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JULY- DEC 2016 • VOL 6 • ISSUE 2

Indian Journal of Comprehensive Dental Care

ENDODONTIC MANAGEMENT OF IMMATURE TEETH WITH NECROTIC PULP- SHIFTING FROM APEXIFICATION TO REVASCULARIZATION

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Abstract

Immature permanent teeth that have lost vitality have traditionally been treated by apexification. Through this technique, the formation of an apical barrier to close the open apex is promoted so that the filling materials can be confined to the root canal. Because tissue regeneration cannot be achieved with apexification, a new technique called regenerative endodontic treatment was presented recently to treat immature permanent teeth. Regenerative endodontic treatment is a treatment procedure designed to replace damaged pulp tissue with viable tissue which restores the normal function of the pulp-dentin structure. After regenerative endodontic treatment, continued root development and hard tissue deposition on the dentinal wall can occur under ideal circumstances. In this review article, the rationale behind revascularization is elaborated along with its protocol and the factors that affect the outcome of the procedure.

Keywords: apexification, immature, revascularization

Date of Submission : 3/2/16 Date of Acceptance : 16/2/16

Introduction

Endodontic management of immature permanent teeth with necrotic pulps and open apices has been a significant challenge, owing to the presence of thin dentin walls and the lack of a natural apical constriction that an obturation material can be placed against. For decades, such teeth have been treated by the apexification procedure, which involved placement of intracanal calcium hydroxide ($Ca(OH)_2$) to induce formation of a calcific barrier at the apex. Despite the widespread use of the $Ca(OH)_2$ based apexification technique, the lengthy treatment period that might require multiple visits and renewal of the intracanal dressing, unpredictability of apical closure and susceptibility of cervical root fracture after prolonged exposure to $Ca(OH)_2$ raised serious concern about the merits of this treatment approach.

More recently, the traditional apexification procedure has been modified by the introduction of artificial apical barrier methods with mineral trioxide aggregate (MTA). Although this approach might considerably shorten the treatment period, improve patient compliance, and result in favorable healing of the periapical tissues, it still cannot stimulate the development of apical closure and thickening of radicular dentin.

On the basis of these considerations, the fate of apexification in future treatment protocols for necrotic immature permanent teeth seemed to be questionable indeed.[1]

The path of endodontic treatment took a sharp turn almost a decade ago, when Iwaya et al showed that continued root development and apical closure in a necrotic immature tooth were possible when successful disinfection of the root canal was achieved.[2]

However, it was in 2004, when Banchs and Trope published a case report describing a new treatment procedure for the management of the open apex called "revascularization." The protocol differs from traditional apexification techniques in that disinfection of the canal is done with both sodium hypochlorite and chlorhexidine and a combination of three antibiotics (ciprofloxacin, metronidazole and minocycline). Unlike traditional apexification or the use of apical barriers, revascularization procedures allow for increase in both the length of the root and root wall thickness.[3]

The current (2012) American Association of Endodontists' *Glossary of Endodontic Terms* defines regenerative endodontics as "biologically-based procedures designed to physiologically replace damaged tooth structures, including dentin and root structures, as well as cells of the pulp-dentin complex."[4]

It can safely be said that regenerative endodontics is a treatment revolution in dentistry- the era in which root canal therapy brings diseased teeth back to life, rather than leaving a "non- vital" or dead tooth in the mouth.[5]

Rationale of Regenerative Endodontics[6]

Regenerative endodontic treatment can occur in infected immature permanent teeth because of mesenchymal stem cells which exist in the apical papilla of immature teeth. These stem cells from the apical papilla (SCAP) are capable of differentiating into odontoblast-like cells forming root dentin.

Another type of mesenchymal cells, which are called dental pulp stem cells (DPSCs) were discovered and isolated earlier, have the ability to differentiate into odontoblast-like cells and form dentin/pulp-like complex when implanted into subcutaneous spaces of immunocompromised mice.

Both SCAP and DPSCs are as potent in osteo/dentinogenic differentiation as mesenchymal cells from bone marrows, whereas they are weaker in adipogenic potential. SCAP and DPSCs show similar features, but they have some differences. SCAP show a significantly greater bromodeoxyuridine uptake rate (an indication of cell proliferation), number of population doublings, and tissue regeneration capacity than DPSCs. These evidences suggest that SCAP derived from a developing tissue may be a superior cell source for tissue regeneration.

Protocol for Regenerative Endodontic Treatment Procedure[5]

Revascularization should include appropriate case selection, with a strict disinfection protocol and use of antimicrobial paste to achieve complete asepsis and blood clot formation in canal space followed by placement of an MTA barrier, or equivalent over blood clot with a final restoration and follow-up at regular intervals.

I) Case selection

Currently there is no evidence-based guideline to help clinicians determine which condition of cases can be treated with this conservative approach. The presence of radiolucency at the periradicular region can no longer be used as a determining factor, nor is the vitality test as in both situation, vital pulp tissue or apical papilla may still present in the canal and at the apex. Logically, any remnant of visible soft tissue that can be visualized under the dental microscope

should give the clinician an incentive to take the conservative approach, even though the soft tissue may be purely granulation tissues. However, one can also not rule out the possibility that there are not any remaining pulp tissues in the very apical part of the canal only because it cannot be detected clinically.

Although case reports on revascularization are largely from teeth with incomplete apical closures, it has also been noted that reimplantation of avulsed teeth with an apical opening of approximately 1.1 mm demonstrate a greater likelihood of revascularization. This is mainly because in enlarged apical foramen there is a high chance of survival of remaining vital pulp in the canal since open apex provides a good communication from pulp space to the periapical tissues, therefore it may be possible for periapical disease to occur while the pulp is only partially necrotic and infected. It is necessary to promote vascularization and maintain initial cell viability via nutrient diffusion and oxygen supply. This finding suggests that revascularization of necrotic pulps with fully formed (closed) apices might require instrumentation of the tooth apex to approximately 1 to 2mm in apical diameter to allow systemic bleeding into root canal systems.[7]

Another obvious consideration is the duration of the infection. The longer the duration of infection lesser will be the number of survived remaining pulp tissue and stem cells. Additionally, the longer the infection there is in the canal, the more likelihood of a deeper penetration of microbial colonies

into dentinal tubules. This renders the disinfection more difficult to accomplish. The technique also shows maximum positive outcome in young adults as younger adult patients generally have a greater capacity for healing.

ii) Disinfection protocol

A successful vital pulp treatment requires a good seal against bacteria, no severe inflammatory reactions, and stable haemodynamics within the pulp. Use of intracanal irrigants with placement of antibiotics for several weeks as a means of disinfection of the canal is a very important step to achieve revascularization.

Calcium hydroxide $Ca(OH)_2$ has been advocated as a root canal disinfectant and for stimulation of hard tissue repair at the apex of infected immature teeth. Several favorable biological properties have been attributed to it when used clinically. It is antimicrobial, it has the ability to dissolve necrotic tissue in the root canal and it can induce apical closure by hard tissue formation. It also acts as a physiochemical barrier, which precludes the proliferation of residual microorganisms and prevents the reinfection of the root canal from the oral cavity.

However, a freshly mixed paste of $Ca(OH)_2$ has a pH of approximately 12.5 and is potentially toxic to not only bacterial cells but human cells too.[8] The use of $Ca(OH)_2$ in revascularization is therefore not without criticism, which are:

1. $Ca(OH)_2$ may destroy the ability to induce the nearby undifferentiated cells to become odontoblasts and damage the remaining pulp tissue, apical papilla and HERS (Hertwig's epithelial root sheath).
2. Direct contact of $Ca(OH)_2$ paste with the tissue which will induce the formation of a layer of calcific tissue which may occlude the pulp space, therefore preventing pulp tissue from regeneration.
3. Even if apexification with $Ca(OH)_2$ is rendered successful owing to its antibacterial properties, the procedure will leave behind a short root with thin dentinal walls with a high risk of root fracture.[9]

The gentle treatment regimen is, therefore, an attempt to conserve any viable tissues that may be remained in the canal system which harbor stem cells, i.e., SCAP in the apical papilla and DPSCs (dental pulp stem cells) in the pulp. Avoidance of trauma to the tissue around the apex is advised. After proper disinfection, the remnants of the survived HERS at the apices of immature teeth may organize the apical mesodermal tissue into root components.

In the first appointment continuous irrigation with NaOCl should be carried out for 30 min at every 5 minutes. This continuous procedure completely disinfects the root canal, as the survival of microorganisms or its toxins will prevent the revascularization procedure.

In the next appointment, after 1 week irrigation of the canal is again carried out for 15 min. If vital tissue is present in the canal the concentration of NaOCl used is 5.25% and if it is not present and revascularization is carried out by blood clot, then the concentration used by most authors is 1.25-2.5%.

Revascularization procedure has also been carried out only with the copious irrigation of the canal without instrumentation. The noninstrumentation procedure using 6% NaOCl and 2% chlorhexidine coronal irrigation has shown to preserve the remaining vital dental pulp stem cells in single step revascularization procedure. Hence it is believed to be critical for pulp revascularization.

However Rossi-Fedele et al have showed that formation of precipitate when chlorhexidine and NaOCl are mixed leading to discoloration and other side effects.[10] Combination of 17% EDTA with 6% NaOCl is safe till now and has shown to be effective for regeneration of pulpal stem cells. Ethylenediaminetetraacetic acid (EDTA) very effectively releases growth factors from human dentin as well as helps in the survival of stem cells of apical papilla.[11,12]

iii) The use of antimicrobial paste

As calcium hydroxide has its own disadvantages in revascularization process, combination of antibiotic paste has been used as an intracanal medicament. By using the antibiotic paste, the pulp tissue is able to fill in the remaining canal space. There is a particular combination of antibiotics which effectively disinfects root canal systems and increases revascularization of avulsed and necrotic teeth. This combination includes metronidazol, minocycline and ciprofloxacin, which is known as triple antibiotic paste. The triple-antibiotics regimen was first tested by Sato et al. to be effective against the Escherichia coli infected dentin in vitro.[13] The same research group also tested their bactericidal efficacy against microbes from carious dentin and infected pulp. They found that the mixture of antibiotics is sufficiently potent to eradicate the bacteria.

The application of antibacterial drugs may represent one method of eradicating bacteria in root canal treatment. This concept is also known as Lesion Sterilization and Tissue Repair (LSTR) therapy. This technique has been developed by Cariology Research Unit of Nigata University School of Dentistry, Japan.[14] Composition and mixing instructions for the tri-antibiotic paste is adapted from Hashino et al.[15]

Antibiotics (3M mix-MP) combines Ciprofloxacin 200mg,

Metronidazole 500mg, Minocyclin 100mg and a carrier (MP): Macrogol ointment or Propylene glycol is used. The combination of drugs has been shown to penetrate efficiently through dentine from prepared root canals, suggesting that topical application of the drug combination may be potent in sterilizing lesions in root canal treatment.

Disadvantages of using antimicrobial paste

The concern of the antibiotic paste is that it may cause bacterial resistance. Also, the paste contains both bactericidal (metronidazol and ciprofloxacin) and bacteriostatic (minocycline) antibiotics. Additionally, minocycline may cause tooth discoloration. Reynolds et al have suggested that the discoloring effect of the minocycline can be minimized by occluding the dentinal tubules in the pulp chamber with a bonding agent, then placing a root canal projector into the chamber, and filling the space between the projector and the dentin with a flowable composite resin. After the resin sets, the projector can be removed and the triple mix antibiotics paste can be placed into the canal in a backfill manner to the level of CEJ.

When discoloration occurs after using the triple antibiotic paste, internal bleaching can be performed during the follow up examinations when evidence of maturation of the tooth has been observed.

Cefaclor instead of minocycline can also be substituted in the paste to avoid discoloration.[16]

In addition, the use of white MTA instead of grey MTA should also be considered.[9]

iv) Blood clot formation in canal space

Revascularization can be carried out with or without the formation of blood clot. As until now no guideline has been proposed for revascularization, it is completely on the clinician to decide whether the canal should be instrumented for inducing blood clot or not depending on the visual or tactile perception of soft tissue remaining within the root canal system. Lack of responsiveness to cold or electric testing is not considered to be indication of loss of vitality, as

most of the revascularization procedures are carried out in immature tooth with open apex. Despite the preoperative irresponsiveness of vitality testing of the tooth, if some vitality is noted during treatment either by sensitivity to instrumentation within the root canal system or by the visual or tactile perception of soft tissue remaining within the root canal system then blood clot is not induced within the canal space, as the remaining vital pulp supplies the stem cells and growth factor responsible for revascularization.

However if there is lack of evidence of residual vital pulp tissue within the root canal system either by tactile or visual perception then treatment is administered with the addition of evoking an intracanal blood clot. Induction of bleeding to facilitate healing is a common surgical procedure. It was first proposed by Ostby in 1961 to induce hemorrhage and form blood clot in the canal space of mature teeth in the hope to guide the tissue repair in the canal. Later in 1974 Myers and Fountain attempted to regenerate dental pulp with blood clot filled in the canal. The mechanism of how a blood clot benefits the root canal revascularization is not entirely clear, although the possible reasons could be that blood clot may act as a natural fibrin scaffold for cell attachment, proliferation, and differentiation to facilitate the regeneration and repair of tissues into the canal. SCAP cells from the apical papilla may migrate into the root canal and produce dentin-pulp complex-like tissue and delivers abundant growth factors within the blood clot, such as platelet-derived growth factor which will aid in revascularization.

Hemorrhage is induced by over instrumentation with either endodontic files or an endodontic explorer penetrating slightly into the remaining pulp tissue or periapical tissue. This procedure induces bleeding into the canal and the bleeding is left for 15 minutes so that the blood would clot in the canal and stopped at a level 3mm below CEJ. MTA is then placed over the blood clot.

At this point, it is unsure of which factors in the blood clot are important. When these factors are isolated, they can be incorporated into a synthetic scaffold that will be easier to for clinicians to manipulate compared with a blood clot. However platelet rich plasma as been tried as a successful clinical alternative. Ding et al. discussed the value of use of PRP in whom it is difficult to produce bleeding in the canal with a file.[17] A recent case report has suggested the possibility of PRP as a potentially ideal scaffold for pulp revitalization in tooth with necrotic pulp and a periapical lesion.[16]

v) MTA barrier, or equivalent, placed over blood clot, Final restoration and follow-up

Once the intracanal infection is controlled and a physical scaffold to promote cell growth and differentiation has been achieved, next important step is coronal seal to prevent reinfection. In revascularization after inducing blood clot, MTA is placed over the clot. If revascularization is carried out without the use of blood clot then after drying the canal with paper point, MTA is placed carefully over the tissues in the root canal. A small piece of collacote may be placed at the pulp chamber to support the MTA cement which is to be placed over it. This is followed by the placement of a wet cotton pellet and temporary filling material. Patient is then recalled after 2- 3 weeks and if the tooth is asymptomatic

then the temporary filling material and the cotton pellet is replaced with a bonded resin restoration or glass ionomer cement.

The use of MTA is for its excellent microleakage-proof property and biocompatibility. Additional placement with glass ionomer/resin provides a double seal, further securing the sealing ability and the integrity of the filled access.

The tooth should be followed up periodically to observe the maturation of the root. If after several rounds of intra-canal irrigation and medication the clinical symptoms show no sign of improvement, i.e., persistent presence of sinus tract, swelling and/or pain, apexification procedure should then be carried out. If no signs of regeneration are present after 3 months, then more traditional treatment methods can be initiated.

Factors that affect the results of regenerative endodontic treatment[6]

There are some factors that affect the results of regenerative endodontic treatment. To achieve successful results of the treatment procedure, a thorough understanding of these factors is very important.

The first factor is the disinfection of the canal. The absence of bacteria is critical for successful revascularization because the new tissue will stop at the level it meets bacteria in the canal space. In necrotic cases with apical periodontitis it must be recognized that the vital tissue might not be normal pulp tissue, despite the fact that root development continues and dentine maturation occurs. In teeth with open apices and necrotic pulps, it is possible that some vital pulp tissue and Hertwig's Epithelial Root Sheath remain. When the canal is properly disinfected, the inflammatory process reverses and these tissues may proliferate.[9]

The second factor is the apex diameter. A tooth with an open apex allows the migration of mesenchymal stem cells into the root canal space, and this could allow host cell homing to form new tissue in the root canal space. An apical opening of 1.1 mm in diameter or larger is beneficial, with natural regenerative endodontic treatment occurring in approximately 18% to 34% of teeth with immature roots.

The third factor is the patient age. Several case reports of regenerative endodontic treatment procedures have generally been limited to patients who are reaching adolescence, mostly aged from 8 - 16 years.[3,18,19,20] Based on these case reports, it would not be advisable to perform regenerative endodontic treatment procedures in children younger than 8 years or older than 16 years.

Conclusion

Regenerative endodontics is a concept and because of the emergence of this concept, clinicians should re- evaluate existing modus operandi while developing the treatment of certain clinical cases. This is principally imperative while dealing with immature teeth, as they still have growth left to accomplish, hence, are more likely to carry potent stem cells that enables the tissue to regenerate and repair better than matured tissues.[5]

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