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Research Paper

Regenerative Endodontics and Minimal Invasive Dentistry Merging Ways: A Review

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***ABSTRACT**: A portion of the pulp-dentin complex is supposed to be repaired and regrow during regenerative endodontic operations (REPs).*
For developing teeth with necrotic pulp and periapical radiolucency, the regenerative endodontic procedure (REP) is regarded as a therapeutic option that can stimulate root development.
Inducing the physiologic replacement of dental tissues and their supporting structures is the goal of regenerative dentistry. Advances in biologic therapies, which employ the concepts of tissue engineering with the spatial and temporal assembly of stem cells, growth factors, and scaffolds to enable the functional regeneration of missing tissue, are largely to thank for the potential of regenerative dentistry.
The transition in caries management from G.V. Black's "extension for prevention" to "minimally invasive" has been facilitated by dental adhesives and restorative materials, improved knowledge of the caries process and remineralization, and changes in caries prevalence.
Given their capacity to preserve the natural tooth structure while working toward the same objective, regenerative and minimally invasive endodontics could be seen as two innovative disciplines combined.
To address two crucial challenges affecting the success of these procedures: conserving tooth structure and ensuring efficient disinfection, it would be necessary to adapt present concepts and protocols in regenerative endodontics to reach this goal.
This review intends to introduce this innovative concept and discuss its realization, challenges, and prospective clinical uses.

***KEYWORDS:** minimallyinvasive, regenerative endodontics, pulp regeneration, scaffolds, stem cells, tissue engineering, disinfection*

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I. INTRODUCTION

Due to its anatomical configuration and the post-mitotic nature of odontoblastic cells, the dental pulp is a highly specialized mesenchymal tissue with a restricted ability for regeneration. A considerable percentage of dentin is lost when the entire pulp is removed, the pulp area is cleaned, and the space is then filled with an artificial substance. This results in a tooth that is no longer alive and is weaker than before. Regenerative endodontics, a new area of contemporary tissue engineering, has achieved promising outcomes by utilizing stem cells in combination with scaffolds and responsive molecules. Recent research suggests that these procedures might herald a paradigm change in endodontic treatments for the conceivable future (Duncan et al., 2019a). In line with this, applications for adult necrotic permanent teeth have progressively begun to appear for REPs, which have long been used as a predictable therapy for immature necrotic teeth (ElKateb et al., 2020; Glynis et al., 2021). The last two years have seen a remarkable rise in publications about REPs citing studies that favor

single-visit methods over those involving numerous visits (Cerqueira-Neto et al., 2021).Ironically propelled forward by a worldwide pandemic, this new path is presently on its way to establishing strong roots in the profession with a conceptual transition from a science of "maybe" to a science that has evolved into normal clinical practice. In this review, we provide a novel idea that combines the disciplines of MIEs and REPs in the expectation that it will pave the way for methods that can both regenerate missing tooth structures and preserve those that are still there.

II. A LESS INVASIVE TERMINALITY IS REGENERATIVE ENDODONTICS.

Regenerative endodontic procedures (REPs) are defined as biologically based procedures designed and performed to repair or replace damaged tooth structures and to regenerate part of the pulp-dentin complex. [(5)]

REP was first established by Nygaard-Ostby in the 1960s, though with low success[(6).] As a result, one of the foremost challenges and most modern problems in regenerative dentistry is REP.The European Society of Endodontology (ESE) and the American Association for Endodontists (AAE) have recently delivered position statements and clinical considerations regarding REP. [(7,8,9)]

According to the American Association of Endodontists (AAE) Clinical Considerations for a Regenerative Procedure, the primary goal of the regenerative procedure is the elimination of clinical symptoms/signs and resolution of apical periodontitis. [(10)].In addition to treating apical periodontitis, this innovative treatment approach also seeks to encourage typical pulpal physiologic activities. As demonstrated in some documented cases, they include ongoing root growth, immunological competence, and normal nociception. Thus, the ultimate objective of these operations is to restore the pulp dentin complex's natural structure and function. [(11)]

The concept of 'Minimally Invasive Dentistry' can be defined as the maximal preservation of healthy dental structures. Within cariology, this concept includes the use of all available information and techniques ranging from an accurate diagnosis of caries, caries risk assessment, and prevention, to technical procedures in repairing restorations. (Ericson *et al*. 2003; Ericson 2007)

The world congress of MID defines minimally invasive dentistry as those techniques, which respect the health, function, and esthetics of oral tissue by preventing the disease from occurring, or intercepting its progress with minimal tissue loss (Nový and Fuller 2008)

The goal of Minimal Invasive Dentistry (MI) is to stop the disease process and then restore lost tooth structure and function, maximizing the healing potential of the tooth. The thought process which underpins this new minimally invasive approach can be organized into three main categories:

• Recognize = Identify patient caries risk
• Remineralize = Prevent caries and reverse non-cavitated caries
• Repair = Control caries activity, maximize healing, and repair damage

The MI approach has been developed because of the many failures associated with traditional operative dentistry. A G.V. Black cavity preparation and the use of amalgam or composite are typically used to restore these cavities after a traditional diagnostic entails finding carious lesions at an advanced stage (frank cavitation).Black cavity preparation and the use of amalgam or composite. Unfortunately, removing the evidence of the disease does not stop the disease process from continuing at other sites. In other words, placing dental restorations does not 'cure' caries.No repair can be thought of as lasting. Unless the ongoing causes of the disease are addressed, restoration failure from recurrent caries is highly likely, and this premature failure results in ongoing restoration replacement, resulting in larger and larger cavities, and weakening of tooth structure. [(12)]

A recent suggestion has been to redefine the definition of regenerative endodontics as follows: "The term regenerative endodontics should embrace the repair, replacement, and regeneration of dentin–pulp lost due to age, disease, trauma or congenital defects to restore normal function" (Duncan et al., 2019b).

Therefore, it may be seen of as a sensible and novel notion to combine MIEs with REPs. On the other hand, the constrained ability to clean and disinfect the root canal system that may be met through the contracted endodontic cavity may complicate the results of REPs (CEC).Hence, if such a strategy is to be employed, considerations must not only be given to how modification of the access cavity will influence adequate disinfection but also should encourage single-visit treatment modalities via the application of biologically inspired and biomimetic scaffolds to guarantee tissue regeneration in a bacteria-free milieu. [(13)]

The idea of tissue engineering is used in regenerative endodontic treatments (REPs) to repair the root canal system to a healthy condition, enabling the continuing growth and regeneration of the root and surrounding tissues (He et al., 2017). The major goals of REPs primarily target the resolution of Apical Periodontitis (AP), induction of apical closure, and increased root canal wall thickness and length of juvenile teeth, intending to conserve and preserve the remaining tooth structure as well as boost its survival (EndodontistsoAAo, 2016).

Regarding these goals, the conservation and maintenance of teeth in a functioning state is a substantially equal goal shared by REPs and MIEs endodontic ideas. To put it another way, MIEs seek to maintain the original tooth structure whereas REPs seek to repair it. [14]

III. NANOMATERIAL-BASED ALTERNATIVES TO CONVENTIONAL IRRIGATION PROTOCOLS

Novel disinfectants such as ozone (Kustarci et al., 2009; Silva et al., 2020b), photodynamic therapy (ZoritaGarcía et al., 2019), and cold atmospheric plasma (Pan et al., 2013; Li et al., 2015) have been tried with variable outcomes and only limited clinical success in the field of endodontics. On the other hand, nanoscience has made significant strides in nearly every area of science and medicine, with an emphasis on endodontic disinfection.

Notably, nanobubble water (NBW) has just been recognised as a promising antibacterial agent with potential applications in a wide range of pharmaceutical, medical, and dental disciplines. It is suggested as a potential agent to improve the antibacterial activity of root canal irrigants at lower noncytotoxic doses in the early stages of the administration of NBW in endodontics.A new catalytic iron oxide nanoparticle-based biomimetic irrigant (IO-NPs) has been developed. The idea was to combine IO-NPs with hydrogen peroxide to demonstrate powerful antibacterial activities that deeply penetrated the full length of dentinal tubules. IO-NPs alone, however, demonstrated only weak bactericidal activity (Bukhari et al., 2018). [15]

Nonetheless, nanoparticles should not be applied with a "one size fits all" approach, given that different materials, formulations, and combinations will generate different properties, both beneficial and adverse. Thus, nanoparticle applications in endodontics have a lot of potentials but there is still some way to go before the basic research translates to clinical studies. [16]

In conclusion, research into nanoparticle-based irrigants may open the door to fresh and cutting-edge endodontic disinfection methods. To fully understand the potential of different nanomaterials to be used as endodontic irrigants, more research is required. Studies should also focus on reducing any potential negative or detrimental impacts while examining the processes for incorporating nanoparticles into irrigation solutions, as well as their long-term antibacterial action and in vivo effectiveness. [17]

IV. SCAFFOLDS WITH DUAL EFFECTS THAT IS ANTIBACTERIAL AND IMMUNOMODULATORY EFFECTS COULD FAVOUR REGENERATION RATHER THAN REPAIR.

Along with a disinfection method that is friendlier to cells, advances in tissue engineering and regenerative medicine, particularly those that concern the fabrication of scaffolds, have laid the groundwork for a dependable and predictable regeneration of the pulp-dentin complex. A scaffold is described as "the support, delivery vehicle, or matrix for aiding the migration, binding, or transport of cells or bioactive compounds utilized to replace, repair, or regenerate tissues" by the American Society for Testing Materials (ASTM; designation F2150). It must perfectly mimic the properties of the original extracellular matrix (ECM) at the nanoscale to control cell activity and promote and direct certain cellular and tissue-level activities. Additionally, to prevent immune reactions, scaffolds should be created using biocompatible and biodegradable materials. [18]

Recent studies have concentrated on creating smart drug delivery scaffolds to improve root canal sanitation and lower the danger of stem cell toxicity (Albuquerque et al., 2017; Bottino et al., 2019). When tested against a dual-species biofilm established inside the root canal, an injectable Platelet-Rich-Fibrin (I-PRF) scaffold that releases antibiotics showed a substantial decrease in the bacterial population. Antibiotics and growth factors were combined in the designed biocompatible autologous scaffold, which could promote regeneration over repair (Rafiee et al., 2020).

A new biomimetic scaffold made of electrospun poly (lactic acid) nanofibers and electro-sprayed polycaprolactone with tannic acid microparticles has recently been the subject of in-vitro research. To fill the empty root canal, this 3D cone-shaped scaffold was created, replicating the natural extracellular matrix. (Terranova et al., 2021). This scaffold has the potential for cell migration, adhesion, and proliferation and may potentially be further loaded with antimicrobial drugs in the next in-vivo research. [17]

The prolonged release of bioactive molecules, which are an essential feature of regenerative endodontics because they control cellular activity such as proliferation, migration, and differentiation, has been proposed as a strategy using nanoparticle-based carrier systems. [19] Nanoparticle-based carrier systems may boost the dissolution and absorption of medicines and bioactive chemicals because nanoparticles have increased solubility, a high surface-area-to-volume ratio, and tiny dimensions. Several polymeric nanocarriers, including those previously mentioned, such as chitosan, Active nanoparticles, as well as regenerative treatments, have been studied in the context of traditional root canal therapy. [20]

V. INNOVATIVE AND CURRENTLY USED INTRACANAL MEDICATIONS FOR REGENERATIVE ENDODONTIC TREATMENT HAVE AN ANTIBACTERIAL EFFECT AND ARE BIOLOGICALLY ACTIVE.

All nonsurgical endodontic operations—and regenerative therapies in particular—face a significant challenge from microbial control inside the root canal space. We need to utilize potent antibacterial agents to minimize or effectively eradicate microorganisms. Strong antibacterial agents, however, are likely to change the canal's environment, leading to less favorable circumstances for cell growth, attachment, and differentiation.

As was previously mentioned, using $Ca(OH)_2$ or antibiotic combinations together might have unfavorable side effects during REPs. The former is in charge of root thinning even after a little time (Bukhari et al., 2018). It has been demonstrated that even when administered at the appropriate clinically indicated dosage, the latter impairs DPSC functioning (Diogenes et al., 2016). A recently developed nanomatrix gel for regulated intracanal administration of antibiotics releases nitric oxide (NO) (Moon et al., 2018). It was proposed that, in contrast to the traditional REP procedure, an intracanal medication that combined the effects of NO and a low dosage of antibiotics would enhance root development and revascularization potential (Kaushik et al., 2015; Moon et al., 2018). [(21)]

There is considerable debate about the use of the term regeneration because existing scientific evidence from histologic studies suggests that the procedures allow for repair instead. This is both a semantic and a biological debate; however, it can be argued that true regeneration as defined by the complete recapitulation of the lost tissue with all its constituents, morphology, function, and molecular markers. [(22)]

A thorough study program focused on each of these elements and their application to our patients will be necessary for the development of regenerative endodontic treatments in the future. Regenerative endodontics' full potential might help millions of patients every year.

VI. CONCLUSION

Eventually, a more optimized treatment outcome might be obtained through this novel biomimetic preservation-regeneration approach and implementing a novel concept of "minimally invasive regenerative endodontic procedures (MIREPs)."

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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