Titanium Tetrafluoride (TiF_4) in the Treatment of Dental Erosion

Tetrafluoreto de Titânio (TiF_4) no Tratamento da Erosão Dental

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Abstract

Dental erosion is a multifactorial pathology that leads to dental substrate loss caused by its exposure to acids of non-bacterial origin. The process begins with a superficial demineralization of enamel, which, when continuously exposed to erosive solutions, can even lead to dentin exposure, causing aesthetic/functional problems to patients, besides increasing the chances of dentin hypersensitivity. Fluoride products, when applied onto dental surface, form a protective physical barrier, which also acts as F ions reservoir. However, against recurrent erosive challenges, this protection has limited effectiveness. Current literature has already proven the capacity of compounds containing polyvalent metal cations associated with fluorides, including titanium tetrafluoride (TiF_4), to form more acid-resistant layers. The ability of the titanium ion to bind simultaneously to F ions and dental tissue allow the formation of a diffusion barrier on the tooth surface, known as glaze, which may protect it against acid demineralization. However, it is still necessary to establish an ideal clinical protocol involving the definition of factors capable of determining the success of the treatment, such as concentration, pH, excipient and form/period of application, as well as frequency for reapplication. The present critical review aims to provide a brief overview of TiF_4's mechanisms of action and discuss the factors that may improve its protection capacity against dental erosion.

Keywords*: Tooth Erosion. Fluorine. Titanium.*

Resumo

A erosão dental é uma patologia multifatorial que leva a uma perda de substrato dental causada pela sua exposição a ácidos de origem não-bacteriana. O processo se inicia com uma desmineralização superficial do esmalte, que, quando da continua exposição a soluções erosivas, pode levar a exposição do esmalte, causando problemas estéticos/funcionais aos pacientes, além de aumentar a chance de hipersensibilidade dentinária. Os produtos fluoretados, quando aplicados sobre a superfície dental, formam uma barreira física de proteção, que também pode agir como reservatório de íons F. Entretanto, frente a recorrentes desafios erosivos, esta proteção tem efetividade limitada. A literatura recente já demonstrou a capacidade de compostos contendo cátions metálicos polivalentes associados a fluoretos, incluindo o tetrafluoreto de titânio (TiF_4), para formar camadas mais ácido-resistentes. A capacidade do íon titânio de se ligar simultaneamente aos íons F e ao tecido dental permite a formação de uma barreira de difusão na superfície dental, conhecida como *glaze*, que a protege contra desmineralização ácida. Entretanto, ainda é necessário estabelecer um protocolo clínico ideal envolvendo a definição de fatores capazes de determinar o sucesso do tratamento, como concentração, pH, veículo e forma/tempo de aplicação, além da frequência para reaplicação. A presente revisão crítica tem como objetivo proporcionar uma breve visão geral dos mecanismos de ação do TiF_4 e discutir os fatores que podem melhorar sua capacidade protetora contra a erosão dental.

Palavras-chave: Erosão Dentária. Flúor. Titânio.

1 Introduction

Dental wear is a multifactorial pathological condition that induces progressive loss of dental hard tissue. Among the non-carious lesions, erosion is caused by the action of non-bacterial acids[1].

These acids, which may have endogenous (eg hydrochloric acid from gastric juice) or exogenous origins (eg acidic foods and drinks), act directly on the dental surface[2]. When exposure to low pH solutions occurs, there is an initial demineralization of mineralized tissue (softening)[3], due to the degree of saturation of the oral cavity in relation to the dental tissue[4].

It has been established that under conditions of pH below 3.5, dental tissue dissolution increases exponentially[5]. However, unlike what occurs in carious lesions, the critical pH for the formation of erosive lesions cannot be defined[2,3]. The critical pH is that at which the fluids present in the mouth are saturated in relation to the dental surface[2]. Although, this is also dependent on other factors, such as the solubility of dental tissue and concentration of minerals present in saliva and acid solution, such as calcium, phosphate and fluoride[3]. Therefore, if an unbalance in the mineral exchange reaction between teeth and fluids of the oral cavity occurs, and the dental tissue is supersaturated regarding the liquids surrounding it, the dental surface demineralization begins.

The dental erosion process is characterized initially by a demineralization of enamel's surface[1], which leads to a superficial softening, followed by a continuous layer-by-layer enamel crystals dissolution [1,3]. This demineralization occurs in a centripetal manner[6], beginning with the interprismatic

area and following through the central region of the prism. The increase of the demineralized area generates a higher surface roughness[7] and decreases the microhardness of dental tissue[8]. In consequence of the alterations caused on surface characteristics, the enamel surface becomes more susceptible to the action of mechanical forces[9]. If the erosive challenge persists, mineral dissolution progresses, which may lead to exposure of the dentin layer.

As in the enamel layer, the inorganic portion of the dentin is also rapidly dissolved by acids action. The mineral loss begins in the peritubular dentin, causing a widening of the dentinal tubules, followed by demineralization of the intertubular dentin[10]. However, the organic portion remains, exposing a dense layer of collagen fibers. Just below this layer is a partially demineralized dentin, followed by healthy dentin[10]. This happens because the organic portion is not affected by oral cavity acids[2] and acts as a diffusion barrier, limiting the ion exchange and consequently, protecting the lower dentin layers from the effects caused by the low pH of the surrounding fluids[11]. This organic matrix is quite resistant to mechanical forces, maintaining not only the coverage, but also its structure against loads up to 4 N during brushing[12]. In this sense, the presence of the organic matrix gives dental erosion its self-limiting characteristic[3].

However, this layer may be degraded by proteolytic enzymes, especially matrix metalloproteinases (MMPs), present in dentin and saliva[13]. This is due to their ability to hydrolyse components from extracellular matrix[14]. After that, mineralized layers are exposed again, allowing the erosion lesion to progress.

Many MMPs have already been identified[13], and MMP-8 seems o be the most collagenolytic enzyme[15]. MMPs are secreted in the form of inactive precursors and require activation through contact with low pH substances to degrade the organic matrix[14,16]. In the case of erosive lesions in dentin, the presence of acids in the oral cavity may lead to exposure of collagen fibrils and activation of MMPs[16]. However, although active, these are not capable of acting under acidic pH. After neutralization of the pH by the saliva buffer capacity, the previously activated MMPs start degrading the collagen matrix[16]. This may end up exposing the partially demineralized dentin layer, which becomes susceptible to acids again and, consequently, to erosion progression[17].

As the erosion process persists, the lesions become larger, and may lead to aesthetic and/or functional problems to patients. Clinically, dentists may encounter wide and shallow lesions[3], which may result even in loss of ideal anatomy and reduction of vertical dimension. In addition, the association between erosion and dentin hypersensitivity is quite frequent[18], since the exposed dentin layer allows stimuli to be propagated through the tubules, causing dentinal fluid movement and painful symptomatology[18].

Since erosion involves loss of tooth structure, after the development of lesions, remineralization is not possible. Depending on the amount of tissue involved, conventional restorative treatment may be necessary[1]. However, with the identification of risk factors concerning diet and patient's health, in addition to early stage lesions, premature diagnosis of the disease may be performed. In these cases, changes in patient's habits added to preventive treatments can protect dental surfaces against acid challenges and reduce erosion progression.

This chapter aims to give the readers an overview of the current literature about the application of fluorides as a treatment to erosion control, emphasizing titanium tetrafluoride's mechanism of action and factors that may influence its protective effect.

2 Development

2.1 How to Prevent and treat Dental Erosion?

Several alternative treatments have been proposed for erosion prevention and control. Among them fluorides may be cited [19,20], the use of antacid solutions[21], high potency lasers[22], adhesives[23] and sealants[24].

Fluorides are known to form a layer of mineral precipitates on the dental surface[6]. Immediately after fluoride application, calcium fluoride-like compounds are deposited onto the teeth. In face of cariogenic challenges, this may be very positive, since fluoride ions are released by the dissolution of the CaF_2-like layer due to the drop in pH of the biofilm[25].

Against erosive challenges, besides fluoride release, the CaF_2-like layer can act as a physical barrier and avoid direct contact between acids and dental surfaces[25]. However, when exposed to significant pH reduction, as occurs on erosion process, this protection may not be efficient and the formation of layers more resistant to acid dissolution is necessary[2]. For this purpose, therapies with agents with high concentrations of fluorides or applications with prolonged time have been shown to be more efficient, since they are able to form thicker, dense and stable layers of CaF_2-like compounds[25]. Although, the protection conferred by fluoride compounds commonly used to prevent carious lesions, such as sodium fluoride and amine fluoride, have still been shown to be limited in cases of erosion[20,26]. For this reason, compounds containing polyvalent metal cations combined with fluorides have been tested.

Besides the fluoride formulas formed with divalent compounds, such as stannous fluoride, tetrafluorides have been investigated, especially titanium (TiF_4).

2.2 Titanium Tetrafluoride

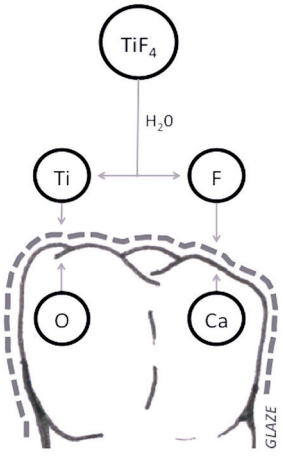
The titanium ion has the ability to form complexes concomitantly with F ions and dental tissues[27]. As a result, TiF_4 action has been widely studied[19,28-30] in Dentistry. In the form of TiF_4, this fluoride presents satisfactory stability and particular mechanism of action in relation to the other fluorides. However, when hydrolyzed, it generates an acidic

solution[31] after the break down of water molecules promoted by the titanium ion and, consequently, releasing H^+ ions, which may lead to a relative cytotoxicity[32]. However, TiF_4, when administered enterally, does not show signs of systemic toxicity[33]. Although, even considering the acidity of the solution, the surface demineralization caused is partial[27] and may favor the penetration of fluoride into the mineralized tissue[34,35].

In addition to fluoride penetration and titanium incorporation into hydroxyapatite[25], other factors also contribute to the protection conferred by TiF_4 to dental tissue. The electrostatic interaction between TiF_4 and acquired film proteins[36] and the presence of organic matrix on the dental surface[37] are capable of positively influencing the incorporation of fluoride by dental tissue[34]. Besides, the formation of an acid-resistant layer occurs on the dental surface[28,29,31,38], which resembles to a *glaze*, and is ultrastructurally composed of numerous spherical particles[31,39].

Due to the high affinity between titanium ions and oxygen atoms, the titanium, once released by the hydrolysis of TiF_4 molecules, can bind to oxygen derived from water or phosphate molecules on the dental surface. After this process, a layer of TiO_2 is formed[40], as shown in Figure 1. Besides, an alternative hypothesis proposes that *glaze* may be composed of organometallic complexes formed between titanium and dental organic matrix[41].

Figure 1 - Hydrolysis of TiF_4 molecules and mechanism of *glaze* layer formation.



Fonte: The authors.

Since TiF_4 enables the formation of this acid-resistant layer, it is responsible for the production of a diffusion barrier and a reservoir of F ions, which may delay the dissolution of dental tissue exposed to acidic challenges[25]. For this reason, its effect on erosion has been studied and has obtained promising results in both enamel[19,20,30,39,42] and dentin[43].

These results are dependent on the concentration, form of presentation, pH and time of application of TiF_4[26,30,39]. However, there is still no consensus as to what the ideal protocol would be. Several combinations have already been tested, but some factors have been more successful than others.

As for the excipient that should be used for TiF_4 application, the simplest would be to incorporate this fluoride into dentifrices, although, it is known that under low pH conditions, the product presents better results in the formation of precipitate on the dental surface and reduction of demineralization[39], maintaining its protection against erosion even after abrasive challenges[43,44].

A lower pH may favor the penetration of F^- ions into the partially demineralized tissue layer[45], since exposure of the organic matrix increases the surface area of dentin and creates diffusion zones[40], which promotes the retention of CaF_2 also in the intratubular region of the dentin[45]. However, this acidity precludes the regular domestic application of TiF_4 at its natural pH (pH 1.2), and its adjustment would be required. On the other hand, a higher pH may compromise TiF_4's action[20] and for that reason applications controlled by the dentist would be the best alternative. In this sense, presentations in the form of solutions[44], gels[22,26,46] and varnishes[30] have been tested, since they allow more precise applications on the lesions, avoiding the contact between the product and soft tissues. Moreover, the greater substantivity of the products in the form of gels and varnishes may positively influence fluoride's effect, since it promotes a longer maintenance of the product on the dental surface and, consequently, may prolong its contact with the teeth[2,46].

As for the ideal concentration, compounds containing 4% of TiF_4 in their composition have obtained better results when compared to lower concentrations, being able to form a thicker and more tenacious *glaze* after treatment[29], to promote greater deposition of CaF_2-like compounds[47], to reduce the surface softening caused by acidic challenges[42] and to promote the release of fluoride into the oral environment for up to 12 h[48]. Besides, prolonged application times, between 2 and 4 minutes, may favor the retention of F^- on the dental surface[35] and decrease mineral loss by dental tissue under acid action[19].

The ideal clinical application frequency has not still been determined, but it is known that TiF_4 is capable of modifying surface morphology since its first application[43], leading to the formation of a smoother surface[49] and covered by precipitate both in enamel[38] and in dentin[50]. However, re-application of the fluoride may favor the reduction of substrate loss after tissue exposure to erosive solutions[43] and to promote certain obliteration of tubule entrance[49], which could also lead to reduction of dentin hypersensitivity.

3 Conclusion

Even though TiF_4 has already been proven to have a unique interaction with the teeth surface, several factors may influence TiF_4's effectiveness in preventing and controlling dental erosion. The fact that it shows better results in its original pH, which is acid, precludes the possibility of its domestic application.

The current literature presents satisfactory results

when TiF_4 is applied onto teeth surface on forms with greater substantivity, longer application times and higher concentrations. Even considering TiF_4 to be a safe alternative of treatment, most studies that evaluated TiF_4 action against erosion were performed *in vitro* and *in situ*. Therefore, in order to make it a product available for commercialization, clinical trials should be conducted to confirm its potential in controlling erosive lesions. Once an ideal clinical protocol for the application of TiF_4 is established, patients will be able to be benefited from its use in dental offices routine.

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