Influence of fixed orthodontic treatment on the menstrual cycle of adult females:
A prospective longitudinal study
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ABSTRACT
Objective: To investigate the influence of fixed orthodontic treatment on the menstrual cycle, including menstrual cycle length (MCL) and duration of menstrual bleeding (DMB), in adult female patients.

Materials and Methods: This was a prospective longitudinal study conducted in Chengdu, China. A total of 164 adult women with normal menstrual cycles were recruited in the study, with 79 patients undergoing orthodontic treatment and 85 serving as controls. Data of MCL, DMB, and accompanying symptoms were collected over six consecutive menstrual cycles in each participant. Student’s t test, Chi-square test, Moses extreme reaction test, and repeated measures analysis of variance were used for statistical analysis.

Results: The MCL of the first menstrual cycle (T1) was significantly elongated by 2.1 ± 0.5 days compared with baseline (P = .003, 95% CI [−3.7, −0.5]). Variability of MCL of the orthodontic group at T1 was also significantly greater (range, 15–46 days) than that of the control group (range, 24–36 days) (P < .05). No significant difference in MCL was found in the subsequent five menstrual cycles (T2–T6) compared with baseline, and no significant differences in DMB or other accompanying symptoms were observed throughout the study.

Conclusion: Fixed orthodontic treatment may influence the MCL of adult females in the first month after bonding, but showed no effect on DMB or subsequent MCL through the follow-ups. (Angle Orthod. 2016;86:475–480.)

KEY WORDS: Orthodontic treatment; Menstrual cycle length; Menstrual bleeding

INTRODUCTION
There has been an increasing demand for orthodontic treatment by adults, especially female, due to its benefits in improving esthetics, self-esteem, and jaw function.1 A German survey has shown that 97% of patients, composed mainly of females, desire to receive orthodontic treatment for esthetic purposes.2 However, while aligning teeth and improving esthetics, orthodontic treatment can cause some adverse events such as pain, discomfort, anxiety, dietary changes, and even damage to oral tissues. These adverse events can lead to stress or psychological changes in patients.3–6

It has been demonstrated that physical as well as psychosocial factors are associated with menstrual disorders, for example, high-density training and changes in nutrition, occupation, and lifestyle.7,8 These factors that induce acute or chronic stress may affect the hypothalamic-pituitary-adrenal axis, cause menstrual disorders directly or indirectly, and eventually affect health, school and work productivity, and social activities.9
Does orthodontic treatment influence the menstrual cycle in female patients? Preliminary data indicate that primary dysmenorrhea is predictive for initial orthodontic pain in female patients and that the rate of tooth movement may vary across the menstrual cycle. Nonetheless, the influence of orthodontic treatment on the menstrual cycle is still largely unknown. Considering that the demand for orthodontic treatment has been growing rapidly worldwide and that the normal menstrual cycle is essential for fertility and maintenance of women’s health, it is important to know whether orthodontic treatment affects the menstrual cycle. This may provide valuable information to both orthodontists and gynecologists and help to interpret menstrual irregularities in patients wearing fixed orthodontic appliances.

The aim of this study was to investigate the influence of orthodontic treatment on the menstrual cycle, including menstrual cycle length (MCL), duration of menstrual bleeding (DMB), and other accompanying symptoms, in adult female patients.

**MATERIALS AND METHODS**

This prospective longitudinal study was approved by the Ethics Committee of West China Hospital of Stomatology, Sichuan University. Subject recruitment started in June 2011 from the Department of Orthodontics of the hospital. All participants provided written informed consent.

The determination of sample size was based on previous studies on menstrual cycles, by setting type I error at 0.05 and type II error at 0.20 (80% power). To account for possible dropouts during the study, we aimed to recruit 164 participants. A total of 420 participants were assessed for eligibility; 256 participants were excluded from the study mainly due to menstrual irregularities, resulting in 164 participants enrolled in the study (79 patients in the orthodontic group and 85 participants in the control group) (Figure 1).

Female orthodontic patients (age, 18–40 years) were informed about the purpose and procedure of the study when they accepted the recommended orthodontic treatment plan. Then the patients who agreed to participate were screened for eligibility before starting treatment. Eligible participants were enrolled in the orthodontic group. Control participants (age, 18–40 years) were recruited among students, nurses, technicians, and staff of Sichuan University at the same time. None of the controls had received orthodontic treatment in the past nor were under additional discomfort (menstrual pain, discomfort in breast or abdomen). All participants were required to keep a consistent standard when collecting information over six consecutive menstrual cycles. Participants’...
information was collected at each orthodontic appointment for the treatment group and by phone call for the controls every month. If the MCL or DMB records over the study period were incomplete, the participants were excluded from the study.

Data were input by EpiData 3.0 (Informer Technologies, Inc, Waltham, Mass) and the MCLs and DMBs were calculated by the statistic technician blindly from each participant’s logbook. Statistical analyses were performed using the Statistical Package (SPSS for Windows, Version 20.0, IBM, Chicago, Ill). The chi-square test and Student’s t test were used to analyze the categorical variables and normally distributed continuous variables, respectively. Repeated measures analysis and two-way ANOVA compared the changes of MCL and DMB between and within groups. The Moses extreme reaction test was used to compare the variability of MCL. A P value of < .05 was considered statistically significant.

RESULTS

During the six-menstrual-cycle observation period, four participants in the orthodontic group and seven in the control group were excluded from the study because of irregular attendance, nonreply to follow-up, use of oral contraceptives, or unwillingness to continue the study, finally resulting in 75 participants in each group for statistical analysis. With this sample size, the power of this study declined to 99.4%. The baselines of the two groups before the study were not significantly different in demographics, age at menarche, MCL, DMB, BMI, or psychological indices of SAS and SDS (Table 1) (P > .05).

The interaction effect between the time factor (different follow-up time points) and the treatment factor (orthodontic group and control group) was significantly different (P < .001). Analysis of the time effect showed that, within the orthodontic group, the MCL was significantly different after orthodontic treatment had commenced (F = 4.1, P = .001), whereas the MCL within the control group did not differ significantly (F = 2.1, P = .07). In the orthodontic group, a significant elongation of MCL of 2.1 ± 0.5 days was observed at the first menstrual cycle (T1) compared with baseline (T0) (P = .003, 95% CI [−3.7, −0.5]) (Figure 2). The MCL at T1 in the orthodontic group was significantly longer than that at T1 in the control group based on the analysis of treatment factor (F = 5.445, P < .05) (Figure 2). The variability of MCL in the orthodontic group at T1 was also significantly wider (range, 15–46 days) than the control group (range, 24–36 days) (P < .05) (Figure 3). No significant difference of MCL was found in the subsequent five menstrual cycles (T2–T6) either between the orthodontic and control groups at each
observational time point (T2–T6) or within groups between the observational points (T2–T6) and baselines (T0) in the two groups (P < .05).

The interaction effect between the time factor and treatment factor in the DMB showed no statistical significant difference throughout the study (F = 0.4, P = .83). There was no significance among different observational time points within each group (F = 2.1, P = .16) nor between the two groups at different time points (F = 2.0, P = .08) (Figure 2). No significant difference in menstrual bleeding amount, menstrual pain, or other symptoms was observed within each group over six menstrual cycles.

DISCUSSION

To our knowledge, this was the first clinical study aiming to assess the influence of orthodontic treatment on menstrual cycles in adult female patients. This prospective longitudinal study followed the participants over six menstrual cycles. We found that the length and variability of the first MCL in the orthodontic group was significantly affected after wearing fixed orthodontic appliances compared with the controls, but not subsequent MCLs (T2–T6). The DMB and other accompanying symptoms were not affected by orthodontic treatment during follow-up.

During the experiment design, some confounders were reported that might have influenced the menstrual cycles, thus the following measures were assessed and analyzed before studying the effects of orthodontic treatment. Regarding the age range in the study, the participants were required to be between 18 and 40 because these groups of women are considered to have more stable menses and reproductive function compared with adolescents.12,16 The subjects were not separated into subgroups because participants between 25 and 40 constituted a relatively small percentage of total subjects (orthodontic, 14.6%; control, 15.8%). Moreover, no significant difference of MCL or DMB at baseline was observed between 18–24-year-old and 25–40-year-old subjects within groups (data not shown). Besides age range, the other possible factors influencing menstrual cycles, including patient’s occupation, ethnicity, marital status, BMI, and psychological condition (SAS and SDS),15,17,18 were also assessed and compared before the study. In brief, all these factors were not significantly different between the two groups, ensuring that the baseline characteristics of the two groups were similar and comparisons after follow-ups were more convincing in both groups.

| Table 1. Comparison of Baseline Characteristics Between Orthodontic Group and Control Group* |
|--------------------------------------------|---------------------------------|---------|
| Orthodontic (n = 75) | Control (n = 75) | P value |
| Age (years)a | 21.8 ± 3.6 | 22.2 ± 3.8 | .5 |
| Occupationb | .9 |
| Student | 57 (76.0%) | 56 (74.7%) |
| Other | 18 (24.0%) | 19 (25.3%) |
| Ethnicitya | .2 |
| Han | 74 (98.7%) | 70 (93.3%) |
| Other | 1 (1.3%) | 5 (6.7%) |
| Marital statusb | .6 |
| Married | 64 (85.3%) | 67 (89.3%) |
| Unmarried | 11 (14.7%) | 8 (10.7%) |
| Age at menarche | 13.0 ± 1.5 | 12.9 ± 1.3 | .8 |
| MCL (days)a | 29.0 ± 2.8 | 29.1 ± 2.6 | .8 |
| DMB (days)a | 5.0 ± 0.9 | 4.8 ± 0.8 | .1 |
| BMI (kg/m²)a | 18.9 ± 1.7 | 19.2 ± 1.7 | .3 |
| SAS (points)a | 39.1 ± 8.3 | 38.0 ± 8.6 | .4 |
| SDS (points)a | 44.7 ± 8.5 | 43.3 ± 9.9 | .4 |

* MCL represents menstrual cycle length; DMB, duration of menstrual bleeding; BMI, body mass index; SAS, Zung Self-Rating Anxiety Scale; SDS, Zung Self-Rating Depression Scale.

a All data represent mean ± standard deviation.

b All data represent number of participants (percentage).

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Figure 2. Changes in menstrual cycle length (MCL) and duration of menstrual bleeding (DMB) with time in the orthodontic and control groups. (a) first MCL of orthodontic group (T1) was increased significantly compared with baseline (T0) (P < .01); (b) first MCL of orthodontic group (T1) was significantly increased compared with MCL in control group at same time point (T1) (P < .05). All data represent mean ± standard error.
The initial fixed orthodontic treatment may cause elongation (2.1 days) and variability of the first month MCL and but not the MCL afterward. Though elongation of the first MCL was statistically significantly different from baseline, the changes of MCL in this study could not be regarded as being clinically significant for oligomenorrhea (abnormal menstrual cycle variation) because by definition, this is a condition wherein menstrual periods occur more than 35 days apart.19

Regarding variability of MCL, the range of the first MCL in the treatment group was more spread out (15–46 days) after wearing fixed orthodontic appliances, whereas the variability of MCL in the control group was more restricted (24–36 days). Clinical attention is important when a menstrual cycle is either shorter than 21 days or longer than 45 days.12,16 When diagnosing menstrual cycle irregularity, gynecologists should keep in mind that there might be a 1-week variability of MCL in patients who just started fixed orthodontic treatment in the previous month. In addition, the elongation and variability of MCL appeared only during the first menstrual cycle; few aberrations were observed during the subsequent menstrual cycles in this study. Moreover, no significant difference of DMB or other accompanying symptoms was observed, suggesting that the effect of orthodontic treatment on DMB may be minor compared with psychological distress or shift work.20,21

The mechanism of the influence of fixed orthodontic treatment on MCL is unclear. Most previous studies have demonstrated that stress and psychological factors have a negative effect on the menstrual cycle.9 For example, changing jobs or working in a stressful job was found to be associated with changes in menstrual cycles.8,22 And about 16% of schoolgirls claimed that they had irregular menses during stressful situations such as school examinations.23 Dietary and nutritional changes were also found to be related to changes in the menstrual cycle.24 Patients usually experience pain, discomfort, and anxiety, and also are given dietary advice by orthodontists during the initial stage of fixed orthodontic treatment.3,25,26 These experiences can cause acute stress and nutritional changes and may thus increase the production of corticotrophin-releasing hormone, leading to an aberration in the menstrual cycle during the first month of wearing fixed orthodontic appliances.27 In this study, after patients got used to the treatment and dietary changes, the menstrual aberration reverted to normal in subsequent menstrual cycles as anticipated.

The results of animal studies suggest that orthodontic treatment may also affect the menstrual cycle through the regulation of estradiol receptor \( \alpha \) (ER\( \alpha \)) or estradiol in periodontal tissues. Previous experiments on rat models have indicated that, when orthodontic force was applied, the levels of ER\( \alpha \) declined while estradiol was elevated during metestrus and diestrus phases, causing a short time elongation of their estrous cycle at the beginning of orthodontic treatment.28,29

One limitation of this study is its reliance on the accuracy of self-reported menstrual cycle dates by the participants. Although estradiol and progesterone testing for monitoring and defining the menstrual cycle phase are considered more accurate, they are relatively invasive so for ethical reasons they were not used in this pilot study.30 The Hawthorne effect may also influence the outcome since the participants were informed of the study design and were aware of being observed. This influence may, however, be minor because the menstrual cycle, compared with other aspects of individual behavior, is less subjectively controlled.20,21 The other factors (classification of malocclusion, tooth extraction, level of crowding, life stage...
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REFERENCES