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CASE REPORT / OLGU SUNUMU

Apexification or Regeneration ? Repair in Endodontics

Apeksifikasyon mu, Rejenerasyon mu? Endodontide Onarım

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Abstract

Regenerative endodontics is a new concept for the management of the permanent immature teeth with necrotic pulps. This procedure enables to replace damaged dentine and pulp-dentin complex within the root structure with healthy tissue. Firstly, elimination of clinical symptoms of the infection then, thickening of the canal walls and continuing root maturation and finally filled with the host's own vital tissue are the main goals of regenerative endodontics. However, apexification is another solution associated with traditional root canal treatment for the teeth with necrotic pulp and immature root development. It involves removal of necrotic and infected tissue from the wide and funnel shape of root canal in immature teeth. The purpose of this article is to review regenerative endodontics and apexification in conjunction within a case.

Keywords: regenerative endodontics, apexification, MTA, immature permanent teeth

Öz

Rejeneratif endodonti, apeksi açık nekrotik pulpalı daimî azı dişlerde uygulanan yeni bir tedavi konseptidir. Bu işlem, kök yapısındaki hasarlı dentin ve pulpa-dentin kompleksinin sağlıklı doku ile değiştirilmesini sağlar. İlk olarak enfeksiyonun klinik semptomlarının ortadan kaldırılması, ardından kanal duvarlarında kalınlaşma sağlanarak kök olgunlaşmasının devam etmesi ve son olarak da hastanın kendi vital dokusu ile kökün doldurulması rejeneratif endodontinin ana hedefleridir. Olgunlaşmamış dişlerde geniş ve huni şeklindeki kök kanalından nekrotik ve enfekte dokunun çıkarılmasını içeren apeksifikasyon işlemi, geleneksel kanal tedavisi ile ilişkili bir başka bir çözümdür. Bu makalede, aynı hasta üzerinde rejeneratif endodonti ve apeksifikasyon işlemleri farklı dişlerde uygulanarak tedavi prosedürü ve sonuçları gözden geçirilmiştir.

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Anahtar Kelimeler: rejeneratif endodonti, apeksifikasyon, MTA, olgunlaşmamış daimî dişler

INTRODUCTION

Root canal treatment is a rational treatment choice in a necrotic tooth. However, it may result in tooth loss, due to high risk of fracture and short root in an immature tooth. So, when the apex is not completely formed, care should be taken to treat necrosis or irreversible pulpitis. Endodontic management of the permanent immature tooth continues to be a challenge for both clinicians and researchers recently. Regenerative endodontics is a new technique for the management of immature and infected root canals and quite popular which results apexo-genesis with apical closure if it is indicated properly.

Conventional root canal treatment is carried out in mature teeth with completely closed apex. But in case of open apex, which residual progenitor pulp cells are not found in necrotic immature teeth, to complete root closure apexification, producing apical plug or regeneration procedure should be performed. Since the dentinal walls are quite thin in these teeth, clinical concerns are related to achieving disinfection as 'aggressive' instrumentation is contraindicated. So, clinician must rely on endodontic irrigants and medicaments mostly. Obturation is quite hard in open apex cases, because of difficulties in controlling the working length. Roots become weaker and fracture or tooth loss is unavoidable in long term due to mechanical instrumentation (Harlamb, 2016).

Apexification is one of the solution conjuncts with conventional root canal therapy in immature necrotic cases. It involves removal of necrotic and infected tissue from the wide and funnel shape of root canal in immature teeth. $Ca(OH)_2$ is the most commonly used materials in treatment of immature teeth due to its high pH and strong antibacterial effect. Also, it's used for induction of an apical barrier. High accomplished

results have been reported in clinical and experimental studies related to Ca $(OH)_2$ applications (Andreasen and Andreasen, 1994). However, although apexification procedure with calcium hydroxide induces apex to close, it does not stimulate the thickness of the entire root dentin. So thin root dentin and large canal are prone to cervical fracture or insufficient root length leading to mobility and subsequent tooth loss in long term (Raldi et al., 2009).

MTA is widely used for apexification due to biocompability, ability to seal and its high pH as apical barrier. It produces an artificial barrier against obturation material to avoid overfilling and condensation forces. Although Ca $(OH)_2$ produces biological barrier, it may weaken the dentin structure and must be replaced at monthly intervals (Yassen and Platt, 2013; Andreasen et al, 2002). However, MTA produces strong barrier and 24 hours after placement, root canal filling can be completed (Torabinejad and Walton, 2009).

Regenerative endodontics is one of the most stimulating improvements in dentistry. It uses the concept of tissue engineering (stem cells from an induced periapical bleeding and scaffold using blood clot, platelet rich plasma or platelet –rich fibrin) to restore the root canals to a healthy state, allowing for continued development of the root and surrounding tissue. The knowledge in the fields of pulp biology, dental trauma, and tissue engineering can be applied to deliver biologically based regenerative endodontic treatment of necrotic immature permanent teeth, resulting in continued root development, increased thickness in the dentinal walls and apical closure. These developments in the regeneration of a functional pulp-dentin complex have a promising impact on efforts to retain the natural dentition, the ultimate goal of endodontic treatment (AAE, 2018).

Nygaard-Ostby performed the first experimental study related to regenerative endodontics in 1961. He extracted an intact tooth and cut off apex; after replantation, he removed the pulp tissue through the crown of dog's teeth. Also, he ensured bleeding from humans' teeth after removal of necrotic pulp tissue, then obturated coronal part of teeth. A new vascular tissue was observed in unfilled apical portion of the experimental teeth (Ostby, 1961). In 1971, Nygaard-Ostby and Hjortdal demonstrated formation of fibrous connective tissue and accumulation of cellular cementum in the root canal after blood clot was created (Nygaard-Ostby and Hjortdal, 1971).

Later in 1978, Skoglund et al. detected occurrence of the revascularization in reimplanted and autotransplanted immature dog's teeth (Skoglund et al., 1978).

The width of the apical foramen is quite important in success of regeneration procedure. Kling et al. indicated that there is no revascularization of permanent teeth with less than 1 mm width of apical foremen which had been avulsed and reimplanted (Kling et al., 1986).

Regeneration procedure should be designed to replace damaged structures such as dentin, root structures and pulp-dentin complex. Since biomechanical preparation cannot be done properly due to thin dentinal wall, irrigation is quite important for elimination infected tissue or debris. 1% NaOCl is optimum and higher percent of NaOCl might be irritant for vital tissue. Usage of EDTA is recommended for effect on PRP and viable cells (Iwaya et al., 2001). Also, triple antibiotic paste (ciprofloxacin, metronidazole and minocycline) is used for disinfection of the root canal. Hoshino et al. found that triple antibiotic paste (ciprofloxacin, metronidazole and minocycline, with and without the addition of rifampicin) effecting sufficiently on eradicating bacteria of the infected dentine in the root canal (Hoshino et al., 1996). Sato et al. found that triple antibiotic paste was effective on disinfection of infected canals (Sato et al., 1996). Allergic reactions or tooth discoloration was detected using of triple antibiotic medication. Kim et al. indicated that minocyclines discolored the coronal tooth structure (Kim et al., 2010). To avoid discoloration, cephalosporin or amocycilin are used instead of minocycline in triple antibiotic paste (Kim et al., 2010). Beside antibacterial effect of antibiotics, several other important effects are found on regeneration such as tetracycline enhances the growth of host cells on dentin via exposure of embedded collagen fibers or grow factors (Terranova et al., 1989). Beside antibiotics, $Ca(OH)_2$ or $Ca(OH)_2$ mixed with chlorhexidine was also used for this purpose. Chueh et al. also found that $Ca(OH)_2$ was effective for elimination of bacteria in regeneration procedure (Chueh et al., 2008). However, usage of Ca $(OH)_2$ was controversial due to its necrosis effect on vital tissue. Meantime, after blood clot was produced, MTA was used as an apical barrier in middle third of the canal in regeneration cases. Iwaya et al. recommended leaving the root canals free of medication for the vital pulp cells which had the potential to proliferate new pulp tissue (Iwayav et al., 2001). The first "revascularization protocol" was proposed by Banchs & Trope as analogous to the regeneration guideline used today (Banchs and Trope, 2004).

Clinical Regenerative Endodontic Procedures

The American Association of Endodontists suggests a Clinical Considerations for a Regenerative Procedure for its members (Figure 1).

AAE Clinical Considerations for a Regenerative Procedure

Revised 4/1/2018

These considerations should be seen as one possible source of information and, given the rapid evolving nature of this field, clinicians should also actively review new findings elsewhere as they become available.

Case Selection:

• Tooth with necrotic pulp and an immature apex.

• Pulp space not needed for post/core, final restoration.

• Compliant patient/parent.

• Patients not allergic to medicaments and antibiotics necessary to complete procedure (ASA 1 or 2).

Informed Consent

• Two (or more) appointments.

• Use of antimicrobial(s).

• Possible adverse effects: staining of crown/root, lack of response to treatment, pain/infection.

• Alternatives: MTA apexification, no treatment, extraction (when deemed nonsalvageable).

• Permission to enter information into AAE database (optional).

First Appointment

• Local anesthesia, dental dam isolation and access.

• Copious, gentle irrigation with 20ml NaOCl using an irrigation system that minimizes the possibility of extrusion of irrigants into the periapical space (e.g., needle with closed end and side-vents, or EndoVac™). Lower concentrations of NaOCl are advised [1.5% NaOCl (20mL/canal, 5 min) and then irrigated with saline or EDTA (20 mL/canal, 5 min), with irrigating needle positioned about 1 mm from root end, to minimize cytotoxicity to stem cells in the apical tissues.

• Dry canals with paper points.

o Place calcium hydroxide or low concentration of triple antibiotic paste. If the triple antibiotic paste is used: 1) consider sealing pulp chamber with a dentin bonding agent [to minimize risk of staining] and 2) mix 1:1:1 ciprofloxacin: metronidazole: minocycline to a final concentration of 1-5 mg/ml. Triple antibiotic paste has been associated with tooth discoloration. Double antibiotic paste without minocycline paste or substitution of minocycline for other antibiotic (e.g., clindamycin; amoxicillin; cefaclor) is another possible alternative as root canal disinfectant. Clinicians should be aware that studies have been done using higher concentrations of TAP/DAP, but a recommendation to a higher concentration can't be made at this time due to limited studies.

• Deliver into canal system via syringe

• If triple antibiotic is used, ensure that it remains below CEJ (minimize crown staining). • Seal with 3-4mm of a temporary restorative material such as Cavit™, IRM™, glassionomer or another temporary material. Dismiss patient for 1-4 week.

Second Appointment (1-4 weeks after 1st visit)

• Assess response to initial treatment. If there are signs/symptoms of persistent infection, consider additional treatment time with antimicrobial, or alternative antimicrobial.

• Anesthesia with 3% mepivacaine without vasoconstrictor, dental dam isolation. • Copious, gentle irrigation with 20ml of 17% EDTA.

• Dry with paper points.

• Create bleeding into canal system by over-instrumenting (endo file, endo explorer) (induce by rotating a pre-curved K-file at 2 mm past the apical foramen with the goal of having the entire canal filled with blood to the level of the cemento–enamel junction). An alternative to creating of a blood clot is the use of platelet-rich plasma (PRP), platelet rich fibrin (PRF) or autologous fibrin matrix (AFM).

• Stop bleeding at a level that allows for 3-4 mm of restorative material.

o Place a resorbable matrix such as CollaPlug™,Collacote™, CollaTape™over the blood clot if necessary and white MTA as capping material.

o A 3–4 mm layer of glass ionomer (e.g. Fuji IX™, GC America, Alsip, IL) is flowed gently over the capping material and light-cured for 40 s. MTA has been associated with discoloration. Alternatives to MTA (such as bioceramics or tricalcium silicate cements [e.g., Biodentine®, Septodont, Lancasted, PA, USA, EndoSequence® BC RRM-Fast Set Putty, Brasseler, USA]) should be considered in teeth where there is an esthetic concern.

• Anterior and Premolar teeth - Consider use of Collatape/Collaplug and restoring with 3mm of a nonstaining restorative material followed by bonding a filled composite to the beveled enamel margin.

• Molar teeth or teeth with PFM crown - Consider use of Collatape/Collaplug and restoring with 3mm of MTA, followed by RMGI, composite or alloy.

Follow-up (6-, 12-, 24-months)

• Clinical and Radiographic exam o No pain, soft tissue swelling or sinus tract (often observed between first and second appointments).

o Resolution of apical radiolucency (often observed 6-12 months after treatment) o Increased width of root walls (this is generally observed before apparent increase in root length and often occurs 12-24 months after treatment).

o Increased root length. o Positive Pulp vitality test response o Recommended yearly follow-up after the first 2 years o CBCT is highly recommended for initial evaluation and follow-up visits

• The degree of success of Regenerative Endodontic Procedures is largely measured by the extent to which it is possible to attain primary, secondary, and tertiary goals:

o Primary goal: The elimination of symptoms and the evidence of bony healing.

o Secondary goal: Increased root wall thickness and/or increased root length (desirable, but perhaps not essential)

o Tertiary goal: Positive response to vitality testing (which if achieved, could indicate a more organized vital pulp tissue)

Fig 1. AAE Clinical Considerations for a Regenerative Endodontic Procedure

Basically, in the success of regenerative endodontic treatment, the clinician should firstly expect to eliminate the symptoms of the infection and heal the bone, then grow the root length and thickness, and finally receive a positive response to vitality test.

In this article, comparative treatment options including regeneration and apexification procedure with open apices of the two maxillary central incisors with history of dental trauma was reported.

Case Presentation

A healthy 8-year-old girl with a history of trauma to her maxillary right and left central incisors was referred to dental clinic of Marmara University, Faculty of Dentistry Istanbul, Turkey. The patient had a history of bicycle injury 2 weeks ago and the crown fractures of #11 and #21 had been restored with composite restoration by a general dentist. The patient's main complaint was pain. Clinically pain was apparent on percussion. Radiographic examination showed no apical pathosis in immature root of the teeth. (Figure 2a) After signed informed consent was obtained from the patient's parent treatment of both teeth was initiated with a canal irrigation of 20 ml of 5.25% NaOCl, without instrumentation and gently dried with paper points. Mixture of triple antibiotic paste was placed in both root canals.

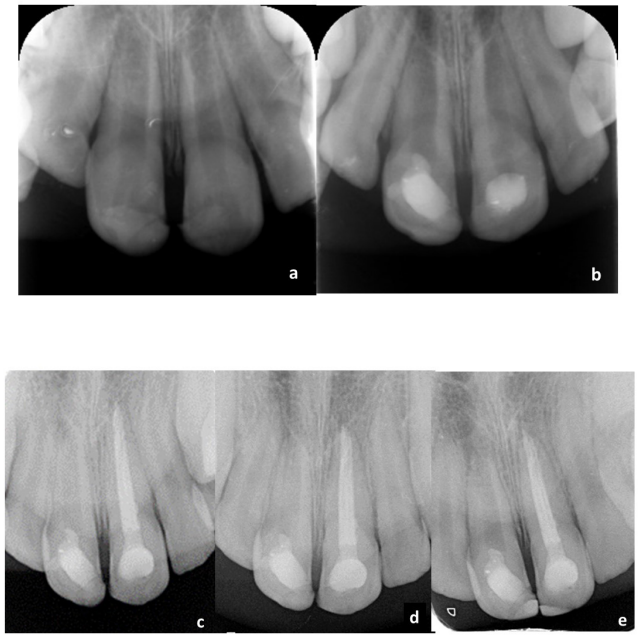

Fig 2. Regenerative and apexification treatment of the 2 central incisors.

a.İnitial radiograph of the patient. b. Regenerative treatment of #11 and apexification of #21. c. Radiograph of one year after regenerative treatment on right maxillary incisor and apexification completed on left maxillary incisor. d. Two years follow up radiograph. e. Three years follow up radiograph.

2 weeks later, the treatment procedure was repeated due to respond to percussion test. Four weeks later, #11 was asymptomatic no longer tender to percussion or palpation, so after irrigation a sterile #20 K-file was used to induce bleeding within the root canal from the periapical tissues. MTA was placed and the tooth restored temporarily and one week later, permanent restoration was done with composite material. However, tooth #21 was still tender to percussion and pain. Apexification procedure was decided to perform on tooth #21 as an alternative approach. A creamy mixed of CaOH were replaced in several appointments for a year, after this period, the root length was increased, thickness of dentinal wall was observed and apical closure was evident on radiograph, so the root canal treatment was completed (Figure 2 b,c).

The case was followed up clinically and radiographically for three years. At follow–up examination of #11 tooth was asymptomatic and functional, respond normal to cold and electrical pulp test but apical closure was not completed yet. Also, tooth #21 was asymptomatic with no periapical pathosis in three years. (Figure 2 d,e)

DISCUSSION

The success of regeneration treatment depends on three criteria: effective disinfection of the root canal, having more than 1 mm size of the apical foramen and the patient's age. Regards to these criteria, tooth #11 was treated successfully.

Kahler et al. investigated 368 published clinical studies of treatment of immature teeth with pulp necrosis (Kahler et al., 2017). They found that $Ca(OH)_2$ apexification treatment is standard endodontic procedure compared to obturating the root apices by MTA. The success rate was found 89.7% in conventional endodontic procedure, whereas 100% in obturated apices with MTA. However, Silujjai & Linsuwanont found 80.77 % success with apexification and 76.47% with regeneration cases (Silujjai and Linsuwanont, 2017). Authors considered success in Regenerative Endodontic Procedure (REP) by degree of apexogenesis including increased root length, increased root thickness and apical closure. They claimed that success rate can be affected due to clinical procedures such as operator skill, material selection and different protocols.

Nowadays regenerative endodontics is considered as the first treatment choice in open apices. However, if the clinical symptoms are not disappeared, apexification with $Ca(OH)_2$

or closure of apex with MTA would be the treatment of choice.

In the present study, clinical symptoms such as swelling of the gingiva and pain in tooth #21 could not be eliminated. So apexification with $Ca(OH)_2$ treatment was preferred to REP. This case allowed us to compare both treatment options. As a result of the treatments, both teeth showed clinical success with increased root width and closed apices. Infection control is one of the success criteria in treatment of necrotic cases with open apices. It seems that race between new tissue and bacteria population in the pulp space result in healing. Almutairi et al. (2019) reviewed failed cases related to regenerative endodontics and found that 79% of these had persistent infections. In vivo studies showed that lack of periapical healing and thin root canal wall caused failure, most probably due to residual bacteria (Almutairi et al., 2019). Although antibiotics or $Ca(OH)_2$ were used for intracanal medication, studies have indicated that most failed cases showed signs and symptoms of infection. When etiology of regenerative treatment cases was investigated, trauma found to be at the highest rate in failure (59%). Dental trauma causes root resorption, and this may induce to damage dental papilla and Herwig epithelial root sheath which may cause the failure of regenerative endodontic treatment.

Controversial results were found related to one-visit REP (Shin et al., 2009). McCabe (2015) and Chaniotis (2016) found successful results with single visit, however failure cases were reported in one visit without use of intra-canal medications.

American Association of Endodontics recommends lower concentration of irrigation solutions and medicaments for eliminating adverse effect of the chemical agents on radicular dentin or viable cells (AAE, 2018).

Alobaid et al. and Shimizu et al. reported crown fractures at the cervical level of immature tooth (Alobaid et al., 2014; Shimizu et al., 2013). Cvek indicated that immature teeth are susceptible to fracture specially in cervical third of the roots (Cvek, 1992). Yassen et al. reported that usage of Ca $(OH)_2$ or antibiotic-based medicament may decrease the fracture resistance of root (Yassen et al., 2013).

This study showed that regenerative treatment procedure can be considered as an alternative to apexification of tooth with immature apices when diagnosed properly. However, lately tissue engineering has been used to regenerate pulp tissue by applying stem cells, bioactive growth/ differentiation factors and biomimetric scaffold. Although so many experimental studies have been published until now, more studies are needed for the success of these types of cells in clinical cases.

CONCLUSION

REP for immature teeth versus Ca $(OH)_2$ apexification/ MTA apical barrier procedures are quite popular and successful results were stated in literature. Potential of regenerative endodontics may benefit millions of patients each year. Although this high success rate of regenerative endodontics, much more effort should be given to reduce the high caries rate in our country and more importance to preventive dentistry in order to reduce early tooth loss. This report offers a good opportunity to compare two different treatment options on teeth with open apices and even though there was success in both treatments, regenerative treatment approach leads to the vitality of the pulp.

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