INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

Regenerative Endodontics: A hype or hope

Dental Science

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ABSTRACT

The advancement of science has contributed significantly to daily aspects of our lives including both our medical and dental care. Traditionally, apexification was used to treat immature necrotic permanent teeth but with the advancement came a newer technology of regeneration in dentistry. Regenerative endodontic treatment is an advanced procedure designed to replace damaged pulp tissue with viable tissue that can restore the normal function of the pulp-dentin structure. These regenerative endodontic techniques involve the use of stem cells, scaffolds and growth factors. Although with the introduction of regenerative endodontics there have been potential benefits to patients but it still fails to re-establish real pulp tissue. This mini review provides an overview of regenerative endodontics and its goals, and the drawbacks that should be considered to affect the efficiency of the treatment

KEYWORDS:

Adult Stem Cells; growth factors, transforming; tissue scaffolds

Abbreviations:

- TGF^{β}: transforming growth factor beta
- SHED: stem cells from human exfoliated deciduous teeth
- Ca(OH)2: Calcium Hydroxide

Introduction

Root canal therapy is an efficient treatment protocol to save teeth with necrotic pulp but the best results are obtained when the diseased or necrotic tissue is substituted with vital pulp tissue through regenerative endodontics. 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 (1) It was in 1952, when Dr. B. W. Hermann used calcium hydroxide for vital pulp therapy in a case report (2), since then concept of regeneration came into knowledge.

Regenerative endodontics involves the use of tissue engineering & these tissues require favorable microbiological control for which superior disinfectants should be used. Many case reports had been published on regenerative endodontics but additional research should be conducted in this field so that efficient and safe method can be established.

As the demand and efficiency of treatment will increase, this can be assumed that the scope of regenerative endodontics may be expanded to replace other dental soft tissues like periapical tissues, periodontal ligaments, gingiva (3). This mini review will provide the types of regenerative endodontic therapies, their drawbacks and the newer technologies which further need research.

Stem Cells

The most widely used cells in regenerative endodontics are stem cells. Stem cells can be defined as an unspecialized cell that can divide continuously & produce cells that can be differentiated into one or more specialized cells (4). Mainly two types of stem cells are used-embryonic stem cells and postnatal stem cells (5).

In spite of greater plasticity of embryonic stem cells (6), postnatal cells are more commonly used now a day because of less legal & ethical issues and also easy availability from host. The dental pulp comprises of no. of stem cells which remain active throughout their life, called pulp stem cells (7,8) and, the one which shed after maturity, called as stem cells from human exfoliated deciduous teeth (SHED) (9,10).

Gronthos *et al.,* in his study reported both in vitro and in vivo in animals that dental pulp stem cells can form ectopic dentin and associated pulp tissue (11,12). Although stem cells promise good results in regeneration, further research is needed as there are no clinical trials conducted and also extracting stem cells is a challenging task.

Growth Factors

Dentinal matrix contains many growth factors which can be released after demineralization of dental tissues. These growth factors may play role in tertiary dentin formation and they also control stem cell activity (13,14). Growth factors playing major role in regenerative endodontics are transforming growth factor beta, platelet derived growth factor, BMPs, Insulin like growth factor (15).

The transforming growth factor beta (TGF^{β}) stimulates secretion of dentinal matrix (16). Bone morphogenic proteins is also considered an important family in tooth development (17) & regeneration (18). It was found that collagen when combined with recombinant human insulin like growth factor-1 can be very useful in forming dentinal bridge & tubular dentin (19). Thus, growth factor play an important role in regeneration and they should be used with stem cells for desired results in regeneration of pulp tissue.

Distribution of cells in scaffold

Scaffold being porous in nature and having three-dimensional structure provides good structural integrity (20). Generally, scaffolds contain stem cells but they should also incorporate growth factors which can enhance the process of tissue development (21). As there is vast microbial population in canal system, scaffolds may also incorporate nutrients and antibiotics to prevent any bacterial growth (22).

Torabinejad and Faras, presented clinical, radiographic, and histologic findings and reported pulp-like vital tissue in human tooth with the use of platelet-rich plasma (PRP) as a scaffold (23).

Revascularization via blood clotting

A treatment done in necrotic root canal systems or endodontically treated tooth to induce angiogenesis. A key step in this process is disinfection of root canal system with irrigants and best possible combination of antibiotics (24-26). After disinfection bleeding is induced in the canal which led to the formation of blood clot which is thought to entrap cells that can form new tissue (27-29).

One important limitation is the unknown concentration of cell strapped in the clot which makes the role of tissue engineering unpredictable.

Unpredictable outcomes

There are reports that show not all cases of pulp regeneration or revascularization are successful. Lenzi and Trope (30) treated an immature maxillary central incisor with necrotic pulp and found empty canal space in a 21 month follow up. Nosrat *et al.* (31) in his case report in which he treated necrotic immature maxillary incisors, reported no development of root and the absence of vital after 6 years.

Even after generation of tissue engineering techniques, studies have shown deposition of hard cementum-like tissue on dentinal walls of root canal (32). Hard tissue formation between coronal MTA and root apex was reported in one more study (33).

Developmental approaches

1. Injectable scaffold delivery: Hydrogels being an injectable scaffold can be easily released into root canal system. It also has non-invasive property (34, 35). Although it is theoretically mentioned they help in pulp regeneration (36) but further research is necessary to make them practically more feasible.

2. **Three-dimensional cell printing:** It is an attractive and powerful technology which offers construction of tissue constructs that mimics the natural features of native tissues. In regenerative endodontics, it can be used to position the cells at correct position and recreate pulp tissue structure (37,38)

3. **Gene Therapy**: Gene therapy has not much evidence till date in regenerative endodontics but genes can be used to enhance the heating potential of pulp tissue (39). They can be combined with stem cells and used for better results. Further research is necessary to develop a safe & efficient gene therapy

Conclusion

Regenerative endodontics which initially looked a hype has generated lot of hopes for future. Though technically challenging but it is an efficient method to save teeth with compromised structural integrity. Presently available case reports are mostly on young patients who already have high stem cell populations and open apices. So, further research including cases of closed apices, and evaluating vitality, histological outcomes is needed to advance the regenerative endodontics to the higher level.

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