



Derleme Makalesi/Review Article

Biochemical Basis of Periapical Bone Healing After Endodontic Treatment

Endodontik Tedavi Sonrası Periapikal Kemik İyileşmesinin Biyokimyasal Temeli

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Öz

Endodontik tedavi sonrası periapikal kemik iyileşmesi, iltihabın çözülmesini, mikrobiyal uyarıların ortadan kaldırılmasını ve kemik yeniden şekillenme mekanizmalarının aktive edilmesini içeren karmaşık bir biyolojik süreçtir. Bu olaylar, inflammatuar medyatörler, sitokinler, büyüme faktörleri ve osteogenez ve osteoklastogenezden sorumlu sinyal yolları da dahil olmak üzere sıkı bir şekilde düzenlenen biyokimyasal bir ağ tarafından kontrol edilir. Periapikal iyileşmenin biyokimyasal temelini anlamak, tedavi sonuçlarını iyileştirmek ve biyolojik temelli endodontik stratejiler geliştirmek için çok önemlidir. Bu derleme, endodontik tedavi sonrası periapikal kemik iyileşmesinin ardındaki moleküler ve biyokimyasal mekanizmalar hakkındaki güncel bilgileri özetlemeyi amaçlamaktadır.

Anahtar Kelimeler: kemik iyileşmesi, İnflammatuar mediatörler, Endodontik tedavi, Periapikal lezyonlar

Abstract

Periapical bone healing after endodontic treatment is a complex biological process that involves resolving inflammation, removing microbial stimuli, and activating bone remodeling mechanisms. These events are controlled by a tightly regulated biochemical network that includes inflammatory mediators, cytokines, growth factors, and signaling pathways responsible for osteogenesis and osteoclastogenesis. Understanding the biochemical basis of periapical healing is crucial for improving treatment results and developing biologically based endodontic strategies. This review aims to summarize current knowledge on the molecular and biochemical mechanisms behind periapical bone healing following endodontic treatment.

Keywords: Bone healing, Inflammatory mediators, Endodontic treatment, Periapical lesions

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Introduction

Apical periodontitis is an inflammatory disease characterized by periapical bone destruction caused by microbial infection of the root canal system¹. Successful endodontic treatment leads to the elimination of intracanal microorganisms and initiates a healing response in periapical tissues. Radiographic resolution of periapical lesions reflects a dynamic biological process rather than a passive repair phenomenon². This process is regulated by biochemical interactions between immune cells, bone cells, and signaling molecules. A detailed understanding of these biochemical mechanisms is crucial for interpreting clinical outcomes and optimizing therapeutic approaches in endodontics³.

Inflammatory Response and Resolution

The initial phase of periapical bone healing involves the resolution of inflammation. During active apical periodontitis, pro-inflammatory cytokines such as interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α), and interleukin-6 (IL-6) are abundantly expressed, promoting osteoclastic activity and bone resorption^{4,5}. Following successful endodontic treatment, the reduction of bacterial antigens leads to a gradual downregulation of these mediators. Concurrently, anti-inflammatory cytokines, including interleukin-10 (IL-10) and transforming growth factor- β (TGF- β), become predominant, creating a microenvironment conducive to tissue repair and bone regeneration⁶.

Role of RANK/RANKL/OPG Pathway in Bone Remodeling

Bone healing in the periapical region is governed by the balance between bone resorption and formation. The receptor activator of nuclear factor kappa-B (RANK), its ligand (RANKL), and osteoprotegerin (OPG) constitute a central biochemical pathway regulating osteoclast differentiation and activity⁷. In apical periodontitis, increased RANKL expression favors osteoclastogenesis and bone destruction⁸. After elimination of infection, a shift toward increased OPG expression inhibits osteoclast activity,

allowing osteoblast-mediated bone formation to predominate. This biochemical shift is a key determinant of periapical lesion resolution⁶.

Growth Factors and Osteogenesis

Growth factors play a pivotal role in periapical bone regeneration. Bone morphogenetic proteins (BMPs), particularly BMP-2 and BMP-7, stimulate osteoblast differentiation and matrix mineralization^{9,10}. Vascular endothelial growth factor (VEGF) contributes to angiogenesis, which is essential for supplying nutrients and oxygen to regenerating tissues¹¹. Transforming growth factor- β not only modulates inflammation but also promotes extracellular matrix production and osteoblastic activity¹². The coordinated action of these growth factors facilitates the replacement of inflammatory tissue with newly formed bone.

Oxidative Stress and Antioxidant Defense

Oxidative stress is another critical biochemical factor influencing periapical healing. During active inflammation, reactive oxygen species (ROS) produced by immune cells contribute to tissue damage and bone resorption¹³. Following endodontic treatment, the reduction in oxidative stress and the activation of antioxidant defense systems—such as superoxide dismutase, catalase, and glutathione peroxidase—support cellular homeostasis and tissue regeneration¹⁴. An imbalance between ROS production and antioxidant capacity may delay or impair periapical healing.

Influence of Endodontic Materials on Biochemical Healing

Endodontic materials can modulate the biochemical environment of periapical tissues. Calcium silicate-based materials and bioceramic sealers release calcium ions and create an alkaline environment, which has been shown to enhance osteoblastic activity and mineralization^{15,16}. These materials may also influence cytokine expression and growth factor release, indirectly supporting bone healing¹⁷. Thus, material selection plays a biologically relevant role in post-treatment periapical tissue responses.

Clinical Implications and Future Perspectives

Understanding the biochemical basis of periapical bone healing provides valuable insights for clinical decision-making. Radiographic healing should be interpreted as a reflection of ongoing molecular and cellular events rather than a simple structural change². Future research focusing on biochemical markers of healing may allow earlier and more accurate assessment of treatment success. Additionally, advances in biomaterials and molecular biology may enable targeted modulation of healing pathways, leading to more predictable clinical outcomes¹⁸.

Conclusion

Periapical bone healing after endodontic treatment is a biologically active and biochemically regulated process involving inflammatory resolution, bone remodeling pathways, growth factor signaling, and oxidative balance. A comprehensive understanding of these mechanisms enhances the clinician's ability to interpret healing patterns and supports the development of biologically driven endodontic therapies. Continued research integrating biochemistry and endodontics will further improve treatment strategies and patient outcomes. long-term success of endodontic treatment. Choudhary et al. (2024) reported that bioceramic sealers exhibit superior penetration into dentinal tubules and significantly reduce bacterial leakage. In the present cases, the rapid resolution of sinus tracts and the absence of recurrence during follow-up may be considered indicators of effective apical and coronal sealing¹⁹.

Recent clinical studies have reported high success rates for root canal treatments performed using bioceramic-based sealers. Chybowski et al. (2018) demonstrated favorable clinical and radiographic outcomes associated with the use of bioceramic sealers. The findings of the present cases at the 3, 6, 12, and 24 month follow-ups are consistent with these reports²⁰.

The limitations of this case report include the small number of cases and the absence of advanced imaging techniques. Nevertheless, the long-term clinical and radiographic

outcomes suggest that bioceramic-based root canal sealers represent a reliable treatment option for teeth associated with intraoral sinus tracts. Further studies with larger sample sizes and longer follow-up periods are warranted to confirm these findings.

Nonsurgical root canal treatment using bioceramic-based root canal sealers appears to be an effective treatment approach for teeth associated with intraoral sinus tracts, resulting in resolution of the sinus tract and successful periapical healing. The biological and physical properties of bioceramic materials contribute to favorable long-term clinical outcomes.

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