Efficacy of Chewing Gum to Reduce Orthodontic Pain Compared to Placebo: A Blinded, Parallel-Group, Preliminary Clinical Trial

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Aims: To quantify the pain experienced by orthodontic patients during the first 10 days of appliance placement, to determine whether chewing gum reduces orthodontic pain compared to placebo, and to examine patients' overall perceptions of the impact of orthodontic pain. **Methods:** Patients bonded with fixed appliances were randomly assigned to one of two groups (gum group [GG] or placebo group [PG]) and then followed for 10 days. The main outcome was a visual analog scale (VAS) pain score, and the secondary outcomes included patients' subjective assessments of overall pain level, the impact of pain on hygiene habits and treatment decision, and the frequency of analgesics consumption. Eighty kits (40 for GG and 40 for PG) were pre-randomized and concealed before patient enrollment using a computer-generated random sequence. Operators and patients were blinded. Data were analyzed using generalized linear models and Mann-Whitney *U*, chi-square, and Fisher exact tests. **Results:** A total of 75 patients were allocated to intervention groups; 37 participated and completed diaries (20 in GG and 17 in PG). No statistically significant differences were detected between the GG and PG groups in any tested variable. Pain negatively affected some patients' oral hygiene practices. A mismatch existed between patient expectations and actual pain experiences. Female patients used analgesics more frequently than male patients ($P = .046$). **Conclusion:** Chewing gum three times per day does not seem to significantly reduce orthodontic pain compared to placebo. Orthodontists should manage their patients' pain expectations. *J Oral Facial Pain Headache 2019;33:301–307. doi: 10.11607/ofph.2192*

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Orthodontic appliance activation causes pain in most, if not all, patients.[1,2] It is in the common interest of the patient and care provider to find interventions that can reduce orthodontic pain. Analgesics have been shown to be useful in reducing orthodontic pain,[3–5] but one concern with the use of analgesics—specifically nonsteroidal anti-inflammatory drugs (NSAIDs)—is the risk of adverse effects, including gastric ulcers. Another concern from an orthodontic perspective is whether these NSAIDs may interfere with the rate of orthodontic tooth movement.[6]

Therefore, it is desirable to find a nonpharmacologic, widely available alternative that has no adverse effects and possibly some positive side effects, such as stimulating saliva or modifying plaque.[7] Proffit's textbook[8] proposes that chewing gum may reduce orthodontic pain through the cycles of PDL compression and decompression that accompany chewing and that it may reduce ischemia. Unfortunately, this topic has not received enough attention in the literature, and studies in this field could benefit from design improvements.[1,9–12] In a recent Cochrane review, Fleming et al[13] indicated the need for more prospective, good-quality studies in this field.

In this blinded, randomized clinical trial, the aims were to quantify the pain experienced by orthodontic patients during the first 10 days of appliance placement, to determine whether chewing gum reduces orthodontic pain compared to placebo, and to examine patients'

overall perceptions of the impact of orthodontic pain. The main research question was: Does chewing sugar-free gum three times per day for 5 minutes reduce initial orthodontic pain compared to placebo?

Materials and Methods

Ethical Clearance, Trial Registration, and Patient Consent

The study design was registered under the number NCT02024139 on (www.clinicaltrials.gov). All patients (or parents) signed an informed consent. The study design was approved by the ethical review committee of the Ministry of Health (MOH) in the State of Kuwait (reference 2183/2013).

Participants

Patients undergoing routine orthodontic treatment at Bneid AlGar Dental Specialty Center and Kuwait University Dental Center who satisfied the eligibility criteria were approached for inclusion in this study. Patient enrollment took place between March 2014 and February 2016.

Patients with fixed maxillary and mandibular orthodontic appliances bonded on the same visit were included. The exclusion criteria were:

- Recent tooth extraction (within 2 weeks)
- Incomplete engagement of archwire into all brackets
- Functional or extraoral appliances
- Bite ramps to relieve occlusion after bonding
- On regular pain medications for chronic problems
- Chronic pain problems
- Mental or cognitive impairments
- Phenylketonuria (ie, unable to chew sugarless gum)

Interventions and Groups. There were two groups in this study: a placebo group (PG) and a chewing gum group (GG). Patients in the PG were asked to rinse for 30 seconds with a fluoridated, alcohol-free mouthwash (Plax Sensitive) three times per day as a placebo. Patients in the GG were asked to use the same mouthwash and to also chew sugar-free chewing gum (Mentos) for 5 to 10 minutes three times per day. Both groups were asked to record pain in a booklet for 10 days. All patients were asked to avoid taking analgesics.

Randomization, Allocation, Concealment, and Blinding

Patient kits were prepared before patient enrollment by the primary investigator (A.A.) and concealed in opaque, sealed bags. A total of 40 kits containing instructions, consent forms, and supplies (mouthwash, visual analog scale [VAS] diaries, pens, and chewing gum) were prepared for the GG, and another 40 kits (same supplies as GG but without the chewing gum) were prepared for the PG. The kits were prepared before randomization, then given random numbers according to the computer-generated sequence. A random sequence was generated in two columns formatted with 40 numbers in each column (www.random.org) to ensure an equal number of patients in each group. Numbers from the first column were used to label GG bags while numbers from the second column were used to label PG bags. The concealed kits were given to participants in order of ascending serial number. The investigator who administered the kits (A.A.A.) and gave instructions to patients discovered the group assignment only at the time of giving patients instructions. Standardized instructions were given to all participants, with the only difference between groups being the use of chewing gum. Operators (S.A.A., S.A.Q., and M.A.) remained blinded, since patient allocation to groups was done after bonding.

Data Collection. Patients were given instructions on how to record pain levels on a 100-mm VAS. Patients were asked to mark an "X" on the VAS according to the pain experienced when biting at 22 time points (at the time of assignment, 3 and 6 hours after bonding, at bedtime on bonding day, and in the morning and at bedtime for the subsequent 9 days). There were also questions regarding adherence to the protocol and use of medication on every page. On the last page of the booklet there were subjective questions regarding the overall pain experience.

Sample Size Calculation. To calculate sample size, the significance level was set at .05, and the power was set at 0.8. Using a standard deviation (SD) of 25 mm on the VAS[14] and a clinically meaningful difference of 25 mm, a total of 34 patients (17 per group) was needed to enter this trial. Anticipating significant dropout from this patient population (from experience), 80 patient kits were prepared.

Validation and Measurement Error. A pilot run of five booklets was conducted for validation. No modifications were done, and these booklets were not included in the final analysis. All VAS responses were measured to the nearest 1 mm by the same blinded investigator using a digital caliper. Intra-examiner reliability of the VAS measurements was assessed using 50 VAS scales measured twice, 10 days apart.

Primary and Secondary Outcomes. The primary outcome measure was the VAS pain score. VAS scores were used to compare groups using generalized linear models (GLMs). The secondary outcome measures included patients' overall subjective assessment of pain and reported frequency of analgesics use.

Appliances Used. All patients in the study received preadjusted appliances (0.022-in MBT prescription) with a 0.014-in nickel-titanium wire engaging all teeth.

Statistical Analyses

Data were entered in Statistical Package for the Social Sciences (SPSS, Windows version 19, by IBM Analytics) and exported to Wizard Pro (Mac version 1.8.15, by Evan Miller). Chi-square and/or Fisher exact tests were used to compare proportions.

Data were also exported to SAS software (Windows Version 9.4, SAS Institute). Generalized linear models (GLMs) with log-link function and gamma distribution were chosen to examine the associations of group, change in time (in days), and gender (male vs female) with VAS pain because the data were non-negative and highly skewed. To allow for observations with 0-mm values to be used in the model, these values were replaced with a value of 0.5 mm (this was only for the GLMs). Thus, the association between pain and variables of interest were presented as a pain scale ratio with 95% confidence interval.

To investigate whether the rate of change in pain (slope) was different between the two groups, interaction terms for the rate of change with time (ie, time multiplied by group) were used in the GLMs. Linear combinations were used to estimate the rate in slope change for each group. Two patients were missing a few VAS scores at some time points; these two patients were excluded from the GLM analyses. The GLMs were applied from bedtime on bonding day onwards and did not include the first three time points (0, 3, and 6 hours), since the time scale of these three points was different from the rest. No statistical test was done for the 0-hour time point, since all observations were 0. In order not to overlook the 3- and 6-hour time points, individual Mann-Whitney *U* tests were carried out, since the data were not normally distributed according to the Shapiro-Wilk test ($P < .001$).

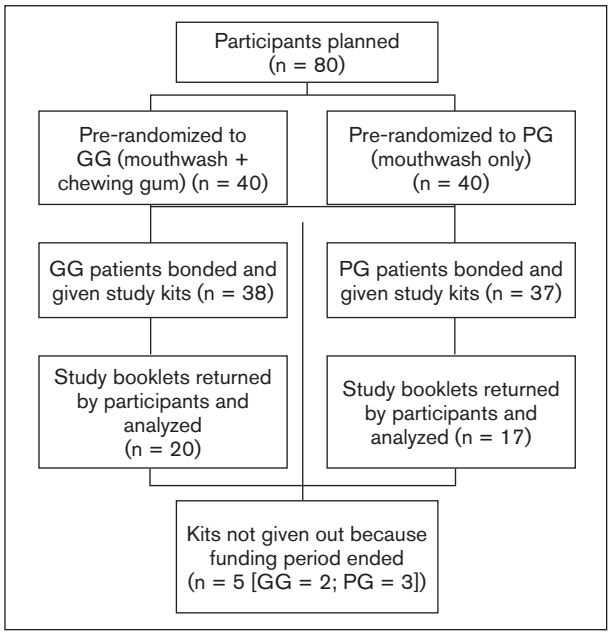

Fig 1 Patient flowchart.

Table 1 Sample Frequencies and Descriptives

	Gender and group distribution, n (%)				
	Male	Female	Unreported	Group totals	*P* value[a]
Gum	5 (27.8)	13 (72.2)	2	20 (54.1)	.915
Placebo	5 (29.4)	12 (70.6)	0	17 (45.9)	
Total	10 (28.6)	25 (71.4)	2	37 (100)	

	Mean age by group				
	n[b]	Mean age (y)	SD	Range (y)	*P* value[c]
Gum	16	16.9	5.12	12–31	.922
Placebo	15	16.1	3.35	12–25	

[a]Chi-square test.
[b]Four patients in the GG and two patients in the PG did not indicate their age.
[c]Using Mann-Whitney *U* test.

Results

Patient Flow

A total of 75 patients were bonded, assigned to a group, and given instructions. Of these patients, 37 participated and completed/returned the study booklets. Patient flow details are shown in Fig 1. Patient recruitment was terminated when the study's funding period ended and before all kits were distributed. The final sample included 10 male and 25 female patients (plus 2 patients who did not indicate gender). Sample descriptives are shown in Table 1. None of the demographic variables were significantly different between groups. All patients indicated complying with the chewing gum and/or mouthwash use protocols.

Measurement Reliability

The reliability of the pain scale measurements was near perfect, with an intraclass correlation coefficient (ICC) of 0.999.

VAS Pain Scores (Primary Outcome)

To summarize the VAS scores obtained at all 22 time points, the scores were displayed as boxplots separately for each group (Fig 2). There were no significant differences in VAS score at the 3- or 6-hour time points according to Mann-Whitney *U* test. The

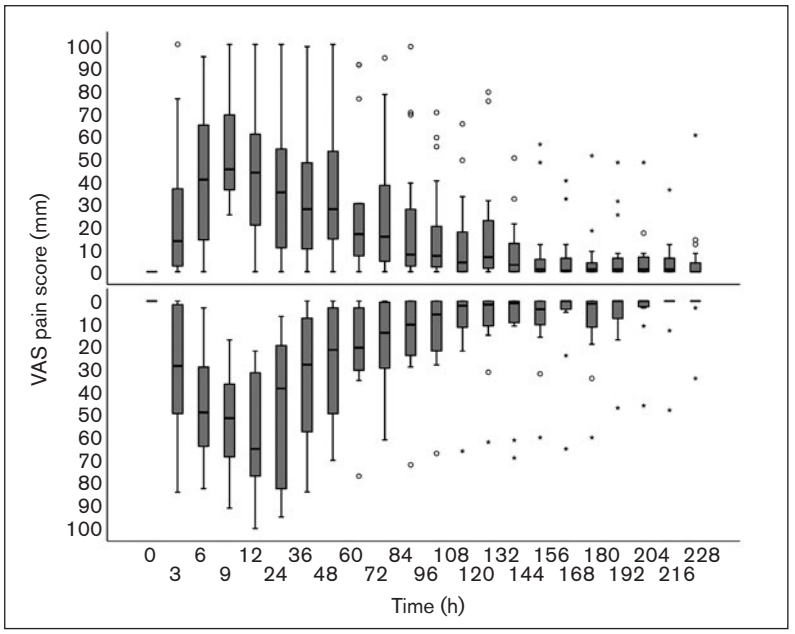

Fig 2 Boxplots of visual analog scale (VAS) pain scores for the different time points. Top: chewing gum group. Bottom: placebo group.

Table 2 Adjusted Generalized Linear Model Examining Association Between Mean Pain and Group

Variable	Ratio	95%	CI	*P* value
Morning				
Group PG vs GG	1.02	0.52	1.99	.96
Time (per d)	0.75	0.69	0.81	< .0001
Male vs female	1.94	.91	4.16	.09
Evening				
Group PG vs GG	0.91	0.48	1.73	.77
Time (per d)	0.74	0.68	0.80	< .0001
Male vs female	1.98	0.92	4.22	.08
Average for the day				
Group PG vs GG	0.96	0.49	1.89	.91
Time (per d)	0.74	0.68	0.80	< .0001
Male vs female	2.03	0.93	4.44	.08

Table 3 Adjusted Generalized Linear Model Examining Association of the Slope of Pain Reduction and Group

Variable	Ratio	95%	CI	Slope *P* value	Interaction *P* value
Morning					
Rate of change GG	0.74	0.68	0.81	< .0001	.91
Rate of change PG	0.75	0.67	0.83	< .0001	
Evening					
Rate of change GG	0.74	0.66	0.83	< .0001	.94
Rate of change PG	0.74	0.66	0.83	< .0001	
Average for the day					
Rate of change GG	0.74	0.66	0.83	< .0001	.92
Rate of change PG	0.74	0.66	0.84	< .0001	

P values for the 3- and 6-hour tests for GG vs PG were .220 and .404, respectively. The *P* values for the 3- and 6-hour tests for male vs female were .529 and .730, respectively.

These remaining time point scores were analyzed using GLMs. The ratios of change in pain for each day for each treatment group are presented in Table 2 together with the *P* values for the interaction terms. In the multivariate GLMs, no associations for group, age, or gender with the overall average pain score were found. Only time predicted the pain score; on average there was a 26% decrease in the VAS score per day.

Linear combinations were used to estimate the rate of slope change for each group. Regardless of time of day (morning or bedtime), there was no difference in slope when comparing the GG to the PG ($P \geq .44$). For example, when comparing the results from the morning pain change, it was found that group GG had a 27% pain reduction per day, while the PG had a 23% pain reduction per day, and the slopes of the two lines were not significantly different from each other. The ratios of change in pain for each day (mornings, evenings, and average) for each treatment group (GG and PG) are presented together with the *P* values for the interaction terms in Table 3.

Subjective Pain Experience, Pain Impact, and Analgesics Use (Secondary Outcomes)

A summary of patients' subjective assessment of the overall pain experience and its impact is presented in Fig 3. There were no statistically significant associations between the patients' responses and their group assignment or gender. Pain had a generally negative impact on the oral hygiene habits of some patients.

Although patients were asked not to use analgesics, data on analgesics use were collected and analyzed. There was no statistically significant difference between GG and PG regarding analgesics use during the first 5 days of bonding ($P = .393$). Female patients used analgesics significantly more frequently than male patients ($P = .046$). A summary of reported use of analgesic medications is presented in Table 4.

Discussion

Pain from tooth movement is an almost constant feature of orthodontic therapy. After placement of the initial archwire, it is reported in the literature that pain is most intense during the first 48 hours of wire placement.[11,15] The results of this study, however, indicate that this may not be very accurate for all patients. VAS peak times displayed significant variation between patients. This is perhaps why looking at the average pain score at each time point may be misleading and why using an overall analysis like GLMs may be more appropriate. Most reports in the literature agree that a period of 1 week is enough for the pain to subside.[11,15] The results from the current study indicate that some patients continue to experience pain throughout the 10-day period.

The results of this study suggest that the use of chewing gum three times per day did not help reduce orthodontic pain. To avoid individual time point tests and multiple comparisons, GLMs examining pain curves were developed. This method is arguably more robust and conservative than using multiple comparison tests or using sample averages.

In a study by Otasevic et al,[1] the use of a bite wafer for reduction of orthodontic pain was compared to avoidance of hard food. Significantly worse VAS pain levels in the first 3 days were reported in the bite wafer group. Although bite wafers might not exactly translate to chewing gum, this study sheds some doubt on the efficacy of chewing to reduce orthodontic pain.

Murdock et al[9] compared the effects of using a bite wafer to using over-the-counter medications (OTC) in reducing pain after placement of initial archwires. Their results indicated that the bite wafer was noninferior to using analgesics. Unfortunately, there was no real control group. Also, bite wafers are not commercially available in all countries.

A study by Farzanegan et al[11] compared the use of ibuprofen, chewing gum, two kinds of bite wafers, and placebo (vitamin pills) in the reduction of orthodontic pain. Due to the limited number of subjects in the study (10 per group), the multiple comparisons, and the inconsistent results obtained, the study failed to unequivocally answer the question of whether chewing gum works.

Benson et al[10] published a clinical trial comparing the use of chewing gum to no intervention on impact, pain, and appliance breakage. Their

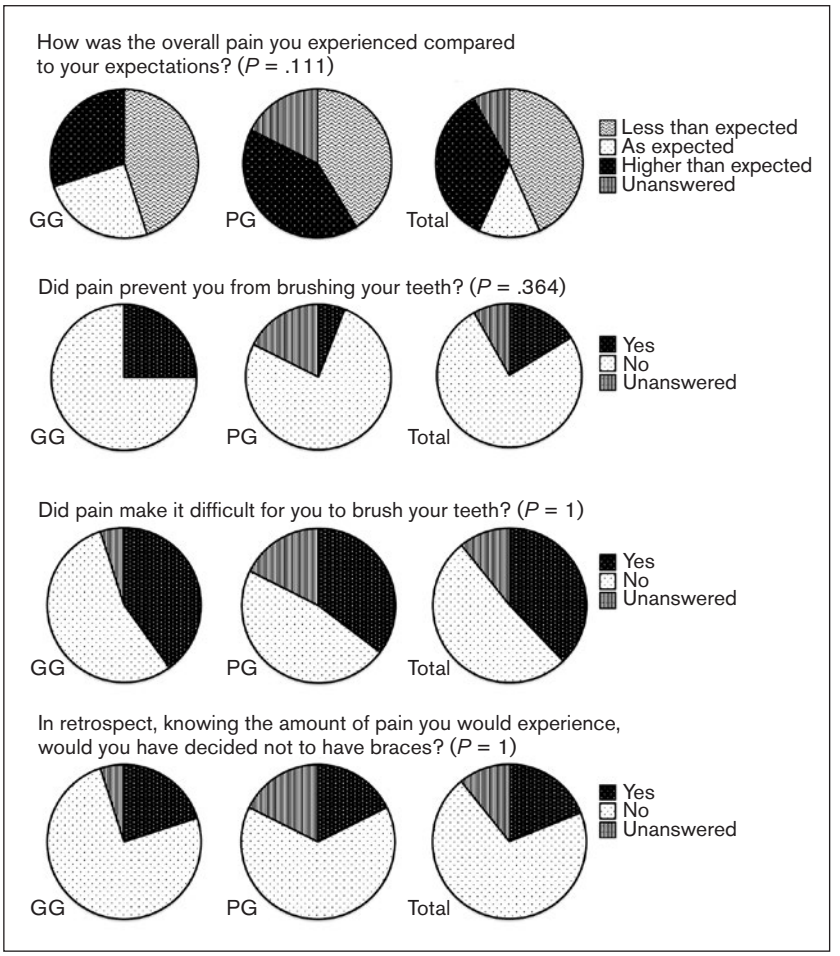

Fig 3 Pie charts indicating the percentage of different answers given by patients to subjective questions. There was no statistically significant difference between the gum and placebo groups (chi-square and/or Fisher exact tests).

Table 4 Frequencies of Analgesics Use by Group and Gender

Used analgesics during the first 5 d	Yes, n (%)	No, n (%)	Unreported, n	*P* value[a]
Gum (n = 20)	6 (30)	14 (70)	0	.393
Placebo (n = 17)	7 (43.75)	9 (56.25)	1	
Total	13 (36.1)	23 (63.9)	1	
Male (n = 10)	1 (10)	9 (90)	0	.046
Female (n = 25)	11 (45.8)	13 (54.2)	1	
Gender not reported (n = 2)	1 (50)	1 (50)	0	
Total	13 (36.1)	23 (63.9)	1	

[a]Using chi-square test.

results seem to indicate that using chewing gum to reduce orthodontic pain may be promising. However, gum use in that study was not standardized. Because there was no placebo group (subjects were not blinded) the placebo effect cannot be excluded. Blinding of operators was also incomplete, and treatment included both one- and two-arch treatments.

Ireland et al published a study in 2016[12] that compared the use of chewing gum plus ibuprofen to only using ibuprofen for pain control. The study, however, had some unfortunate design choices despite its huge scale. The use of chewing gum and ibuprofen was not standardized; in fact, patients in the experimental group were asked to chew gum "if required" to control pain, and to use ibuprofen if they did not get enough "relief" from the gum. The control group used an intervention known to reduce pain, which was also not standardized. Hence, that study[12] leaves the question unanswered.

Orthodontic pain had an important impact on patients, with 6% indicating it prevented them from brushing and 38% indicating it made it difficult to brush. In fact, about 19% of patients reported that they would have decided against having orthodontic treatment had they known the level of pain in advance. It has also revealed a mismatch between patients' expectations and the amount of pain they experienced, with only 13.5% of patients indicating that the pain matched their expectations.

As analgesics were shown to have an effect on orthodontic pain,[3–5] attempts were made to control for analgesics by asking patients to avoid them. However, if patients did not fully comply with this request, they were asked to report their use of analgesics. All patients' results were analyzed on an intention-to-treat basis whether they used analgesics or not. The extent to which analgesics use was controlled for in other studies was variable.[1,10,11] Analgesics use was similar between the GG and PG. The fact that female patients were found to use analgesics significantly more than male patients suggests that research on the role of gender in pain perception in orthodontics might be important. Some evidence exists in the literature that female individuals may have higher sensitivity to pain.[16]

Limitations

Achieving the number of planned enrolled patients was challenging at the two study locations because of the limited number of orthodontists and the very limited proportion of cases receiving maxillary and mandibular braces on the same day. Hence, despite the 2-year enrollment period, only 75 patients were approached.

A major limitation of this study was the high patient nonparticipation rate. A total of 38 patients decided not to fill out the booklet and declined to participate in the study after they were given the supplies and instructions. Those patients did not provide any data points at all. Effectively, it is as if those patients declined to participate from the beginning. This is outside the control of the authors. What is within the authors' control is accurate reporting and presentation of data. The strict inclusion and exclusion criteria of the study made it challenging to recruit a high number of patients. By using a booklet that the patient filled out, the compliance and return rate of this study may be comparable to that of a survey, which is commonly lower than a clinical measurement study. Due to the nature of the free service provided with its long appointment intervals, patient motivation was not ideal. In retrospect, using fewer time points could have improved patient participation; however, it would not have allowed detailed information gathering regarding dynamic pain changes. The nonparticipation rate was similar in both groups. Fortunately, despite the high rate of failure to participate, the minimum sample size required according to the sample size calculation was achieved.

Group assignment became known to the author providing the kits (A.A.A.) at the time of giving instructions. This author, who is not an orthodontist, had no influence on patient treatment, data entry, or analysis. Since the assignment happened after bonding and since this author played no part in treating the patients, this was unlikely to influence the results. It was not possible to blind the person who gave the instructions without compromising the blinding of patients. By making the group assignment known to this author, it was possible to keep PG patients blinded to the use of chewing gum by the GG.

Data on the level of tooth irregularity at baseline were not collected. However, randomization should ensure that baseline characteristics are distributed similarly between the groups. Also, the age range of the patients in the sample was wide, but it did reflect the population treated at the study's locations.

The fact than some patients used analgesics despite being asked not to might potentially have an impact on these results. This limitation is unfortunately extremely difficult to avoid. Excluding patients who used analgesics would compromise sample size and would probably be a risk for bias as well. Hence, the data were analyzed on an intention-to-treat basis, as originally planned.

Conclusions

Chewing gum three times per day did not seem to significantly reduce orthodontic pain compared to placebo; but a larger scale trial with higher percent-

age of participation might be needed to corroborate this finding.

Orthodontists should set their patients' expectations at the right level regarding orthodontic pain.

Further studies are needed to investigate the mechanisms of interaction between chewing and nociception in the periodontium and to elucidate the role of gender in orthodontic pain perception.

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