The adjuvant effect of a mouthwash containing green tea and hyaluronic acid on the peri-implant parameters: a pilot short-term clinical evaluation

Efeito do uso adjunto de um colutório contendo chá verde e ácido hialurônico sobre parâmetros clínicos peri-implantares: estudo piloto de acompanhamento curto

Efecto del uso adjunto de un enjuague bucal que contiene té verde y ácido hialurónico sobre los parámetros clínicos periimplantarios: estudio piloto a corto plazo

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ABSTRACT

The aim of this pilot study was to evaluate the adjuvant effect of a mouthwash containing green tea and hyaluronic acid on the peri-implant clinical parameters in full arch implant-supported fixed prosthesis users. Eleven patients with a total of 75 implants that supported 6 lower total fixed prostheses and 7 upper total fixed prostheses agreed to participate in this short-term pilot study. Patients were submitted to clinical analysis of the implants at baseline and 10 days after initial product use. The probing depth, level of the peri-implant mucosa, clinical attachment level, peri-implant mucosa inflammation index and visible plaque index in each of the 6 sites were evaluated. To perform these analyses all, the prostheses were unscrewed during both intervention points. In general, the newly-developed mouthwash was shown to be safe to use with no signs of negative side effects. Additionally, biofilm and inflammation index were both reduced, with changes in the peri-implant mucosa marginal level due to inflammation reduction. It can be concluded that the mouthwash containing green tea and hyaluronic acid successfully reduced biofilm accumulation and inflammation around dental implants in full arch implant-supported fixed prosthesis safely in a short-term evaluation period.

KEYWORDS: Dental implants. Oral hygiene. Hyalutonic acid.

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RESUMO

O objetivo deste estudo piloto foi avaliar o efeito adjuvante de um colutório contendo chá verde e ácido hialurônico nos parâmetros clínicos peri-implantares em usuários de próteses fixas implantossuportadas de arcada completa. Onze pacientes com um total de 75 implantes que suportavam 6 próteses fixas totais inferiores e 7 próteses fixas totais superiores concordaram em participar neste estudo piloto de curto prazo. Os pacientes foram submetidos à análise clínica dos implantes no início do estudo e 10 dias após o uso inicial do produto. A profundidade de sondagem, nível da mucosa peri-implantar, nível de inserção clínica, índice de inflamação da mucosa peri-implantar e índice de placa visível foram avaliados em 6 sítios ao redor de todos os implantes. Para realizar essas análises, todas as próteses foram desenroscadas durante os dois períodos de intervenção. Em geral, o colutório recém-desenvolvido mostrou-se seguro para uso, sem sinais de efeitos colaterais negativos. Além disso, o biofilme e o índice de inflamação foram reduzidos, com alterações no nível marginal da mucosa peri-implantar devido à redução da inflamação. Pode-se concluir que o colutório contendo chá verde e ácido hialurônico reduziu com sucesso o acúmulo de biofilme e a inflamação ao redor dos implantes dentários em próteses fixas implantossuportadas de arcada completa com segurança em um período de avaliação de curto prazo.

PALAVRAS-CHAVE: Implantes dentários. Higiene bucal. Ácido hialurônico.

RESUMEN

El objetivo de este estudio piloto fue evaluar el efecto adyuvante de un enjuague bucal que contiene té verde y ácido hialurónico sobre los parámetros clínicos periimplantarios en usuarios de prótesis fijas implantadas con arco completo. Once pacientes con un total de 75 implantes que soportaban 6 prótesis totales fijas inferiores y 7 prótesis totales fijas superiores aceptaron participar en este estudio piloto a corto plazo. Los pacientes fueron sometidos a un análisis clínico de los implantes al inicio del estudio y 10 días después del uso inicial del producto. La profundidad de sondaje, el nivel de la mucosa periimplantaria, el nivel de inserción clínica, el índice de inflamación de la mucosa periimplantaria y el índice de placa visible se evaluaron en 6 sitios alrededor de todos los implantes. Para realizar estos análisis, se desenroscaron todas las prótesis durante los dos periodos de intervención. En general, el enjuague bucal desarrollado recientemente demostró ser seguro de usar, sin signos de efectos secundarios negativos. Además, se redujo el biofilm y el índice de inflamación, con cambios en el nivel marginal de la mucosa periimplantaria debido a la reducción de la inflamación. Se puede concluir que el enjuague bucal que contiene té verde y ácido hialurónico redujo con éxito la acumulación de biopelícula y la inflamación alrededor de los implantes dentales en prótesis fijas sobre implantes con arco completo en un período de evaluación a corto plazo.

PALABRAS CLAVE: Implantes dentales. Higiene bucal. Ácido hialurônico.

INTRODUCTION

Oral rehabilitation with prostheses supported by osseointegrated implants has been increasingly applied for treatment of all types of edentulism[1]. However, cleaning the oral cavity poses a significant challenge for patients, such that chemical control of the biofilm is an indispensable condition for maintaining peri-implant health[2], especially in elderly patients who are impaired by limitations in their ability to access regions below the full arch implant-supported prostheses[3-4]. For these patients it is necessary to complement their biofilm control with easier-to-dissipate agents, such as mouthwash[5].

Most of the range of chemical agents used by patients traditionally have fluorides or chlorhexidine when used as mouthwashes[6-7]. Both compounds have shown their efficiency in controlling gingival inflammation[6-8]. However, fluorides have been shown to alter titanium surfaces, which can generate negative repercussions on the components used for rehabilitation (Implants and abutments)[9]. Besides that, chlorhexidine can cause side effects such as changes in palate and pigmentations in restorations and teeth, which affects patient compliance with the use of these products[6-7].

From this perspective, the search for alternative chemical agents for cleaning implant-supported prostheses that do not interfere with the chemical stability of the components used in implant-supported rehabilitation is necessary. The use of herbal medicines as active agents to control gingival inflammation and the reduction of oral biofilm has been applied with positive clinical outcomes[10-13]. In this context, the use of a compound based on green tea deserves notice, since it has shown to be highly biocompatible[14], with good potential for biofilm control[12,14] and inflammation reduction[10] in patients with gingivitis.

In addition to the use of herbal medicines, another alternative for stimulating repair processes associated with inflammation reduction can be carried out through the use of bioactive substances such as hyaluronic acid. It has recently been shown that hyaluronic acid has the potential to be used in the treatment of inflammatory conditions by promoting healing and the repair process during the treatment of periodontal disease[15] and in the treatment of ulcers in the oral cavity[16], which may occur due to its bacteriostatic, anti-inflammatory, and antioxidant effects[17].

Thus, the aim of this pilot study is to clinically evaluate the short-term safety, antibiofilm, and anti-inflammatory adjuvant effects of a new mouthwash containing green tea and hyaluronic acid in patients with full arch dental implant-supported fixed prosthesis.

MATERIAL AND METHODS

General Procedures, Eligible Criteria, and Pilot Design

This study was approved by the ethical committee of the Federal University of Uberlândia under the protocol number 549.913. All the patients read and sign the informed consent term. In this pilot study, a new mouthwash containing green tea and hyaluronic acid (New Dental Care, São Paulo, Brazil) was tested in patients with full arch implant-supported fixed prosthesis. Eleven patients were evaluated before and after 10 days of the professional biofilm control consisting of the removal of the screwed prosthesis, the execution of the peri-implants analysis, and scaling and polishing of the implants and prosthesis. All these patients experienced a gap of more than one year since their last maintenance visit, and all of them were diagnosed with mucositis. All the patients were instructed regarding the oral hygiene procedure and product use during the entire experimental procedure. The patients were also instructed to use 10 ml of the mouthwash 3 times every day after the oral hygiene procedure.

The inclusion criteria for the patients in this pilot study were: having dental implants undergoing total rehabilitation with permanent prosthesis installed for at least 12 months, within the age range of 18 to 60 years, and systemically healthy. Smoking, decompensated diabetics and history of radiotherapy or chemotherapy were exclusion criteria.

Mouthwash Formulation

The new dental care (NDC) mouthwash tested in this pilot study had the following chemical composition: glycerin, sodium benzoate, xylitol, glucoside lauryl, sodium lauryl sulfate, hyaluronic acid, polyvinylpyrrolidone K 30, salicylate dimethylsilanediol (DSBC), green tea extract (camellia sinensis), tetrashodic pyrophosphate, ricin hydrogenate oil, saccharin, EDTA, mint aroma, blue dye CI42090, yellow dye CI 19140, purified water.

Clinical Evaluation

Six sites per implant (mesio-buccal, buccal, disto-buccal, mesio-palatine-lingual, palatine/lingual, disto-palatine/lingual) were analyzed, before and after 10 days of the professional biofilm control and NDC mouthwash use. The following clinical parameters were evaluated: 1) probing depth (PB) - distance from the peri-implant margin to the bottom of the peri-implant sulcus/pocket; 2) peri-implant mucosa marginal level (PML) - distance from the peri-im-

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plant mucosa margin to the bottom of the peri-implant sulcus/pocket; 3) clinical attachment level (CAL) - distance from the implant platform to the bottom of the peri-implant sulcus/pocket; 4) inflammation index (II)[18] - Score 0 = absence of inflammation; Score 1 = mild inflammation - slight color change in the gingival margin associated with a small change in soft tissue texture; Score 2 = moderate inflammation - marginal soft tissue with an aspect of vitrification, redness, edema and hypertrophy; Score 3 = severe inflammation - abundant redness or hypertrophy associated with spontaneous bleeding; 5) biofilm index (BI)[19]: Score 0 = absence of biofilm; Score 1 = biofilm detected only by probing; Score 2 = moderate presence of visible biofilm; Score 3 = abundant presence of visible biofilm or formation of dental calculus.

Statistical Analysis

All the data followed a normal distribution. Then, a paired t-test was used to compare the initial and final values of the clinical attachment level, gingival/mucosal marginal level, probing depth, inflammation and biofilm index. A 5% ($p < 0.05$) significance level was used for all comparisons. The software GraphPad Prism 6 (San Diego, CA, USA) was used to perform the statistical analysis.

RESULTS

The 11 patients with full arch implant-supported fixed prosthesis presented a total of 75 implants, 6 mandibular total fixed prosthesis and 7 maxillary total fixed prosthesis. Two patients showed CAL higher than 3 mm (patients 5 and 9) at the baseline. After treatment, all patients demonstrated a reduction in the BI and II, with the exception of patient number 10. In general, use of the NDC mouthwash was associated with the reduction of the BI and II, and an increase in the PML and CAL. Tables 1 and 2 show the peri-implant parameters at the baseline and after 10 days of NDC mouthwash use. Table 3 shows the mean and standard deviation of the peri-implant parameters at baseline and after 10 days of NDC mouthwash use. There were statistically significant differences ($p < 0.05$) between the baseline and 10-day mark for BI (10 Days = 0.79 ± 0.50, Baseline = 1.74 ± 0.77), II (10 Days = 0.56 ± 0.39, Baseline = 1.46 ± 0.80), CAL (10 Days = 2.29 ± 1.28, Baseline = 2.09 ± 1.22) and (10 Days = 0.65 ± 0.80, Baseline = 0.50 ± 0.85). The Figure 1 shows the clinical aspect before and after 10 days of the use of the mouthwashes.

Table 1 - Baseline parameters of the patients that used the mouthwash.

Patient	Number of Implants	Location	PB	PML	CAL	BI	II
1	5	Mandible	1.36	1.96	3.33	3.00	2.20
2	4	Maxilla	0.79	0.00	0.79	1.20	0.54
3	5	Mandible	1.20	0.60	1.80	1.20	0.30
4	8	Maxilla	1.72	-0.77	0.95	0.97	1.81
5	7	Maxilla	2.66	1.73	4.40	2.02	2.45
6	12	Mandible/Maxilla	0.87	-0.30	0.59	0.41	0.29
7	11	Mandible/Maxilla	2.71	0.19	2.90	2.31	2.45
8	7	Maxilla	1.85	0.52	2.30	2.76	1.80
9	4	Mandible	1.70	1.41	3.12	1.75	1.70
10	4	Mandible	1.29	0.25	1.54	1.79	1.04
11	8	Maxilla	1.27	0.00	1.27	1.79	1.50

PB - probing depth (mm); PML - peri-implant mucosal level (mm); CAL - clinical attachment level (mm); BI - biofilm index; II - inflammation index.

Table 2 - Peri-implant parameters of the patients after 10 days of NDC mouthwash use.

| Patient	Number of Implants	Location	PB	PML	CAL	BI	II
1	5	Mandible	1.30	2.10	3.40	0.66	0.13
2	4	Maxilla	0.65	0.00	0.65	0.29	0.12
3	5	Mandible	1.26	0.68	1.94	0.56	0.93
4	8	Maxilla	1.72	-0.14	1.58	0.43	0.64
5	7	Maxilla	2.87	1.81	4.68	1.14	1.14
6	12	Mandible/Maxilla	0.81	-0.09	0.72	0.00	0.00
7	11	Mandible/Maxilla	2.87	0.28	3.15	1.06	0.93
8	7	Maxilla	2.04	0.60	2.64	0.59	0.42
9	4	Mandible	1.90	1.55	3.45	1.29	0.87
10	4	Mandible	1.50	0.40	1.90	1.79	0.79
11	8	Maxilla	1.15	0.00	1.15	0.95	0.27

PB - probing depth (mm); PML - peri-implant mucosal level (mm); CAL - clinical attachment level (mm); BI - biofilm index; II - inflammation index.

Table 3 - Mean and standard deviation of the peri-implant parameters at baseline and after 10 days of NDC mouthwash use.

Parameter/Period	Baseline	After 10 days
PB	1.58 ± 0.63	1.64 ± 0.73
PML	0.50 ± 0.85	0.65 ± 0.80*
CAL	2.09 ± 1.22	2.29 ± 1.28*
BI	1.74 ± 0.77	0.79 ± 0.50#
II	1.46 ± 0.80	0.56 ± 0.39#

PB - probing depth (mm); PML - peri-implant mucosal level (mm); CAL - clinical attachment level (mm); BI - biofilm index; II - inflammation index.
*Higher values than the baseline; # Lower values than the baseline - Paired t-test ($p < 0.05$).
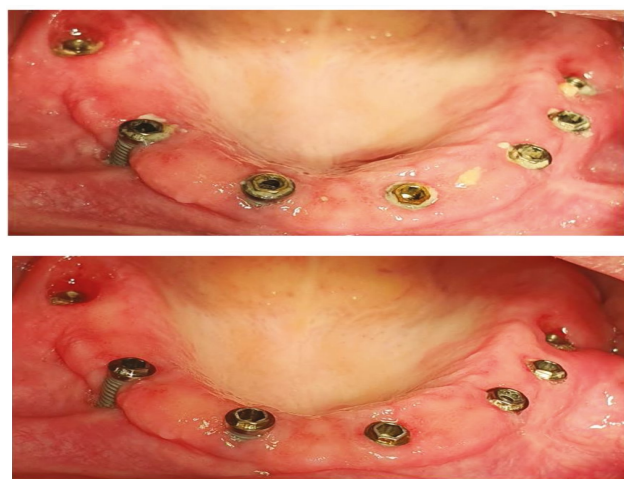
Figure 1 - Clinical aspect at the baseline and after the use of the mouthwashes for 10 days.

DISCUSSION

In general, the results of this pilot study have shown that the use of a mouthwash containing green tea and hyaluronic acid, as an adjuvant treatment, was associated with a reduction in the amount of biofilm and inflammation in patients using full arch implant-supported fixed prosthesis. These results indicate that use of this agent as a clinical option for chemical control of bacterial biofilm is promising in this population.

Full arch implant-supported fixed prosthesis users normally previously presented conditions of total tooth loss for a considerable time and are previous users of removable total or partial prosthesis[20-21]. The oral hygiene procedure becomes substantially more complex when these patients receive a fixed prosthesis into the oral cavity[22], as was easily noted in the patients of this pilot study. In fact, oral hygiene was considered poor in 9 of the 11 patients, since they presented an average of biofilm index above 1 in the baseline period, which clearly demonstrates the unmet need to improve the oral hygiene in this population.

The reduction of the amount of biofilm and inflammation was associated with a 10% increase in the clinical attachment level, associated with the apical migration of the peri-implant mucosa margin, as expected given that the inflammation reduction is associated with hyperplasic tissue[23] retraction. The active agents of the mouthwash used in this study may have influenced the occurrence of these effects: these findings are in accordance with a clinical study which showed that the use of a green tea-based toothpaste reduced inflammation and loss of clinical attachment after treatment of periodontal disease, and this effect was associated with an anti-oxidant effect of the substance[24]. Additionally, it was found that green tea reduced the expression of pro-inflammatory cytokines in LPS-stimulated keratinocyte cultures[25]. Furthermore, the use of hyaluronic acid as a chemical agent present in mouthwashes has shown that this product decreases inflammation in patients with gingivitis[26], and this effect may explain the findings of an in vitro study, which demonstrated that hyaluronic acid reduced the expression of proinflammatory cytokines in fibroblast cultures stimulated by P.gingivalis by suppressing the MAPK and NF-κB signaling pathways[27].

It is important to note that no side or adverse effects, such as the changes in palate or pigmentations in restorations and teeth commonly seen with the use of chlorhexidine mouthwashes[7] were reported by the patients. The NDC mouthwash was well tolerated by the subjects, and did not cause any undesirable reaction in the oral cavity tissues, corroborating the product safety. Furthermore, some patients related that the use of the NDC was pleasant associated with a good taste. However, this impression was subjective and require more information´s in future.

This study has some drawbacks that must be taken into account when interpreting our data. This is a pilot study with limited sample size, absence of a control group, and short follow-up time. These characteristics obviously generate a large number of biases and effects that may have interfered with the results obtained. In addition, the fact that patients underwent professional biofilm control certainly influenced the findings of the biofilm and inflammation scores. In the future, a randomized controlled clinical trial with a larger sample size and longer follow-up evaluations should be performed to assess the real effect of the use of this mouthwash on maintaining peri-implant health. However, the encouraging outcome of this study, as well as the safety and absence of side effects, showed that the mouthwash with green tea and hyaluronic acid has a potential to be an alternative in maintaining the health of soft tissue around dental implants.

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CONCLUSION

According to the results of this short-term clinical study, it can be concluded that the use of the NDC mouthwash with green tea and hyaluronic acid demonstrated promising results as an adjuvant treatment of mucositis and for health maintenance of the soft tissue around dental implants, promoting reduction of the biofilm and inflammation index with no signs of undesirable side effects.

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