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Nonsurgical Endodontic Management of Large Periapical Lesion with Cold Ceramic: A Literature Review and Case Series

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Introduction: The purpose of this review is to investigate the contribution of non-surgical endodontic treatment in the healing process of large periapical lesions as well as looking over other potential non-surgical endodontic treatment options**. Materials and Methods**: two females and one male patient were referred to the private office, complaining of having pain in the anterior maxillary region which was pertinent to the presence of a large periapical lesion, and subsequently were managed by a non-surgical endodontic approach using cold ceramic. The archive of PubMed and Google Scholar databases was also searched for finding relevant articles in which a nonsurgical endodontic approach was performed to improve the healing process of large periapical lesions. **Results**: Clinical examination of the case series subjects revealed no signs and symptoms following treatment while relative improvement of the lesion and apical closure was apparent in radiographs 7 months, 9 months, and 4 years subsequently. In twenty-two reviewed clinical trials, a total number of 107 teeth with large periapical lesions were treated by nonsurgical endodontic approaches using MTA, biodentine, gutta-percha, and bioceramic iRoot Bp plus. Complete healing occurred in 38 cases (35.5%) after 12-17 months. **Conclusions**: Although surgical interventions have been used previously in the management of large periapical lesions, a nonsurgical endodontic approach with cold ceramic seems to be effective, leading to complete healing of the periapical lesion in treated subjects. Further clinical research is recommended to identify the effectiveness of cold ceramic for the treatment of extensive periapical lesions.

Keywords: Cold Ceramic; Great Lesion; Nonsurgical Endodontic; MTA; Regenerative Endodontic Treatment; Root Canal Treatment

Introduction

Periapical lesions are commonly noticed on conventional radiographs of the patients which may potentially cause tooth pain as well. More than 90% of these lesions can be classified as granuloma, radicular cysts, or abscesses [1]. Periapical periodontitis occurs as a result of pulpal inflammation and subsequent necrosis of the dental pulp tissue. Microorganisms infiltrate the necrotic pulp and cause apical bone loss and periodontal ligament deterioration. More than 90% of periapical lesions can be classified as granuloma, radicular cyst, and abscess [2]. Toller hypothesized that periapical cyst growth is related to the hydrostatic pressure of an enclosed liquid which stimulates osteoclastic activity [1].

The periapical radiolucent lesions can be detected as cysts in the case of being larger than 200 square meters, being related to one or two non-viable teeth, being round in radiograph with specific boundaries, and aspiration or drainage of straw-colored liquid through the accessed cavity [3]. Large apical lesions can receive non-surgical endodontic treatment or endodontic surgery, otherwise, it leads to tooth extraction [4]. If the apical lesion fails to respond to intracanal endodontic treatments, surgical intervention should be contemplated; these procedures include periradicular curettage, apical resection along with simpler techniques such as marsupialization and tube decompression [5].

According to Strindberg's criteria, RCT is deemed to be successful when a uniform and healthy lamina dura, normal PDL contour and width, and resolution of periapical radiolucent defect appear radiographically. Moreover, there should be no pain or swelling clinically [6]. Previous findings showed that large apical lesions can be treated with non-surgical endodontic treatments directly approaching the root canal system so that drainage through the access cavity can be achieved [4]. Periapical surgery is the ultimate choice in extreme cases with persistent periapical lesion that do not respond to conventional endodontic procedures [2].

After the introduction of ultrasonic microsurgical systems and new obturating materials in early 1995, there has been an improvement in the healing rate of apical surgery with root-end filling; however, it remains around 80-90% [2, 7].

The characteristics of an ideal root canal filling material include biocompatibility, ease of manipulation, proper sealing, lack of shrinkage, impermeability to fluids, antibacterial activity, radiopacity, and no discoloration of the tooth [8]. While being the most commonly used obturating material, gutta-percha has some disadvantages including lack of adhesion to the dentin and low elastic properties, which may cause shrinkage of the material away from the root canal walls [7].

Bioceramics are biocompatible materials that are available in three forms: putty, paste, and sealer. The Bioceramics hydration process produces compounds such as hydroxyapatite, which is capable of inducing tissue regeneration and acts as a temporary mesh framework for hydroxyapatite deposition. Bioceramics with calcium silicate base like MTA, cold ceramics, Bioaggregate, biodentine, iRoot Fs/So can be named [9].

MTA is a bioceramic material that was first introduced by Mahmoud Torabinejad for root perforation repair. It can also be used as a pulp capping agent, filling material for horizontally fractured teeth, and apical barrier in immature permanent teeth with an open apex [10]. MTA has shown superior properties as a gold standard over the previously used materials in root canal filling and periapical surgery such as glass ionomer, amalgam, and cold ceramic [11]. Imperceptible solubility, high pH along with a slight expansion during the setting process of MTA could lead to the destruction of microorganisms [12].

However, MTA use is technically sensitive and prone to displacement and subsequent microleakage due to its slow setting process [15]. Other drawbacks of MTA are discoloration potential and the presence of bismuth oxide, a toxic element, in the material composition [12].

"Cold Ceramic" is a biocompatible ceramic with a major elemental component of calcium hydroxide that was first introduced in 2000 [8]. The alkalinity of cold ceramic improves its antibacterial activity [12]. This bioceramic can be used in the pulp capping of vital teeth, repairing root perforations, and forming an apical barrier in immature permanent teeth [16].The initial setting time of this material is 15 min, and it becomes fully set within 24 h in the presence of moisture. It has better sealing ability than MTA, glass ionomer, and amalgam in blood-contaminated areas; however, the sealing ability of cold ceramic is similar to MTA in dry and saliva contamination conditions [15].

Therefore, cold ceramic could be a more sensible option as a root-end filling material rather than MTA since it has a faster initial setting and better sealing [15].

The following paragraphs represent a case series study in which large periapical lesions were successfully managed through a nonsurgical endodontic approach using cold ceramics.

Literature Review

A structured electronic database search was organized from February 1994 until August 2022. The databases of PubMed and Google Scholar were searched for articles in which a nonsurgical endodontic approach has been undertaken for the management of large periapical lesions. The MESH terms used in the search were as follows: (large periapical lesion) OR (large periapical radiolucency) AND (conservative endodontic treatment) OR (nonsurgical endodontic approach) OR (minimal invasive endodontic treatment) OR (Cold ceramic) OR (bioceramic). Twenty-two relevant primary types of research were identified including one clinical trial and twenty-one case reports/series. The total number of treated teeth was 107 over a 28 years period, indicating the difficulty of treating and monitoring large periapical lesions.

Table 1. Description of periapical index scores (adapted from Orstavik *et al.* [13] ; and Penesis *et al.* [14])

PAI score	Description of radiographic findings
1	Normal periapical structures
2	Small changes in bone structures
3	Change in bone structure with mineral loss
4	Periodontitis with well-defined radiolucent area
5	Severe periodontitis with exacerbating features

Table 2. Demographic information, time of follow up, PA index of patients

	Age	Gender	Universal tooth number	Time of follow up	PAI before	PAI after
Case 1	14	male	9	9 months	4	1
Case 2	32	female	7	7 months	4	3
Case 3	41	female	10	1 years	4	3
				4 years		2

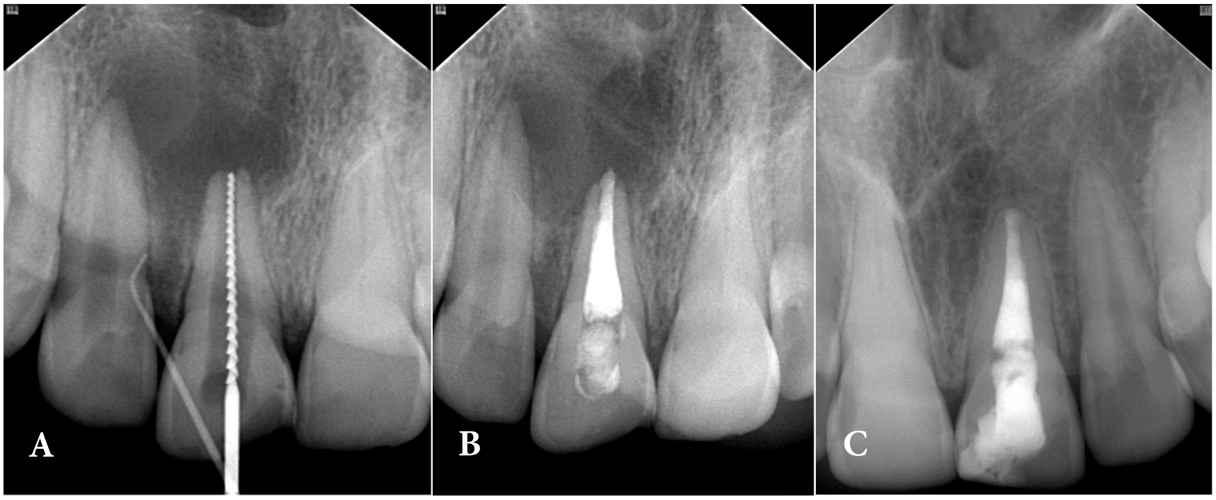

Figure 1. *A*) Sinus tract tracing and working length measuring of the left maxillary central incisor; *B*) Obturation of the root canal with cold ceramic; *C*) Recall radiograph after 9 months showed bone regeneration and normal PDL

EDTA was used in eight cases throughout the chemical preparation of the root canal while 2.5% hypochlorite sodium was the main irrigant in others. Applied intracanal medicaments comprised a triple antibiotic paste and calcium hydroxide that was used in four and eighty-two cases, respectively to improve disinfection following chemo-mechanical preparation [17-20]. Apical plugging of the root canal was performed using MTA, Biodentine, cold ceramic, and iRoot BP Plus [21-23]. Out of ten cases that were treated with MTA apical plug and sealer, complete healing was identified in five cases after an average of 17 months, whereas in the other half, healing was apparent after 18 months on average [2, 19, 20, 24-30]. Biodentine and iRoot BP plus were used in two cases, both showing complete healing after one year [22, 23]. Thirty-two cases out of seventy-nine, in whom gutta-percha was used as the obturating material, also demonstrated complete healing after one year [4, 18, 31-33].

Cold ceramic was used in three cases already as an apexification material showing healing and bone regeneration after six, two, and one year [21, 34, 35].

According to the Calisken *et al.* clinical review, of the forty-two teeth with large periapical lesions that had received drainage from the root canal, calcium hydroxide as the intracanal medication, and finally gutta-percha for obturation, thirty-one showed complete healing 8-24 months following the treatment [36].

Radiographic assessment

The periapical status of the endodontic treatment was evaluated by the periapical index (PAI) scoring system given by Orstavik [13]. Table 1 represents the description of PAI scores.

Case Presentation

Case 1

A 14-year-old male presented with soft tissue swelling who was otherwise healthy. Clinical and radiographic examination revealed the presence a buccal fistula and a large periapical lesion in relation to the left maxillary central incisor, sensitivity to palpation and percussion without any mobility (the pocket depth was 4mm), and mild external root resorption in the apical region. The tooth had also no response to the vitality/sensibility tests implying the necrosis of the pulp while the adjacent teeth were all vital. The decision was made to obturate the canal with cold ceramic

After providing local anesthesia, the access cavity was prepared under operating microscope without using a rubber dam since the patient found it uncomfortable. Exploration of sinus tract and working length determination was carried out simultaneously using a gutta-percha cone. Sinus tract tracing revealed the communication of the lesion with the oral cavity through a defect on the buccal aspect of the left maxillary central incisor (Figure 1A).

Next, cleaning and shaping of the root canal were performed up to K-file #80 hand file (Mani, Tochigi, Japan) using a combination of 6% NaOCl as the main irrigant with normal saline for final irrigation. The apical portion of the canal was filled with cold ceramic in compliance with the manufacturer's instructions; the cold ceramic (SJM, Yazd, Iran) was transferred to the root canal with an MTA carrier and then condensed using Plugger #25 (Dentsply Maillefer, Ballaigues, Switzerland). During the same appointment, the remaining portion of the canal was obturated with gutta-percha *via* lateral condensation technique so that the placement of a post and core would be feasible. The pulp chamber was temporarily restored with Cavit (Figure 1B). No antibiotics were prescribed.

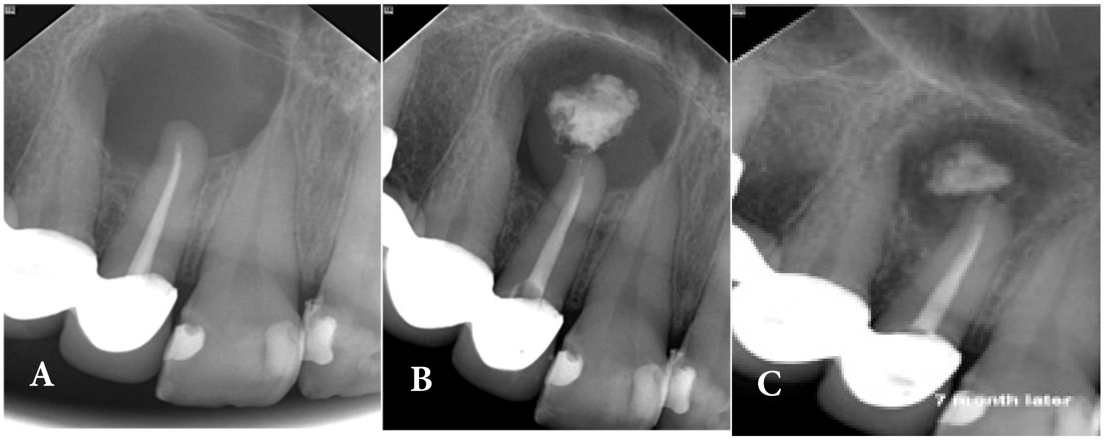

Figure 2. A) Radiograph of endodontically treated right maxillary lateral incisor with a large periapical lesion; *B*) Root canal obturation with cold ceramic; *C*) Recall radiograph after 7 months exhibited periapical bone formation

Follow up

During the 9-month recall evaluation, the patient had no pain or discomfort on palpation. The radiographic examination revealed remarkable periapical healing along with bone regeneration and complete apical closure. Moreover, the normal appearance of the apical periodontal ligament increased the thickness of the root canal walls, and the formation of a cementum-like tissue near the apical end of the root was observed radiographically (Figure 1C).

Case 2

A 32-year-old female was referred to the private dental office with facial swelling and a symptomatic right maxillary lateral incisor that had been endodontically treated previously. Her medical history was non-contributory. Clinical examination revealed that periodontal probing depths were within normal limits and the tooth was sensitive to palpation and percussion without increased mobility. Radiographic examination demonstrated resorption of the palatal aspect of the alveolar bone and a large periapical cystic lesion with persistent exudate (Figure 2A).

At the first treatment appointment, 1mL buccal infiltration of 4% articaine with 1: 100,000 adrenaline was administered for local anesthesia. The access cavity was then prepared with an operating microscope through which suppurative fluid straw-colored fluid with cholesterol crystals visible by unaided eye flowed outward. Complete removal of the existing filling material was performed using an F1 file and chloroform. The working length was subsequently determined and the root canal was shaped up to F3 (Dentsply Maillefer, Ballaigues, Switzerland) file under constant irrigation.

The root canal was temporarily filled with calcium hydroxide due to the persistent discharge from the root canal system. The application of calcium hydroxide as an intracanal disinfectant was repeated four times along with irrigation of the root canal with 6% NaOCl and normal saline. As the intracanal exudation disappeared during the fifth appointment, the root canal was filled with cold ceramic, carrying it with an MTA carrier, and condensed with plugger #20 in adherence to the manufacturer's instructions. The quality of the final obturation was less than ideal due to the diffusion of cold ceramic particles in the periapical space (Figure 2B). The pulp chamber was then temporarily restored with Cavit and no antibiotics were prescribed.

Follow up

Recall radiographs after 7 months revealed that almost two-thirds of the periapical radiolucency had been resolved and filled with trabecular bone (Figure 2C).

Case 3

A 41-year-old female presented to a private office, complaining of pain in her left maxillary lateral incisor region and mild swelling of the lips. A review of her medical history confirmed the presence of rheumatoid arthritis. Clinical examination demonstrated tenderness of the tooth to percussion or palpation, normal periodontal probing depths, and necrosis of the teeth besides the sensitivity of all the adjacent teeth to cold pulp testing. A large periapical lesion as well as external apical root resorption was noticed in the radiographic examination and there was no significant tooth mobility despite the resorption of the buccal and palatal surfaces of the tooth. At the first treatment appointment, 0.4 mL buccal infiltration of 2% lidocaine with 1: 100,000 adrenaline was administered. Straw-colored fluid with cholesterol crystals visible by unaided eye discharged from the exposed pulp was observed during the preparation of the access cavity. The

Figure 3. *A*) Left maxillary lateral incisor with a large periapical lesion; *B*) Unsuccessful cold ceramic obturation with extensive penetration of the material into the periapical area; *C*) Placement of calcium hydroxide into the root canal following cold ceramic removal; *D*) Satisfactory cold ceramic obturation; *E*) Recall radiograph after one year suggesting insufficient bone regeneration; *F*) Recall radiograph after four years showed bone regeneration

working length was then determined with H-file #25 (Mani, Tochigi, Japan) and the root canal was prepared up to F3 file under copious irrigation with normal saline (Figure 3A). Obturation of the root canal was not performed as the tooth showed constant exudation even after root canal instrumentation.

Calcium hydroxide was placed into the root canal in an attempt to reduce the total number of bacteria surviving even after chemo-mechanical preparation and control the outflow of inflammatory exudate. In the next two subsequent appointments, calcium hydroxide was replaced as the tooth was symptomatic yet. After seven days, the root canal was filled with cold ceramic in compliance with the manufacturer's instructions despite the presence of some exudate discharge from the root canal system. Radiographic evaluation showed that the coronal portion of the root canal was solely filled with cold ceramic and the majority of the material was pushed into the periapical area (Figure 3B). Therefore, the cold ceramic was removed *via* ultrasonic file and calcium hydroxide was put into the root canal (Figure 3B). No antibiotics were prescribed. During the next appointment, the last effort was made to obturate the root canal with cold ceramic although persistent exudation was still present (Figure 3D). According to the radiographic assessment, acceptable obturation and apical seal were essentially achieved.

Follow up

Recall radiograph after one year was not satisfactory in terms of healing of the periapical lesion (Figure 3E), although the patient had no relevant symptoms; therefore, surgical endodontic intervention was not undertaken. Radiograph at 4-year follow-up (Figure 3F) demonstrated adequate healing of the periapical lesion and bone regeneration along with the induction of apical closure. Compared with the previously mentioned case, the periapical lesion persists for a longer time which can be contributed to the presence of cholesterol crystals and consequential delay in the healing process.

Discussion

Root canal infection occurs as a result of bacterial invasion into the dental pulp[5]. Chronic periapical inflammation results in the formation of periapical radiolucent bony lesions [18]. Periapical lesion that is well-defined radiographically, greater than 200 square millimeters in size, involved with one or more non-vital teeth, and producing a straw-colored fluid upon aspiration or through the accessed root canal system is considered as a radicular cyst with the incidence of almost 100%. [37].

The incidence of periapical cysts varies between 10% and 55%. The enlargement of the cyst is associated with the increased hydrostatic pressure of the fluid within the cyst (Toller *et al.*)(36). Large periapical cystic lesions are more prevalent in the maxilla rather than the mandible as traumatic dental injuries most frequently affect anterior maxillary teeth. Furthermore, most radicular cysts range in size from 5 to 15 mm while the lesion may enlarge more than 15 mm in the maxilla [38].

The management of large periapical lesions is the subject of prolonged debate [36]. Untreated or poorly treated periapical lesions can lead to serious complications such as pathological fracture of the jaw, osteomyelitis, and Ludwig's angina [39]. It has been proposed that large periapical lesions are less likely to heal after non-surgical root canal treatment [36]. The treatment options range from conventional RCT, marsupialization, and decompression to surgical removal of the lesion[3]. All periapical lesions should be initially treated with nonsurgical surgical procedures to minimize the burden of surgical intervention.

Root canal treatment has reportedly a success rate of 85% in establishing periapical health. It can be postulated that radicular cysts might respond successfully to non-surgical endodontic treatments since 40% of periapical lesions are cystic [36]. According to Strindberg criteria, non-surgical endodontic treatment is considered successful when the periapical lesion size reduces, an intact lamina dura and PDL is present, and the patient has no pain and swelling [6]. Surgical endodontic treatments such as curettage and apical resection should be performed as the last attempt for persistent lesions after rolling out morphological abnormalities and failure of conventional root canal treatment [5, 40].

The best way to shrink the lesion is usually to reduce the pressure (decompression). Re-curettage should be performed, in order to prevent damage to nearby structures such as the mandibular nerve [38].

Large periapical lesions are often associated with persistent intracanal exudate which makes non-surgical endodontic treatment challenging. Therefore, the materials applied would need to have particular characteristics such as moisture compatibility and ability to set in a wet environment, adequate sealing, antibacterial properties, and release of osteoinductive factors to counteract bone loss.

Although gutta-percha is the most commonly used root canal filling material, a number of studies have reported the failure of gutta-percha obturation due to insufficient sealing ability. [24] Therefore, it seems that a root canal filling with gutta-percha would be unpredictable, especially in the presence of a large periapical lesion.

Alternatively, calcium hydroxide can be used which has reportedly led to periapical healing within 1-3 months [5]. However, calcium hydroxide possesses some drawbacks including the need for frequent replacement of the material, greater solubility, and alteration of dentin mechanical properties which can predispose the treated tooth to root fracture [21].

Several biocompatible ceramics have been introduced in recent years [21]. Bioceramics contain nanocrystals with diameters of 1-3 nanometers which prevent microbial adhesion. Alkaabinah *et al.* stated that bioceramics produce different compounds such as hydroxyapatite during the hydration process which in turn could initiate a regenerative response by absorbing osteoinductive substances [12].

Among biocompatible materials, MTA, Cold ceramic, and bioaggregate biodentine are calcium silicate-based bioceramics [12]. MTA has been used for pulp capping, root perforation repair, and induction of apical barrier formation on immature teeth. It offers excellent sealing ability due to its expansion properties, antimicrobial effect, ability to set in a moist environment, and proper marginal adaptation to root canal walls [24]. Moreover, MTA has yielded promising results in root canal retreatments to the extent that it has become the gold standard for this procedure [24].

Alkaline pH and calcium ions are necessary for the production of calcified tissue. Based on the histological results of animal studies, if factors affect cell-material interactions, cementum is formed. Some studies showed that the process of cementogenesis on MTA needs 3-6 months. More intense inflammation of periapical tissues is related to weaker cementogenesis probably due to the relation of inflammation to acidic pH, which has an inappropriate effect on setting reactions and mechanical properties of MTA, which probably also affects the capacity of cementogenesis [41]. On the other hand, tooth discoloration induced by both white and gray MTA is one of its main drawbacks. The presence of toxic heavy metals like bismuth oxide, long setting time with the possibility of subsequent coronal leakage, and difficulty in manipulation especially during the treatment of large periapical lesions are some other shortcomings of the MTA. Due to the aforementioned reasons, it seems rational to use alternative materials for the treatment of large periapical lesions [41].

Cold ceramic is another calcium hydroxide-base biocompatible ceramic that was first introduced in 2000 [8]. Cold ceramic has favorable characteristics including biocompatibility, radiopacity, ability to set in the presence of moisture while maintaining its physical properties, and gradual increase in the alkalinity of the environment with pH change from 7.36 to 11.16 after 7 days. Cold ceramic initial and final setting times are 15 min and 24 h, respectively so that adequate sealing could be achieved in moisture-contaminated conditions as is the case with large periapical lesions [8, 12]. Both cold ceramic and MTA increase the alkaline phosphatase activity and promote bone formation [42]. Evidence from the case of apexification with cold ceramic showed PDL formation at the root end and tissue regeneration [21].

Numerous animal and in vitro studies have shown that cold ceramic has excellent potential for clinical application. In a study It was consumed that significantly lower microleakage occurred with the cold ceramic as an apical barrier than with calcium hydroxide, using a dye penetration technique to investigate the quality of the apical seal [8, 43]. It seems that both cold ceramic and MTA had similar marginal adaptation and apical sealing ability in dry and saliva-contaminated environments while the mean interfacial adaptation and sealing in blood-contaminated environments were better with cold ceramic[43] (45). In a study using cold ceramic, GIC, Pro Root, and MTA (Dentsply, Tulsa Dental, Johnson City, Tennessee, USA) in furcal perforation, the adjacent periodontal tissues were less inflamed in cold ceramic and MTA groups after 3 months which cold ceramic exhibited less tissue inflammation after 30 days[16] (44).

In an animal study, in the presence of cold ceramic, in addition to new bone, cementum, and PDL were observed in more than half of the samples, while super EBA and IRM could not create cementum and PDL. ProRoot MTA regenerated significantly more PDL and cementum-like material than cold ceramic. Bone formation was evident in the radiographic image after 4 months [41].

Cold ceramic had several advantages over MTA including ease of manipulation, no discoloration of the dentin, low toxicity, better apical sealing in certain circumstances, and less microleakage and inflammatory responses [8, 12, 16, 43]. Sealing ability of cold ceramic, even in the presence of blood, has led us to consider this material as the root canal filling material in the treatment of teeth with large periapical lesions where possible contamination with blood and other tissue fluids is anticipated.

According to the aforementioned case reports, however, periapical healing, bone regeneration, and approximate apical closure along with the absence of signs and symptoms were observed in the 9-month and 4-year follow-up of the first and third reported cases, respectively. Moreover, the normal appearance of the apical periodontal ligament, remarkable increase in apical thickness of the root canal walls, and formation of cementum-like mineralized tissue at the apex had been achieved.

Additionally, it seems that the root length in the first presented case was increased beyond the apical limit of the cold ceramic. Also, due to the short-term inflammation caused by cold ceramic, cementation can be disturbed, because cementogenesis has the opposite relationship with periradicular inflammation. [41]

As presented in the second and third cases, filling materials were extended through periapical tissue which reduces the prognosis of the treatment [44]. According to the poor handling properties and longtime setting of MTA, extrusion is more likely in the periapical space [45]. When canal filling materials contact with periapical tissues, they may cause inflammation[46]. Sealers containing eugenol or paraformaldehyde cause more inflammation. Low cytotoxicity and induction of mineralization and solubility are desirable features, which explains the lack of interference with MTA extrusion, although the solubility of MTA is controversial [26]. Overfilled MTA can be absorbed and does not interfere with the recovery of periapical tissues, although gross overfilling of material into the apical filling space is not recommended and should be avoided [47]. Nosrat reported three clinical cases in which a large increment of MTA was extruded. Afterward, the teeth were tender to palpation of the soft tissue [46]. Some clinical cases reported the failure of the treatment following MTA extrusion after a 6-month recall [48].

As cold ceramic and MTA are both with calcium hydroxide-base, the aforementioned complications could be predicted in cold ceramic extrusion but need more studies to be established. Unpublished clinical observation and the outcome of this case series showed that cold ceramic extrusion approximately not bring about periapical lesions and cause further healing. Under all the declared circumstances, the treatment results of cases 2 and 3 were favorable.

In all of the cases, remarkable resolution of periapical radiolucency occurred at the same time the clinical signs and symptoms disappeared, indicating that substantial healing has been achieved.

Conclusions

According to the final results of the presented cases, cold ceramic can be an attractive alternative for the treatment of large periapical lesions due to its enhanced physical properties.

Conflict of Interest: 'None declared'.

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