⁶

Elumalai et al., Niranjana et al., Vidal et al., Martens et al., Sharma et al.,¹³ Pruthi et al.) from 11 case reports placed Biodentine™ plug at the tip of apical, and only 1 case of modified apexification by Songtrakul et al. put a 3 mm Biodentine™ plug at 4-5 mm coronal from the apical tip (the details are the first 1-2 mm apical tip was emptied, then 3 mm of collagen matrix was placed).^{13,18,36-42} That modified apexification was carried out with the reason to promote the continuation of root development because the results of traditional apexification treatments previously carried out by researchers did not provide the expected results (lack of promoting the further apical root development). The result proved satisfactory, 8 out of 10 cases (including 1 case that used Biodentine™ material) showed the results of advanced apical development that is increase in wall thickness, increase in length of apical root, and apical closure.¹¹

In 9 articles (Sinha et al., Khetarpal et al., Nayak & Hasan, Sharma et al.,³⁶ Niranjana et al., Vidal et al., Sharma et al.,¹³ Songtrakul et al., Pruthi et al.) of 11 case reports used Biodentine™ as an apical plug with a gutta-percha obturation material, while other case reports (Martens et al. & Elumalai et al.) used Biodentine™ as a full canal obturation material.^{13,18,36-42} Based on in vitro study of Girish et al. which compared fracture resistance between the group that used MTA/Biodentine™ as an apical plug (followed by obturation using gutta-percha) with MTA/Biodentine™ group used as full canal obturation material, it was found that using MTA/Biodentine™ as a full obturation material showed significantly higher fracture resistance ($P < 0.05$).⁴⁴ The in vitro study conducted by Darak et al. reported similar results, that is the apexification with full obturation system using Biodentine™ was better than the apexification system using Biodentine™ apical plug followed by obturation using gutta-percha.⁴⁵

A total of 7 articles (Sinha et al., Khetarpal et al., Nayak & Hasan, Sharma et al.,³⁶ Elumalai et al., Vidal et al., Martens et al.) from 11 case reports did not use matrix prior to Biodentine™ placement, while 4 other case reports (Niranjana et al., Sharma et al.,¹³ Songtrakul et al., Pruthi et al.) used a resorbable matrix such as collagen and platelet-rich fibrin (PRF) at the apical tip that was followed by placement of the Biodentine™ plug.^{13,18,36-42} The discussion case of Nayak & Hasan reported that

the placement technique of Biodentine™ as an apical plug is sensitive, so it is important to be careful so the material used is not extruded into the periapical area which has the potential to harden before it disintegrates and reabsorbed. In the case report of Martens et al., there was extrusion of Biodentine™ into the periapical area, but the extruded material can slowly be absorbed over time. On the other hand, the placement of the matrix becomes important to prevent the unexpected impact which is inflammatory process persistence, that ultimately complicates tissue repair. The use of an external matrix such as collagen is recommended to retrieve the root outer shape and simplify adaptation of the plug material. The collagen matrix has a hemostatic effect and can absorb moisture completely in 10-14 days (thus gradually allows new bone to fill the defects).³⁹ PRF is an external matrix that can induce osteoblasts, periodontal ligament cells, gingival fibroblasts, and pulp cells by its properties which is osteoinductive, osteoconductive, and easily absorbed. PRF has been shown to increase bone regeneration and soft tissue maturation.⁴⁶

In 11 case reports, it was found that overall apexification treatment (from access opening; cleaning and shaping; the placement of Biodentine™ plugs; obturation; to post-endodontic restoration) was carried out with a total of more than 1 visit. However specifically for the placement of obturation material, all reports mentioned that obturation was performed immediately after the setting of Biodentine™ plug (12-15 minutes).^{13,18,36-42} This indicates that obturation can be performed directly (same visit) after Biodentine™ placement as the apical plug. One of apexification materials using MTA drawbacks is the long setting time (2 hours 45 minutes), so the clinicians must wait for obturation at the next visit (2-step apexification). This is certainly become additional value for Biodentine™ because the setting time is quick, around 9-12 minutes only. The shorter setting time is influenced by its good physical characteristics such as small particle size; modified composition consisting of calcium chloride as an accelerator and water reducing agents. This proves that Biodentine™ supports single visit apexification treatment (beyond follow up).^{18,39,41,42,46}

The patient's preoperative condition in the 11 case report articles have been reported in

vary, including pain, fracture, discoloration, swelling, discharge of pus, presence of sinus tract, pain on percussion and palpation, and radiolucent lesions in periapical area. After apexification treatment was conducted, the clinical and radiographic outcomes of 11 case reports assessed variably within 3 weeks – 3 years. In 8 case reports (Sinha et al., Khetarpal et al., Nayak & Hasan, Vidal et al., Martens et al., Sharma et al.,¹³ Songtrakul et al., Pruthi et al.) mentioned complete follow-up treatment outcomes (both clinical and radiographic aspects), but 3 other case reports (Sharma et al.,³⁶ Elumalai et al., Niranjana et al.) only highlight the radiographic treatment outcomes and did not mention clearly the clinical condition of the patient after treatment (it was not clear whether asymptomatic, or no discoloration, or no pus, etc.).^{13,18,36-42} On the clinical aspect, 8 case reports declared various good results, such as no more pain and swelling; absence of pus and sinus tracks; the function and aesthetics of the restored tooth; and no discoloration. On the radiographic aspect, 11 case reports informed varied and satisfying results, including the healing of radiolucent lesions in the periapical, regeneration of periradicular tissue, further root growth (formation of calcified apical barrier, increase in thickness of the apical dentin wall, and increase in length of apical root).^{13,18,36-42} Rao stated that the calcified barrier was formed from apexification can be cementoid, osteoid, or osteodentine.⁸ However, in the case report articles which claimed that the radiographic results of the formation of a calcified barrier, it is not clearly stated about the type of tissue formed. This probably due to the need for further examination such as histological examination to determine the type of calcification barrier. Songtrakul et al. mentioned that a calcified barrier can be formed due to the survival of HERS and based on 2 of 8 cases in his study with the result no calcification barrier formation, presumably due to severe damage to HERS.¹¹ Hertwig's epithelial root sheath (HERS) influence and has responsibility for promoting root development including the increase in length, wall thickness, and narrowing of the apical part. If necrosis occurs, it will stop the blood supply to HERS.¹ In addition, Rao stated that the toxin product from the necrotic pulp will result in the death of HERS cells.⁸ This ultimately disrupts the process of further root development. As a result,

immature teeth finally have wide root canals with open apices characteristics.^{1,8} Overall, 11 case reports showed satisfactory treatment results in the Biodentine™ apexification procedure according to clinical and/or radiographic outcomes.^{13,18,36-42}

Based on the assessment of study quality (SORT) from AFP, 11 case reports were categorized in Level 3 (other evidence) with a strength of recommendation C (weak).²⁹ Furthermore, based on a critical appraisal of each case report according to JBI's indicators (full assessments can be seen in Table 2 and Table 3), 6 articles (Sinha et al., Khetarpal et al., Nayak & Hasan, Sharma et al.,³⁶ Elumalai et al., Vidal et al.) categorized as low risk of bias (meets > 75% of overall assessment) and 5 articles (Martens et al., Niranjana et al., Sharma et al.,¹³ Songtrakul et al., Pruthi et al.) categorized as moderate risk of bias (meets 50% - 74% of the overall assessment).³⁴

Although 11 case report articles generally showed that the apexification treatment using Biodentine™ showed good results, the articles with this study design were still at the bottom level of the evidence-based pyramid. The published clinical research articles on the use of Biodentine™ as apexification material are still available in limited number. Until this review study conducted on the 4 previously mentioned databases, the authors have not found any experimental studies discuss about the

effectiveness of Biodentine™ as apexification material for nonvital immature teeth at the level of a randomized controlled trial/RCT (study design that placed at the top of the evidence-based pyramid, under meta-analysis and systematic review). Therefore, the authors suggest that experimental clinical studies (RCT level) of apexification using Biodentine™ in nonvital immature teeth can be carried out further to obtain better level of evidence.

Conclusion

Based on the review of clinical and radiographic treatment results of 11 case reports, Biodentine™ is effective to use as an alternative apical plug material for nonvital immature teeth apexification treatment with its advantages such as short setting time, supporting the formation of calcified apical barrier, and healing of periapical lesions.

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Declaration of Interest

The authors declare that there is no conflict of interest.

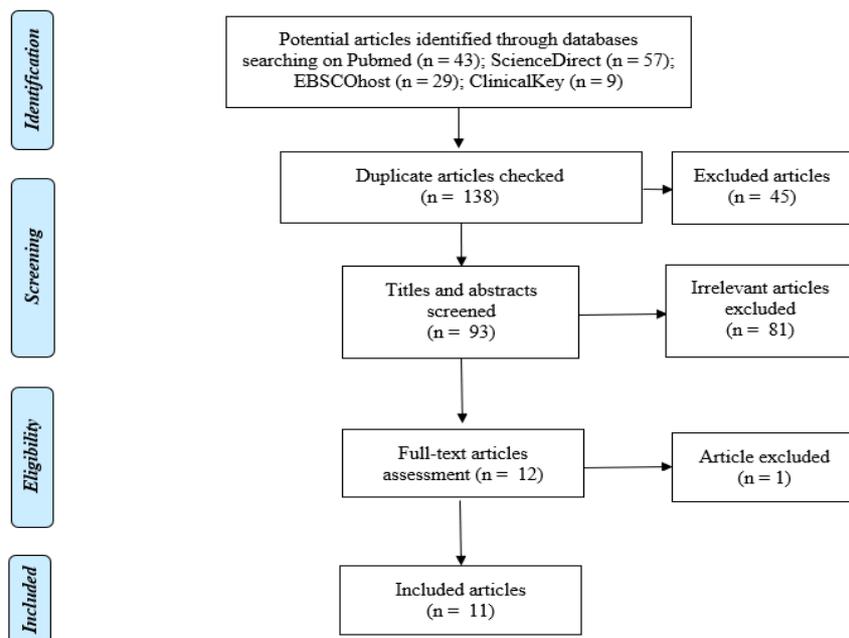


Figure 1. PRISMA flow diagram for this rapid review study.

Author (Year)	Country	Study Design	Sample/Participant(s) (gender; age*; teeth; cause of nonvital)	Follow-up Results
Sinha <i>et al.</i> ¹⁸ 2014	India	Case report	Male, 18 y.o., #8, trauma > 10 years ago	Clinical (3 weeks): complete sinus tract healing and no other clinical symptoms Radiographic (1 year): healing of the periapical radiolucent lesion and formation of calcified barrier at the tooth apex
Khetarpal <i>et al.</i> ⁴⁰ 2014	India	Case report	Male, 15 y.o., #10, trauma at age 8	Clinical (18 months): the patient's function is good, no clinical symptoms and sinus tract Radiographic (3 months): healing of periapical lesions and bone formation; 18 months: complete periapical radiolucent lesions healing and periradicular tissue regeneration
Nayak & Hasan ³⁹ 2014	India	Case report	Male, 20 y.o., #9, trauma 10 years ago	Clinical and radiographic (1 year): revert of aesthetics and function, no clinical signs of periradicular abnormalities, formation of a thin layer of calcified barrier at the apex
Elumalai <i>et al.</i> ³⁷ 2015	India	Case report	Female, 17 y.o., #9, trauma 9 years ago	Radiographic (9 months): early healing of periapical lesions was better in Biodentine™-treated teeth than MTA; but in the long-term healing, MTA is better
Sharma <i>et al.</i> ³⁶ 2015	India	Case report	Male, 14 y.o., #9, trauma 6 years ago	Radiographic (6 months): healing of periapical lesion
Niranjana <i>et al.</i> ⁴¹ 2016	India	Case report	Female, 8 y.o., #8, Trauma	Radiographic (6 and 12 months): root growth and increase of dentin thickness in teeth treated with Biodentine™ material were better than MTA
Vidal <i>et al.</i> ¹⁸ 2016	Mexico	Case report	Male, 9 y.o., #9, trauma 1 month ago	Clinical (3, 6, and 18 months): asymptomatic, no discoloration Radiographic (3, 6, and 18 months): continuity of the periodontal membrane space without periapical radiolucent lesions, adequate of apical development
Martens <i>et al.</i> ³⁸ 2016	Belgium	Case series	Case 1: Caucasian Male, 8 y.o., #9, trauma few weeks ago	Clinical: no symptoms, swelling and pus disappear Radiographic (12 and 24 months): healing of periapical lesions
			Case 2: Caucasian Male, 9 y.o., #8, trauma 10 months ago	Clinical (12 and 24 months): asymptomatic, no other subjective complaints Radiographic (24 months): healing of periapical lesions
			Case 3: Caucasian Male, 9 y.o., #9, trauma	Clinical: asymptomatic; Radiographic (12 and 24 months): slow resorption of extruded Biodentine™ in periapical area; periapical lesion healing
Sharma <i>et al.</i> ¹³ 2018	India	Case series	Case 1: Female 39, y.o., #9, childhood trauma	Clinical (3 months): asymptomatic Radiographic (3 months): periapical lesions healing partially; 6 months: complete healing of periapical lesions and closure of the apex with a hard tissue barrier formation
			Case 2: Female 45, y.o., #9, childhood trauma	Radiographic (3 and 6 months): healing of periapical lesions
			Case 3: Male, 15 y.o., Caucasian, #9, trauma 10 months ago, N.A†	Radiographic (3 months): healing of periapical lesions; 6 months: increased bone density, apical repair
Songtrakul <i>et al.</i> ¹¹ 2019	US	Case series	10 cases in total. Case with Biodentine™ (Case 5): 18 y.o., #18, caries	Clinical and radiographic (2 years): no clinical signs, healing of periapical lesions, increased wall thickness and apical length; apical closure
Pruthi <i>et al.</i> ⁴⁶ 2020	India	Case series	3 cases in total. Case with Biodentine™'s apexification (Case 1): Female, 17 y.o., #8 & #9, trauma 10 years ago	Clinical and radiographic (3 years): no clinical symptoms, good function, healing of periapical lesions

Table 1. Study characteristics of 11 articles. *Age in years (y.o. = years old), † N/A = data not available.

Critical appraisal tools of JBI ³⁰	Sinha <i>et al.</i> ¹⁸ 2014	Khetarpal <i>et al.</i> ⁴⁰ 2014	Nayak & Hasan ³⁹ 2014	Elumalai <i>et al.</i> ³⁷ 2015	Sharma <i>et al.</i> ³⁶ 2015	Niranjana <i>et al.</i> ⁴¹ 2016	Vidal <i>et al.</i> ¹⁸ 2016
1. Were patient's demographic characteristics clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Was the patient's history clearly described and presented as a timeline?	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes
3. Was the current clinical condition of the patient on presentation clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Were diagnostic tests or assessment methods and the results clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Was the intervention(s) or treatment procedure(s) clearly described?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Was the post-intervention clinical condition clearly described?	Yes	Yes	Yes	Unclear	Unclear	Unclear	Yes
7. Were adverse events (harms) or unanticipated events identified and described?	No	No	No	No	No	No	No
8. Does the case report provide takeaway lessons?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Overall (%)	87.5%	75%	87.5%	75%	75%	62.5%	87.5%

Table 2. Critical appraisal of 7 case report articles.

Critical appraisal tools of JBI ³¹	Martens et al. ³⁸ 2016	Sharma et al. ¹³ 2018	Songtrakul et al. ¹¹ 2019	Pruthi et al. ⁴⁶ 2020
1. Were there clear criteria for inclusion in the case series?	Yes	Yes	Yes	Yes
2. Was the condition measured in a standard, reliable way for all participants included in the case series?	Yes	Yes	Yes	Yes
3. Were valid methods used for identification of the condition for all participants included in the case series?	Yes	Yes	Yes	Yes
4. Did the case series have consecutive inclusion of participants?	No	No	No	No
5. Did the case series have complete inclusion of participants?	No	No	No	No
6. Was there clear reporting of the demo- graphics of the participants in the study?	Yes	Yes	Yes	Yes
7. Was there clear reporting of clinical information of the participants?	Yes	Yes	Yes	Yes
8. Were the outcomes or follow-up results of cases clearly reported?	Yes	Yes	Yes	Yes
9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?	No	No	No	No
10. Was statistical analysis appropriate?	N/A	N/A	N/A	N/A
Overall (%)	60%	60%	60%	60%

Table 3. Critical appraisal of 4 case series articles.

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