The Rationale for the Application of Bone Grafts in Periapical Surgery: A Review

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ABSTRACT
Following periapical surgery, restoration of the destroyed bony architecture is a pre-requisite. Previous studies had shown that supplementing with artificial bone substitutes, growth factors or barrier membranes in the osseous defects is essential in influencing the healing following surgical intervention. This review is intended to focus on whether tissue regeneration with the aid of bone grafts coupled with a membrane barrier will suffice or is there a need for recruiting progenitor/stem cells. A literature search was conducted on several medical databases. All studies that used bone graft following periapical surgery were included. Around 38 relevant articles were selected for this review. Literature shows that the mere use of a membrane barrier and/or bone graft following surgery would not yield the desired outcome. Previous studies show that some substitutes are capable of generating progenitor/stem cells and induce the undifferentiated mesenchymal cells to differentiate. Bone augmentation with the aid of bone graft materials along with biologically active molecules in addition to a mechanical barrier in the form of a membrane would enhance the healing of periapical tissues following periapical surgery. Better bone fill, gain in clinical attachment level is achieved with the use of various grafts as compared to non grafted sites.

Key Words: Endodontics, Periapical surgery, Allogenous bone grafts, PRF, Guided tissue regeneration, Vital tooth

INTRODUCTION
A periapical pathology inevitably results in the presence of a nonvital tooth which is left unattended. This ultimately will result in osseous destruction in the periapical area. It is also a familiar observation that despite an accurately accomplished endodontic treatment failure can be encountered due to microbial infection. This can lead to the formation of a periapical lesion as a result of an inflammatory response to bacterial infection within the root canal. An important goal in periapical surgery is to enrich healing along with removing the unhealthy tissues.

Periapical surgery not only eliminates the unhealthy tissues in the periapical region but also cleanses the root surface along with contouring the surrounding bone. However, few studies have suggested that the healing of the tissues by the newly formed tissue generally fails to fully restore the architecture of the pre-existent bone. The concept of tissue regeneration has been introduced to improve the quality of healing. The kind of cells that repopulates the wound initially determines the quality of healing. Literature shows that the use of either bone graft materials or incorporation of biologically active molecules in addition to the placement of a mechanical barrier following periapical surgery enhances tissue regeneration in the periapical tissues.

BONE GRAFTS
It is a well-known fact that periapical lesions that are relatively small in size would heal satisfactorily with the aid wound healing but larger lesions would require recruitment of stem cells and their differentiation. In huge osseous defects, insufficient osseous regeneration occurs.

Numerous studies in the past have demonstrated a better outcome with regards to tissue healing following periapical surgery with the aid of regenerative technique using bone graft compared to the same lesions without regenerative techniques. It is believed that a simple enucleation of the periapical cyst usually leaves a bony defect. Because the maxilla demonstrates a relatively high regenerative capacity,
optimal obliteration of this osseous defect in presence of a background of an inflammatory reaction may be hindered.\(^9\)

Inadequate or less optimal bone healing results when the regenerative technique is not employed due to the invagination of overlying tissue into the osseous defect, preventing osteogenesis.\(^{10}\) According to Jansson et al., the survival rates of periapical surgery was found to be 68% in molars and 77% in single-rooted teeth over 10 years.\(^{11}\) This highlights the fact that augmentation with the aid of bone grafts is essential to facilitate optimal tissue healing in the periapical region following periapical surgery.

Augmented bone graft plays a key role by acting as a template for osteogenesis and slowly resorb to permit replacement by new bone.\(^{12}\) Bone grafts have either osteogenic, osteoinductive or osteoconductive properties.\(^{13}\) Hydroxyapatite can be considered to be a very effective alloplastic material particularly in large bone destruction caused by periradicular lesion where it can facilitate effective bone replacement in the later stages as well as provide functional support to the tooth in the initial stages.\(^{10}\) A recent study evaluated bone regeneration in the periapical region using Platelet-rich fibrin (PRF) and nanocrystalline hydroxyapatite with collagen in combination with PRF and their effects on healing and concluded that the combination of PRF and nanocrystalline hydroxyapatite with collagen produced a significantly faster bone regeneration and that conventional technique and PRF were less predictable with its healing response.\(^{13,14}\)

**BIOLOGICALLY ACTIVE MOLECULES**

PRP play a critical role in enhancing wound healing due to the discharge of some growth factors via \(\alpha\) granules.\(^{12,14}\) These growth factors generally act both locally and systemically.\(^{15}\) It increases early wound strength by enhancing collagen synthesis and angiogenesis.

Few studies suggested that the use of a triple antibiotic paste for canal disinfection along with PRF strengthens the effectiveness of sterilization in carious teeth, infected dentin, periapical lesions and necrotic pulp.\(^{16}\) Huang et al. in his study concluded that PRF can multiply pulp cells in addition to enhancing the expression of osteoprotegerin and Alkaline phosphatase activity.\(^{17}\)

In vitro studies have demonstrated that PRF has shown no cytotoxicity toward many normal cells present in the periapical region.\(^{18}\) A recent study showed that the PRF membrane has a slow sustained release of growth factors for 7-28 days.\(^{19}\)

A recent study used PRF with tricalcium phosphate (TCP) bone graft for treating a periapical cyst and advocated that usage of PRF and TCP together would yield enhanced results than the usage of biomaterials alone.\(^{20}\) Study done by Keswani et al on the revascularization of immature pulp apices concluded that PRF acts as a biological connector for neoangiogenesis and vascularization.\(^{21}\) This highlights the fact that augmentation with the aid of bone grafts coupled with biologically active molecules is essential to facilitate optimal tissue healing in the periapical region following periapical surgery.

**BARRIER MEMBRANES**

To prevent invading of the overlying soft tissue into the osseous defect, it is advisable to use a mechanical barrier on top of the defect. This would create an environment for the cells to repopulate into the defect.\(^{22}\) Resorbable membranes are available alternatives to non-resorbable membranes.\(^{23}\) They are resorbed by proteolytic enzymes and excreted via kidney.\(^{24}\) An in vitro study advocated that resorbable membranes stimulate cellular proliferation more than non-resorbable membranes.\(^{25}\)

Literature shows that collagen membrane coupled with a bone graft significantly enhances the preservation of alveolar bone.\(^{26}\) Membranes containing greater than 5% metronidazole show antibacterial activity deprived of any cytotoxic effects.\(^{27}\)

Amnion membrane is derived from the human placenta. It incorporates growth factors presenting anti-inflammatory and antimicrobial properties.\(^{28}\) The thickness of the amnion membrane is less than collagen membranes which assist a proper adaption over the osseous defect.\(^{29,30}\) Amnion membrane facilitate the proliferation of endothelial cells and angiogenesis in addition to recruitment of mesenchymal progenitor cells assisting accelerated wound healing.\(^{31,32}\)

**Inference**

The application of graft materials in the form of hydroxyapatite, tricalcium phosphate or xenograft alone would lead to the formation of fibrous encapsulation of the graft material and thereby interfere with the ideal healing in the periapical tissues following surgical intervention.\(^{32}\) It is believed that a blood clot plays a key role in stabilizes the wound matrix in the event of wound healing. Platelet alpha granules of PRP act as a source of growth factors that facilitate cellular proliferation and bone formation.\(^{33}\) PRF facilitates the preservation of the integrity of the bone graft material by revascularizing the bone graft particles through neo-angiogenesis.\(^{2,34}\) Once PRF starts resorbing slowly it releases growth factors that maintain a viable field to enhance healing.\(^{35,36}\) In addition to this placement of a barrier membrane would avoid the invagination of soft tissue into the osseous defect thereby enhancing the wound healing.
RECENT ADVANCES

Conventional periapical surgical generally results in a big osseous defect. With the aid of the 3D printed template, the osseous defect resulted in surgical intervention is limited to 3–4 mm. This confines injury to osseous tissues resulting in less bleeding, less postoperative complications, shorter healing time and better prognosis.37

A recent study employed Cone Beam Computed Tomography(CBCT) imaging, 3D printing technology and a 3D surgical guide designed with computer-aided software. A hollow trephine bur was used to perform the osteotomy, resection of the root, and enucleation of the lesion. The intact cortical plate was salvaged and used as a graft along with plasma-rich fibrin acquired preoperatively from the patient’s blood. The positioning guide allowed the clinicians to precisely achieve targeted tissues and shorten the procedure time. Modified soft tissue management helped achieve a small surgical wound for uneventful healing.38

CONCLUSION

Guided tissue regeneration acts as an adjunct to surgical intervention that can employ an extensive range of biomaterials. Augmentation with the aid of bone graft materials along with biologically active molecules in addition to a mechanical barrier in the form of a membrane would enhance the healing of peripheral tissues following periapical surgery. We conclude that that better bone fill, gain in clinical attachment level are achieved with the use of various grafts as compared to non grafted sites.

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