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Apexification Treatment with a Mixture of Calcium Hydroxide and Hydroxyapatite

Zastosowanie mieszaniny wodorotlenku wapnia i hydroksyapatytu w metodzie apeksyfikacji

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A – research concept and design, B – collection and/or assembly of data, C – data analysis and interpretation, D – writing the article, E – critical revision of the article, F – final approval of article, G – collection of references

Abstract

Background. Multi-appointment apexification using calcium hydroxide (CH) is the best known effective method of treatment. However, shortening the therapeutic procedure is desired.

Objectives. The assessment of apexification efficacy when using a mixture of CH-based material and hydroxyapatite (HA).

Material and Methods. Treatment based on the apexification technique was conducted in 12 incisors and 1 molar of 13 patients. In the research the mixture of CH-based material and HA powder was used. The mixture was cyclically exchanged and the presence of mineral barrier was clinically verified.

Results. Successful apical barrier formation was noted in 100% cases qualified for research. The average treatment time reached 6.77 months.

Conclusions. A mixture of CH and HA effectively stimulates the apexification process. However, further research is required to find if an admixture of hydroxyapatite accelerates the periapical mesenchymal cells' organisation in relation to CH based-apexification (*Dent. Med. Probl.* 2014, 51, 1, 65–71).

Key words: apexification, calcium hydroxide, hydroxyapatite.

Streszczenie

Wprowadzenie. Wieloseansowa apeksyfikacja z zastosowaniem wodorotlenku wapnia jest najlepiej poznaną skuteczną metodą leczenia. Dokłada się jednak starań w celu skrócenia długoterminowego postępowania w leczeniu zębów z nieuforzonymi wierzchołkami korzeni.

Cel pracy. Ocena procesu apeksyfikacji po zastosowaniu mieszaniny wodorotlenku wapnia i hydroksyapatytu.

Materiał i metody. Apeksyfikację przeprowadzono u 13 pacjentów w 12 zębach siecznych i 1 zębie trzonowym. W badaniach zastosowano mieszaninę wodorotlenku wapnia i hydroksyapatytu, którą cyklicznie wymieniano i jednocześnie przeprowadzano kliniczną kontrolę pod kątem obecności bariery wierzchołkowej.

Wyniki. Pomyślną apeksyfikację zanotowano w 100% przypadków zakwalifikowanych do leczenia. Średni czas leczenia wyniósł 6,77 miesiąca.

Wnioski. Mieszanina wodorotlenku wapnia i hydroksyapatytu jest skutecznym materiałem odontotropowym w procesie apeksyfikacji. Potrzebne są jednak wnikliwe badania, czy domieszka hydroksyapatytu przyspiesza transformację mezenchymy okołowierzchołkowej w stosunku do procesu zachodzącego z udziałem samego wodorotlenku wapnia (*Dent. Med. Probl.* 2014, 51, 1, 65–71).

Słowa kluczowe: apeksyfikacja, wodorotlenek wapnia, hydroksyapatyt.

Treatment of immature necrotic teeth is always a procedure of uncertain prognosis. The recently applied one-step apexification method us-

ing mineral trioxide aggregate (MTA) is not always successful [1–3]. Many authors point to the necessity of continuing research into this materi-

al [1, 4, 5]. The economic aspect is also important as this method remains unavailable for a certain group of patients requiring apexification. Multiappointment apexification with calcium hydroxide, which has been commonly applied for decades, is considered the most effective method, mainly due to infection control in canals having an irregular structure [1, 6, 7]. Despite good treatment results, which are almost always reflected in the formation of apical barrier, this method has a few drawbacks. The biggest disadvantage is a long treatment period, during which the weakened canal walls may be broken, the patient may not return for follow-up and, in some cases, there are no conditions for the broken tooth crown reconstruction [1, 4, 7, 8].

Attempts are being undertaken to find a new way of treatment or a material the use of which would shorten the time of apical barrier formation. The application of such materials as: IRM, liofilized dentin, tricalcium phosphate, bone growth factors, bone proteins and other materials have been applied with various effects [9, 10]. Unfortunately, these endeavours did not bring the expected results, and CH was still considered the only effective way to induce apexification. Investigations into the effect of CH alone, as well as CH with HA on rabbit bone, which were conducted in our clinic revealed higher effectiveness of the mixture [11]. A similar mixture has been already applied in endodontic treatment of periodontitis [12]. The osteoconductive potential of HA, emphasised by other authors, might accelerate apical closure [13, 14].

Material and Methods

Thirteen patients aged from 6 years and 10 months to 10 years and 3 months, whose 12 upper central incisors and 1 mandibular first molar were subjected to apexification (the total of 14 roots), were qualified for treatment. The children were selected from Department of Pediatric Dentistry of Silesian Medical University.

The cause of incisors treatment was injury. In the case of 8 teeth it was Ellis class II crown fracture accompanied by a rupture of nervovascular bundle, as after a time the teeth were affected by pulp necrosis. In another 4 teeth the injury caused Ellis class III crown fracture, but the necessity to apply the apexification method resulted from four different reasons: simultaneous haematoma of pulp, delayed medical intervention, in the third case – not to apply the biological method by the dentist giving first aid, and in the fourth tooth – failure of apexogenesis procedure. The molar was treated due to chronic apical periodontitis

resulting from caries. Summing up, 4 teeth with irreversible pulpitis, 3 – with uncomplicated necrosis, 1 – with acute apical periodontitis and 5 – with chronic apical periodontitis were subjected to research.

During the first visit the degree of teeth roots development was evaluated by preoperative radiograph, according to classification of Moorrees, Fanning and Hunt [15]. In 3 teeth (3 roots) the development stage $R_{1/2}$ was noted, in 5 teeth (5 roots) – $R_{3/4}$, and in the remaining 5 teeth (6 roots) – $R_{CA_{1/2}}$.

Next the pulp remains were removed, the pulp chamber was prepared and the canal was initially cleaned. Then, basing on the radiograph with the file in the canal, the working length was determined – 1 to 2 mm shorter than the radiographic apex [16]. The canal was cleaned by the gentle retrograde method with copious irrigation with 0.5–1% sodium hypochlorite and then it was carefully dried. Before the proper stimulation therapy began, CH powder – Biopulp® (Chema-Elektromet, Rzeszów, Poland) mixed with saline or, in the cases of acute apical periodontitis, the antibiotic-steroid paste – Dexadent® (dexamethason aceticum, framycetin sulfate, polymyxin B sulphate, Chema-Elektromet) was placed into the canal for a period of 1–2 weeks.

During another visit, the whole canal was filled with an *ex tempore* prepared thick mixture of CH-based material – Calcicur® (VOCO GmbH, Cuxhaven, Germany) and HA powder – Ha-Biocer® (Chema-Elektromet, Rzeszów, Poland), using an amalgam carrier and large size paper points. The mixture filling was radiographically examined. Next a sterile cotton pellet and a temporary filling of glass ionomer cement Ketac Molar® (3M Espe, St Paul, MN) were placed on the material.

Follow-up appointments were established at 3-month intervals [8, 17–19]. During each visit the material was completely removed from the canal, the presence of the barrier was carefully detected with a 35 ISO file and examined by radiograph. If the presence of hard tissue in the apex area was clinically diagnosed, the treatment was considered completed. If, however, a soft, frequently painful tissue was palpable in the root apex area, which indicated complete or partial absence of the barrier, the canal space was dressed with CH-HA mixture for another observation period. The long-term stimulation therapy was continued until the root apex or a hard calcific barrier, enabling the canal to be filled, was formed. Depending on the final shape of canal lumen after apexification, two methods of obturation with use of AH Plus® sealer (Dentsply DeTrey, Konstanz, Germany) were applied. In the cases when dentine walls

were parallel or convergent, the canals were filled by lateral condensation with gutta-percha. If the canal space was irregular, most frequently taper-shaped, the warm gutta-percha technique Obtura II® (J. Morita Corporation, Osaka, Japan) was used. Since that moment the tooth was subject to clinical and radiological follow-ups due to a possibility of post-traumatic resorption, periapical radiolucency presence or root fracture.

Results

In all 13 patients (100.00%) subjected to treatment, the apexification process was completed with a positive result. In 6 teeth (46.15%) a complete root apex development was achieved. In the remaining 7 cases (53.85%) the presence of a mineral barrier was noted. The roots of 5 teeth with a formed apex reached a proper length, whereas 1 root appeared to be shorter than that in a contralateral tooth. In all 7 cases with a calcified barrier induced by the apexification technique the tooth root length was shorter than the physiological one.

An apical barrier was formed in all the teeth with roots at $R_{1/2}$ stage, whereas in 5 cases with roots at $R_{3/4}$ stage the formation of a barrier was observed in 3 and the formation of an apex – in 2 teeth. In the case of $RcA_{1/2}$ stage, an apex was formed in 4 teeth and a barrier – only in 1 tooth.

Increased thickness of root canal walls compared to their size recorded at the time of injury was not observed in any of the patients during the apexification process. Therefore, the shape of canal lumen did not change along its walls. Radiological examination only revealed proliferation of calcific tissue around the canal apex having a shape of the already mentioned barrier or root apex.

Ingrowing of mineral tissues into the canal space and subsequent shortening of the working length over the whole treatment period was not observed in any of the teeth. In 7 cases (6 incisors and 1 molar – 9 canals) the working length did not change, while in the remaining 6 incisors it increased by 0.5 to 3.5 mm – an average of 1.75 mm.

The period of treatment lasted the shortest of 2 and the longest of 14 months – an average of 6.77 months. The necessary number of check-ups during which the mixture was exchanged reached 1 to maximum 4.

An analysis of the number of roots cured at particular time intervals showed that in as many as 5 of them the apexification was completed within 3 months. In a period of 6 months the treatment was completed in another 4 cases. In 2 roots the process of apexification lasted from 7 to 9 months, and in the remaining 3 cases – 10 to 14 months.

The shortest average period of treatment – 4.67 months – was reached for roots with necrotic pulp, and the longest – for canals with pulpitis – 7.50 months. In the case of acute periodontitis the treatment took 6 months, whereas in teeth with chronic periapical inflammation the average treatment period was 6.29 months.

An analysis of the influence of root development degree at the time of injury on a period required for effective apexification revealed that the shortest average time of treatment – 3.71 months was noted for roots at the most advanced development stage $RcA_{1/2}$. It turned out to be shorter than the average apexification time in the case of teeth at $R_{1/2}$ root development stage – 7.33 months and teeth with roots at $R_{3/4}$ development stage, in which treatment was completed within an average time of 9.20 months.

The results of observations of the age of patients at the time of injury and its influence on the time necessary to form a periapical calcific barrier showed no differences between the average period of treatment in different age groups. When apexification started at the age of 6.5–7.5 years, the average treatment time reached 7.33 months, whereas in the group of children aged 7.5–8.5 years this time was 6 months, between 8.5–9.5 years of age – 7.33 months and over 9.5 years of age – 6.5 months.

In the first year, 5 months after treatment completion, one patient suffered an oblique root fracture when using the tooth, which resulted in its extraction. In the remaining 12 cases, clinical and radiological follow-up after 12 months revealed no clinical signs of failure, no periapical radiolucency connected with periodontitis or root resorption and no symptoms of fracture.

Two selected clinical cases have been presented in the Fig. 1 and 2.

Discussion

For many years it has been known that pulp necrosis in a tooth undergoing odontogenesis does not lead to its loss. The apexification procedure enables final canal obturation and the restoration of tooth crown, which is frequently damaged due to injury. As the use of other materials has not become widespread, CH remains the most effective material for apexification. MTA, which is gaining popularity, cannot always be used according to its indications. It is difficult to insert this non-resorbable material around the canal apex without placing it behind the wide apex opening. Many researchers emphasize the importance of precise MTA insertion in the canal [16, 20, 21]. On the other hand, slight overextrusion of a biocom-

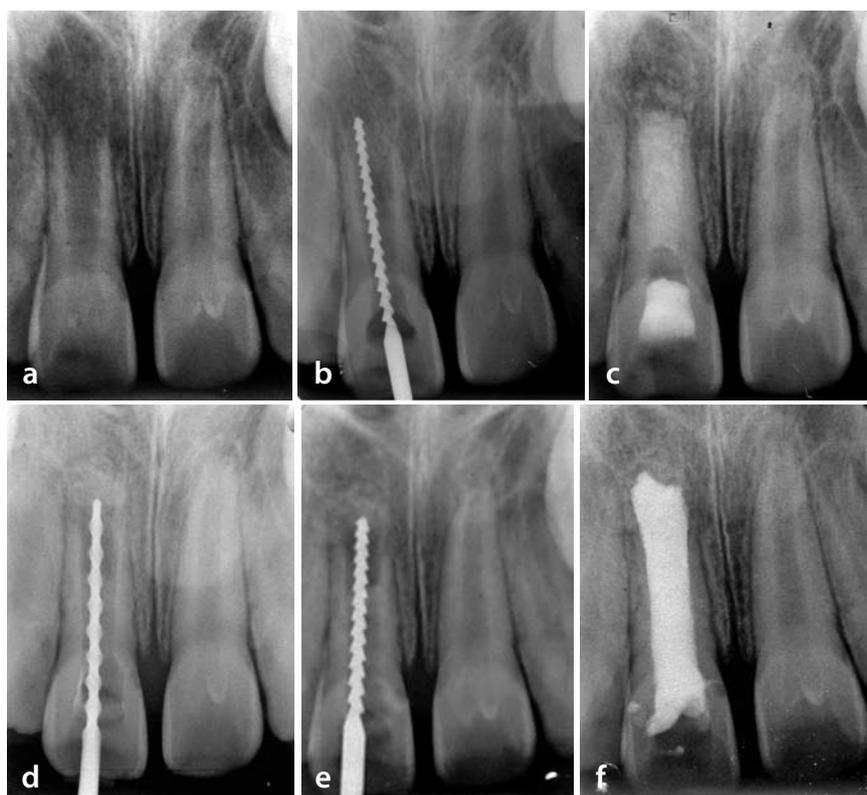


Fig. 1. a) a diagnostic radiograph of a traumatized tooth 11 R1/2; b) working length determination; c) a radiographic control of $\text{Ca}(\text{OH})_2$ + HA intracanal medication; d) and e) radiographic and clinical control of apical barrier formation after 3 and 6 months respectively; f) radiographic determination of canal's final filling after 10 months of treatment

Ryc. 1. a) zdjęcie diagnostyczne zęba 11 po urazie R1/2; b) pomiar długości roboczej; c) kontrola radiologiczna wypełnienia kanału mieszaniną $\text{Ca}(\text{OH})_2$ i HA; d) i e) radiologiczna i kliniczna kontrola obecności bariery wierzchołkowej po odpowiednio 3 i 6 miesiącach obserwacji; f) ocena ostatecznego wypełnienia kanałowego po 10 miesiącach leczenia



Fig. 2. a) a diagnostic radiograph of tooth 46 R3/4; b) working length measurement; c) a radiographic control of $\text{Ca}(\text{OH})_2$ + HA intracanal medication; d) a follow-up after 6 months: the mesial canals filled after 3 months of treatment; apical barrier in a distal canal determined after next 3 months; e) the radiographic control of the last canal's final filling; f) the radiograph taken 1 year after the completion of apexification treatment

Ryc. 2 a) zdjęcie diagnostyczne zęba 46 R3/4; b) pomiar długości roboczej; c) kontrola radiologiczna wypełnienia kanału mieszaniną $\text{Ca}(\text{OH})_2$ i HA; d) kontrola po 6 miesiącach leczenia: kanały mezjalne wypełnione po 3 miesiącach leczenia; bariera wierzchołkowa w kanale dystalnym zarejestrowana po następnych 3 miesiącach; e) kontrola radiologiczna ostatecznego wypełnienia kanału; f) zdjęcie po 12 miesiącach od zakończenia apeksyfikacji

patible and (or) resorbable material doesn't interfere with the process of healing [16, 19]. Excellent odontotropic properties of CH are unquestionable. The application of its *ex tempore* mixture with HA in endodontic treatment, which has been men-

tioned by Sędrowicz et al [12], encouraged Postek-Stefańska et al [11] from our department to undertake experimental research. The mixture grafted into the bone of a rabbit's mandible showed its excellent osteoinductive effectiveness compared to

other materials placed in the same conditions. In the vicinity of the mixture, greater accumulation of more mature newly-formed trabeculae was observed in comparison with areas where CH and HA were grafted separately. And although new bone formation after implantation of HA was not faster than the process of its self-regeneration, an admixture of CH, and, in consequence, a probable increase of the environment alcalization, considerably contributed to the stimulation of mesenchymal cells towards a more intense osteogenesis. In their clinical and experimental research, many authors enriched HA implants with various osteoinductive biologically active substances [13, 14, 22].

Bearing the above in mind, the authors of this work ventured to use the above mentioned mixture in the multiple-visit apexification method applied in clinical research. Previously the two substances had not been used jointly in the apexification procedure. In our studies, a 100% effectiveness was achieved in the stimulated development of an apex or barrier closing the canal lumen. A similar or slightly worse result was obtained by the authors who used CH for apexification [18, 23, 24]. Farhad and Mohammadi [25] claim that CH effectiveness is so high that there is no need to use it jointly with other materials. However, endeavours are continued to make the time of apexification as short as possible, because shortening of the treatment time contributes to a reduced risk of complications during a long-term therapy and enables quick strengthening and restoration of the tooth. Sheehy and Roberts [26] described investigations conducted in a few clinical centres. Their review shows that the authors of older studies used *ex tempore* preparations of CH. The time of apexification noted by Heithersay (1970) was 14–75 months, Cvek (1972) – 18.2 months, Chawla (1986) – 12 months in 35% and 6 months in 65% of cases, and by Yates (1988) – 9 months. In later investigations, ready-made CH materials were applied. In the research conducted by Ghose et al. (1987) the treatment lasted 3–10 months, by Mackie et al. (1988) – 7.8 months, by Kleier et al. (1991) – 1 to 30 months, and by Mackie et al. (1994) – 5.1 months [as cited in 26]. Dominguez Reyes et al. [18] achieved apexification within an average time of 12.19 months. In research conducted at our department by Jodłowska et al. [24], the average time of apexification using CH material Calcicur, similarly to that achieved by some researchers, was relatively long, reaching 14.23 months. The maximum treatment time they noted – 23 months – is too long and involves a risk of root walls fracture as well as the patient's failure to come to check-ups. The mixture of Calcicur and Ha-Biocer, applied in this study, brought the expected result, as the average time of treatment

reached 6.77 months, i.e. more than twice shorter than in the cases treated in the same clinical conditions (by the same method) with Calcicur. In 8 (8 teeth – 10 canals) of 13 patients subjected to treatment, apexification was completed within the first 6 months of treatment. The maximum apexification time in this group reached 14 months and was similar to the average time noted for patients treated by Jodłowska et al with Calcicur alone [24]. However, further investigations are necessary to find if an admixture of HA accelerates the process of periapical mesenchymal cells' organisation to form a barrier.

Few authors give a clear opinion on whether the rate of barrier formation can be influenced by the condition of pulp and periapical tissues at the beginning of treatment, the apical width of the canal, i.e. the root development stage, patient's age or the kind of injury. In view of numerous publications on the impact of pulpitis and periodontitis on the conditions of Hertwig's root sheath and other structures responsible for odontogenesis, it remains an unquestionable fact that properly conducted apexification is successful despite the abovementioned pathological processes [16]. However, a question arises as to whether the degree of inflammatory changes advancement exerts any influence on the rate of apical barrier formation. This dependence is frequently defined as an influence of time lapse between injury and the beginning of treatment on the effectiveness or duration of the apexification process [27]. Our observations imply that in the vast majority of cases these correlations are identical, as chronic periodontitis was observed in teeth in which treatment was applied after a long period of 10–15 months following the injury (Fig. 1). Although it may be difficult, early diagnosis of complications caused by injury undoubtedly prevents inflammatory changes from diffusing. Thater and Marechaux [27] report that endodontic treatment acceleration favours apexification. However, they did not present a statistical analysis of their results, and in many cases they treated the duration of apexification was short although a lot of time passed from the date of injury, and vice versa – it was long despite the quickly undertaken treatment [27]. Mackie et al [23] as well as Lee et al [28], basing on their research, found that the extent of pathological process in periapical tissues has no influence on the rate of apical barrier formation. Dominguez Reyes et al [18] quote the opinions of other authors claiming that the existence of inflammatory changes larger than 5mm in periapical tissues contributes to a delay in apexification and that the formed barrier has an irregular structure. The authors, however, did not observe a similar correlation in their own research.

Numerous publications quote consistent opinions on the correlation of the treatment time and the degree of root apex development, i.e. the more advanced development of the root, the shorter the time needed for apexification [18, 23, 29].

As far as the patient's age is concerned, it is difficult to draw unambiguous conclusions due to different observations of clinical research authors. Basing on their investigations, Mackie et al. [23] concluded that the time of treatment shortens with the patient's age. In a group aged 6–8 years, the average apexification time was 10.1 months, in a group aged 9–10 years – 9.1 months, whereas in a group of children aged 11–15 years it was significantly shorter – 4.8 months. Rafter [29] notices that other authors did not have similar observations. Dominguez Reyes et al. [18] cite other researchers' investigations and claim that the time of apexification is not dependent on the patient's age.

The conducted research seems to indicate that apexification duration does not depend on the abovementioned factors. In all the cases in which treatment began in a period when the root development was the most advanced – at $R_{C_{1/2}}$ stage, apexification lasted for a short time, irrespective of the condition of the pulp and periapical tissues, although the patients' age differences reached 3 years. However, in one incisor at $R_{3/4}$ stage of root development in a 10-year-old patient diagnosed as suffering from pulpitis the treatment lasted as many as 14 months – 8 months longer than in an incisor with chronic periodontitis at $R_{1/2}$ development stage in a patient aged 7 years and 6 months.

As the research does not allow the authors to draw clear-cut conclusions concerning the influence of pulp and periapical tissues' condition as well as the degree of tooth development or patient's age on the duration of apexification, it seems advisable to consider other factors which made the treatment with a mixture of CH and HA shorter compared to therapy based only on CH. The biological activity of CH is commonly known and understood. The anti-inflammatory effect due to

contraction of capillaries, neutralization of the acid products of inflammation, stimulation of alkaline phosphatase and long-term antimicrobial properties favour the process of regeneration [4, 16, 28, 29]. On the other hand, thanks to the osteoconductive properties of HA, this biomaterial can be successfully used as a scaffold for the newly formed tissue. The HA could be used as an "artificial apical stop" in the one-visit method. The above research did not indicate shortening of the working canal length during treatment, which may occur in the case of stimulation with a high solubility material, e.g. CH when hard tissues can deposit in the apical portion of the canal [30]. The presence of HA in the mixture most probably served as an apical barrier for the tissues which may grow into the canal in a process similar to osteoinduction. However, when deprived of antimicrobial properties, it cannot effectively fight the bacteria which survived despite the applied antiseptic treatment. Possibilities of disinfection the canal in immature teeth are limited due to its thin walls and non-typical shape. At the same time, by shortening the duration of treatment, the one-visit method eliminates many inconveniences and complications related to long-term treatment. Jodłowska et al. [31] applied Ha-Biocer in canals of 5 single-rooted teeth. After a 9-month observation, in 3 cases without complications they left the periapical part of hydroxyapatite and filled the remaining part with gutta-percha. In one patient the radiological examination, which was continued for 6 years after treatment completion, revealed proper condition of the tooth and periapical tissues. The authors of the above research presume that the observed failure might have been due to the lack of HA antibacterial properties [31]. Although the commercially available MTA meets the requirements, it cannot be applied in all cases and is relatively expensive [4, 16, 20, 32]. Therefore, application of HA enriched with CH as an artificial apical stop could also be taken into consideration. Further investigations are necessary, though.

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