Original Article

Tooth movement, orofacial pain, and leptin, interleukin-1β, and tumor necrosis factor–α levels in obese adolescents

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ABSTRACT

Objectives: To evaluate tooth movement, orofacial pain, and leptin, interleukin (IL)–1β, and tumor necrosis factor (TNF)–α cytokine levels in the gingival crevicular fluid (GCF) during orthodontic treatment in obese adolescents.

Materials and Methods: Participants included adolescent patients aged 12–18 years: group 1, obese (n = 30), and group 2, nonobese controls (n = 30). They were evaluated before (T_0) and after 1 hour (T_1), 24 hours (T_2), and 1 week (T_3) of fixed appliance bonding. Periodontal examination (T_0), collection of GCF (T_1, T_2, T_3), and evaluation of Little's irregularity index (T_0, T_3) were performed, and a visual analog scale was used to measure pain (T_1, T_2, T_3). Evaluation of IL-1β, TNF-α, and leptin cytokines was performed using a Luminex assay. Mann-Whitney and *t*-tests were used for intergroup comparisons, and a generalized estimating equation and cluster analyses were used for comparisons among observation times ($P < .05$).

Results: The obese group had a higher prevalence of probing depth of ≥4 mm and bleeding on probing. Orthodontic tooth movement was similar in both groups. Peak of pain was at T_2 in both groups and was higher in the obese patients. TNF-α showed a slight increase at T_1, followed by a gradual decrease at T_2 and T_3 in both groups. The obese group had a higher concentration of IL-1β before and during orthodontic treatment. There was no difference in tooth movement between obese and control patients during the first week of orthodontic treatment.

Conclusions: Obese adolescents had a greater subjective report of orofacial pain after 24 hours of orthodontic treatment and higher concentrations of IL-1β proinflammatory cytokine before and during tooth movement as compared with nonobese control adolescents. (*Angle Orthod.* 2022;92:95–100.)

KEY WORDS: Obesity; Tooth movement; Inflammation; Interleukin-1β; Tumor necrosis factor–α

INTRODUCTION

Obesity and its associated comorbidities are increasingly prevalent among adolescents. Childhood and adolescent obesity are associated with health consequences later in life, including adult overweight/obesity[1] and cardiovascular, musculoskeletal, and endocrine diseases.[2]

Patients with obesity suffer from chronic inflammation accompanied by elevated inflammatory cytokines, suggesting that these individuals display a dysfunctional immune response. Elevated inflammatory cytokines interleukin (IL)–1β, IL-6, and tumor necrosis factor (TNF)–α are primarily produced by an increased number of macrophages in obese adipose tissue, and their altered circulating levels have been reported in patients with obesity, contributing to local as well as systemic chronic inflammation.[3]

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Encountering obese patients who undergo orthodontic treatment is becoming more common, as the incidence of individuals who are obese and overweight is increasing worldwide.[4] The effect of oral habits on cranial and maxillofacial growth and development is dependent on the nature, onset, and duration of the habits. Orofacial pain may negatively affect adolescents. Widespread pain may indicate changes related to central sensitization, partially explaining the relationship between obesity and comorbidities with painful conditions.[5]

The tooth movement induced by fixed orthodontic appliances causes a change of the microbiome and subsequent infections, such as an inflammatory response in the periodontium. Orthodontic appliances make it more difficult to keep teeth clean and induce plaque accumulation. The events leading to tooth movement are complex and include interactions between cells in the alveolar bone and the periodontal ligament. Tooth displacement and bone-remodeling activity are consequences of an inflammatory process induced by mechanical stimulus.[6]

Therefore, both adipose tissue and the inflammation generated by orthodontic tooth movement alter the levels of TNF-α, IL-1β, and leptin, which are simultaneously related to obesity and tooth movement.[7,8] However, there are no reports about the relationship between orthodontic treatment and inflammatory cytokines, periodontal status, and orofacial pain in obese adolescents. Thus, this study aimed to prospectively investigate the impact of obesity on orthodontic tooth movement regarding the changes in inflammatory cytokines, periodontal conditions, and orofacial pain.

MATERIALS AND METHODS

Design and Participants

This was a prospective cohort study in which data were collected before and after bonding of the fixed orthodontic appliances (1 hour, 24 hours, and 1 week). The study was approved by the Committee of the Faculty of Dentistry of Bauru (CAAE 68559617.8.0000.5417).

The sample consisted of 60 adolescent patients aged 12 to 18 years, divided into two groups: group 1, obese ($n = 30$; 16 female, 14 male), and group 2, nonobese control ($n = 30$; 17 female, 13 male). Recruitment and clinical evaluations were carried out at the Orthodontic Clinic of the Faculty of Dentistry of Bauru. Eligibility criteria were orthodontic records indicating the use of fixed orthodontic appliances, between 12 and 18 years of age at the beginning of orthodontic treatment, permanent dentition, and Little's irregularity index between 3 and 12 mm. Exclusion criteria were regular use of anti-inflammatory drugs, treated with antibiotics in the past 6 months, smoker, and pregnant or breast-feeding.

Anthropometric Evaluation

Measurements of body mass and body composition were performed using Inbody 230 Multifrequency Tetrapolar Bioimpedanciometer (Biospace, Rio de Janeiro, Brazil), with 100 g of precision and a maximum capacity of 250 kg.[9] Height was measured using a stadiometer attached to the wall with an accuracy of 0.1 cm. The diagnosis of nutritional status through body mass index (BMI) was performed using the BMI percentile, obtained through growth curves according to sex and age,[10] using the World Health Organization AnthroPlus software 1.0.4 (https://pt.freedownloadmanager.org/Windows-PC/WHO-AnthroPlus-GRATUITO.html).

Clinical Evaluation

Clinical evaluations were performed at four time points: before fixed appliance bonding (T_0) and at 1 hour (T_1), 24 hours (T_2), and 1 week (T_3) after bonding of appliances. At T0, evaluation of Little's irregularity index, collection of gingival crevicular fluid (GCF), and a periodontal examination (probing depth, gingival bleeding index, and presence of calculus) were performed. The fixed appliance consisted of 0.022 $\times$ 0.028-inch Roth prescription metal brackets (Morelli, Sorocaba, Brazil). After bonding, 0.014-inch NiTi arch wires were inserted and tied with elastomeric or metal ligatures, when necessary.

To assess probing depth, the distance from the gingival margin to the most apical point of the gingival sulcus/pocket was considered. The periodontal probe was introduced with light pressure, parallel to the tooth axis. The probing depth and blooding on probing were evaluated at three sites: mesial, central, and distal on the buccal and palatal/lingual surfaces of all teeth, except the third molars.[11]

At T_1, T_2, and T_3, the visual analog scale (VAS) was used to evaluate pain, and GCF was collected. In addition, at T_3, Little's irregularity index was measured.

Little's Irregularity Index

Little's irregularity index was measured on the mandibular dental model with a digital caliper (model/code 500-144B, Mitutoyo, Suzano, Brazil) with an accuracy of 0.01 mm, parallel to the occlusal plane. Little's irregularity index consisted of measuring the linear displacement of the anatomical contact points between adjacent mandibular incisors, and the sum of the five measurements is the irregularity index. This measure represented the distance by which the

Table 1. Anthropometric Characteristics of Participants Stratified by Group[a]

	G1 Obese, Mean ± SD (Min–Max)	G2 Eutrophic, Mean ± SD (Min–Max)	*P*
Age, y	14.06 ± 2.24 (12–18)	14.56 ± 1.73 (12–18)	.14
Weight, kg	74.98 ± 20.08 (47.9–127.4)	53.33 ± 9.10 (40.5–76.6)	.00*
Height, m	1.63 ± 9.13 (1.45–1.84)	1.65 ± 8.30 (1.85–1.50)	.83
BMI, kg/m^2	25.05 ± 3.13 (20.72–28.04)	19.90 ± 2.00 (18.30–22.72)	.00*
WHR	0.93 ± 0.07 (0.80–1.08)	0.81 ± 0.04 (0.75–0.90)	.00*
SMM	26.35 ± 7.22 (15.9–42.8)	23.94 ± 5.28 (16.8–35.5)	.19
Fat mass	29.74 ± 12.17 (10.8–59.0)	10.93 ± 4.42 (10.8–23.0)	.00*
Body fat, %	37.0 ± 6.9 (15.6–52.3)	20.17 ± 7.3 (7.8–33.8)	.00*
Protein mass	9.4 ± 2.4 (6.0–14.9)	8.6 ± 1.8 (6.2–12.5)	.18
Mineral mass	3.3 (2.1–5.0) ± 0.8	3.0 (2.3–4.4) ± 0.6	.06
Total body water	34.9 (22.1–54.5) ± 8.9	32.0 (23.2–46.0) ± 6.5	.24

[a] BMI indicates body mass index; SMM, skeletal muscular mass; WHR, waist-to-hip ratio.
* Statistically significant at $P < .05$.

contact points must be moved to achieve alignment[12] and was used in this study indirectly to measure the amount of tooth movement in the groups. Similar intergroup changes in the index would indicate similar amounts of tooth movement.

VAS for Orofacial Pain

Pain sensitivity was evaluated after 1 hour, 24 hours, and 1 week of fixed appliance bonding (T_1, T_2, T_3) using a VAS in which the patient scored the intensity of pain experienced from 0 to 10.[13] The volunteers were instructed not to use any analgesic medications within 1 week of fixed appliance bonding.

GCF Collection

GCF was collected with sterile absorbent paper cones. For collection, supragingival plaque removal was performed, followed by isolation with cotton rolls and drying with an air syringe for 5 seconds. After preparation, absorbent paper cones (#30, Tanari, AM, Brazil) were inserted into the gingival sulcus at a 1 mm depth for 30 seconds, distal to the six mandibular anterior teeth (central and lateral incisors, and canine). If the paper ends were contaminated with blood or saliva, they were discarded.

Immediately after collection, the paper cones were transferred to Eppendorf tubes containing 200 μL of buffered saline (phosphate-buffered saline) with 0.1% Tween 20 solution (USB Corp, Cleveland, Ohio) and 1 μL of protease inhibitor cocktail (Sigma-Aldrich, St Louis, Mo). The tubes were shaken for 30 minutes and centrifuged at 10,000 rpm for 5 minutes and then stored at −80°C for further laboratory analysis.

Laboratory Stage

Evaluation of IL-1β, TNF-α, and leptin in the GCF was performed using Luminex xMAP for multiple assays, using the appropriate kit (Cat. No. HADK2-MAG-61K, Millipore Corporation, Billerica, Mass), with reading of the plates by MagPix equipment (Luminex Corporation, Austin, Tex), following the protocol indicated by the manufacturer.

Mann-Whitney and *t*-tests were used for intergroup comparisons, and a generalized estimating equation and cluster analyses were used for interphase comparisons ($P < .05$).

RESULTS

The obese group (G1) showed significantly higher values for weight, BMI, waist-to-hip ratio, fat mass, and percentage body fat as compared with the controls (G2; Table 1). The participants were stratified according to their periodontal status. G1 had a significantly smaller percentage of 0- to 3-mm probing depths and a significantly greater percentage of 4- to 5-mm probing depths and bleeding sites than G2 did (Table 2).

Crowding was similar in the groups, both initially and after 1 week of treatment (Table 3). There were significant decreases in crowding after 1 week of treatment in both groups.

Pain intensity was greater at all time points for the obese group; however, the difference between groups was significant only at T2 (Table 4).

The obese group had significantly higher concentrations of IL-1β cytokine than the control group did. The concentration varied significantly with time (Table 5). TNF-α cytokine varied significantly with time.

Table 2. Periodontal Parameters by Group[a]

	G1 (n = 30) Obese	G2 (n = 30) Eutrophic	*P*
PD, mm	2.13 ± 0.34	2.07 ± 0.25	.39
PD 0–3 mm, % sites	97.44 ± 4.35	98.05 ± 3.45	.00*
PD 4–5 mm, % sites	0.53 ± 1.00	0.21 ± 0.52	.00*
% Calculus, teeth	7.97 ± 8.64	5.90 ± 6.78	.48
% BOP, sites	11.27 ± 5.92	6.50 ± 3.76	.00*

[a] BOP indicates bleeding on probing; PD, probing depth.
* Statistically significant at $P < .05$.

Table 3. Little's Irregularity Index: Initial (T_o) and After 1 wk of Orthodontic Treatment (T_3)

	T0	T3	Group	Time	Group × Time
Dental crowding, mm					
G1	4.90[a] (4.01–5.79)	3.50[b] (2.67–4.33)	.43	.00*	.72
G2	4.50[a] (3.75–5.25)	3.03[b] (2.38–3.68)			

[a,b] Indicates statistically significant differences
* Statistically significant at $P < .05$.

DISCUSSION

This longitudinal study showed that tooth movement triggered greater orofacial pain after 24 hours of orthodontic treatment in obese adolescents.

Obesity is a pathologic condition associated with excess adipose accumulation and the production of systemic proinflammatory factors, which lead to chronic subclinical inflammation.[14] In this study, BMI[15] and body composition (fat mass, skeletal muscle mass, water)[16] were assessed using bioimpedance tests. The BMI of the group of obese adolescents was significantly higher than the nonobese control group (Table 1), with an average of 37.6% fat in body composition and 20.17%, respectively. Therefore, it is highly recommended to assess not only the BMI but also the percentage of fat mass.[16]

In the present study, the periodontal condition was evaluated before bonding the orthodontic appliances. The probing depths and the number of sites with 4- to 5-mm pockets were significantly higher in obese individuals (Table 2). A recent systematic review reported there was a tendency for greater probing depths in obese adolescents and found an association between obesity and periodontitis.[17] The adverse effect of obesity on the periodontium can be mediated by proinflammatory cytokines, such as interleukins, adipokines, and numerous other bioactive substances that are produced by adipose tissue, which are involved in the pathophysiology of obesity and periodontitis.[7] Therefore, the differences in periodontal parameters at baseline of the obese group were already expected and were difficult to eliminate.

Obese adolescents had a higher prevalence of sites with bleeding on probing (BOP) (Table 2). BOP has been widely used as a sign of gingival inflammation and active periodontal disease and is used for the purpose of determining periodontal health.[18] The findings of the present study were in agreement with a previous study[19] that demonstrated that 32.1% of obese patients had a prevalence of sites with BOP greater than 25%, compared with only 7.6% of nonobese patients; however, there was no evaluation of the probing depth in that study. The prevalence of BOP was higher compared with the present study because of methodological differences. The current study investigated BOP at six sites per tooth, in addition to two additional sites.

The periodontal condition can be aggravated by the presence of dental crowding due to the difficulty in cleaning. The present study included patients who needed orthodontic treatment because of the presence of mandibular crowding, regardless of the anteroposterior relationship of the basal bones. The groups had similar initial crowding (Table 3). These results were in agreement with the findings of a previous study[20] in which there was no significant difference in maxillary and mandibular dental crowding in obese and nonobese adolescents aged 13 years. According to that study, obese and nonobese patients had similar needs for orthodontic treatment.

Obese patients perceived greater pain at all of the times evaluated, with a peak and significantly greater intensity than the control group after 24 hours (Table 4). A previous, prospective cohort study[21] assessed the influence of obesity on perceived orofacial pain in adolescents undergoing orthodontic therapy using fixed appliances and showed that obesity was associated with higher pain levels and consumption of analgesics compared with controls. These studies suggest that obesity influenced tooth movement by affecting bone remodeling and also affected orthodontic therapy–related parameters such as pain perception.

In addition, obesity was associated with changes in adipokine, leptin, and resistin levels[22] in the GCF, all of which have been reported to influence bone remodeling and the function of osteoblasts/osteoclasts.[23] Leptin had numerically higher concentrations in the obese group at the four time points evaluated (Table 3). This higher concentration in obese people can be explained by the fact that leptin is synthesized from adipose tissue.[24] One hypothesis would be a possible adaptation with a change in the response of obese people to the obesogenic environment based on a previous study in which rats were the experimental model.[25]

Table 4. Comparison of the Mean Visual Analog Scale Scores for Perceived Pain, by Group and Time

	G1	G2	P
T1	0.53 ± 0.25	0.10 ± 0.98	.110
T2	6.57 ± 0.26	5.13 ± 0.44	.006*
T3	1.07 ± 0.32	0.43 ± 0.14	.074

* Statistically significant at $P < .05$.

Table 5. Comparisons of Leptin, IL-1β, and TNF-α Cytokine Concentrations Over Time, Within and Between Groups

	T0	T1	T2	T3	Group	Time	Group × Time
Leptin, pg/mL							
G1	14.9 (10.6–19.2)	14.8 (11.5–18.0)	12.0 (11.4–12.5)	13.0 (11.5–14.4)	.08	.30	.41
G2	11.9 (11.3–12.4)	11.8 (11.4–12.0)	11.5 (11.3–11.7)	11.7 (11.4–12.0)			
IL-1β, pg/mL							
G1	10.3 (5.0–15.6)	12.8 (6.9–18.7)	20.1 (12.4–27.7)	17.9 (7.5–28.2)	.01*	.00*	.61
G2	4.47 (2.9–6.0)	3.4 (1.7–5.0)	11.5 (3.9–19.0)	12.2 (5.6–18.8)			
TNF-α, pg/mL							
G1	0.47 (0.29–0.65)	0.90 (0.73–1.07)	0.80 (0.55–1.05)	0.40 (0.15–0.65)	.28	.00*	.34
G2	0.37 (0.19–0.54)	0.63 (0.44–0.83)	0.60 (0.33–0.87)	0.50 (0.26–0.74)			

* Statistically significant at $P < .05$.

There were decreases in leptin concentrations in relation to baseline at T_1 and T_2, with a slight increase at T_3 in both groups. A decrease IN leptin concentration in the GCF after 1 hour and 24 hours after bonding of fixed appliances suggested that leptin may be one of the mediators responsible for tooth movement.[26]

The decrease in leptin levels at the beginning of tooth movement might possibly be explained by the fact that leptin inhibits genesis and action of osteoclasts.[27] This decrease in GCF leptin concentration might be consequent to tissue resorption in the compressed and tension sites or even secondary to possible cell necrosis in the periodontal ligament during orthodontic treatment.[28]

The correlation between salivary leptin and the slow tooth movement rate in obese individuals was presented previously.[29] However, the current results demonstrated that the tooth movement was similar in both groups (Table 3). The obese group had the highest concentration of IL-1β cytokine 24 hours after bonding, while this occurred at 7 days in the control group. According to a systematic review,[7] the IL-1β cytokine level peaked after 24 hours. On the other hand, another study reported that the peak was reached in 7 days.[30] However, IL-1β is one of the chemical inflammatory mediators that induces secretion of substances that cause pain.[31] This fact can be confirmed by the intergroup difference in the levels of cytokine and pain since obese individuals in the present study reported peak pain after 24 hours, coinciding with the peak concentration of IL-1β.

In both groups, there was an increase in the concentration of TNF-α cytokine at T_1 and T_2 in relation to baseline, with a decline at T_3. This behavior followed the pattern described in a systematic review,[8] in which all evaluated studies showed an increase in the first 24 hours after bonding of fixed appliances, with a decline after 1 week. As was found in the current study, the application of orthodontic forces caused an immediate increase in the levels of inflammatory mediators responsible for bone resorption (IL-1β and TNF-α) after 1 hour, reaching the peak in 24 hours, which supports the role of inflammation in initial tooth movement.[30] On the other hand, leptin levels decreased in the first week. The hypothesis would be that this was caused by leptin's inhibition of bone resorption, which is desirable at the beginning of tooth movement.

Despite the limitations of this investigation, the results contribute to the scientific literature, since there are few studies associating excess weight, pain, and orthodontic tooth movement. The relationship between obesity and orthodontic treatment, especially in relation to tooth movement, remains unexplained because of the scarcity of studies in this area. Therefore, clinical protocols should not yet be changed, and tooth resorption should not be considered to be associated with obesity, as scientific data are insufficient.

CONCLUSIONS

- Obese adolescents displayed higher orofacial pain after 24 hours of orthodontic treatment and higher concentrations of IL-1β proinflammatory cytokine before and during tooth movement than nonobese adolescents did.
- There was no difference in tooth movement between obese and nonobese patients during the first week of orthodontic treatment.

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DISCLOSURE

The authors declare no conflict of interest.

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