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Effect of obesity on tooth movement using an orthodontic device and changes in inflammatory cytokines, periodontal tissues, and orofacial pain

A. ALNAZEH

Department of Orthodontics, Faculty of Dentistry, King Khalid University, Abha, Saudi Arabia

Abstract. – OBJECTIVE: This study aimed to investigate the effect of obesity prospectively on tooth movement via an orthodontic device and changes in inflammatory cytokines, periodontal tissues, and orofacial pain.

SUBJECTS AND METHODS: Prospective design in which data was gathered at baseline T0, 1 hour, 24 hours, and 1 week after the application of fixed orthodontic appliances. The total sample size was 60 participants aged between 12 to 18 years and divided into 2 groups based on the inclusion and exclusion criteria. Anthropometrical estimation was made using a bioimpedance meter. A clinical assessment was performed before the application of fixed appliance bonding (T0) one hour after bonding (T1), after 24 hours (T2), and finally after one week (T3). At T0 little irregularity index was assessed, gingival crevicular fluid (GCF) was collected and periodontal examination including probing depth (PD), gingival bleeding (GB), and the presence or absence of calculus were measured. Orofacial pain was assessed at three levels: 1 hours, 24 hours, and 1 week after application of fixed orthodontics using a visual analog scale. For inter-group comparison, Mann-Whitney and *t*-tests were used and for interphase, comparison cluster analysis was performed. The level of significance was $p<0.05$

RESULTS: The participants in obese groups were significantly higher in terms of weight, BMI, WHR, FM, and BF than in the non-obese group ($p<0.05$). Obese participants had significantly more PD 4-5 mm (0.64±0.23 mm) and significantly higher BoP compared to non-obese participants (0.13±0.10 mm). Little's irregularity index at T0 and T3 showed no significant difference among obese and non-obese participants. The inflammatory cytokines level of IL-β was higher in the obese group compared to non-obese groups.

CONCLUSIONS: The intensity of orofacial pain was higher in obese participants after 24 hours along with high levels of IL-β pro-inflammatory cytokines before and during orthodontic treatment. No difference was noted in tooth movement in both obese and non-obese during orthodontic treatment in the first week.

Key Words:
Proinflammatory cytokines, Obesity, Orthodontic tooth movement, Orofacial pain, Adults.

Introduction

Obesity is a public health concern for developed and developing countries[1]. Obesity is considered to be a risk factor for many other co-morbidities in adolescents[2]. These co-morbidities may range from cardiovascular, musculoskeletal, hypertension, and various endocrine diseases[2]. Evidence highlights that obese individuals suffer from chronic inflammation along with raised cytokine levels which may result in a delayed immune response[3]. Raised inflammatory cytokines may include tumor necrosis factor-alpha (TNF-α), Interleukin-1β (IL-β), Interleukin-6 (IL-6), and leptin[4]. These cytokines are produced by an augmented count of macrophages in adipose tissues of obese individuals with altered circulating levels deferring immune response and contributing to systemic inflammation[5].

Obese individuals undergoing orthodontic treatment are now commonly seen, as awareness and knowledge concerning oral care and aesthetics are growing. Oral habits affect maxillo-facial and cranial growth and development[6], which are directly related to nature, duration, and onset of habit. Pain in the orofacial region harmfully influences adolescents[7]. Extensive pain indicates an alteration in central sensitization, explaining an association between over-weightiness and co-

Corresponding Author: Abdullah Alnazeh, JBO; e-mail: Aalnazh@kku.edu.sa

morbidities linked to painful conditions[8,9]. Orthodontic-induced tooth movement results in the variation of the microbiome following infection, such as a provocative response in the periodontal tissues[6,10]. Fixed orthodontics devices hinder dental cleaning which results in plaque buildup. Tooth movement is a complicated process and includes a connection between the alveolar bone, cells (osteoclast and osteoblast), and periodontal ligament[11]. Displacement of teeth and remodeling of bone are consequences of seditious response tempted by a power-driven stimulus[12].

Adipose tissues along with orthodontic tooth movement induce inflammation altering the levels of TNF-α, IL-β, IL-6, and leptin which are directly related to obesity and tooth movement[13-15]. However, a lack of evidence exists between fixed orthodontic treatment, orofacial pain, periodontal status, and inflammatory cytokines in obese adolescents. Thus the present study aimed to investigate the effect of obesity prospectively on tooth movement *via* an orthodontic device and changes in inflammatory cytokines, periodontal tissues, and orofacial pain.

Subjects and Methods

Participants and Study Design

The present study followed a prospective design in which data was gathered at 1 hour, 24 hours, and 1 week after the application of fixed orthodontic appliances. The present study was approved by the Ethical Research Committee of King Khalid University (IRB/KKUCOD/ETH - 2022/23/027). The study followed the Declaration of Helsinki which is in line with the ethical principles involving human subjects. Written consent was made to sign by all involved participants.

The total sample size was 60 participants aged between 12 to 18 years and divided into 2 groups. Clinical evaluation and scrutinization were performed by the department of orthodontics of King Khalid University based on the inclusion and exclusion criteria. The subjects were categorized into two groups 30 each. Group 1 is obese (18 female and 12 male) and non-obese (20 female and 10 male). Shortlisting of the participants was performed based on the inclusion and exclusion criteria. The participants included were based on the following included criteria. Participants whose dental records indicated fixed orthodontic treatment in the age range 12-18 years at the start of treatment; participants having permanent dentition; Little's irregularity index between 3 to 12 mm; willing participants with flexible hours. The exclusion was based on the following criteria: use of anti-inflammatory drugs regularly; medical systemic conditions; individuals who didn't consent; pregnant; breastfeeding participants and individuals who used antibiotics in the last six months.

Anthropometrical Estimation

230 Multifrequency Tetrapolar Bioimpedanciometer (BIC) was used for measuring body composition and body mass. The precision of BIC was 100 g and the capacity of 250 kg. Stadiometer was used for measuring height having an accuracy of 0.1 cm. Body mass index (BMI) percentile was used to analyze nutritional status through BMI using growth parameters related to age and sex from WHO AnthroPlus 1.0 (https://who-anthroplus.informer.com/).

Clinical assessment, Little's Irregularity Index, and VAS for Orofacial Pain

A clinical assessment was performed at four points in time. Before the application of fixed appliance bonding (T0) and one hour after bonding (T1), after 24 hours (T2), and finally after one week (T3). At baseline i.e., before bonding, T0 Little's irregularity index was assessed, gingival crevicular fluid (GCF) was collected and periodontal examination including probing depth (PD); gingival bleeding (GB), and presence or absence of calculus were measured. Fixed orthodontic treatment consisted of metallic brackets 20-24 g and 0.028 inches (Denmark Dental Platinum Plus Bracket, India). Bonding of brackets was followed by insertion of NiTi 0.014 inch archwires inserted and tied with elastomeric ligatures. PD was assessed as gingival margin distance to apex of the gingival sulcus. PD and GB were assessed at three sites mesially, distally, and centrally both palatally and buccally in all the teeth except the third molars. At points, T1, T2, and T3 pain were assessed using a visual analog scale also GCF was collected simultaneously. At point T3 i.e., after 1-week little irregularity index was measured.

The measurement of Little's irregularity index was performed using a digital caliper on the mandibular model corresponding to the occlusal plane. The Little's irregularity index measures rectilinear dislodgment of the functional connexion points between together mandibular incisor teeth and the summation of measurements is the

Table I. Characteristics of participants in the group.

Anthropometric characteristics	Obese participants mean ± SD (min-max)	Non-obese participants mean ± SD (min-max)	*p*-value
Age (years)	14.22 ± 2.47 (12-18)	14.65 ± 2.21 (12-18)	**.11**
BMI kg/m^2	25.85 ± 3.25 (19.49-28.68)	19.48 ± 2.47 (17.68-23.55)	**.00***
Height m	1.55 ± 9.47 (1.74-1.88)	1.68 ± 8.74 (1.98-1.68)	**.87**
Weight kg	77.58 ± 21.88 (49.8-128.5)	54.25 ± 9.54 (41.25-77.55)	**.00***
Waist to hip ratio WHR	0.98 ± 0.09 (0.84-1.01)	0.80 ± 0.02 (0.77-0.99)	**.00***
Skeletal muscular mass SMM	27.24 ± 7.11 (15.8-43.6)	24.25 ± 5.11 (17.4-36.9)	**.22**
Fat mass (FM)	30.44 ± 13.55 (11.8-60.4)	11.55 ± 4.22 (11.9-24.5)	**.00***
Body fat % (BF)	38.5 ± 7.4 (16.4-54.8)	20.88 ± 7.5 (7.1-34.9)	**.00***
Protein mass (PM)	10.8 ± 1.9 (7.1-15.2)	8.9 ± 1.9 (6.8-13.4)	**.20**
Minerals mass (MM)	3.6 ± 0.9 (2.2-5.1)	3.1 ± 0.4 (2.1-4.1)	**.08**
Total body water	36.21 ± 8.10 (23.5-56.21)	33.1 ± 6.9 (24.5-47.6)	**.28**

little irregularity index. The measurement is used to quantify tooth movements in a group. Changes in the intergroup of index specify similar tooth movement.

Orofacial pain was assessed at three levels. T1 one hour, T24 hours, and 1 week after application of fixed orthodontics using a Visual analog scale. The intensity of pain was measured from 0 to 10. The directions were given to the participants to avoid analgesics during this period.

Collection of GCF

Sterile absorbent paper cones (#45 New Delhi, India) were used for the collection of GCF. Initially, removal of supra gingival plaque was performed from (distal to six mandibular, central, lateral, and canines). This was followed by drying for 5 sec and isolation with sterile cotton rolls. After isolation, the absorbent cones were interleaved into the sulcus of gingiva at a depth of 1 mm for 45 sec. If the absorbent paper was contaminated with saliva or blood they were wasted.

After collection, the absorbent paper cones were transported into Eppendorf tubes holding 200 mL of phosphate buffer saline along with 0.1% of tween solution (Thermo Fisher Scientific, Waltham, MA, USA) and a 1µL protease inhibitor cocktail (DMSO solution, Sigma Aldrich, St. Louis, MO, USA). The tubes were centrifuged for 300 sec at 12000 rpm and then stored at -90°C for further supplementary examination.

Statistical Analysis

Luminex xMAP for multiple assays was used for the assessment of IL-β, TNF-α, and leptin in GCF. The readings of plates were performed using MagPix equipment (Luminex Corporation, Austin, TX, USA). The protocol was used as recommended by the manufacturer. For inter-group comparison, Mann-Whitney and *t*-tests were used and for interphase, comparison cluster analysis was performed. The level of significance was $p<0.05$.

Results

Table I demonstrates the anthropometric characteristics of participants in two groups, obese and non-obese. The participants in obese groups were significantly higher in terms of weight, BMI, WHR, FM, and BF than in the non-obese group ($p<0.05$).

On assessing PD Table II. Obese participants had significantly more PD 4-5 mm (0.64±0.23

Table II. Periodontal parameters in obese and non-obese.

Periodontal parameters	Obese participants (n = 30)	Non-obese participants (n = 30)	*p*-value
PD mm	2.35 ± 0.21	2.04 ± 0.14	**0.47**
PD 0-3 mm	96.47 ± 4.26	97.31 ± 3.97	0.00*
PD 4-5 mm	0.64 ± 0.23	0.13 ± 0.10	0.00*
% Calculus teeth	9.25 ±3.47	7.39 ± 3.04	**0.67**
% BoP	14.26 ± 5.66	7.29 ± 4.21	0.00*

Probing depth (PD); Bleeding on Probing (BoP). Statistically significant at $p < 0.05$.

Table III. Littles irregularity index measured T0 and T3.

Dental crowding mm	T0	T3	Group	Time	Group x Time
Obese	4.70 (4.25-5.77)[a]	3.25 (2.04-4.29)[b]	.48	.00*	0.78
Non-obese	4.30 (3.21-5.28)[a]	3.10 (2.39-3.62)[b]			

Same letter ([a] and [b]) denote no significant difference .Statistically significant at $p < 0.05$.

mm) and significantly high BoP compared to non-obese participants (0.13±0.10 mm). Similarly, PD between 0-3 mm was significantly less in obese compared to non-obese ($p<0.05$).

Little's irregularity index at T0 and T3 showed no significant difference among obese and non-obese participants. However, a significant decrease in crowding was noted in both groups at T3 i.e., after one week. Pain assessment using VAS at T2 i.e., 24 hours after fixed orthodontic appliance exhibited a significant difference between obese and non-obese participants ($p<.05$). However, generally, the intensity of pain was higher in obese participants. (Table III- IV)

The inflammatory cytokines level of IL-β was higher in the obese group to non-obese groups. Fluctuation in concentration was seen with time (Table V). Similarly, the cytokine TNF-α showed variation in time which was also found to be significant ($p<.05$) (Table V).

Table IV. Pain assessment using a visual analog scale (VAS) at TI, T2, and T3 among obese and non-obese participants.

Time	Obese	Non-obese	*p*-value
T1	0.85 ± 0.32	0.44 ± 0.11	.258
T2	7.20 ± 0.24	6.11 ± 1.22	.006*
T3	1.56 ± 0.33	0.88 ± 0.18	.074

Same letter ([a] and [b]) denote no significant difference .Statistically significant at $p < 0.05$.

Discussion

The findings of the present longitudinal study showed that obese participants experienced orofacial pain after 24 hours of fixed orthodontic appliance. Obesity is an excessive accumulation of adipose tissue associated with an upsurge of systemic proinflammatory cytokines leading to chronic inflammation subclinically[10,16]. In the existing study, BMI and body composition including FM, SMM, and water were evaluated using a bioimpedance test. BMI in the present study was significantly higher in obese participants undergoing fixed orthodontic treatment compared to non-obese. Therefore, for better assessment and treatment planning, BMI along with other indicators of body composition needs to be assessed. These include BF, SMM, FM, and body water.

In the existing study, obese participants had significantly more PD 4-5 mm (0.64±0.23 mm) and significantly high BoP compared to non-obese participants. The precise explanation of this outcome is still unclear and dubious. Recent studies by Atabay et al[17] and Huang et al[18] proclaim that obese individuals have more periodontal destruction due to high oxidative stress

Table V. Levels of cytokines at T0 to T3 within and between groups.

Cytokine level	T0	T1	T2	T3	Group	Time	Group x time
Leptin pg/mL							
Obese	15.9 (10.9-19.4)	15.1 (12.4-17.9)	12.5 (11.9-12.8)	13.7 (11.8-14.9)	.09	.40	.51
Non-obese	11.6 (11-12)	11.1 (11-12)	11.1 (11.1-11.9)	11.9 (11.5-12)			
IL-β pg/mL							
Obese	11.43 (5.21-16.47)	12.5 (6.7-18.1)	21.1 (12.8-27.9)	16.8 (8.8-24.9)	.01*	.00*	.61
Non-obese	3.45 (2.5-6.5)	3.11 (1.58-6.25)	11.0 (4.0-18.5)	12.5 (6.6-19.5)			
TNF-α pg/mL							
Obese	0.57 (0.21-03.385)	0.99 (0.60-1.22)	0.85 (0.21-1.88)	0.50 (0.10-0.65)	.30	.00*	0.31
Non-obese	0.21 (0.11-0.58)	0.51 (0.30-0.90)	0.45 (0.23-0.91)	0.60 (0.20-0.60)			

Statistically significant at $p < 0.05$.

in periodontal tissues. Moreover, the periodontal immune response in obese individuals is compromised plummeting the infiltration and activation of immune cells and macrophages aggravating periodontal conditions[18]. A current systematic review by Khan et al[19] endorses the findings of the present study of higher PD in obese participants compared to non-obese. Similarly, the prevalence of BoP was also higher in obese individuals compared to non-obese. A possible explanation for this conclusion is the escalation of pro-inflammatory cytokines IL-β and TNF-α. Both the cytokines are documented as an indication of an inflammatory systemic condition[4,10]. Another contributing factor to increased BoP or worsening periodontal condition is dental crowding which may create a barrier to maintaining good oral hygiene[20].

Based on little irregularity index at T0 and T3 showed no significant difference among obese and non-obese participants. However, a significant decrease in crowding was noted in both groups at T3 i.e., after one week. In the current study patients who needed fixed orthodontic treatment had mandibular crowding regardless of the anterior-posterior relationship of basal bones[21]. The verdict of the current study was in line with the previously reported work by Giuca et al[22] who narrated that obese and non-obese participants were the same in terms of needs for orthodontic treatment.

Pain assessment using VAS at T2 i.e., 24 hours after fixed orthodontic appliance exhibited a significant difference between obese and non-obese participants ($p<.05$). However, generally, the intensity of pain was higher in obese participants. The findings of the present study were in harmony with the previously reported prospective cohort by Yan et al[24] who claimed obese participants with a fixed orthodontic appliance had high utilization of analgesics and aggravated intensity of orofacial pain[23]. The findings of the present and previous work by Yan et al[24] suggest that tooth movement by bone remodeling and pain perception are influenced by obesity.

The level of leptin was higher in obese participants from T0, T1, T2, and T3 compared to non-obese. A peptide in nature hormone leptin maintains the reproductive system, intake of food, and body mass. The higher concentration of leptin in obese participants may be associated with the synthesis of this hormone by white adipose tissues and fat cells[15]. Obesity results in high levels of leptin, which acts as a pro-inflammatory cytokine and amplifies the process of insulin resistance[10,25,26]. However, it was surprising to note that the level of leptin decreased at T1 and T2 from baseline in both obese and non-obese participants. A downward trend in the levels of leptin may initially indicate that at the start of tooth movement leptin impedes osteoclastic activity with an increase in resorption of leptin in the sites of tension and compression in the periodontal tissues during tooth movement[27-29]. Similarly, obese participants had the highest IL-1β after 24 h of bonding. IL-β is one of the proinflammatory mediators that result in the secretion of substance that induces pain. This finding can be confirmed by the present study as obese individuals experienced high pain after 24 h. Moreover, recent work by Elangovan et al[30] found a direct co-relation between WHP ratio and IL-β[30,31]. The outcome of the present study also supports this finding. At T1 and T2 the concentration of cytokine TNF-α in both obese and non-obese groups was higher compared to the starting point. However, a descent was observed at T3. This is the same pattern as seen in a systematic review by Kapoor et al[32]. It is believed that orthodontic forces application increased inflammatory mediators' liable for bone resorption reaching a peak at 24 h and then a gradual decline. This response supports the role of inflammation in the initial movement of the tooth[33].

Limitations

The present study is subjected to some inherent limitations. The association between obesity and orthodontic-induced tooth movement is still difficult to explain due to the lack of studies in this area. More randomized control trials (RCT) are compulsory to extrapolate the findings of the present study. Dental clinicians must educate obese patients seeking orthodontic treatment regarding the link between obesity and tooth movement and periodontal tissue inflammation.

Conclusions

The intensity of orofacial pain was higher in obese participants after 24 hours along with high levels of IL-β pro-inflammatory cytokines before and during orthodontic treatment. No difference was noted in tooth movement in both obese and non-obese during orthodontic treatment in the

first week.

Conflict of Interest
The author declares no conflict of interest.

Informed Consent
Written consent was signed by the participating individuals who were told about the purpose of the study and were allowed to withdraw at any point in time.

Funding
No funding was received for the study.

Data Availability
Data can be made available on request.

Ethics Approval
The present study was approved by the Ethical Research Committee of King Khalid University (IRB/KKUCOD/ETH - 2022/23/027). The study followed the Declaration of Helsinki which is in line with the ethical principles involving human subjects

ORCID ID
A. Alnazeh: 0000-0002-2381-2285

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