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Original Article

A double-blinded randomized clinical trial of pain perception during orthodontic treatment

Ensaio clínico randomizado duplo cego de percepção da dor durante tratamento ortodôntico

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Resumo

Introdução: A movimentação ortodôntica pode causar sintomatologia dolorosa, principalmente nas fases iniciais do tratamento. **Objetivo:** Este estudo teve como objetivo comparar o desempenho da goma de mascar e do ibuprofeno no controle da dor durante o período inicial do tratamento ortodôntico. **Material e método:** Foi desenvolvido um ensaio clínico randomizado cego, com razão de alocação de 1:1, com pacientes com idade ≥18 anos. O tamanho da amostra foi estabelecido considerando um nível de significância de 5% e poder do teste de 80%, resultando em um mínimo de 30 voluntários por grupo (n=90). Os participantes foram pareados quanto ao sexo, idade, gravidade da má oclusão, definida pelo Componente de Saúde Bucal (DHC) do Índice de Necessidade de Tratamento Ortodôntico (IOTN), e apinhamento, determinado pelo índice de irregularidade de Little. A amostra foi distribuída aleatoriamente em três grupos: Grupo I (controle) placebo; Goma de mascar Grupo II; e Grupo III Ibuprofeno. A percepção da dor foi avaliada pela Escala Visual Analógica (EVA) nas primeiras 24, 36 e 48 horas após a ativação do aparelho ortodôntico. Os dados foram analisados por modelos lineares generalizados para medidas repetidas no tempo. **Resultado:** Não foi observada diferença estatisticamente significativa (p>0.05) entre os grupos para os métodos de terapia da dor avaliados em 24, 36 e 48 horas pós-ativação. **Conclusão:** Não houve diferença entre o método utilizado para controle da dor durante o tratamento ortodôntico.

Descritores: Dor; aparelos ortodônticos fixos; analgésicos; RCT.

Abstract

Introduction: Orthodontic movement can cause painful symptoms, especially in the early stages of treatment. **Objective:** This study aimed to compare the performance of chewing gum and ibuprofen in pain control during the initial period of orthodontic treatment. **Material and method:** A randomized blind clinical trial, with an allocation ratio of 1:1, was developed with patients aged ≥18 years old. The sample size was established considering a significance level of 5% and test power of 80%, resulting in a minimum of 30 volunteers per group (n=90). Participants were paired regarding sex, age, the severity of malocclusion, defined by the Dental Health Component (DHC) of the Index of Orthodontic Treatment Need (IOTN), and crowding, determined by Little's irregularity index. The sample was randomly allocated to three groups: Group I (control) placebo; Group II chewing gum; and Group III Ibuprofen. Pain perception was evaluated by the Visual Analog Scale (VAS) in the first 24, 36, and 48 hours after activation of the orthodontic appliance. The data were analyzed by generalized linear models for repeated measures in time. **Result:** No statistically significant difference (p>0.05) was observed among the groups for the methods of pain therapy evaluated in 24, 36, and 48 hours post-activation. **Conclusion:** There was no difference among the method used for pain control during the orthodontic treatment.

Descriptors: Pain; fixed orthodontic appliances; analgesics; RCT.

INTRODUCTION

The tooth movement in orthodontic treatment may cause painful symptoms[1-3]. The level of pain reported varies from one individual to another and may be considered an important factor in discouraging patients from seeking orthodontic treatment[4]. Furthermore, it is known that approximately 30% of patients interrupt treatment due to pain in the initial stages of tooth movement[5]. The cause of pain in the initial stage of treatment is the inflammation induced in the periodontal ligament, interfering in releasing mediators such as prostaglandins that lead to hyperalgesia[1-3].

The orthodontist may recommend using drugs to control pain experiences, such as ibuprofen, which attenuates the signs of inflammation inhibiting the cyclooxygenases, preventing the production of Prostaglandins and Thromboxane A2. Some studies have proved that this medication is efficient in controlling pain during orthodontic treatment[2,6,7]. In addition, as nonpharmacological methods for pain control, the literature has reported the use of chewing gum, bite wafers (viscoelastic plates)[2,7,8], laser application[9], ketoprofen, and xylocaine[10].

Some studies investigating the use of chewing gum to diminish pain during the initial period of orthodontic treatment reported less ingestion of drugs during this stage[7,11,12]. Chewing gum use promotes an increase in blood flow in periodontal tissue that decreases the activity of inflammatory mediators and pain responses[1]. However, no studies have previously compared the effect of placebo, chewing gum, and ibuprofen treatment in subjects matched for gender, age, and severity of the malocclusion. Therefore, this randomized clinical trial aimed to compare the performance of chewing gum and ibuprofen in pain control during the initial period of orthodontic treatment.

MATERIAL AND METHOD

Trial Design and Any Changes After Trial Commencement

The present study was a double-blinded, placebo-controlled randomized clinical trial, with an allocation ratio of 1:1. There were no changes after trial commencement.

Participants, Eligibility Criteria, and Settings

This study was previously approved by the Research Ethics Committee (CAAE#2.370.450/2017). Patients of both sexes and aged between 18 and 25 were selected from February to November 2017 in the Department of Orthodontics.

All patients in the initial stage of orthodontic treatment were invited to participate in the study and were selected according to the following inclusion criteria: patients with complete permanent dentition, except for third molars, and an initial stage of fixed orthodontic treatment -full upper and lower fixed appliances fitted and 0.014-in round Nitinol wire. Exclusion criteria were: intellectual limitation, hypersensitivity to sorbitol, mannitol, xylitol, and ibuprofen; hypersensitivity reaction to aspirin or other non-steroidal anti-inflammatory drugs. Volunteers with asthma, urticarial, peptic ulcer, and/or cardiac problems and patients who reported temporomandibular disorder symptoms. All patients read and signed the informed consent document. Also, oral and written explanations about this study were supplied to the patients or their guardians. No rewards were given for participation, which was voluntary.

Sample Size Calculation

The sample size calculation considered the design of repeated measures in time and was based on the three null hypotheses: absence of difference between the groups as regards pain; absence of difference between the times as regards pain and absence of interaction among the groups and times as regards pain. The sample size analysis was performed using SAS (SAS Institute, NC, USA), considering previous studies[2,7-9,13,14], level of significance of 5% and effect size of 0.25, resulting in a minimum of 90 volunteers to reach the minimum test power of 0.80 for the three null hypotheses. The primary outcome measure for this trial component was pain during the initial stage of orthodontic treatment.

Randomization

The volunteers were randomized into three groups with 30 individuals in each group, as follows: Group I - Control-Placebo; Group II - Chewing Gum; and Group III- Ibuprofen; and paired as regards sex, age, the severity of malocclusion, and degree of crowding ($p>0.05$) by the Chi-square test, as may be observed in Table 1. In addition, for the sample pairing, the severity of malocclusion was evaluated by the Dental Health Component (DHC) of the Index of Orthodontic Treatment Need (IOTN)[15] and the degree of crowding Little's irregularity index[16]. Finally, the patients were randomly divided into Group I, II, and III with a randomizer program (www.randomizer.org) whom random numbers used to generate a sequential allocation list.

Table 1. Comparison among the studied groups relative to age, sex, severity of malocclusion and degree of crowding

Variable	Group			p-value
	Group I (Placebo)	Group II (Gum)	Group III (Ibuprofen)	
	n (%)			
Sex				
Female	20 (66.7)	19 (63.3)	20 (69.0)	0.8993
Male	10 (33.3)	11 (36.7)	9 (31.0)	
Severity of malocclusion				
Low	14 (46.7)	13 (43.3)	14 (48.3)	0.9270
High	16 (53.3)	17 (56.7)	15 (51.7)	
Degree of crowding				
Low	12 (40.0)	10 (33.3)	14 (48.3)	0.5070
Moderate	13 (43.3)	15 (50.0)	8 (27.6)	
High	5 (16.7)	5 (16.7)	7 (24.1)	
	Median (minimum value-maximum value)			
Age	19.0 (12.0;-29.0)	17.0 (11.0;-26.0)	20.0 (11.0;-30.0)	0.2913

Intervention

Sequential, closed envelopes were delivered to the operator after parental/guardian consent to participate in the study. The envelopes had the name of the pain therapy to be used in a double-blind manner. In addition, each envelope contained the Visual Analog Scale (VAS)[17,18] and a form with instructions for filling. The VAS consisted of a horizontal 10-cm line, with the classification with no pain and extreme pain at either end. Next, the patients were instructed to mark a vertical line and the VAS, which best represented their pain intensity. Afterward, the distance from the

beginning of the line (which corresponded to zero) to the place marked by the respective patient was measured, and a numerical classification was obtained. Finally, the VAS scores were evaluated to three-time points: 24 hours, 36 hours, and 48 hours after the orthodontic intervention[17]. The determination of the evaluated times was based on the previous studies[6,7,9,11].

Group l was instructed to use the placebo (capsules containing a harmless substance, similar to the capsules that contained ibuprofen; composed of 49% cellulose microcrystalline 102, 40% corn starch, and 1% aerosil) one hour after the orthodontic session, every 8 hours for 48 hours. Group II was instructed to use the chewing gum pellets for 10 minutes every 4 hours for 48 hours. Finally, group III had to use 400mg ibuprofen one hour after the orthodontic session, every 8 hours for 48 hours.

Blinding

Blinding of patient and operator was performed. The pain control method was placed in a sealed envelope with specific codes. The codes were kept by another person who was not involved in these processes. Therefore, both operator and patient were unaware of the study's objectives.

Statistical Methodology

Exploratory analysis indicated that the pain perception data did not meet the presuppositions of parametric analysis. Thus they were analyzed by generalized linear models for repeated measures in time. All the analyses were performed with the SAS statistical program, considering the level of significance of 5%.

RESULT

A CONSORT diagram demonstrating patient flow through the trial is shown in Figure 1. Of the 135 patients examined, 33 did not fulfill the inclusion criteria. One hundred two (102) randomized volunteers were selected in three groups: Group 1 (placebo), 32 in Group II (chewing gum), and 34 in Group III (ibuprofen).

Group 1 completed the intervention with 30 volunteers; there were 4 segment losses and 2 treatment interruptions. Group 2 completed the intervention with 30 volunteers; there were 2 segment losses. Finally, Group 3 completed the intervention with 29 volunteers; there were 5 segment losses and 2 treatment interruptions.

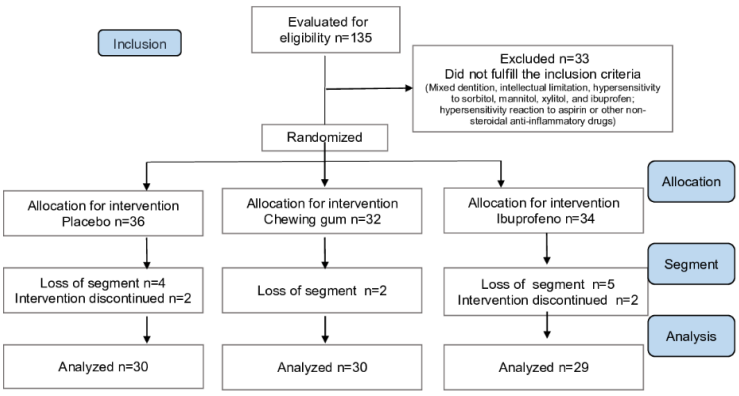

Figure 1. CONSORT diagram showing patient flow during the trial.

Table 2 and Figure 2 show the median of pain (VAS) considering group and time. According to the results, there was no statistically significant difference between the times and the groups concerning pain perception (VAS) in the four stages evaluated (p>0.05).

Table 2. Median (minimum value – maximum value) of pain (VAS) considering group and time

Group	Time			
	Before medication	24 hours after activation and medication	36 hours after activation and medication	48 hours after activation and medication
Placebo (G I)	4.0 (0.0; 9.0) Aa	2.0 (0.0; 9.0) Aa	4.5 (0.0; 9.0) Aa	2.0 (0.0; 9.0) Aa
Gum (G II)	4.0 (0.0; 10.0) Aa	4.0 (0.0; 10.0) Aa	4.0 (0.0; 9.0) Aa	4.0 (0.0; 10.0) Aa
Ibuprofen (G III)	4.0 (1.0; 10.0) Aa	4.0 (1.0; 8.0) Aa	4.0 (0.0; 9.0) Aa	3.0 (0.0; 10.0) Aa

p(group)=0.3907; p(time)=0.0705; p(group x time) = 0.4333. Means followed by the same letters (lower case in the Vertical direction and capital letters in the horizontal direction) did not differ among them (p>0.05).

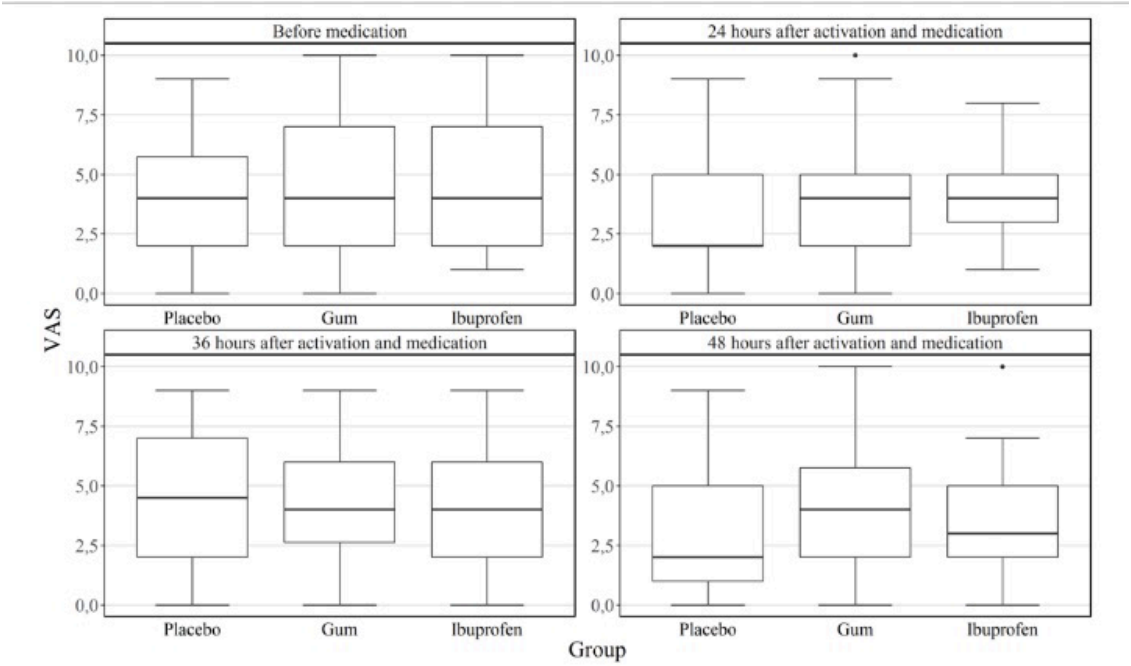

Figure 2. Box plot of pain perception by the VAS scale considering group and time.

DISCUSSION

The beginning of orthodontic treatment results in the patient's experience with some degree of pain caused by the induction of tooth movements and, this factor may be an aspect that limits adhesion to treatment[1-5]. Pain control during treatment has been proposed by different methods, with or without medication. Thus, this randomized controlled trial evaluated the performance of chewing gum and ibuprofen in the pain control assessed by collecting data before and after the orthodontic intervention has taken place. The participants were randomly selected, and the trial was performed in a controlled way, ensuring that all factors other than the intervention were considered equal.

Placebo is an inert substance that produces a positive or adverse effect on the individual health but does not have a proven pharmacological or alternative action. Therefore, this substance can cause a placebo effect in a specific context, resulting from a response to analgesia by a non-analgesic substance[19]. In the present study, the option was to use a placebo with the same

posology as Ibuprofen. This concern met the need for standardization and reproducibility of clinical trials, directly comparing the groups[20]. The intervention with placebo showed no statistically significant difference, showing that the action of the placebo resulted in a similar effect in pain control[21].

Although previous studies have used chewing gum as a form of controlling pain[7,11,12], and the inflammatory response[1], this method also presented no statistically significant differences in pain control, when compared with ibuprofen[7,11,12], which is considered an efficient medication in the control of pain[6,7,9,11,12], and the reference method in comparison with the others alternative methods used in this study. Thus, this is the first study that evaluated intervention groups with placebo, chewing gum and ibuprofen, in a sample of volunteers matched for sex, age, and severity of malocclusion and crowding, eliminating the bias of previous studies to identify a population for which a statistically significant impact of the outcome was feasible and probable.

Our findings showed that the methods studied for pain control in the initial stage of orthodontic therapy did not differ. First, however, a discussion of clinical considerations is appropriate. Although the pain of orthodontic origin is related to the release of mediators such as prostaglandins that lead to hyperalgesia[1,3], this perception of pain is subjective, suggesting that extrinsic factors can mitigate the results to reduce stress and induce endorphins arising from a good quality of life. Intrinsic factors such as the use of medications and practical actions that regulate the production of cortisol modulate the production of prostaglandins[22,23]. Thus, a probable limitation of the study was not to include the perception of individual pain in selecting participants.

Considering pain is a multifactorial factor, and a significant influence on individual perception, pain control in the early stages of orthodontic treatment should be expanded. In addition, factors such as stress and quality of life must be considered.

CONCLUSION

There was no difference among the method used for pain control during the orthodontic treatment, showing that non-medicated methods may be adequate for pain control in Orthodontics.

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CONFLICTS OF INTERESTS

The authors declare no conflicts of interest.

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