Assessment of adherence to preventive treatment of plaque-induced oral diseases using sugar-free gums: a controlled clinical trial[1]

Evaluación de la adhesión al tratamiento preventivo de enfermedades bucales inducidas por placa bacteriana mediante el uso de gomas de mascar sin azúcar: ensayo clínico controlado[1]

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Abstract

Keywords: tooth decay, chewing gum, cariostatic agents, adherence to treatment, public health

Introduction: the aim of this study was to assess the adherence to a preventive treatment of plaque-induced oral diseases using two sugar-free gums, establishing their effect on cariogenic bacteria counts as a biological marker of treatment response. ***Methods:*** a double-blind, randomized, parallel-group, controlled intervention study was conducted in 96 young adult university students in an experimental period of 30 days. Participants were distributed into two groups and given a chewing gum with either pentitol or hexitol + CPP-ACP complex to be taken three times a day for 20 minutes after conventional oral hygiene. Saliva samples were collected at baseline to evaluate counts of *Streptococcus mutans* (SM) and *Lactobacillus* spp. A survey was conducted at the end of the experimental period to assess the levels of adherence to treatment, remeasuring bacterial counts. ***Results:*** SM counts showed statistically significant differences between the study groups at the end of the experimental period, with a decreasing tendency in both groups. Intragroup difference was observed in patients who took pentitol gum with a marked reduction in SM counts. ***Conclusion:*** the final estimate of adherence to treatment showed that the type of chewing gum patients were given had no influence and therefore such gums can be used, considering the therapeutic agents that most contribute to patient's particular case and preferences.

Resumen

Palabras clave: caries dental, gomas de mascar, agentes cariost ticos, adherencia al tratamiento, salud p blica

Introducci n: el objetivo consisti en evaluar la adherencia a un tratamiento preventivo de enfermedades bucales inducidas por placa bacteriana, utilizando dos gomas de mascar sin az car y establecer su efecto sobre recuentos de bacterias cariog nicas como indicador biol gico de los efectos del tratamiento. ***M todos:*** se realiz un estudio de intervenci n, doble ciego, de grupos paralelos, aleatorizado controlado, en 96 adultos j venes universitarios, en un per odo experimental de 30 d as. Los participantes fueron distribuidos en dos grupos con asignaci n de una goma de mascar con pentitol o con hexitol + complejo CPP-ACP que deb an ser consumidas 20 minutos/tres veces al d a despu s de la higiene oral convencional. Al inicio del estudio fueron recolectadas muestras de saliva para evaluar recuentos de *Estreptococos* del grupo mutans (SM) y *Lactobacillus* spp. Al finalizar el per odo experimental, se realiz una encuesta para evaluar los niveles de adherencia al tratamiento y los recuentos bacterianos fueron medidos nuevamente. ***Resultados:*** Los recuentos de SM mostraron diferencias estad sticamente significativas entre los grupos de estudio al final del per odo experimental, con tendencia hacia la disminuci n en ambos grupos. Se observ diferencia intragrupo en los pacientes que consumieron la goma de mascar con pentitol, con marcada reducci n de los recuentos de SM. ***Conclusi n:*** la estimaci n final de la adherencia al tratamiento mostr que el tipo de goma de mascar asignada al paciente no tuvo influencia y, por lo tanto, estas pueden ser utilizadas teniendo en cuenta los agentes terap uticos que m s aporten al caso particular del paciente y las preferencias del mismo.

INTRODUCTION

Dental caries and gingivitis are significant oral health problems associated with the presence of bacterial biofilm.[1] The incidence of these diseases remains high among the population,[2] with the dental profession devoted to implementing intervention and prevention measures such as brushing, flossing, fluoride rinses, and toothpastes. Chewing gums with sugar substitutes have been part of these measures, as the stimulation of salivary secretion produced by mastication improves the mechanical cleansing of bacterial plaque and can increase pH levels and saliva buffering capacity.[3]

The chewing gums used for prevention contain mixtures of sweeteners instead of common sugar (sucrose), including polyalcohols like hexitol (mannitol) and pentitol (xylitol). Xylitol has proven to interfere with the process of dental caries,[4] and has therefore been used in preventive programs aimed at preschool and school children, seeking to decrease vertical transmission of microorganisms or to reduce their counts and thus the risk of tooth decay.[5]

A histological study found out that the use of mannitol and sorbitol in chewing gum can contribute to the remineralization of the surface of teeth with white spot lesions.[4] Overall, the use of sugar-free gum may reduce the rates of bacterial plaque, *Streptococcus mutans* (SM) and *Lactobacillus* spp. counts in both plaque and saliva, suggesting that their regular use (especially those sweetened with xylitol) may reduce the risk of dental caries —even in patients undergoing orthodontic treatment—, common among children, adolescents and young adults.[6]

More recently, the CPP-ACP nanocomplex (casein phosphopeptide amorphous calcium-phosphate) has been added to chewing gums. Morgan et al in 2008 have found that this component has an anti-cariogenic effect by decreasing bacterial plaque and can help re-mineralize the surface of white spot lesions in radiographic follow-ups.[7]

Regardless of the active ingredients added to chewing gums, their use as a preventive strategy require patient engagement, monitoring frequency and chewing time indications. This collaboration is known as adherence to treatment and is defined by the World Health Organization (WHO) as the extent with which patients follow medical instructions,[8,9] which implies their collaboration with the health care plan and incorporates beliefs and attitudes as factors reflected in the outcomes of therapy.[10]

So far, no method of evaluating adherence to treatment is considered fully reliable, and therefore combinations can be used for better evaluation, taking into account the variables that can directly or indirectly influence compliance, such as complexity of medical instructions, treatment's side effects, length and costs, patient-practitioner interaction, and patient education level.[11]

Treatments that require the patient to discontinue habits or develop new behaviors entail lifestyle changes and therefore have higher rates of non-adhesion.[8,9] It is well known that one of the foundations for maintaining and improving oral health is the monitoring of preventive measures, but achieving this is challenging. The available literature on compliance with preventive measures is scarce and the existing evaluations show limited follow-up of routines that require the use of conventional tools such as brushing, flossing and fluorinated products, even when clear and precise instructions are given—as practitioners claim—to remember the importance of following such measures.

This study analyzes the effect of two chewing gums added with different therapeutic components on salivary counts of *Streptococcus mutans* (SM) and *Lactobacillus spp.*, evaluating the participants' compliance with the instructions given, in order to determine the effect on treatment and to establish whether the provided gum produced any difference in treatment adherence.

METHODS

The study complied with the ethical guidelines of the Helsinki Declaration and was evaluated and approved by the Institutional Ethics Committee of the Universidad de Antioquia School of Dentistry (24th June-2010). In addition, this project was registered on the website clinical trials.gov with number NCT01578603.

To determine adherence to the preventive treatment of oral diseases by using chewing gum with sugar substitutes, a double-blind, parallel-group, controlled, randomized intervention study was conducted in a sample of 96 young adult students from the Universidad de Antioquia School of Dentistry at Medell n (Colombia), with an experimental period of 30 days, previously published by Mart nez-Pab n et al.[12]

Sample size was calculated based on an earlier study related to the effect of chewing gums on oral health.[13] There was an increase of 10% to keep estimates at an optimal level of accuracy (5%), avoiding the possible effect of sample size reduction due to exclusions and dropouts.

Subjects with at least 22 teeth and overall good health were included. The exclusion criteria were as follows: the presence of systemic disease as stated in the medical history,

orthodontic appliances, chronic inflammatory disorders of the skin and oral mucosa, any systemic conditions that could affect the dental and periodontal status, chronic use of antibiotics, antiseptic mouthwashes and medications that could affect salivary flow, prior maxillofacial exposure to radiation, and temporomandibular joint disorders.

Assessment of the presence of tooth decay was performed using the ICDAS diagnostic system,[14] in order to make a homogeneous distribution of patients with cavitated caries in the study groups.

Participants were randomly distributed into two study groups: 1 (pentitol-sweetened gum) and 2 (hexitol-sweetened chewing gum added with CPP-ACP complex), masking the gum that each group was given (pellets of same color and size). Similarly, the study objective and potential risks were clearly explained, obtaining the participants' informed consent.

All patients were given oral hygiene instructions, and each was provided with a kit containing 1,500 ppm fluoride toothpaste, brush and floss, all of the same characteristics. They personally received the same instructions regarding the consumption of chewing gums: take 2 chewing gum pellets for 20 minutes three times a day (morning, noon and evening) after conventional oral hygiene (brushing with 1,500 ppm fluoride toothpaste three times a day and flossing once a day).

Bacterial counts of *Streptococcus mutans* (SM) and *Lactobacillus spp.* were done before and after the intervention. Each participant's saliva sample was collected, measuring saliva flow rate, pH levels and buffer capacity in a standardized manner. The microbiological analysis was conducted at the Laboratory of Microbiology of the Universidad de

Antioquia School of Dentistry, after ten-fold serial dilutions, inoculating 100 µL in mitis-salivarius agar to detect SM and rogosa agar for *Lactobacillus spp.* The agar plates were incubated in anaerobiosis with 5% CO_2 for two days at 37 °C. After incubation, the plates were observed with a stereomicroscope (Carl Zeiss, Oberkochen, Germany) to detect the colonies of SM and *Lactobacillus spp.*, reporting the amount found as Colony Forming Units (CFUs) per mL of saliva.

Participants were asked not to make additional dietary changes, receive no dental prophylaxis, and avoid any oral hygiene adjuvants or commercial chewing gums other than those provided by the researchers during the 30-day trial period.

At the end of the intervention period, a survey was conducted to assess treatment adherence levels, using a test modification validated by Morisky-Green-Levine[15] to assess adherence to drug use for chronic diseases. This test assesses patient's attitudes towards therapy. It includes four questions that explore patient's full compliance with the therapeutic instructions given by the practitioner, alternating with questions not directly related to treatment. In this survey, the first two questions seek to defocus patient's attention and the next questions assess treatment adherence levels.[15]

The responses were analyzed in order to identify the potential difficulties that prevented individuals from adhering to treatment as instructed. By adapting the Morisky-Green-Levine test,[15] the following variables were considered:

1. Consumption of other chewing gums different from those provided

2. Difficulties in chewing the gums provided

3. Compliance with consumption at the indicated times

4. Suspension of the use of chewing gums because they made participants sick

Based on these variables, three levels of adherence were established: compliant, semi-compliant and non-compliant. A patient who responded to variables 1, 2 and 4 negatively and to variable 3 affirmatively was considered compliant. One who answered two to three of the questions as expected was considered semi-compliant, and one who only answered one or none of the questions as expected was considered as non-compliant.

The Statistical Package for Social Sciences (SPSS®, Chicago Inc. v. 19) was used for descriptive and inferential statistical analysis. Quantitative variables are given in averages and standard deviations, and qualitative variables in percentages. Demographic and microbiological variables are related to the level of adhesion, assuming a statistical significance lower than 5%.

RESULTS

To assess adherence to preventive treatment using chewing gum, a sample of 96 students from the Universidad de Antioquia School of Dentistry was evaluated, distributing it into two groups according to the chewing gum provided.

The study groups' demographic characteristics are shown in Table 1. It was identified that the groups are comparable in gender distribution, but age distribution showed a statistically significant difference, which can be explained because of sample randomization but does not prevent the outcome variables comparison between both groups before and after the intervention.

Table 1. Sociodemographic conditions of the study population

Variable	Group 1 (pentitol) n=48	Group 2 (hexitol + CPP-ACP) n=48	Total n=96	p^∞
Age (actual years) (average and SD)	20.9 (19-22)	19.4 (18-20)	X = 20.15	<0.01¥
Sex (N° and %)	M: 14 F: 34	M: 16 F: 32	M: 30 F: 66	>0.01∞

¥ Test of homogeneity of variance
∞ Pearson's Chi²
Source: by the authors

The comparison of initial counts of SM showed statistically significant differences between the study groups, while the *Lactobacillus spp* counts between the groups were similar in the initial test.

The comparison before and after inter-group intervention showed statistically significant differences in SM counts with a decreasing tendency; however, this decrease was more marked in group 1 (pentitol), reaching an average 1.5E+1 CFU/mL, corresponding to 99.9% less SM compared to the initial bacterial load. In the initial evaluation, there were 6 subjects with negative SM counts, while after the intervention 31 had negative counts in both groups.

The *Lactobacillus* spp. counts did not show intra- or intergroup statistically significant differences, perhaps because 33 subjects of the total sample had negative counts at baseline. At the second moment of evaluation, the number of individuals with negative counts increased to 40, so the intervention did not achieve a statistically significant reduction on already low counts (Table 2).

Table 2. Inter- and intra-group comparison of average microbiological counts through the study period

Parameter	Group 1 (Pentitol) (n=48)	Group 2 (Hexitol/CPP-ACP) (n=48)	p value¥
SM Counts (UFC/mL)			
Baseline (average) (SD)	3.0E+7 (6.0E+6 − 1.0E+8)	2.0E+7 (4.0E+6 − 5.0E+7)	,000
Final (average) (SD)	1.5E+1 (0.0E+0 − 3.3E+5)	1.0E+7 (2.3E+6 − 2.0E+8)	,000
p value£	,004	,005	
Lactobacillus spp count (UFC/mL)			
Baseline (average) (SD)	3.0E+1 (0.0E+0 − 2.5E+4)	1.1E+2 (0.0E+0 − 1.2E+5)	>0.05
Final (average) (SD)	3.0E+1 (0.0E+0 − 8.0E+2)	2.5E+1 (0.0E+0 − 1.4E+3)	>0.05
p value£	,735	,582	

¥ Levene's test for equality of variances
£ t-test for equality of means
Source: by the authors

Table 3 shows the results of the modified Morisky-Green-Levine test used for the evaluation of adherence to chewing gum treatment and the follow-up to the specific instructions participants were given. The final estimate of treatment adhesion levels showed that there are no statistically significant differences between the study groups and that the most common level among participants was medium compliance in the group that used chewing gum with pentitol and good compliance in the group that used chewing gum with hexitol (41.6%) (Table 4).

Table 3. Comparison of the modified Morisky-Green-Levine test results among study groups

Test questions to evaluate adherence to treatment		*Study group*		*p*-value
		Group 1 (Pentitol) n = 48	Group 2 (Hexitol/CPP-ACP) n = 48	
There were difficulties in taking the chewing gums[a]	Yes	29 (60.4%)	21 (43.7%)	0.117[¥]
	No	19 (39.6%)	27 (56.3%)	
You were able to meet the hours indicated for chewing[a]	Yes	45 (93.7%)	41 (85.4%)	0.18[¥]
	No	3 (6.3%)	7 (19.6%)	
You had to stop using the chewing gums because they made you sick[a]	Yes	8 (6.7%)	8 (6.7%)	1.0[¥]
	No	40 (83.3%)	40 (83.3%)	
You used other chewing gums[a]	Yes	19 (39.5%)	21 (43.7%)	0.18[¥]
	No	29 (60.5%)	27 (56.3%)	

[a] Values given in n (%) of subjects
[¥] Pearson's Chi^2
Source: by the authors

Table 4. Treatment adherence levels achieved by study participants

Study group	Compliance[b]			Total	*p*-value
	Compliant	Semi-compliant	Non-compliant		
Group 1 (Pentitol)	13 (27.1%)	25 (52.1%)	10 (20.8%)	48	>0.05[§]
Group 2 (Hexitol/CPP-ACP)	19 (39.5%)	15 (31.2%)	14 (29.2%)	48	>0.05[§]
Total	32 (33.3%)	40 (41.6%)	24 (25.0%)	96	
p-value	>0.05[§]	>0.05[§]	>0.05[§]		

b Values given in n (%) of subjects
[§] McNemar's Chi^2
Source: by the authors

DISCUSSION

Dental caries uses a significant part of the economic resources, not only in public health programs such as mass fluoride administration and preventive measures to reduce the high rates of dental caries among the population,[2] but also and mainly in the search of a cure. Efforts have been made to achieve a more effective control of risk factors, implementing complementary tools for regular oral care when teeth brushing is not enough to control bacterial plaque buildup.[16]

Chewing gums increase salivary secretion rate and sweep off bacterial plaque, an effect that can be used as an adjuvant of conventional oral hygiene,[3] with advantages in population groups such as patients with oral cancer, xerostomy, Sjogren's syndrome, Parkinson's

disease, menopause, smoking, use of some drugs (about 400 of them), alcoholism, diabetes Mellitus (type 1), radiation therapy, chemotherapy, and hypothyroidism.[17]

Sugar-free gums have been used as a vehicle to administer various substances for therapeutic purposes, including calcium, bicarbonate, carbamide, chlorhexidine, fluorine, xylitol, and the CPP-ACP complex.[3-7] It has been demonstrated that some of these substances have protective properties for the oral cavity, such as xylitol in the control of tooth decay; however, there is concern over the lack of consensus on recommendations for use, which modifies the dosage and perhaps the preventive effect.[18]

In this study, the comparison of *Lactobacillus* spp. counts did not show significant statistical differences between the study groups, perhaps because counts were very low at baseline and because of the high percentage of patients with negative counts both at baseline and at the end of the test. The opposite was for SM counts, as a significant statistical difference was found between the study groups at the end of the test, caused by a marked reduction in final counts in the group of patients who took pentitol-added chewing gums, in which there was a marked intragroup difference, with a surprising final average of just 15 CFU/mL in those who initially had an average of 30.000.000 CFU/mL.

Studies have shown that the use of sugar-free gums added with pentitol produce biochemical changes such as modification in oral pH, buffer capacity, salivary flow, and enamel remineralization,[3] as well as in counts of microorganisms involved in the development of carious lesions,[5] which exceeds the mechanical sweeping effect of the potential control of specific bacteria related to the onset of tooth decay.[19]

While chewing gums may have important effects in the composition and stimulation of salivary flow in the short term, they have not been found to influence the sustained increases in these parameters over time, hence the importance of continuous consumption if they are to be used as a preventive strategy of bacterial plaque-induced oral diseases; therefore, their proper use depends on the monitoring of the indications of chewing frequency and time.[8,10]

The absence of intragroup changes in those who used chewing gums with hexitol + CPP-ACP complex is similar to the findings of other studies, in which the main benefit was in terms of dental tissue remineralization,[7,20] rather than changes in microbiology or bacterial plaque.

The literature shows an inverse relationship between the behavioral changes needed to follow a treatment and the necessary patient's adherence for success. For example, treatments that require modifying old habits to adopt new beneficial behaviors require significant lifestyle changes, and therefore have higher rates of non-adherence than less demanding treatments.[8,9]

The consumption of chewing gums has been considered by some as an unhealthy habit; it can be classified as a parafunction and produces gastric discomfort in some samples studied; therefore, its use has been discouraged in many environments,[21] yet many other find it pleasant, making it easier for people to incorporate the consumption of such gums into their lives as a habit more easily than other therapies, which is why it has been used, for example, for tobacco cessation.[22]

It is necessary to find a balance between the patient's expectations, needs, and tastes and what the practitioner considers the

ideal treatment and needed education for a therapeutic strategy to be implemented.

In this study, adverse effects occurred in 8.0% of the participants of each group, with gastric discomfort being the most common problem. 52% of participants reported some difficulty in following the indicated treatment, citing reasons such as "because of my studies in the morning", "I forgot it at lunch", "I went on a trip and forgot the gums", "I had a virosis for a week" and "my stomach ached and I had a reflux." Of those who reported failure to meet the schedule for taking the chewing gums (n = 10), 2% did not report a reason for forgetting it.

Only 16.3% (n = 11) of participants took the chewing gums during the indicated time without forgetting it any day, meaning that the rest failed to take them at least 1 day because they forgot to. This is why the most frequent level of compliance among participants in both study groups was semi-compliance.

Treating systemic diseases requires a strict monitoring of medical recommendations for proper control, as lack of adhesion reduces the benefits of treatment, creates a bias in clinical evaluation in terms of treatment efficiency, and leads to the modification in the prescription of medicines.[23] In contrast, in a preventive treatment using chewing gums added with safe substances,[24] forgetting to take the gums in one month had no effects on the final treatment outcome (there were no significant statistical differences in bacterial count between compliant and semi-compliant patients) and therefore average compliance can be considered sufficient to achieve the sought benefits.

The common denominator of most interventions seeking to improve adherence to treatment is that patients should be encouraged to be active participants in their health care. It is therefore recommended for them to participate in treatment planning and definition of goals to be achieved so that their priorities, lifestyles, resources, and potential obstacles in treatment compliance can be considered.[10]

The thoughts, attitudes towards disease and treatment, motivation and ability to understand, memorize, and follow the instructions given are also decisive factors, and therefore practitioners must be prepared to constantly reinforce the information. Similarly, certain attitudes toward dental care, such as anxiety or fear, can have a negative impact on self-care. Professional-patient communication is particularly important; therefore, the dentist's attitude can affect the effectiveness of treatment, potentially contributing to greater adherence by listening to patients and giving clear instructions and recommendations.[25]

Despite lack of patient adherence being so common, it is not usually highlighted by health professionals, as there are limitations to understanding this phenomenon, such as knowledge of the factors that determine it.[26] While oblivion was the reason that many patients reported for not to fully comply with the instructions given to take the chewing gums, it should be highlighted that the patient's mind is not a blank board in which the practitioner can record prescriptions and indications. On the contrary, we should remember that there are psychological and social factors that operate in an extremely complex way in each patient to achieve compliance and follow-up of medical or dental indications, and failure to achieve full compliance suggests failure to produce changes in patient attitudes and behaviors.[27]

Treatment adherence decreases when the number of drugs and frequency of

administration increases, with the occurrence of adverse effects when treatment is prolonged. Interference with habits, either during work hours or at certain times in the patient's social life, leads to some of them not taking the medication or doing so at a different schedule than recommended.[28]

Achieving good treatment compliance is a challenge in medicine and dentistry, especially in children and youths.[25] Although this study included a controlled process of instructions to each patient to inform them of the conditions of treatment, not all of them adhered to the directions even in the relatively short therapy period (30 days). The study was aimed at a young population able to understand the detailed therapy instructions given by a professional responsible to comply with such measures. The modification of the Morinsky-Green-Levine test made it possible to identify that the chewing gum given to each group did not produce differences in the follow-up of the therapeutic instructions (Table 3), which is important when considering that the intensity of the sweetness of pentitol is different and this can lead to greater acceptance or rejection of the product.

Considering that pentitol sweetness is different, that there is no difference in the evaluation of treatment follow-up between the tested chewing gums, and the marked reduction in MS counts, the pentitol chewing gum is an adjuvant to be considered for the management of patients with special needs.

CONCLUSIONS

— The studies on the variables that may influence adherence to treatment should be expanded, in this case in the treatment of young people and patients with special needs, in order to strengthen the preventive programs and to offer alternatives to complement oral hygiene habits.

— The absence of differences in adherence to treatment between the used sugar-free gums suggests that therapists may choose the one whose components are most favorable to treatment and are more accepted by patients.

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CONFLICT OF INTEREST

The authors declare that during the implementation of this project or the drafting of the manuscript there was any interest other than the proper development of the research project. They also state that they have no relation with the commercial houses producing the chewing gums used. One of the authors (MCMP) is part of thematic coordinators of Revista Facultad de Odontolog a Universidad de Antioquia, but transparency in the editorial processing of the manuscript has been guaranteed since she did not participate in such process.

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