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BEYOND SILVER DIAMINE FLUORIDE: EMERGING ZINC-BASED STRATEGIES FOR CARIES ARREST WITHOUT TOOTH DISCOLORATION

ALÉM DO FLUORETO DIAMINO DE PRATA: ESTRATÉGIAS EMERGENTES BASEADAS EM ZINCO PARA A INTERRUPÇÃO DA CÁRIE SEM DESCOLORAÇÃO DENTÁRIA

MÁS ALLÁ DEL FLUORURO DIAMINO DE PLATA: ESTRATEGIAS EMERGENTES BASADAS EN ZINC PARA LA DETENCIÓN DE LA CARIES SIN DECOLORACIÓN DENTAL

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ABSTRACT

Objective: To explore emerging zinc-based strategies as alternatives to silver diamine fluoride (SDF) for caries arrest, with a focus on maintaining efficacy while avoiding tooth discoloration.

Methodology: A narrative review of the literature was performed using databases such as PubMed, Scopus, and Web of Science. Studies investigating zinc-based compounds and their antimicrobial, remineralizing, and anti-cariogenic properties were included. Data were qualitatively analyzed to compare these approaches with conventional SDF therapy.

Results: Zinc-based formulations have shown promising antimicrobial activity against cariogenic bacteria, particularly Streptococcus mutans, and demonstrate the ability to inhibit biofilm formation. Additionally, these compounds contribute to enamel remineralization and dentin stabilization. Unlike SDF, zinc-based agents do not cause undesirable black staining,

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which is a major limitation of SDF in aesthetic zones. However, the current evidence is largely derived from in vitro and preliminary clinical studies, with limited long-term clinical validation.

Conclusion: Zinc-based strategies represent a promising alternative for caries management, particularly in patients where aesthetics are a concern. While early findings are encouraging, further well-designed clinical trials are necessary to establish their long-term effectiveness and safety. Their integration into minimally invasive dentistry could expand treatment options beyond traditional SDF.

Keywords: Dental Caries. Zinc Compounds. Caries Arrest. Remineralization. Antimicrobial Agents. Silver Diamine Fluoride Alternatives. Biofilm Inhibition. Minimally Invasive Dentistry.

RESUMO

Objetivo: Explorar estratégias emergentes baseadas em zinco como alternativas ao fluoreto diamino de prata (SDF) para a interrupção da cárie, com foco em manter a eficácia enquanto se evita a descoloração dentária.

Metodologia: Foi realizada uma revisão narrativa da literatura utilizando bases de dados como PubMed, Scopus e Web of Science. Foram incluídos estudos que investigaram compostos à base de zinco e suas propriedades antimicrobianas, remineralizantes e anticariogênicas. Os dados foram analisados qualitativamente para comparar essas abordagens com a terapia convencional com SDF.

Resultados: Formulações à base de zinco demonstraram atividade antimicrobiana promissora contra bactérias cariogênicas, particularmente Streptococcus mutans, e apresentaram capacidade de inibir a formação de biofilme. Além disso, esses compostos contribuem para a remineralização do esmalte e estabilização da dentina. Diferentemente do SDF, agentes à base de zinco não causam escurecimento indesejável, que é uma limitação importante do SDF em zonas estéticas. No entanto, as evidências atuais derivam, em grande parte, de estudos in vitro e estudos clínicos preliminares, com validação clínica de longo prazo ainda limitada.

Conclusão: Estratégias baseadas em zinco representam uma alternativa promissora para o manejo da cárie, especialmente em pacientes nos quais a estética é uma preocupação. Embora os achados iniciais sejam encorajadores, são necessários mais ensaios clínicos bem delineados para estabelecer sua eficácia e segurança a longo prazo. Sua integração na odontologia minimamente invasiva pode ampliar as opções de tratamento além do SDF tradicional.

Palavras-chave: Cárie Dentária. Compostos de Zinco. Interrupção da Cárie. Remineralização. Agentes Antimicrobianos. Alternativas ao Fluoreto Diamino de Prata. Inibição de Biofilme. Odontologia Minimamente Invasiva.

RESUMEN

Objetivo: Explorar estrategias emergentes basadas en zinc como alternativas al fluoruro diamino de plata (SDF) para la detención de la caries, con énfasis en mantener la eficacia evitando la decoloración dental.

Metodología: Se realizó una revisión narrativa de la literatura utilizando bases de datos como PubMed, Scopus y Web of Science. Se incluyeron estudios que investigaron

compuestos a base de zinc y sus propiedades antimicrobianas, remineralizantes y anticariogénicas. Los datos fueron analizados cualitativamente para comparar estos enfoques con la terapia convencional con SDF.

Resultados: Las formulaciones a base de zinc han mostrado una actividad antimicrobiana prometedora contra bacterias cariogénicas, particularmente Streptococcus mutans, y demuestran capacidad para inhibir la formación de biofilm. Además, estos compuestos contribuyen a la remineralización del esmalte y a la estabilización de la dentina. A diferencia del SDF, los agentes a base de zinc no causan tinción negra indeseable, que es una limitación importante del SDF en zonas estéticas. Sin embargo, la evidencia actual proviene en gran medida de estudios in vitro y estudios clínicos preliminares, con validación clínica a largo plazo aún limitada.

Conclusión: Las estrategias basadas en zinc representan una alternativa prometedora para el manejo de la caries, especialmente en pacientes en los que la estética es una preocupación. Aunque los hallazgos iniciales son alentadores, se requieren más ensayos clínicos bien diseñados para establecer su eficacia y seguridad a largo plazo. Su integración en la odontología mínimamente invasiva puede ampliar las opciones de tratamiento más allá del SDF tradicional.

Palabras clave: Caries Dental. Compuestos de Zinc. Detención de la Caries. Remineralización. Agentes Antimicrobianos. Alternativas al Fluoruro Diamino de Plata. Inhibición del Biofilm. Odontología Mínimamente Invasiva.

1 INTRODUCTION

Dental caries remains one of the most prevalent chronic diseases worldwide, affecting individuals across all age groups and representing a significant public health burden. Despite advances in preventive strategies and restorative techniques, the global prevalence of untreated caries in permanent teeth continues to be high, particularly in low- and middle-income countries, where access to dental care is often limited (Kassebaum et al., 2017). The contemporary paradigm of caries management has shifted from a purely surgical-restorative approach toward a minimally invasive and preventive model, emphasizing early detection, risk assessment, and the arrest or reversal of carious lesions (Fejerskov et al., 2015). Within this context, non-invasive therapeutic agents have gained increasing attention as effective tools for managing caries without the need for extensive operative intervention.

Among these agents, silver diamine fluoride (SDF) has emerged as a highly effective and widely studied option for caries arrest. SDF combines the antimicrobial properties of silver ions with the remineralizing effects of fluoride, resulting in a dual mechanism of action that inhibits bacterial activity and promotes the formation of more resistant mineral phases in demineralized dental tissues (Horst et al., 2016). Numerous clinical studies and systematic reviews have demonstrated the efficacy of SDF in arresting both coronal and root caries lesions, particularly in pediatric and geriatric populations (Gao et al., 2016). Its simplicity of application, low cost, and effectiveness make it especially valuable in community-based and low-resource settings.

However, despite its clinical benefits, the widespread adoption of SDF is significantly limited by a major aesthetic drawback: the irreversible black staining of treated carious lesions. This discoloration results from the formation of silver oxide and other silver compounds within the demineralized tooth structure, which can be particularly problematic in anterior teeth and in patients with high aesthetic demands (Horst et al., 2016). As a result, both patients and clinicians may be reluctant to use SDF in visible areas, restricting its applicability in routine clinical practice. This limitation has driven the search for alternative materials that can achieve comparable antimicrobial and remineralizing effects without compromising aesthetics.

In recent years, zinc-based compounds have emerged as promising candidates in the field of minimally invasive caries management. Zinc is a biologically relevant trace element with well-documented antimicrobial properties and a recognized role in mineral metabolism. In the oral environment, zinc ions have been shown to inhibit the growth of cariogenic bacteria, including Streptococcus mutans, by interfering with metabolic pathways, enzyme activity, and biofilm formation (Lynch, 2011). Additionally, zinc can modulate

demineralization–remineralization dynamics, contributing to the stabilization of dental hard tissues and potentially enhancing resistance to acid attacks.

The incorporation of zinc into dental materials and therapeutic agents has been explored in various forms, including zinc oxide nanoparticles, zinc-substituted hydroxyapatite, and zinc-containing varnishes and pastes. These formulations have demonstrated promising antimicrobial and anti-biofilm effects in vitro, as well as the ability to promote remineralization of enamel and dentin (Hernández-Sierra et al., 2008; Ten Cate, 2013). Importantly, unlike silver-based compounds, zinc does not cause significant discoloration of dental tissues, making it a more aesthetically acceptable alternative for patients.

Nanotechnology has further enhanced the potential of zinc-based strategies by enabling the development of nanoscale delivery systems with improved bioavailability and targeted activity. Zinc oxide nanoparticles (ZnO-NPs), in particular, have attracted considerable attention due to their high surface area, enhanced antimicrobial efficacy, and ability to disrupt bacterial membranes and biofilms (Hernández-Sierra et al., 2008). These properties make them especially suitable for applications in caries prevention and arrest. Moreover, the combination of zinc with other bioactive agents, such as fluoride or calcium phosphate compounds, may produce synergistic effects that further enhance therapeutic outcomes.

Despite these promising findings, the current body of evidence supporting zinc-based strategies remains limited, particularly in terms of clinical validation. Much of the available research is derived from in vitro studies or short-term experimental models, which may not fully capture the complexity of the oral environment. Factors such as saliva composition, dietary habits, and patient-specific variability can significantly influence the effectiveness of these agents in vivo. Furthermore, there is a lack of standardized protocols for evaluating the caries-arresting potential of zinc-based formulations, making it difficult to directly compare results across studies. Another important consideration is the need to balance antimicrobial efficacy with biocompatibility and safety. While zinc is generally regarded as safe at physiological concentrations, excessive exposure or inappropriate formulations could potentially lead to cytotoxic effects or disruption of the oral microbiome. Therefore, careful optimization of concentration, delivery mechanisms, and formulation is essential to ensure both effectiveness and safety in clinical applications.

From a translational perspective, the development of zinc-based alternatives to SDF represents an important step toward expanding the therapeutic arsenal available for minimally invasive dentistry. Such strategies have the potential to address one of the key limitations of SDF namely, tooth discoloration while maintaining or even enhancing its

beneficial properties. However, the successful integration of these materials into clinical practice will require robust evidence from well-designed randomized controlled trials, as well as long-term studies assessing durability and patient-centered outcomes.

Given the growing interest in aesthetic, non-invasive caries management and the limitations associated with existing therapies, there is a clear need to critically evaluate emerging alternatives. In this context, the present narrative review aims to explore the current evidence on zinc-based strategies for caries arrest, compare their mechanisms and effectiveness with those of silver diamine fluoride, and identify key gaps and future directions for research. By providing a comprehensive and critical overview, this study seeks to contribute to the development of more effective and aesthetically acceptable approaches to caries management.

2 METHODOLOGY

A narrative review was conducted to explore the potential of zinc-based compounds as alternatives for caries arrest. Electronic databases, including PubMed (MEDLINE), Scopus, and Web of Science, were systematically searched for studies published up to 2025. The search terms included combinations of “zinc,” “dental caries,” “caries arrest,” “remineralization,” and “antimicrobial.”

Studies were considered eligible if they evaluated the antimicrobial, anti-cariogenic, or remineralizing effects of zinc-based materials in dental contexts. Both in vitro and in vivo studies, as well as relevant review articles, were included to provide a comprehensive overview.

Articles unrelated to dentistry or lacking relevance to caries management were excluded. Due to the narrative nature of the review, study selection was guided by scientific relevance and thematic contribution. Findings were synthesized qualitatively, emphasizing mechanisms of action, comparative effectiveness with silver diamine fluoride, and current limitations. No formal risk of bias assessment was conducted.

3 RESULTS

The analysis of the selected literature revealed that zinc-based compounds exhibit significant antimicrobial, anti-biofilm, and remineralizing properties, positioning them as promising alternatives to silver diamine fluoride (SDF) for caries arrest.

3.1 ANTIMICROBIAL ACTIVITY AGAINST CARIOGENIC BACTERIA

Multiple studies have demonstrated that zinc ions and zinc-based nanoparticles possess strong antimicrobial effects, particularly against Streptococcus mutans, a key pathogen in dental caries. Zinc interferes with bacterial glycolysis, enzyme activity, and membrane integrity, ultimately reducing acid production and bacterial viability.

In vitro investigations have shown that zinc oxide nanoparticles (ZnO-NPs) exhibit dose-dependent antibacterial activity, often comparable to or exceeding that of conventional agents (Hernández-Sierra et al., 2008). Similarly, a study by Aydin Sevinç and Hanley (2010) reported that ZnO nanoparticles significantly inhibited S. mutans growth and reduced biofilm formation on dental surfaces. Moreover, zinc has been shown to disrupt quorum sensing and extracellular polysaccharide synthesis, which are critical for biofilm maturation (Allaker & Memarzadeh, 2014). These mechanisms contribute to the prevention of bacterial adhesion and colonization, key steps in caries progression.

3.2 BIOFILM INHIBITION AND MODULATION

Zinc-based formulations not only inhibit planktonic bacteria but also significantly affect biofilm architecture and viability. Studies indicate that zinc reduces biofilm thickness and metabolic activity, impairing the structural integrity of cariogenic biofilms.

For instance, Osorio et al. (2012) demonstrated that zinc-containing dental materials reduced bacterial penetration and biofilm formation in dentin. Additionally, zinc ions have been shown to inhibit matrix metalloproteinases (MMPs), enzymes involved in dentin collagen degradation, thereby contributing to the preservation of dentin structure during caries progression (Tjäderhane et al., 2013).

3.3 REMINERALIZATION POTENTIAL

Zinc plays a crucial role in modulating demineralization–remineralization dynamics. Zinc-substituted hydroxyapatite and zinc-containing formulations have been shown to promote mineral deposition and enhance enamel resistance to acid challenges.

According to Lynch (2011), zinc can integrate into the crystal lattice of hydroxyapatite, improving its stability and reducing solubility under acidic conditions. Furthermore, in situ and in vitro studies suggest that zinc, when combined with fluoride or calcium phosphate systems, enhances remineralization outcomes through synergistic effects (Ten Cate, 2013). A study by Hara et al. (2014) also indicated that zinc-containing solutions reduced enamel demineralization and facilitated partial remineralization, although the effects were less pronounced than those observed with high-concentration fluoride therapies.

3.4 COMPARISON WITH SILVER DIAMINE FLUORIDE

SDF remains one of the most effective agents for caries arrest due to its dual antimicrobial and remineralizing mechanisms. Clinical studies consistently report high caries arrest rates, often exceeding 80% in primary teeth (Gao et al., 2016). However, its major limitation is the formation of black stains due to silver precipitation.

In contrast, zinc-based agents do not produce intrinsic discoloration of dental tissues, making them more suitable for use in aesthetically sensitive areas. While zinc demonstrates comparable antimicrobial properties in vitro, its clinical efficacy in caries arrest has not yet reached the level of evidence established for SDF.

3.5 LIMITATIONS OF CURRENT EVIDENCE

Despite promising findings, the majority of studies on zinc-based strategies are limited to laboratory or short-term experimental models. There is a lack of well-designed randomized controlled trials evaluating long-term caries arrest outcomes in vivo. Additionally, heterogeneity in formulations, concentrations, and delivery systems complicates direct comparison across studies. Variability in experimental conditions, such as pH cycling models and biofilm composition, further limits the generalizability of results.

4 DISCUSSION

The findings of this review highlight the growing potential of zinc-based strategies as alternatives to conventional silver diamine fluoride in the management of dental caries. One of the most relevant advantages of zinc lies in its ability to provide antimicrobial and anti-biofilm effects without causing the aesthetic compromise associated with tooth discoloration. This characteristic positions zinc-based agents as particularly attractive for use in anterior teeth and in patients with high aesthetic expectations.

From a mechanistic perspective, zinc appears to act through multiple complementary pathways, including disruption of bacterial metabolism, inhibition of biofilm formation, and stabilization of the dentin matrix. This multimodal activity resembles, to some extent, the dual mechanism observed with SDF, although mediated through different biochemical interactions. In addition, the capacity of zinc to inhibit matrix metalloproteinases suggests an important role in preserving dentin integrity, which is critical in slowing lesion progression. Another important aspect is the integration of zinc into remineralization processes. Although its remineralizing effect may not be as potent as high-concentration fluoride therapies, zinc contributes to the formation of more stable mineral phases and may enhance the effects of other remineralizing agents when used in combination. This opens the possibility of

developing synergistic formulations that combine zinc with fluoride or calcium phosphate systems to optimize clinical outcomes.

Despite these promising features, the current evidence base remains limited. Most available studies are laboratory-based, and their results may not fully translate to the complex conditions of the oral environment. Factors such as saliva composition, dietary habits, oral hygiene, and microbiome diversity can significantly influence the performance of these agents in vivo. Furthermore, there is a lack of standardized protocols for evaluating caries arrest, which makes it difficult to compare zinc-based strategies directly with established treatments such as SDF. Another challenge lies in optimizing the formulation and delivery of zinc-based compounds. The concentration of zinc must be carefully controlled to balance antimicrobial efficacy with biocompatibility, as excessive levels may lead to cytotoxic effects or disruption of the oral microbial balance. Advances in nanotechnology offer promising solutions in this regard, allowing for controlled release systems and improved targeting of cariogenic biofilms.

From a clinical standpoint, zinc-based strategies should not yet be considered replacements for SDF, but rather as complementary or emerging alternatives. Their use may be particularly justified in cases where aesthetics are a primary concern or where patients refuse SDF treatment due to staining. However, robust clinical trials with long-term follow-up are essential to validate their effectiveness, safety, and durability.

5 CONCLUSION

Zinc-based compounds represent a promising and innovative approach for the management of dental caries, offering antimicrobial, anti-biofilm, and remineralizing properties without the undesirable tooth discoloration associated with silver diamine fluoride. While current evidence supports their potential as effective agents in minimally invasive dentistry, their clinical applicability remains limited by the lack of high-quality, long-term studies.

Future research should focus on well-designed randomized controlled trials, standardized evaluation protocols, and the development of optimized formulations that maximize efficacy while ensuring safety. The integration of zinc-based strategies into clinical practice may ultimately expand the therapeutic options available for caries management, particularly in situations where aesthetic considerations are paramount.

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