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The Effect of Nicotine Lozenge Over Teeth Bleaching During Cigarette's Addiction Treatment

Efecto de Comprimido de Nicotina sobre el Blanqueamiento Dental Durante el Tratamiento de Adicción al Cigarrillo

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ABSTRACT: The aim of this study was to evaluate the effect of nicotine lozenge on teeth staining with/without bleaching in animal model study. A total of 15 Wistar rats were exposed in an acrylic container to 10 cigarettes smoke three times a day for 8 minutes per time, and sacrificed after 60 days. A total of 30 incisor teeth were treated (n=10) as the following: Group-1: in-office bleaching, at-home bleaching and immersion in artificial saliva; group-2: in-office bleaching, at-home bleaching and immersion in nicotine lozenge solution and in artificial saliva; group-3: immersion in nicotine lozenge solution and in artificial. The specimens of all groups were photographed using a stereomicroscope at T1) immediately after the extraction and before any treatment; T2) after one month of the treatment; and T3) after two months of the treatment. Four equidistant points of each specimen were analyzed using CMYK shade guide. The data were analyzed one-way ANOVA test followed by Tukey test for multiple comparisons with ($a \leq 0.05$). In group-1, there was a significant difference of the color saturation of specimens between T1 and T2, and between T1 and T3 readings ($P<0.0001$). In group-2, there was a significant difference of the color saturation of specimens between T1 and T2, between T2 and T3 readings ($P<0.0001$). In group-3, there was a significant difference of the color saturation of specimens between T1 and T2, and between T1 and T3 readings ($P<0.0001$). The usage of nicotine lozenge promotes teeth lighting with/without bleaching.

KEY WORDS: nicotine lozenge, teeth bleaching, nicotine addiction.

INTRODUCTION

Tobacco smoking is a global habit that increases the risk of tooth discoloration (Zhao *et al*., 2019). It is considered as a risk factor of periodontitis, peri-implantitis, caries, alveolar osteitis and halitosis, and it can cause benign and malignant tumors (Ford & Rich, 2021).

Many patients suffer from smoking addiction caused by nicotine, the main component of tobacco, because of its psychoactive action, as it reaches the highest levels in arterial blood in up to 10 seconds and modulate behavior (Pomerleau, 1992). Its action in the central nervous system decreases after being metabolized, causing the need to smoke again to keep the concentration high (Benowitz, 2009).

Conversely, nicotine gum, lozenge or tablet have a slower onset of action, resulting in less reinforcement value making them suggestable alternatives for cigarettes (Pomerleau, 1992), associated with cognitive behavioral therapy for addicted smokers (Etter, 2009), as the replacement of nicotine present in cigarettes has advantages in allowing less intoxication by other substances present in cigarettes, and the use of nicotine gum and / or lozenge tends to decrease after a period (Shiffman *et al*., 2004).

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Smokers complain of tooth discoloration (Zanetti *et al*., 2019) and increasingly demanding teeth bleaching to solve aesthetic problems related to the darkening of tooth enamel, resulting mainly from exogenous pigments (Joiner & Luo, 2017). The bleaching material has an oxidizing agent, hydrogen peroxide (H2O2) or carbamide oxide, its mechanism depends on degrading extracellular matrix and oxidizing chromophores in enamel and dentin (Kwon & Wertz, 2015).

Patients who undergo the smoking addiction treatment may request teeth bleaching while still consuming nicotine lozenge or tablet where precautions are necessary to avoid further tooth staining. To the best of our knowledge, there is only one study in the literature that evaluated the effect of nicotine tablet over the tooth staining (Whelton *et al*., 2012). Therefore, the aim of this study was to evaluate the effect of nicotine lozenge on teeth staining with and without bleaching in animal model study.

MATERIAL AND METHODS

Animals. This study was approved by the Research Ethics Committee of the Institute of Science and Technology of São Paulo State University (ICT-UNESP) under protocol CEUA nº 07/2015. The experiments were conducted in accordance with the relevant guidelines.

A total of 15 Wistar rats (Botucatu, SP, Brazil) (Rattus norvegicus, variation albinus, Wistar) 90-days old, weighing around 250 to 300 grams, were kept in cages at room temperature. They were fed with ration (GuabiNutrilabor®, Mogiana alimentos, São Paulo, SP, Brazil) and ad libitum water.

Exposure to Smoke. The rats were exposed to tobacco in an acrylic container (45x25x20cm) in 3 cycles of 5 animals per time. The rats were exposed to the smoke of 10 cigarettes with a concentration of 1.3 mg of nicotine, 16.5 mg of tar and 15.2 mg of carbon monoxide three times a day for 8 minutes per time. The acrylic container consists of 2 chambers connected by a hole. In the first one, lit cigarettes are kept. In this part there is also an entrance where air is pumped, forming a stream that moves the smoke to the second chamber, where the animals are kept. In the second chamber there is another orifice that gives vent to the pumped air (César-Neto *et al*., 2003; de Geus *et al*., 2018). The rats were anesthetized with ketamine (75 mg/kg, Vetaset; Fort Dodge Animal Health Ltd, São Paulo, Brazil) and xylazine (50 mg/kg, Coopazine; Coopers Ltd Brazil, São Paulo, Brazil) by intramuscular injection and sacrificed 60 days after the daily exposure to smoke.

Experimental groups. A total of 30 incisor teeth were extracted and randomly divided into three groups (n=10) as the following (Table I):

· Group 1: In the first month the specimens were submitted to: I) in-office bleaching only in the first day using hydrogen peroxide 35 % (Whiteness HP, FGM Produtos Odontológicos, Joinville, SC, Brazil) for three bleaching sessions of 15 minutes, totalizing 45 minutes of contact with the specimens, according to the manufacturer's instructions and as detailed previously (Costa *et al*., 2021); II) at-home bleaching using 10 % carbamide peroxide 10 % (Whiteness Perfect, FGM Produtos Odontológicos, Joinville, SC, Brazil) 10h per day for a total of 30 days; and III) immersion in artificial saliva 14h per day which was prepared according to the formulation of Göhring *et al*. (2004) and consisted of hydrogen carbonate (22.1 mmol/L), potassium (16.1 mmol/L), sodium (14.5 mmol/L), hydrogen phosphate (2.6 mmol/L), boric acid (0.8 mmol/L), calcium (0.7 mmol/L), thiocyanate (0.2 mmol/L), and magnesium (0.2 mmol/L), with a final of pH 7.0 (Borges *et al*., 2019). In the second month, the specimens were immersed in artificial saliva 24h per day.

· Group 2: In the first month the specimens were submitted to: I) in-office bleaching only in the first day; II) at-home bleaching 10h per day for a total of 30 days; and III) immersion in nicotine lozenge solution 14h per day for a total of 30 days, which was prepared daily by macerating a nicotine lozenge (NiQuitin® Pastilhas 2mg, GSK GlaxoSmithKline, London, England) in a container filled with 15 mL of artificial saliva. In the second month, the specimens were immersed in nicotine lozenge solution 10h per day and in artificial saliva 14h per day.

· Group 3: Specimens were immersed in nicotine lozenge solution 10h per day and in artificial saliva 14h per day for a total of 60 days without a previous bleaching.

Table I. The experimental groups protocol.

Experimental groups	Bleaching	Immersion
Group 1	With	In artificial saliva
Group 2	With	In solution of artificial saliva + nicotine lozenge
Group 3	Without	In solution of artificial saliva + nicotine lozenge

Shade evaluation. The specimens of all groups were photographed in a stereomicroscope (Zeiss Stemi 2000-C, Jena, Germany): T1) immediately after the extraction and before any treatment (baseline); T2) after one month of the treatment (with/without bleaching); and T3) after two months of the treatment (with/without bleaching).

Four equidistant points of each specimen were analyzed at the three times of evaluation (baseline, after one month and after two months) and the photographic images were analyzed with the aid of the Adobe Photoshop program (Adobe Systems Inc.) (Silva *et al*., 2013), which made it possible to evaluate the percentages of pigments through an assay using CMYK shade guide (Bentley *et al*., 1999; Zhang *et al*., 2010). The results were submitted to statistical analysis, using the one-way ANOVA test followed by Tukey test for multiple comparisons with ($a \leq 0.05$) using GraphPad Prism 6 (La Jolla, CA, USA).

RESULTS

In group 1, there was a significant difference of the color saturation of specimens between T1 and T2, and between T1 and T3 readings ($P < 0.0001$) (Table II). Thus, the association of in-office and at-home bleaching after the smoke cessation as in group 1 is effective in reducing discoloration saturation after 1 and 2 months.

In group 2, there was a significant difference of the color saturation of specimens between T1 and T2, between T2 and T3, and between T1 and T3 readings ($P < 0.0001$) (Table II). In group 3, there was a significant difference of the color saturation of specimens between T1 and T2, and between T1 and T3 readings ($P < 0.0001$) (Table II).

Table II. The mean values of color saturation of the experimental groups at three times readings. Upper-case letters mean statistical difference inter-groups (different treatments), and lower-case letters mean statistical difference intra-groups (different readings).

	Group 1	Group 2	Group 3
Time 1	(194.1) Aa	(181.0) Aa	(179.9) Aa
Time 2	(129.1) Ab	(133.1) Ab	(144.8) Ab
Time 3	(133.6) Ab	(154.1) Bc	(152.9) Bb

DISCUSSION

Smoking causes tooth discoloration because of the deposition of extrinsic pigmentation over enamel surface or because of the cigarette smoke penetration into the dental tissues (de Geus *et al*., 2018), making many smokers looking for tooth bleaching including in-office and at-home techniques using different bleaching agents (de Geus *et al*., 2017; da Silva *et al*., 2018). Even more, addicted smokers demand teeth bleaching while undergoing the addiction treatment using nicotine lozenge. The aim of this study was to evaluate the effect of nicotine lozenge on teeth staining with and without bleaching in animal model study.

In this study, all the animal were kept in an acrylic container, in contact with cigarette smoke, for two months simulating the related methodology in the literature (César-Neto *et al*., 2003; de Geus *et al*., 2018) where it was observed that this method allows the deposition of nicotine on the external surface of the enamel promoting extrinsic pigmentation.

Hydrogen peroxide 35 % was indicated for teeth bleaching because of coffee, cola-based soft drink, wine, beetroot and tobacco staining using the in-office technique (Silva *et al*., 2013), as well, carbamide oxide 10 % applied in a tray and worn by the patient overnight for at least 2 weeks in what so-called at-home bleaching technique (Meireles *et al*., 2012).

The effectivity of the association of in-office and at-home bleaching technique in reducing the teeth discoloration cannot be overemphasized (Rezende *et al*., 2016). In this study, it was noticed in group 1 that this association was effective in reducing the discoloration, and this effectivity remains stable after 2 months of application (Table II). In a clinical study, it was observed that only the at-home bleaching was effective in removing extrinsic stains from diet and cigarette smoke in smokers patients (de Geus *et al*., 2015). However, a more recent study reenforce the use of in-office bleaching using 35 % hydrogen peroxide to achieve a more efficient removal of nicotine staining (de Geus *et al*., 2018). These results are affected by the bleaching agent, concentration, exposure time, sessions number and activation method (Torres *et al*., 2013; Kwon & Wertz, 2015; Joiner & Luo, 2017; Torres *et al*., 2019; Memari Trava *et al*., 2020).

To the best of our knowledge, there are no studies in the literature evaluating the effect of nicotine lozenge usage over the teeth staining. Nicotine lozenges and gums, often used to aid in the treatment of smoking addiction, are dissolved in the mouth and remains in contact with the teeth and the surrounding

tissue (Whelton *et al*., 2012). In the present study, it was found that the application of nicotine lozenge without any bleaching agent resulted in decreasing teeth staining as in group 3 (Table II). in the literature, it was found that nicotine gum and lozenge promotes teeth lighting by different degrees with a greater efficacy by the nicotine gum in a clinical study (Whelton *et al*., 2012), and in an in vitro study using bovine teeth, similar results were found (Moore *et al*., 2008).

In the present study, it was found also that the association of in-office and at-home bleaching in addition to lozenge consumption as in group 2 is effective in reducing discoloration saturation after 1 and 2 months . Thus, it may be indicated theassociation of both techniques for teeth bleaching during the cigarette's addiction treatment using nicotine lozenge.

CONCLUSIONS

· Teeth bleaching by in-office and at-home techniques is effective during cigarette's addiction treatment.

· The usage of nicotine lozenge promotes teeth lighting with and without bleaching.

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RESUMEN: El objetivo de este estudio fue evaluar el efecto de comprimidos de nicotina sobre la tinción de los dientes con/sin blanqueamiento en un estudio de modelo animal. Un total de 15 ratas Wistar fueron expuestas en un recipiente acrílico al humo de 10 cigarrillos tres veces al día durante 8 minutos por vez, y sacrificadas después de 60 días. Se trataron un total de 30 dientes incisivos (n=10) de la siguiente manera: Grupo-1: blanqueamiento en consultorio, blanqueamiento en casa e inmersión en saliva artificial; grupo-2: blanqueamiento en consultorio, blanqueamiento en casa e inmersión en solución de comprimidos de nicotina y en saliva artificial; grupo-3: inmersión en solución de nicotina en comprimidos y en artificial. Los especímenes de todos los grupos fueron fotografiados utilizando un microscopio estereoscópico en T1) inmediatamente después de la extracción y antes de cualquier tratamiento; T2) después de un mes del tratamiento; y T3) a los dos meses del tratamiento. Se analizaron cuatro puntos equidistantes de cada espécimen utilizando la guía de colores CMYK. Los datos se analizaron con la prueba ANOVA unidireccional seguida de la prueba de Tukey para comparaciones múltiples con ($a \leq 0,05$). En el grupo 1, hubo una diferencia significativa de la saturación de color de las muestras entre T1 y T2, y entre las lecturas T1 y T3 ($P<0,0001$). En el grupo 2, hubo una diferencia significativa de la saturación de color de las muestras entre T1 y T2, entre las lecturas de T2 y T3 ($P<0.0001$). En el grupo 3, hubo unadiferencia significativa de la saturación de color de las muestras entre T1 y T2, y entre las lecturas T1 y T3 ($P<0,0001$). El uso de comprimidos de nicotina promueve la iluminación de los dientes con/sin blanqueamiento.

PALABRAS CLAVE: comprimidos de nicotina, blanqueamiento dental, adicción a la nicotina.

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