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SYSTEMIC EFFECTS OF ENDODONTIC TREATMENT: IMPROVEMENTS IN GLYCEMIC CONTROL, LIPID PROFILE, AND INFLAMMATORY MARKERS

EFEITOS SISTÊMICOS DO TRATAMENTO ENDODÔNTICO: MELHORIAS NO CONTROLE GLICÊMICO, PERFIL LIPÍDICO E MARCADORES INFLAMATÓRIOS

EFECTOS SISTÉMICOS DEL TRATAMIENTO ENDODÓNTICO: MEJORAS EN EL CONTROL GLUCÉMICO, PERFIL LIPÍDICO Y MARCADORES INFLAMATORIOS

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ABSTRACT

Objective: To critically synthesize current evidence on the systemic effects of root canal treatment (RCT), particularly its impact on metabolic and inflammatory biomarkers associated with cardiometabolic diseases.

Methodology: A narrative review was conducted based on recent clinical, translational, and mechanistic studies investigating the relationship between apical periodontitis, endodontic treatment, and systemic health outcomes. Relevant literature was identified through electronic databases and institutional reports, with emphasis on longitudinal clinical studies evaluating changes in circulating biomarkers following successful RCT.

Results: Apical periodontitis has been consistently associated with increased systemic inflammatory burden, bacteremia, and alterations in metabolic pathways linked to cardiometabolic risk. Successful RCT appears to mitigate these effects by eliminating the

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infectious source. Longitudinal evidence demonstrates improvements in glycemic control, including significant reductions in blood glucose levels, as well as short-term improvements in lipid profiles such as cholesterol and fatty acids. Additionally, reductions in systemic inflammatory markers have been observed following treatment, supporting a decrease in overall inflammatory burden. These findings suggest a biological link between oral infection control and systemic metabolic regulation.

Conclusion: Current evidence indicates that successful root canal treatment may contribute to improved systemic health by reducing inflammation and positively influencing metabolic parameters. Although causality cannot yet be firmly established, these findings reinforce the concept of oral-systemic interconnection and highlight the importance of integrating dental care into broader strategies for cardiometabolic disease prevention.

Keywords: Root Canal Treatment. Apical Periodontitis. Systemic Inflammation. Glycemic Control. Lipid Profile. Cardiometabolic Risk. Biomarkers. Endodontic Therapy.

RESUMO

Objetivo: Sintetizar criticamente as evidências atuais sobre os efeitos sistêmicos do tratamento endodôntico (RCT), particularmente seu impacto em biomarcadores metabólicos e inflamatórios associados às doenças cardiometabólicas.

Metodologia: Foi realizada uma revisão narrativa com base em estudos clínicos, translacionais e mecanísticos recentes que investigam a relação entre periodontite apical, tratamento endodôntico e desfechos sistêmicos de saúde. A literatura relevante foi identificada por meio de bases de dados eletrônicas e relatórios institucionais, com ênfase em estudos clínicos longitudinais que avaliaram alterações em biomarcadores circulantes após o sucesso do RCT.

Resultados: A periodontite apical tem sido consistentemente associada a um aumento da carga inflamatória sistêmica, bacteremia e alterações em vias metabólicas relacionadas ao risco cardiometabólico. O tratamento endodôntico bem-sucedido parece mitigar esses efeitos ao eliminar a fonte infecciosa. Evidências longitudinais demonstram melhorias no controle glicêmico, incluindo reduções significativas nos níveis de glicose sanguínea, bem como melhorias de curto prazo no perfil lipídico, como colesterol e ácidos graxos. Além disso, reduções em marcadores inflamatórios sistêmicos foram observadas após o tratamento, sugerindo diminuição da carga inflamatória global. Esses achados indicam uma ligação biológica entre o controle da infecção oral e a regulação metabólica sistêmica.

Conclusão: As evidências atuais indicam que o tratamento endodôntico bem-sucedido pode contribuir para a melhoria da saúde sistêmica ao reduzir a inflamação e influenciar positivamente parâmetros metabólicos. Embora a causalidade ainda não possa ser firmemente estabelecida, esses achados reforçam o conceito de interconexão oral-sistêmica e destacam a importância da integração da saúde bucal em estratégias mais amplas de prevenção de doenças cardiometabólicas.

Palavras-chave: Tratamento Endodôntico. Periodontite Apical. Inflamação Sistêmica. Controle Glicêmico. Perfil Lipídico. Risco Cardiometabólico. Biomarcadores. Terapia Endodôntica.

RESUMEN

Objetivo: Sintetizar críticamente la evidencia actual sobre los efectos sistémicos del tratamiento endodóntico (RCT), particularmente su impacto en biomarcadores metabólicos e inflamatorios asociados a enfermedades cardiometabólicas.

Metodología: Se realizó una revisión narrativa basada en estudios clínicos, traslacionales y mecanicistas recientes que investigan la relación entre la periodontitis apical, el tratamiento endodóntico y los resultados de salud sistémica. La literatura relevante fue identificada mediante bases de datos electrónicas e informes institucionales, con énfasis en estudios clínicos longitudinales que evaluaron cambios en biomarcadores circulantes tras el éxito del RCT.

Resultados: La periodontitis apical ha sido consistentemente asociada con una mayor carga inflamatoria sistémica, bacteriemia y alteraciones en las vías metabólicas relacionadas con el riesgo cardiometabólico. El tratamiento endodóntico exitoso parece mitigar estos efectos al eliminar la fuente infecciosa. La evidencia longitudinal demuestra mejoras en el control glucémico, incluyendo reducciones significativas en los niveles de glucosa en sangre, así como mejoras a corto plazo en el perfil lipídico, como colesterol y ácidos grasos. Además, se han observado reducciones en marcadores inflamatorios sistémicos tras el tratamiento, lo que sugiere una disminución de la carga inflamatoria global. Estos hallazgos indican una relación biológica entre el control de la infección oral y la regulación metabólica sistémica.

Conclusión: La evidencia actual indica que el tratamiento endodóntico exitoso puede contribuir a mejorar la salud sistémica al reducir la inflamación e influir positivamente en los parámetros metabólicos. Aunque la causalidad aún no puede establecerse de forma definitiva, estos hallazgos refuerzan el concepto de interconexión oral-sistémica y destacan la importancia de integrar la salud bucal en estrategias más amplias de prevención de enfermedades cardiometabólicas.

Palabras clave: Tratamiento Endodóntico. Periodontitis Apical. Inflamación Sistémica. Control Glucémico. Perfil Lipídico. Riesgo Cardiometabólico. Biomarcadores. Terapia Endodóntica.

1 INTRODUCTION

Apical periodontitis is a chronic inflammatory disorder of microbial origin characterized by infection of the root canal system and a sustained host immune response in periapical tissues. Although traditionally considered a localized condition, increasing evidence suggests that apical periodontitis may contribute to systemic inflammation through the dissemination of bacteria, endotoxins, and inflammatory mediators into the bloodstream (Gomes et al., 2013; Cotti et al., 2011). This systemic spillover may promote low-grade inflammation, a key mechanism underlying the development and progression of cardiometabolic diseases.

The concept of oral-systemic interconnection has gained substantial attention over the past decades, particularly regarding the role of chronic oral infections as potential modifiers of systemic health. In this context, apical periodontitis has been associated with elevated levels of circulating inflammatory biomarkers and an increased risk of systemic conditions such as cardiovascular disease (Caplan et al., 2006; Liljestrand et al., 2016). These associations are biologically plausible, given that persistent endodontic infections can act as reservoirs of pathogenic microorganisms capable of inducing endothelial dysfunction, immune activation, and metabolic disturbances.

Chronic inflammation is a well-established contributor to insulin resistance and dysregulation of glucose metabolism. Therefore, the presence of untreated apical periodontitis may negatively influence glycemic control, particularly in individuals with pre-existing metabolic disorders. Similarly, systemic inflammation may interfere with lipid metabolism by altering hepatic function and promoting oxidative stress, potentially leading to unfavorable lipid profiles. These pathways suggest that endodontic infections may play a role in the broader network of cardiometabolic risk factors.

Root canal treatment (RCT) is the standard therapeutic approach for eliminating intracanal infection and resolving apical inflammation. By removing microbial biofilms and sealing the root canal system, successful RCT aims to eliminate the primary source of infection. Beyond local healing, it has been hypothesized that effective endodontic treatment may reduce systemic inflammatory burden and subsequently improve metabolic parameters. Emerging clinical evidence supports this hypothesis, indicating that resolution of apical periodontitis may be associated with reductions in inflammatory markers and improvements in systemic health indicators (Aminoshariae & Kulild, 2016; Gomes et al., 2013).

Despite growing interest in this topic, the available evidence remains heterogeneous, with variations in study design, population characteristics, and outcome measures. Furthermore, the causal relationship between endodontic treatment and systemic improvements has not yet been firmly established. Therefore, a critical synthesis of current

data is essential to better understand the extent to which root canal treatment may influence systemic biomarkers related to inflammation and cardiometabolic health.

The aim of this narrative review is to critically evaluate the current evidence on the systemic effects of root canal treatment, with a particular focus on its impact on glycemic control, lipid profile, and inflammatory markers, while also exploring underlying biological mechanisms and identifying existing gaps in the literature.

2 METHODOLOGY

This narrative review aimed to provide a comprehensive and critical overview of the current evidence regarding the systemic effects of root canal treatment (RCT) in patients with apical periodontitis. A literature search was conducted in major electronic databases, including PubMed/MEDLINE, Scopus, and Web of Science, to identify relevant studies published in English.

The search strategy combined controlled vocabulary and free-text terms related to endodontic infection and systemic outcomes, including “root canal treatment,” “apical periodontitis,” “systemic inflammation,” “cardiovascular disease,” “glycemic control,” and “metabolic biomarkers.” Additional articles were identified through manual screening of reference lists of selected studies.

Eligible studies included clinical trials, observational studies, and translational research investigating the association between apical periodontitis, endodontic treatment, and systemic biomarkers. Review articles were also considered to support the discussion and provide contextual background. No strict restrictions on publication date were applied; however, emphasis was given to recent and high-impact evidence. Study selection and data extraction were performed qualitatively, focusing on key outcomes such as inflammatory markers, glycemic parameters, lipid profiles, and other circulating biomarkers. Due to the narrative nature of this review, no formal risk of bias assessment or meta-analysis was conducted. The findings were synthesized descriptively to highlight trends, biological plausibility, and existing knowledge gaps.

3 RESULTS

3.1 APICAL PERIODONTITIS AND SYSTEMIC INFLAMMATORY BURDEN

A consistent body of evidence indicates that apical periodontitis is associated with elevated systemic inflammatory markers, supporting its role as a contributor to low-grade systemic inflammation. A systematic review and meta-analysis demonstrated that individuals with apical periodontitis present significantly higher circulating levels of inflammatory

mediators compared to healthy controls (Gomes et al., 2013). These findings suggest that endodontic infections may act as chronic inflammatory reservoirs capable of influencing systemic immune responses.

Mechanistically, bacterial components such as lipopolysaccharides and other virulence factors can enter the bloodstream from infected root canals, triggering immune activation and cytokine release. This systemic dissemination has been linked to increased levels of acute-phase proteins and pro-inflammatory cytokines, which are known to play central roles in the pathogenesis of cardiometabolic diseases. Observational studies further support this association, demonstrating correlations between the presence of endodontic lesions and systemic inflammatory conditions (Cotti et al., 2011).

3.2 EFFECTS OF ROOT CANAL TREATMENT ON SYSTEMIC INFLAMMATORY MARKERS

Longitudinal evidence suggests that successful root canal treatment is associated with a reduction in systemic inflammatory burden. Clinical studies have reported decreases in circulating inflammatory biomarkers following the resolution of apical periodontitis, indicating that elimination of the infectious focus may attenuate systemic immune activation.

Interventional data demonstrate that patients undergoing effective endodontic treatment exhibit reductions in markers such as C-reactive protein and other inflammatory mediators, particularly in the short-term post-treatment period. These findings align with the hypothesis that removal of chronic oral infection reduces systemic exposure to inflammatory stimuli. Furthermore, systematic evidence supports the notion that treatment of apical periodontitis may contribute to normalization of inflammatory profiles, although the magnitude of this effect varies across studies (Gomes et al., 2013).

3.3 IMPACT ON GLYCEMIC CONTROL

Emerging evidence highlights a potential relationship between root canal treatment and improvements in glycemic control. Chronic inflammation is a known contributor to insulin resistance, and the presence of apical periodontitis may exacerbate metabolic dysregulation. In this context, resolution of endodontic infection has been associated with reductions in blood glucose levels and improved glycemic markers.

Observational and longitudinal studies suggest that patients with diabetes or impaired glucose metabolism may experience measurable improvements in glycemic control following successful root canal treatment. These improvements are thought to be mediated by the reduction in systemic inflammatory burden, which may enhance insulin sensitivity. Supporting

this concept, epidemiological data have demonstrated associations between endodontic disease and diabetes-related outcomes, reinforcing the biological plausibility of this interaction (Caplan et al., 2006).

However, the evidence remains heterogeneous, with variability in study populations, follow-up periods, and glycemic assessment methods. While some studies report significant reductions in fasting glucose or glycated hemoglobin levels, others show more modest or non-significant changes. This inconsistency highlights the need for standardized clinical trials to better define the magnitude and clinical relevance of these effects.

3.4 CHANGES IN LIPID PROFILE

The relationship between endodontic infection and lipid metabolism has also been explored, although the available evidence is more limited and less consistent compared to inflammatory and glycemic outcomes. Inflammatory processes are known to influence lipid homeostasis by altering hepatic metabolism, promoting oxidative modification of lipoproteins, and affecting lipid transport mechanisms.

Some clinical studies have reported short-term improvements in lipid parameters, including reductions in total cholesterol and alterations in fatty acid profiles following root canal treatment. These changes may reflect a decrease in inflammation-driven metabolic disruption. Additionally, the systemic inflammatory response associated with apical periodontitis has been implicated in the pathogenesis of atherosclerosis, further supporting a potential link between endodontic infection and lipid metabolism (Liljestrand et al., 2016).

Nevertheless, the evidence remains inconclusive, with variability in reported outcomes and limited longitudinal data. Differences in patient characteristics, baseline metabolic status, and methodological approaches may account for these inconsistencies. As such, further research is required to clarify the extent to which root canal treatment influences lipid metabolism.

3.5 ASSOCIATION WITH CARDIOVASCULAR RISK

Several studies have investigated the potential association between apical periodontitis, endodontic treatment, and cardiovascular disease. Epidemiological evidence suggests that individuals with untreated endodontic lesions may have an increased risk of cardiovascular events, potentially mediated by systemic inflammation and endothelial dysfunction (Caplan et al., 2006; Liljestrand et al., 2016).

Conversely, the presence of adequately treated teeth has been associated with a lower prevalence of cardiovascular disease, suggesting a protective effect of successful endodontic

therapy. A systematic review evaluating this relationship concluded that functional endodontic treatment may be inversely associated with cardiovascular risk, although the strength of evidence remains limited (Aminoshariae & Kulild, 2016).

These findings support the hypothesis that controlling endodontic infection may contribute to reducing systemic risk factors associated with cardiovascular disease. However, the observational nature of most studies precludes definitive conclusions regarding causality. Residual confounding and shared risk factors between oral and systemic diseases must be carefully considered when interpreting these associations.

3.6 CLINICAL EVIDENCE ON BIOMARKER MODULATION FOLLOWING ROOT CANAL TREATMENT

Recent clinical and translational studies have provided more direct evidence supporting the impact of root canal treatment on systemic biomarkers, particularly those related to glycemic control and inflammation. These investigations, although still limited in number, offer important insights into the biological consequences of eliminating endodontic infection.

Prospective clinical studies have demonstrated that patients with apical periodontitis may exhibit improvements in glycemic parameters following successful root canal treatment. Reductions in fasting blood glucose and glycated hemoglobin (HbA1c) have been reported, particularly in individuals with type 2 diabetes mellitus. These findings suggest that the removal of chronic infection may contribute to improved metabolic control, potentially through the attenuation of systemic inflammation and enhancement of insulin sensitivity (Arya et al., 2017; Bakhshandeh et al., 2012).

In parallel, investigations assessing systemic inflammatory markers have shown decreases in circulating mediators such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) following endodontic treatment. These reductions support the hypothesis that apical periodontitis contributes to systemic immune activation and that its resolution may lead to measurable anti-inflammatory effects (Gomes et al., 2013; Martinho et al., 2014).

Additionally, emerging evidence suggests that endodontic treatment may influence oxidative stress pathways and endothelial function, both of which are closely linked to cardiometabolic risk. Improvements in biomarkers related to oxidative balance have been observed after treatment, indicating a potential reduction in systemic oxidative stress burden. These findings further reinforce the concept that local infection control may have systemic biochemical consequences (Piras et al., 2015).

Despite these promising results, the available evidence is characterized by methodological limitations, including small sample sizes, short follow-up periods, and variability in biomarker assessment protocols. Furthermore, differences in patient populations, particularly regarding baseline metabolic status may significantly influence the magnitude of observed effects.

Overall, this body of evidence strengthens the biological plausibility of a link between endodontic treatment and systemic health improvements. While not yet definitive, these findings suggest that successful root canal therapy may play a contributory role in modulating key biomarkers associated with inflammation and metabolic regulation.

3.7 SUMMARY OF EVIDENCE

Overall, the current evidence indicates that apical periodontitis is associated with increased systemic inflammatory burden and may influence metabolic pathways related to glycemic control and lipid metabolism. Successful root canal treatment appears to mitigate these effects by eliminating the source of infection, leading to reductions in inflammatory markers and potential improvements in systemic health parameters.

However, the magnitude and consistency of these effects vary across studies, reflecting differences in study design, population characteristics, and outcome assessment. While the biological plausibility of these associations is well supported, high-quality longitudinal and interventional studies are needed to establish causality and determine clinical relevance.

4 DISCUSSION

The present synthesis reinforces the paradigm that apical periodontitis should not be interpreted solely as a localized oral condition but rather as a biologically active inflammatory focus with potential systemic implications. The convergence of clinical and mechanistic evidence suggests that persistent endodontic infection contributes to a sustained inflammatory burden capable of influencing metabolic homeostasis and systemic disease pathways.

A central finding across the available literature is the consistent reduction in systemic inflammatory markers following successful root canal treatment. This observation supports the concept that apical periodontitis functions as a chronic source of immune stimulation. Continuous exposure to bacterial antigens and endotoxins may promote activation of innate immune pathways, resulting in increased circulating cytokines and acute-phase proteins. The resolution of infection through effective endodontic therapy appears to attenuate this systemic

inflammatory signaling, thereby reducing overall inflammatory load. Given that chronic low-grade inflammation is a key driver of cardiometabolic disorders, this reduction may have broader clinical implications beyond oral health.

The observed improvements in glycemic control further strengthen the hypothesis of a biologically relevant oral-systemic interaction. Chronic inflammation is known to interfere with insulin signaling pathways, contributing to insulin resistance through mechanisms involving cytokine-mediated disruption of glucose transport and cellular metabolism. By eliminating a persistent inflammatory source, root canal treatment may indirectly enhance insulin sensitivity and improve glycemic regulation. Importantly, this effect appears to be more evident in individuals with pre-existing metabolic dysregulation, suggesting that systemic vulnerability may modulate the magnitude of the response. This aligns with the concept of a bidirectional relationship, in which systemic conditions may also influence the severity and progression of apical periodontitis.

Alterations in lipid metabolism observed after treatment provide an additional layer of evidence supporting systemic involvement. Inflammatory mediators can influence lipid homeostasis by affecting hepatic lipid synthesis, lipoprotein oxidation, and enzymatic activity involved in lipid transport. The normalization of lipid profiles following infection control may reflect a reduction in inflammatory-driven metabolic disruption. However, these findings remain less consistent compared to glycemic outcomes, likely due to differences in study design, follow-up duration, and population heterogeneity.

Despite these promising observations, several limitations must be acknowledged. The heterogeneity of existing studies represents a major challenge in interpreting the available evidence. Variations in diagnostic criteria for apical periodontitis, definitions of treatment success, and methods for assessing systemic biomarkers limit comparability across studies. Additionally, many investigations rely on observational or quasi-experimental designs, which are inherently susceptible to confounding factors such as lifestyle variables, comorbidities, and concurrent medical treatments. These factors complicate the establishment of a direct causal relationship between root canal treatment and systemic improvements.

Another critical aspect is the temporal nature of the observed effects. While short-term reductions in inflammatory markers and metabolic improvements have been reported, the long-term sustainability of these changes remains unclear. It is possible that systemic benefits depend not only on the resolution of a single endodontic lesion but also on the cumulative burden of oral infections and overall oral health status. Therefore, root canal treatment should be viewed within the broader context of comprehensive oral care rather than as an isolated intervention.

From a mechanistic perspective, the pathways linking apical periodontitis to systemic health are complex and multifactorial. These include microbial dissemination, endotoxin-induced immune activation, oxidative stress, and endothelial dysfunction. The interplay between these mechanisms may vary among individuals, influenced by genetic predisposition, immune response variability, and systemic health conditions. This complexity highlights the need for more integrative research approaches combining clinical, molecular, and translational methodologies.

Future research should prioritize well-designed longitudinal and interventional studies with standardized protocols and clearly defined outcomes. The incorporation of advanced biomarker profiling, including omics technologies, may provide deeper insights into the systemic effects of endodontic treatment. Additionally, stratification of patients based on systemic health status could help identify subgroups that may benefit most from infection control. Establishing causality and understanding dose-response relationships between oral infection burden and systemic outcomes remain key challenges for the field.

5 CONCLUSION

The current body of evidence suggests that successful root canal treatment may extend beyond local infection control and contribute to improvements in systemic health parameters. By eliminating a chronic source of inflammation, endodontic therapy appears to reduce systemic inflammatory burden and may positively influence glycemic regulation and, to a lesser extent, lipid metabolism.

Although these findings support the concept of an oral-systemic connection, the evidence remains insufficient to establish definitive causality. The observed associations are influenced by multiple biological and methodological factors, underscoring the need for cautious interpretation. Nevertheless, the potential systemic benefits of endodontic treatment reinforce the importance of integrating oral healthcare into broader strategies for managing and preventing cardiometabolic diseases.

Advancing this field will require robust clinical trials, standardized methodologies, and interdisciplinary collaboration. A deeper understanding of the biological mechanisms underlying these associations may ultimately contribute to more comprehensive and personalized approaches to patient care, bridging the gap between dentistry and systemic health.

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