Original Article

Prevalence of Nickel Allergy and Longitudinal Evaluation of Periodontal Abnormalities in Orthodontic Allergic Patients

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ABSTRACT

Objective: To determine the prevalence of nickel allergy in a sample of orthodontic patients and longitudinally compare the clinical periodontal status of these individuals with that of a group of nonallergic patients.

Materials and Methods: The initial sample consisted of 96 patients selected randomly from a databank of patients who sought orthodontic care at a teaching institution. Following the selection and beginning of treatment, periodontal status was assessed over a 12-month period (one evaluation every 3 months— T_1 , T_2 , T_3 , T_4) using the Loe index. The evaluations were performed blindly by a single, calibrated examiner and were followed by prophylaxis and orientation regarding oral hygiene. The prevalence of nickel allergy was determined by the patch test 9 months after the beginning of treatment and occurred in 16 individuals (17.2%). Two groups were then established: the allergic group (AG, n = 16) and the age-paired nonallergic control group (NAG, n = 16). Data were analyzed using the Mann-Whitney *U*-test and Friedman's analysis of variance (ANOVA) tests ($P \le .05$).

Results: Significant differences were present between groups at the T_3 and T_4 evaluations for the LOE index (P = .045 and .009), with allergic individuals showing higher mean values than nonallergic individuals (hyperplasia, change in color, and bleeding). No significant differences were found in the intragroup evaluations between the four evaluations (P > .05).

Conclusions: The results suggest a cumulative effect from nickel throughout orthodontic treatment associated with clinically significant periodontal abnormalities in allergic individuals over time. (*Angle Orthod.* 2009;79:922–927.)

KEY WORDS: Nickel; Allergy; Orthodontics

INTRODUCTION

Adverse reactions stemming from the use of fixed and removable orthodontic appliances have been a

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Accepted: October 2008. Submitted: August 2008. © 2009 by The EH Angle Education and Research Foundation, Inc. concern for orthodontists and researchers in the healthcare field.^{1–5} Nickel has often been pointed out as a biological sensitizer capable of causing short- and long-term sensitivity reactions (type IV immune response, cell-mediated by T lymphocytes).⁶

Clinical abnormalities, such as gingivitis, gingival hyperplasia, lip desquamation, burning sensation in the mouth, metallic taste, angular cheilitis, and periodontitis, may be associated with the release of nickel from orthodontic appliances.^{7,8} Thus, the study of adverse reactions to nickel in such appliances acquires singular importance, as austenitic stainless steel is the most often employed metal for the confection of orthodontic appliances and contains 8% to 20% nickel in its composition.^{9,10} Furthermore, it is estimated that 10% to 30% of women and 1% to 3% of men have a hypersensitive reaction to nickel.¹¹

Although recent studies have addressed the influence of nickel in the development of immune reactions in orthodontic patients, evidence on manifestations and the consequences that this material can have on

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oral and general health have been somewhat inconsistent.^{12–14} Part of this problem can be explained by different study designs, small sample sizes, and different assessment methods, thereby leading to conflicting results and compromising the clinical application of such information. Specifically, the periodontal aspects of this issue have been rather under-explored in the literature.

During orthodontic treatment, sensitive patients are at greater risk of oral discomfort, which hinders both hygiene and treatment.¹⁵ The warm, moist, aerobic status of the mouth offers a favorable environment for the activity of microorganisms. As orthodontic appliances hamper oral hygiene, dental biofilm accumulates with greater facility on tooth surfaces as well as on the appliance itself in most patients. When this biofilm is thicker and has been present for a longer amount of time, there is an increase in the anaerobic status, thereby further favoring the corrosion of the metals in the appliance.¹⁶

The aim of the present study was to determine the prevalence of individuals with nickel allergy in a population of orthodontic patients and to longitudinally compare the periodontal status of these individuals to a group of nonallergic patients.

MATERIALS AND METHODS

Ninety-six individuals awaiting orthodontic treatment at a specialization course in orthodontics of the Lavras University Center (Lavras, MG, Brazil) were randomly selected for participation in the study. All participants were white; 58 (60%) were female and 32 (40%) were male; ages ranged from 10 to 43 years.

All individuals began orthodontic treatment at the same time (throughout the same month of January 2006). Prior to the placement of the appliances, all participants received prophylaxis with a bicarbonate spray as well as orientation on oral hygiene. Morelli brand braces (Sorocaba, SP, Brazil) were attached; these braces contain the following composition: 16% to 18% chrome, 10% to 14% nickel, and 2% to 3% molybdenum.

The clinical gingival characteristics such as color and volume were assessed. A standardized millimeter probe was used to determine the presence or absence of gingival bleeding at the upper and lower first premolars at three different points on the vestibular, lingual, mesial, and distal faces. First premolars were selected due to their location at the halfway point of each quadrant of the oral cavity. For this assessment, the LOE index was employed to take into account qualitative changes in the gingival tissue.^{17,18} The Loe index score was based on the mean values of four first premolars multiplied by three sites per tooth. The mean value is used to classify the patient into one of four categories. This index has the following scores: 0— normal gums; 1—mild inflammation, slight change in color, mild edema, no bleeding upon probing; 2—moderate inflammation, reddish appearance, mild edema, bleeding upon probing; and 3—severe inflammation, reddish appearance, evident edema, ulceration, tendency toward spontaneous bleeding. Patients with at least two of the classifications of each previous item were classified in the more severe category.

Assessments of periodontal status were carried out by a single, blinded, duly calibrated (Kappa > 0.90) examiner at regular 3-month intervals for 12 months (total of four evaluations— T_1 , T_2 , T_3 , T_4) with braces in place. Additionally, prophylaxis with a bicarbonate spray was performed in each session (following the periodontal evaluation).

The skin patch test was used for the diagnosis of nickel allergy. According to the allergy evaluation standards of the Brazilian Medical Association and the Federal Medicine Council (Brazilian Study Group on Contact Dermatitis, 2000), this is the most efficient method for confirming the etiologic diagnosis of allergic contact eczema. This method consists of a 2 cm \times 2 cm patch (Finn Chambers, Tuusula, Finland) attached to the dorsal region of the patient at two different points placed 10 cm apart, following cleansing of the skin with cotton soaked in alcohol (Figure 1). Due to the extensive area involved, an ideal amount of the gel (standardized by the manufacturer) containing a 5% nickel sulfate antigen (solid petroleum jelly) (FDA allergenic, Rio de Janeiro, RJ, Brazil, Importer and Distributor; Epitest Ltd Oy, Tuusula, Finland) remained for 48 hours. During the placement of the patches, patients were instructed to remove them if they experienced any reaction beyond the expected and to seek the researchers in charge as well as the municipal medical emergency room. After 48 hours, the patches were removed and only one reading was made in compliance with the norms of the International Contact Dermatitis Research Group (ICDRG).19 Guidelines of ICDRG are: (-) Negative; (+) discrete erythema with some papules; (++) erythema, papules, and vesicles; and (+++) intense erythema, papules, and vesicles. All patients considered negative presented no clinical condition visible to the naked eye, and all patients considered positive presented erythema, edema, papules, and blisters (+++) (Figure 2).

Nine months following the beginning of treatment, the prevalence of patients with a nickel allergy was determined using the patch test. At this time, one individual with intraoral piercing, one who abandoned treatment for personal reasons, and one who was pregnant were excluded from the study. Sixteen individuals (17.2%) were determined to have nickel allergy



Figure 1. Site of patch test.

and formed the allergic group (AG). Among the nonallergic individuals, 16 patients were randomly selected to form the age-paired control group (NAG).

Intergroup (allergic and control) and intragroup gingival indexes were compared on the four evaluation sessions using the Mann-Whitney *U*-test and Friedman's analysis of variance (ANOVA), respectively. Dunn's correction was used to adjust *P* values for multiple testing. Nonparametric tests were applied since the LOE index is a qualitative method. So, the values



Figure 2. Positive reaction to patch test.

for the 0, 1, 2, and 3 scores cannot be used as ordinary variables. Differences were considered significant with $P \leq .05$. The study received approval from the Research Ethics Committee of the Lavras University Center, under process number 0117.0.189.000-06.

RESULTS

There was a 17.2% prevalence of nickel allergy (16 individuals), 94% (15) of which occurred in female patients and 6% (1) in male patients. Table 1 displays the mean values found for the groups with regard to periodontal status, as assessed by the LOE index. There were significant differences between groups in the T_3 and T_4 evaluations ($P \le .05$). Table 2 displays the intragroup findings of the different evaluation times. There were no significant differences among the different evaluation times within groups (P > .05).

DISCUSSION

The prevalence of nickel allergy in the present study was 17.2%, and the vast majority of allergic individuals were female. The allergic group presented only one man because only one was positive for the patch test. This is in agreement with findings described by other authors.²⁰ The greater sensitivity to nickel on the part of women is related to environmental exposure, such as contact with detergents, jewelry, and other metallic objects, whereas such sensitivity in men is related to professional exposure, especially those who handle nickel.²¹

Nickel is widely used in orthodontics.²² However, few studies address the influence of this metal on periodontal health, especially in a longitudinal fashion. Despite gingival inflammation being considered an allergic reaction to metals in orthodontic appliances,²³ the

Table 1. Mean Gingival Index (GI) and Standard Deviation (SD) Values Based on the Loe Classification (1967) and Comparison Between Allergic Group (AG) and Nonallergic Control Group (NAG) in Four Evaluation Sessions (T_1 : 3 Months; T_2 : 6 Months; T_3 : 9 Months; and T_4 : 12 Months)



* $p \le 0.05$ Statistically significant difference

a,^b Different letters on same line indicate significant difference ($p \le 0.05$)

onset of periodontal disease depends mainly on the accumulation of biofilm. The placement of orthodontic braces influences the accumulation of biofilm and colonization of bacteria, thereby being more prone to inflammation and bleeding.24 This characteristic indicates that the inflammatory conditions of the disease may be transitory, stemming from variations in the degree of oral hygiene of the individual. This emphasizes the need for this type of study over a 12-month period in order to track the condition over time. In the present study, the LOE index was employed to verify periodontal status. Additionally, the plaque index was thought to be used as well since plague is known as the most important indicator of gingivitis. However, the plaque index is totally influenced by oral hygiene right before the evaluation, and if the patient dedicatedly brushed his teeth before evaluation, it would bias the results.

The results of the present study suggest that nickel can influence inflammatory reactions throughout orthodontic treatment. Such reactions are characterized by gingival hyperplasia, changes in color, and gingival bleeding upon probing. The scores between the two groups did not differ at T_1 and T_2 , which suggests that both groups were the same in periodontal status before treatment. Differences only appeared in T_3 (after 9 months), and this can justify why nickel allergy could be involved in this mechanism. The fact that statistical differences between the allergic and control groups occurred on the T_3 and T_4 evaluations (9 and 12 months after beginning treatment, respectively) indicates a cumulative effect of nickel throughout orthodontic treatment.

The type and duration of oral exposure to nickel alloys capable of initiating an adverse reaction is controversial. Metal ions in the saliva can be swallowed prior to causing a reaction or may be absorbed in the mouth, and the amount of nickel released from the dental alloys is significantly lower than that consumed as part of food ingestion.3,25 In the present study, periodontal abnormalities only differed between groups after 9 months, demonstrating that the reaction is dependent on exposure time. The release of nickel from orthodontic appliances has been demonstrated in a number of in vitro studies.26 The release of 40 mg of nickel per day occurs with appliances spanning the entire mouth. However, the daily consumption of nickel in the diet ranges from 300 mg to 600 mg, which suggests a predominantly local rather than systemic effect of nickel. Analysis of Ni-specific T-cell clones generated from peripheral blood mononuclear cells (PBMC) and the skin of allergic patients have suggested that both CD4⁺ and CD8⁺ T cells are involved in the immune response to nickel.27 In vitro responses to nickel have been shown to involve the activation of Ni-specific T cells, followed by the proliferation and induction of both Th1-type (eg, interleukin [IL]-2 and interferon [IFN]-g) and Th2-type (eg, IL-4, IL-5, and IL-13) as well as regulatory (eg, IL-10) cytokines.28-32 IL-10 was formerly described as a Th2-type cytokine with regulatory

Table 2. Comparison of Gingival Index of LOE Values Over a 12-Month \mbox{Period}^a

Friedman's ANOVA	IG	P Value*
AG	IG (T ₁ , T ₂ , T ₃ , T ₄)	.088
NAG	IG (T ₁ , T ₂ , T ₃ , T ₄)	.277

 $\ensuremath{\,^{a}}$ IG indicates intragroup; AG, allergic group; NAG, nonallergic control group.

* P > .05. There was no statistically significant difference.

effects on Th1-type cytokine production,³³ and has been shown to be produced in comparable amounts by cell types other than T cells, including monocytes, macrophages, and dendritic cells. It has the capability to counteract the allergic reactions mediated by Th1type cytokines.

More than a direct sensitizing agent of skin and mucosa, nickel appears to alter periodontal status, acting as a modifying factor of periodontal disease in sensitive patients. The increase in the LOE index over time $(T_3 \text{ and } T_4)$ in the allergic group may suggest nickel adhesion to endogenous macromolecules, thereby stimulating the proliferation of monocytes, macrophages, and cytotoxic cells, which may influence the periodontal inflammatory response.34,35 Furthermore, nickel induces T lymphocytes to produce cytokines, including interferon IF- λ as well as interleukins IL-2, IL-5, and IL-10, thereby stimulating tissue proliferation, which may favor gingival hyperplasia.³⁶ It would therefore be plausible to presuppose that the continuous release of small amounts of nickel to the epithelium could be an initiating factor of gingival over-growth induced by orthodontic therapy.37

Orthodontic treatment with braces containing nickel does not always have a direct allergic affect on gingival tissue.²² However, the results of the present study indicate that nickel is potentially able to exercise an influence over the periodontal status of allergic orthodontic patients. Further studies addressing the humoral aspects of such individuals are needed, thereby allowing a better understanding of the exact nature of the immunological systemic reactions involved in the inflammatory process in allergic patients.

CONCLUSIONS

- The prevalence of patients with nickel allergy was expressive in the sample studied (17.2%).
- The results suggest a cumulative effect of nickel throughout orthodontic treatment and that this effect is associated with clinically significant periodontal abnormalities.

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