MANAGEMENT OF IMMATURE TEETH – A PARADIGM SHIFT FROM APEXIFICATION TO APEXOGENESIS

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ABSTRACT: Apexification has been a routine procedure for treating immature non-vital teeth with apical pathosis. Even with the advent of single visit apexification procedure using MTA as an apical barrier, no apexification method can produce the outcome that apexogenesis can achieve. Two new clinical concepts have emerged recently. A revascularization procedure is one approach, in which new vital tissue is expected to form in the cleaned canal space, allowing continued root development in terms of both length and thickness. The other approach is the tissue engineering technology to implant or regenerate the pulp tissue. This article will review the recent concepts in the treatment of immature teeth with non-vital pulps.
KEYWORDS: apexification, apexogenesis, blunderbuss apex, revascularization, regenerative endodontics.

INTRODUCTION

One of the aims of root canal treatment is to fill the canal system completely in order to prevent re-infection. In young children, carious or traumatically exposed pulp eventually undergoes necrotic degeneration, either because vital pulp therapy was not attempted, was not successful or was not feasible. As root development takes almost 2 years after the tooth has erupted into the oral cavity, injury to the young developing tooth results in a short root with a wide canal that can be either divergent or parallel and is associated with flared or cylindrical root apex. The term “blunderbuss apex” is specifically used to indicate an open or flaring apex, resembling the barrel of a blunderbuss rifle[1].

Although root canal therapy is the choice of treatment for an immature non-vital tooth, it is not possible to achieve a good apical seal due to an open apex and a good lateral seal due to the abnormal width and shape of the root canal. For many years, the open apex had been managed by customized gutta–percha cone method with or without apical surgery and retrograde filling procedures. The unfavourable crown root ratio and very thin dentinal walls of an immature tooth would be further affected by this surgical approach, leading to complications in post-endodontic restoration or even to root fracture.

A non–surgical approach called apexification has been reported by various authors since 1960[1,2,3]. In this procedure obliteration of the open apex takes place at the root end by the induction of a calcific barrier, against which root canal obturation is performed. Placement of a biologically active and tissue compatible material in a clean canal environment is thought to stimulate and accelerates cell differentiation to form calcific barrier Calcium hydroxide $Ca(OH)_2$ with or without other antiseptics, freeze-dried allogenic dentine powder, true bone ceramic, tricalcium phosphate, Osteogenic protein, collagen, calcium phosphate gel, Bone morphogenic protein and Mineral trioxide aggregate (MTA) are the materials that have been evaluated extensively[1]. However, since it’s introduction in 1962, Calcium hydroxide has been repeatedly proven to be an effective medicament for root-end closure. Recently, Single-visit apexification procedure or apical barrier method, using MTA is gaining popularity.

The clinical decision to perform apexogenesis or apexification for immature teeth appears to be unambiguous with the teeth containing vital pulp being subjected to apexogenesis and teeth having non-vital pulp being subjected to apexification. But recently, these specific guidelines were called into question by certain clinical observations showing that apexogenesis may occur in teeth which have non-vital pulps. Revascularization procedure of infected, immature teeth has been documented to stimulate regeneration of apical tissues and to induce apexogenesis, and is emerging as a new treatment modality for such teeth, (Iwaya et al 2001).[2,3] This method emphasizes that a clean canal environment is the pre-requisite for hard tissue induction.

On another front, major developments have taken place in an attempt to regenerate pulp tissue by two basic research methods namely tissue engineering and stem cell biology. The isolation and characterization of dental pulp stem cells, stem cells from exfoliated deciduous teeth

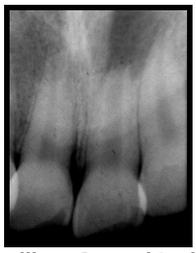

Fig.1. Maxillary Central Incisor with Open-apex

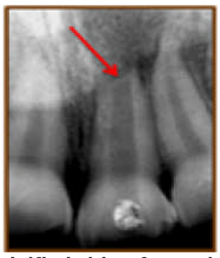

Fig.2.Calcific bridge formation with $Ca(OH)_2$ after 7 months

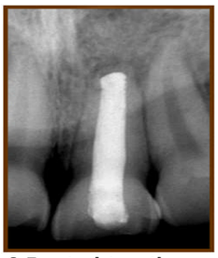

Fig.3 Post-obturation x-ray

and stem cells from apical papilla have capitalized on the possibility for pulp / dentine regeneration. Because of the wide–open apex of the immature teeth, vascularization via apical ingrowth of blood vessels into an engineered construct containing stem cells may facilitate a successful regeneration of pulp / dentine within the canal space[2].

Apexification does not allow regeneration of vital tissues in the canal space, whereas the revascularization or tissue regeneration approaches provide a chance to regain biological tissue recovery and growth. This article will overview the changing concept of treating immature teeth using revitalization rather than apexification and the current status of pulp tissue engineering and regeneration.

Apexification

Apexification can be defined as a "method to induce a calcific barrier in a root with an open apex or the continued apical development of teeth with incomplete roots and a necrotic pulp." (American Association of Endodontics, 2003)[3]. It has been suggested that "Maturogenesis" is a more appropriate term than apexification, because not only the apex but the entire root is allowed to mature as in a non-traumatized tooth (Weisleder R, Benitez CR, 2003).

Apexification procedure primarily involves debriding the canal short of the apex, without disturbing the apical tissues and placement of a biocompatible agent to stimulate the hard tissue formation. The prime objective of apexification is to obtain an apical stop for compaction of the obturating material.

In non-vital immature teeth with periapical lesion, the Hertwig's root sheath (HERS) may get destroyed completely and root formation cannot occur in a natural way. In these situations, the viable cementoblasts or the undifferentiated fibroblasts in the periapical tissue and the periodontal ligament may differentiate into hard tissue producing cells. However, these undifferentiated cells may require a chemical stimulant to differentiate, which has to be in contact with the tissue but should not be forced into it. This results in the formation of a calcific bridge at /or short of the apex**(Fig.1, Fig.2, Fig.3 and Fig.4)**

Calcium hydroxide has been the first choice material for apexification (Rafter 2005) to induce the formation of calcific barrier. The osteogenic potential of $Ca(OH)_2$ was first documented by Mitchell and Shankhwalkar in 1958[4], by implanting the material in rat's connective tissue. They observed that calcified material was seen to be deposited even in an area where no preexisting hard tissue was present. Taking advantage of this property of $Ca(OH)_2$, apexification in a non-vital incisor was documented by Kaiser in 1962 and later popularized by Frank in 1966[5].

Immature teeth undergoing apexification are disinfected with irrigants like Sodium hypochlorite, Chlorhexidine, EDTA and Iodine–Potassium-Iodide (Rabter 2005). The canal is then filled with $Ca(OH)_2$, paste once every 3 months. $Ca(OH)_2$, has a strong antimicrobial action as it releases hydroxyl ions which can chemically alter and effect on the lipopolysaccharide of bacterial cellular components (Safari and Nichols 1993, Barthel et al 1997, Nelson–Filho et al 2002, Jiang et al 2003). The high p^H (12.2–highly alkaline) of $Ca(OH)_2$, was considered to be a contributing factor for it's osteo-inductive property (Javelet et al 1985). However, the time taken for apical barrier formation with $Ca(OH)_2$, apexification was often as long as 6-24 months. Conditions such as age, presence of symptoms or periradicular pathology may effect the time needed to form an apical barrier.

The calcific barrier that results from apexification has been reported to be porous or of a "Swiss Cheese Configuration", resembling dentine – Osteodentine or Cementum –Osteocementum or bone. In the absence of the Hertwig's root sheath, under $Ca(OH)_2$ stimulation, the resultant mass has been reported to mimic dentine. Under the influence of HERS, the mass has been reported to have features of cementum. Without the placement of any medicament, the mass has been found to be more like bone.

There are several limitations in $Ca(OH)_2$ induced apexification procedure, that include :-

- Unpredictable and lengthy course of treatment leading to the vulnerability of the temporary

coronal restoration to re-infection (Magura et al 1991).

- Multiple visits involved in this treatment requires a high level of patient compliance.

Long term intra canal $Ca(OH)_2$ dressing can also make the tooth brittle because of its hygroscopic and proteolytic propertics (Cvek 1992; Andreason et al 2002). Cvek reported that 4 years after $Ca(OH)_2$, apexification, fractures ranged from 77% of the most immature teeth to 28% of the most fully developed teeth[4].

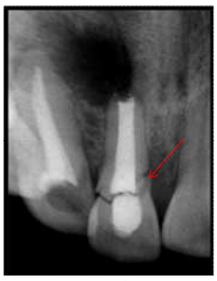

Fig.4.Sub-gingival fracture of central incisor, after $Ca(OH)_2$ apexification

The barrier formed with $Ca(OH)_2$ is often porous and not continuous or compact. Thus it requires obturation of the canal after apical barrier formation with all its inherent problems of achieving a fluid–tight seal without splitting the tooth. With it's high p^H, $Ca(OH)_2$ is known to be toxic to vital cells (Spanberg L, 1969). By filling the canal with $Ca(OH)_2$, a physical barrier is formed, that prevents migration of multipotent undifferentiated mesenchymal cells into the canal (Cvek, 1992) and regeneration of tissues at the lateral dentinal walls.

For these reasons, one visit apexification has been suggested by Morse et al in 1990. Mineral trioxide aggregate (MTA) has been proposed as a material suitable for single visit apexification (Toranbinejad and Chavian, 1993; Shabahand and Toranbinejad 2000; Moroto et al 2003), as it combines biocompatibility, bacteriostatic action with farourable sealing ability. Cleaning of the root canal followed by its apical seal with MTA makes the rapid placement of a bonded restoration within the root canal possible, that may prevent potential fractures of immature teeth[2]. **(Fig.5)**

Though a better outcome may be achieved with MTA and bonded restorations, no apexification method can strengthen the remaining tooth structure with apical maturation with increased thickness of the root. Thus, alternative approaches that allow the increase of root thickness and length should be persued.

Revascularization

Regeneration of tissues rather than replacement with artificial substitutes is an emerging and exciting field in the health sciences. The concept of revascularization was introduced by Ostby in 1961. Later in 1966, Rule and Winter documented root development and apical barrier formation in cases of pulpal necrosis in children. Iwaya et al (2001) and Banchs and Trope (2004) demonstrated the advantages of this treatment modality, which resulted in a radiographically apparent normal maturation of entire root and clinical healing of periapical abscesses in immature teeth. A clinical pilot study by Sha et al, 2008, demonstrated 93% resolution of periradicular radiolucencies with revascularization procedure. Thickening of lateral dentinal walls was seen in 57% of cases and increased root length in 71% of cases. None of the cases presented with pain, reinfection or radiographic enlargement of pre-existing periapical lesions[1]**.(Fig.5, Fig6, and Fig.7)**

The development of normal, sterile granulation tissue within the root canal is thought to aid in revascularization and stimulation of cementoblasts or the undifferentiated mesenchymal cells at the periapex, leading to the deposition of a calcific material at the apex as well as lateral dentinal walls. Infection control in immature non-vital teeth is achieved with minimal instrumentation, depending more on copious irrigation with Sodium hypochlorite, Chlorhexidine or Povidone – Iodine. Use of antibiotic paste containing ciprofloxacin, metronida zole and minocycline was suggested by some authors[4].

Root formation which is influenced by the HERS disintegrates and remains as a remnant near the apex. HERS is highly resistant to infection and even with pulpal necrosis also, it is possible that apical tissue containing viable root sheath can continue the nomal root formation and lengthening. It is also possible that the apical pulp tissue may remain vital, despite the necrosis of the remaining tissue that may be responsible for continued root growth.

If the pulp, HERS and apical papilla are completely lost, the root may still gain some level of thickness by the ingrowth of cementum from the periapical areas onto the internal root canal dentine walls. Additionally, this cementum ingrowth is accompanied by PDL and bone tissue (Kling et al, 1986; Andreason et al 1995)[2].

The biggest advantage with revascularization procedure is that of achieving continued root development and strengthening of the root as a result of reinforcement of lateral dentinal walls with deposition of new dentine / bone like tissue. The procedure requires shorter treatment time, that means after control of infection, it can be completed in a single visit. Obturation of the root canal is not required, avoiding the danger of splitting the root during lateral condensation[5].

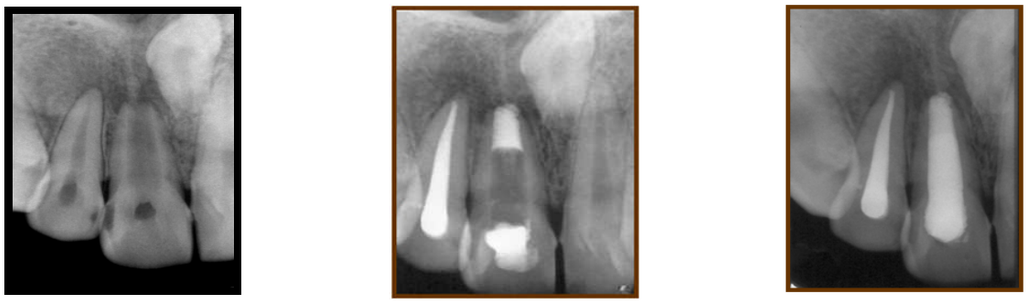

Fig.5. Maxillary central incisor treated with single visit apexification with MTA

The revascularization procedure is not feasible in teeth with entire canal calcification. In cases where the final restorative treatment requires post placement, revascularization is not the right treatment option because the vital tissue in the apical two third of the canal cannot be violated for post placement.

Pulp / Dentine Tissue Engineering and Regeneration

The new protocol of revascularization treatment in which a haemorrhage is induced to fill the canal with blood clot as a scaffold to allow generation of live tissues, coincides with the recent concept of regenerative medicine[2].

A landmark study in animals conducted by Gronthos et al in 2000, demonstrated both in vitro and in vivo that dental pulp stem cells (DPSCs) were capable of forming ectopic dentin and associated pulp tissue. Potential sources to obtain autologous cells for pulp / dentine tissue regeneration include – DPSC, Stem Cells from Apical Papilla (SCAP) and Stem cells from exfoliated deciduous teeth (SHED). Immature third molars are one of the best sources for DPSC's and SCAP. They give rise to odontoblast like cells and ectopic dentin as seen in in-vivo study models (Sonoyama et al 2006). SHED also produce ectopic dentine in-vivo (Miura et al, 2003).

While vascularization is imperative in an engineered tissue, it was considered that the use of angiogenic inducing factors such as vascular endothelial growth factor (VEGF) could enhance and accelerate pulp angiogenesis. Artificial synthetic scaffolds like co-polymer of D, L-Lactide and glycolide can be fabricated with impregnated growth factors such as VEGF and / or platelet derived growth factor(PDGF). The size of the apical opening will affect the ingrowth of blood vessels into the engineered pulp tissue and the larger the opening the more likely that angiogenesis can occur. Therefore, immature teeth with open apices are the best candidates for pulp tissue regeneration.

When regenerating pulp and dentine, the dentine should be located peripherally to the pulp, not within it. The scaffold that carries the stem cells should not induce dentine formation randomly within the regenerated pulp. From the observations made by Nor 2006, Cordeiro et al 2008, it appears that stem cells seeded in the scaffold will be attracted to the dentinal wall, differentiate into odontoblast–like cells and extend their cellular processes into the dentinal tubules. It was speculated that transforming growth factor-beta (TGF-β) is released by the dentine and this attracts and induces the differentiation of odontoblasts (Huang et al, 2006). They also demonstrated that new dentine–like or osteodentine structure can deposit on to the existing dentine throughout the entire canal wall in an in-vivo pulp engineering study model[2].

Another challenge associated with the regenerative pulp therapy includes neural regeneration. Schwann Cells appear to release neurotrophic growth factors and play a role in recruitment of sensory and sympathetic nerves during reinnervation. Thus the pulpal nerve fibers contribute to angiogenesis, extravasation of immune cells and regulate inflammation to minimize initial damage, maintain pulp tissue and strengthen pulpal defense mechanism. It was shown that members of bone morphogenetic proteins (BMPs) have beneficial effects on nerve regeneration[6].

CONCLUSION

The complete restoration of the physiologic, structural and mechanical integrity of the native pulp-dentine complex is the ultimate goal of endodontic treatment. Apexification procedure may no longer be the preferred first option to treat immature permanent teeth with non vital pulps. Induced generation and regeneration of vital tissues in the pulp space can thicken the root structure leading to a stronger tooth with a potentially reduced fracture risk. The progress of pulp / dentine regeneration so far has been promising and is likely to work in the not so distant future.

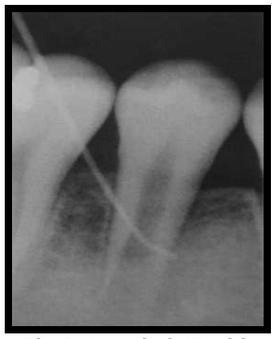

Fig.6 Non-vital 45 with open-apex

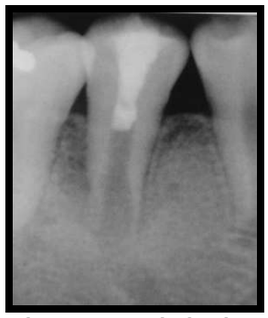

Fig.7 Revascularization procedure

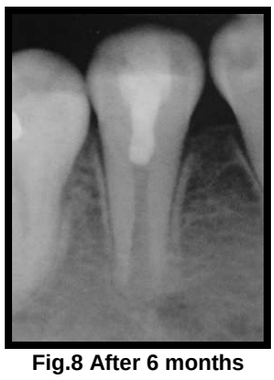

Fig.8 After 6 months

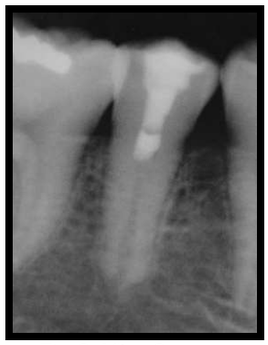

Fig.9 After 2 years

Fig.6,7,8&9-Revascularization

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