Original Article

Primary dysmenorrhea is potentially predictive for initial orthodontic pain in female patients

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ABSTRACT

Objective: To investigate the relationship between primary dysmenorrhea (PD) and orthodontic pain in female patients, and to test the hypothesis that the intensity and duration of orthodontic pain could be roughly predicted by severity of PD.

Materials and Methods: One hundred twenty college females were enrolled and put into one of three groups—mild (Mi), moderate (Mo), or severe (S)—according to level of menstrual pain. Intensity of the orthodontic pain was measured by visual analog scale (VAS) on days 1, 2, 4, 7, 14, and 28 after archwire placement.

Results: As the intensity of orthodontic pain declined with time, the three groups demonstrated different changes during the initial week. Mi had the lowest VAS scores, whereas S possessed the highest scores. In contrast, Mo stayed in between. Significantly positive correlations were found between the severity of PD and the intensity of orthodontic pain at each time point within the first 2 weeks. In addition, though the majority of subjects reported disappearance of pain by the end of the second week in both Mi and Mo, a large proportion of females still perceived pain in S.

Conclusion: Females with higher levels of menstrual pain tended to perceive orthodontic pain with higher intensity and more prolonged duration. Thus, PD could potentially serve as a reference to predict orthodontic pain in clinical settings. (*Angle Orthod.* 2014;84:424–429.)

KEY WORDS: Orthodontic pain; Primary dysmenorrhea; Visual analog scale; Prediction

INTRODUCTION

Recently there has been an increase in demand for orthodontic treatment. The number of patients is skyrocketing, and females constitute the majority. However, in contrast to males, females are more vulnerable to orthodontic pain, a negative experience that more than 90% of the patients complain of during orthodontic treatment.[1,2] According to previous research, the intensity of pain that females perceived was stronger than that perceived by males, which was seen from days 3 to 7 after administration of orthodontic forces. In addition, the pain persisted longer in women. By the day 7, only approximately 25% of male patients reported pain, but, in contrast, >50% of the female patients were still reporting pain.[2–4] Therefore, it is of great necessity to predict the possible pain of female patients so that orthodontists can take measures to control the pain in clinical settings.

Pain is an individualized perception that differs among subjects. Prediction of pain is difficult in clinical settings because of these individual variations. Although a few previous studies reported the predictive power of a series of psychological factors[5] and

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personality traits[5,6] for orthodontic pain, the prediction was made based on a plethora of psychological scales that can hardly be navigated without the professional assistance of a psychologist. Furthermore, it was time consuming to collect and analyze the data for each patient, which seemed impractical in orthodontic clinics, considering the large number of patients an individual doctor treats on a daily basis.

Primary dysmenorrhea (PD) is a common symptom among adolescent girls and adult women, the prevalence rate of which is as high as 90%.[7] Defined as a cramping pain or discomfort in the lower abdomen at the onset of menstruation in the absence of any identifiable pelvic disease, PD is a relatively stable perception of pain that most female orthodontic patients are already acquainted with. Furthermore, PD is reported to be caused by an increased level of pain mediators such as prostaglandin,[7–9] which is the same one that induces orthodontic pain.[10–12]

Thus, we hypothesized that PD could be a reference to predict the orthodontic pain of female patients. The aim of the study was to investigate the relationship between the severity of PD and the intensity of orthodontic pain in females. We also attempted to analyze whether the severity of PD could indicate duration of orthodontic pain.

MATERIALS AND METHODS

Subjects

The study was approved by the bioethics committee of the university. Informed consent was obtained from each participant. The inclusion criteria were (1) female college student who started their orthodontic treatment in West China Hospital of Stomatology during the period 2009 to 2012; (2) mild crowding ($<$4 mm) of each jaw treated by fixed appliance without extraction of any teeth; (3) no other malocclusions except crowding; (4) no pregnancy or abortion; (5) no gynecological organic diseases, confirmed by a pelvic ultrasound examination; (6) regular monthly menstrual experience; (7) menstrual discomfort/pain that had remained stable for at least half a year; (8) agreement not to take any analgesics during the period of study. Individuals were excluded if they (1) had undergone previous orthodontic treatment, (2) had used analgesics within 3 days prior to orthodontic treatment, (3) had recently experienced a toothache, (4) exhibited excessive anxiety according to the Trait-Anxiety Inventory (T-AI) score ($\geq$57),[13] or (5) had a cold pressor test (CPT) that displayed abnormal pain threshold ($<$3 sec or $>$60 sec) and abnormal pain tolerance ($>$5 min).[14]

In total, 124 females were enrolled in the study. Before grouping, they were asked to finish an 11-point numeric rating scale (NRS), from *no pain* (0) to *worst pain* (10), to score the feeling of menstrual pain experienced within half a year. The patients were then grouped according to the values on the NRS: 0 for *no pain* (N), 1–3 for *mild pain* (Mi), 4–6 for *moderate pain* (Mo), and 7–10 for *severe pain* (S).[15] No one rated 0 for their menstrual experience, so the subjects were assigned to one of three groups. There were 43 subjects in Mi, 51 in Mo, and the remaining 30 in S.

Methods

Prior to orthodontic treatment, dental casts of the subjects were obtained, and the malocclusions were analyzed in terms of arch length discrepancy (ALD) and peer assessment rating (PAR) scores. In addition, baseline questionnaires were administered to all participants. The questionnaires included assessment of pain threshold and pain tolerance level by CPT, of anxiety level by T-AI, of personality traits by Eysenck personality questionnaire (EPQ),[16] and of motivation for treatment by motivation questionnaire.[2]

To be specific, CPT was done by requiring a participant to place their hand in the cold pressor for as long as they could. Once pain was present, the time was recorded as pain threshold. Once the pain was unbearable, the time was subtracted by threshold as the pain tolerance level. T-AI measured trait anxiety using 20 items scored by a participant from 1 to 4, demonstrating *never*, *sometimes*, *usually*, and *always*, respectively. The higher the total score was, the higher the level of anxiety the participant possessed as a trait. EPQ assessed personality trait by four scales with a total of 88 items, which included an extraversion (E) scale with 21 items, a neuroticism (N) scale with 23 items, a psychoticism (P) scale with 21 items, and a lie (L) sale with 20 items. The participants completed the questionnaire by answering *yes* or *no* for each item, and four scores were calculated for each scale demonstrating different dimensions of temperament for a participant. The motivation questionnaire was characterized by two questions in terms of their willingness to bear high levels of pain and to accept extended treatment time, each on a five-step scale from 1, *definitely yes*, to 5, *definitely no*. A motivation score, summed by the two assessments, was calculated to demonstrate how important the participant felt it was to get aligned teeth.

The orthodontic treatment was initiated within 1 week after the latest menstrual period ended. All patients received 0.014-inch nickel-titanium (ClassOne Orthodontics, Carlsbad, Calif) archwires for both the upper and lower arch to initiate aligning immediately after bracket (Xinya Corp, Hangzhou, China) bonding. They were given routine instructions on dietary habits and

Table 1. Comparison of Malocclusion and Baseline Parameters Among the Groups[a]

	Mi (n = 42)		Mo (n = 48)		S (n = 30)	
	Mean	SD	Mean	SD	Mean	SD
NRS*	2.3	0.8	5.0	0.8	7.4	0.6
Ages	22.3	3.3	21.5	2.9	22.8	3.4
ALD, mm						
Upper arch	−2.3	1.1	−1.8	1.5	−2.5	1.7
Lower arch	−2.2	1.7	−2.9	2.0	−2.5	2.1
PAR scores	6.8	3.7	8.0	3.3	7.2	2.9
CPT, s						
Pain threshold	30.1	26.5	27.6	23.3	25.5	20.3
Pain tolerance	203.2	178.3	197.3	171.8	165.3	160.3
EPQ						
Extraversion	12.3	2.9	11.9	3.3	11.0	3.2
Neuroticism	9.5	3.8	9.9	4.5	11.9	4.4
Psychoticism	9.3	3.6	9.8	4.0	10.3	3.5
Lie	9.7	2.5	9.9	2.7	9.5	2.5
T-AI	36.9	8.1	38.5	8.7	41.9	10.2
Motivation	6.3	2.2	6.1	2.6	5.3	2.0

[a] Mi indicates mild; Mo, moderate; S, severe; SD, standard deviation; NRS, numeric rating scale; ALD, arch length discrepancy; CPT, cold pressor test; EPQ, Eysenck personality questionnaire; T-AI, Trait-Anxiety Inventory score.

* $P < .05$, indicating a significant difference in NRS (PD) among the three groups.

oral hygiene maintenance. No intervention for pain was prescribed.

The intensity of orthodontic pain was measured on the evening of days 1, 2, 4, 7, 14, and 28 after archwire placement by telephone interviews. The participants were reminded to complete a 100-mm visual analog scale (VAS), with the lower end indicating *no pain* and the upper end indicating *extreme pain*. The VAS scores before insertion of the initial archwires were not recorded.

Statistical Analysis

The statistical analysis was performed by SPSS Statistics version 20 (IBM Corp, New York, NY). Baseline parameters of the three groups were calculated, and analysis of variance tests were applied to evaluate whether these parameters were balanced.

The VAS scores were calculated as nonparametric statistics, because of a skewed distribution of the data. To evaluate the general differences among the three groups during the overall period, a general linear model for repeated measures was applied. The intergroup difference at each time point was compared by a Kruskal-Wallis rank-sum test with statistical significant level set at $P < .05$.When the Krusakal-Wallis rank-sum test yielded significant results, indicating that at least one group was significantly different from the others, a Dunnet multiple comparison test was performed for multiple-group comparison to determine which group significantly differed. The statistically significant level was set at $P < .05$.

To assess the correlation between the VAS of orthodontic pain and the NRS of PD at each time point, correlation analysis was carried out to yield the Spearman rank correlation coefficient.

As the number of subjects who scored a VAS of 0 met the criteria for the chi-square test from day 7 on, the test was used to compare the percentages of subjects who reported no pain among the three groups at each time point on days 7, 14, and 28. Statistical significance was set at $P < .05$. When the chi-square test yielded significant results, indicating that at least one group was significantly different from the others, chi-square tests for fourfold tables were performed for multiple group comparison to determine which group significantly differed. The statistically significant level was adjusted according to Bonferroni correction as $P < .017$.

RESULTS

Of the total 124 females enrolled, four subjects (one in Mi and three in Mo) were excluded because they failed to record the VAS score at every required time point. The dropout percentage was 3.2%, which was considered within the acceptable limit. Descriptive analysis of malocclusion and baseline parameters is given in Table 1. NRS for PD differed significantly between groups because of the way we grouped the subjects. Except for that, no significant difference was seen in terms of age, ALD, PAR scores, pain threshold and tolerance, anxiety level, personality trait, and motivation between the three groups, indicating that baseline levels were generally balanced.

The general linear model for repeated measures showed that VAS scores demonstrated intergroup differences during the overall period. As Figure 1

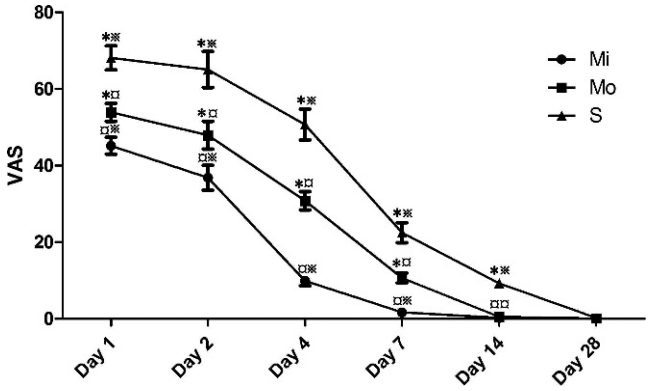

Figure 1. Changes of orthodontic pain on days 1, 2, 4, 7, 14, and 28 after archwire placement in the three groups. Significant intergroup difference at each time point was set at $P < .05$. * indicates significant differently from Mi; ※, significantly different from Mo; ¤, significantly different from S.

shows, pain intensities exhibited a downward tendency along the time, but the changes in pain intensity were significantly different between the three groups. The intergroup comparison at each time point showed that Mi had the lowest VAS scores during the first 7 days. In contrast, S possessed the highest VAS scores, and those of Mo stayed in between. On day 14, the VAS score of Mo declined to a similar level as that of Mi, while that of S remained higher. By day 28, the three groups shared a similar level of VAS scores.

The results of correlation between NRS scores and reports of pain intensity (VAS scores) are presented in Table 2. Significantly positive correlations were found between NRS for PD and VAS scores reported on days 1, 2, 4, 7, and 14, indicating that the more severe the PD was, the more intense the orthodontic pain would be at the first five time points.

Percentages of patients who reported no pain (VAS = 0) for the last three time points are shown in Table 3. The chi-square tests demonstrated a significantly higher proportion of people reporting no pain on day 7 in Mi than in Mo and S. This proportion of pain-free subjects in Mo approached that of Mi at the end of the second week, whereas this proportion in S did not approach that of Mi until day 28. Thus, though the pain was not perceived by a majority of patients in Mi on day 7, it was still perceived by almost all patients in Mo and S. When only a tiny minority of patients reported pain in Mi and Mo on day 14, a large majority of females in S still suffered from orthodontic pain. The result indicated that orthodontic pain tended to persist among subjects with a higher intensity of PD.

DISCUSSION

An important finding of our study was the good correlation between NRS scores of menstrual pain and VAS scores of orthodontic pain within the initial 2 weeks after force initiation. The females who had experienced heavier PD were prone to report more intense pain during the initial 2 weeks of orthodontic treatment. They also tended to have prolonged pain experiences in contrast to those who reported milder PD.

Prediction of females' orthodontic pain is necessary for both medical and social reasons. However, the existing methods of prediction are not convenient enough for widespread application in clinical settings. A simple method to predict orthodontic pain is thus required. In the present study, we evaluated PD, a pain experience common to most female patients. We confined our subjects to college students so that the ages and educational backgrounds of the subjects were similar. We assigned the subjects to one of three groups based on the established classifications for NRS in terms of PD. Orthodontic treatment was initiated within 1 week after the latest menstrual period ended to prevent concurrence of PD that might have interfered with assessment of orthodontic pain. The orthodontic force was balanced among groups by confining the extent of malocclusion and the size of initial archwire, because the magnitude of force was previously reported to be associated with orthodontic pain.[17] In addition, the baseline parameters that were considered to influence orthodontic pain were balanced among the groups, primarily due to a rigorous selection of subjects.

Our results exhibited differences in reported pain between the three groups, which were further confirmed by correlation analysis. The heavier the PD was, the higher the level of orthodontic pain a patient might perceive. This tendency was especially of clinical significance for the initial few days after archwire placement because it was the period when the pain was most intense for the majority of patients. Our results also revealed differences in pain duration according to severity of PD. In our study, the percentage of patients whose pain disappeared was

Table 2. Correlation Between the Severity of PD (NRS) and the Intensity of Orthodontic Pain (VAS) at Different Time Points[a]

	VAS Day 1	VAS Day 2	VAS Day 4	VAS Day 7	VAS Day 14	VAS Day 28
Correlation coefficient	.69	.64	.84	.85	.69	.18
P value	<.000*	<.000*	<.000*	<.000*	<.000*	.051

[a] PD indicates primary dysmenorrhea; NRS, numeric rating scale; VAS, visual analog scale.
* $P < .05$, indicating a statistically significant correlation between NRS and VAS.

Table 3. Comparison of the Percentage of Subjects That Reported No Pain Among the Groups on Days 7, 14, and 28[a]

	Percentage of Subjects Reporting No Pain (VAS = 0)				
	Mi	Mo	S	χ^2	*P* Value
Day 7	61.9%	8.3%	3.3%	44.12	<.001*
Mi vs Mo				28.92	<.001*
Mo vs S				25.62	<.001*
Mi vs S				0.77	.644
Day 14	90.5%	83.3%	16.7%	52.23	<.001*
Mi vs Mo				0.99	.368
Mo vs S				33.62	<.001*
Mi vs S				39.63	<.001*
Day 28	95.5%	93.8%	90.0%	0.79	>.672
Mi vs Mo				0.10	1.000
Mo vs S				0.37	.670
Mi vs S				0.74	.643

[a] VAS indicates visual analog scale; Mi, mild; Mo, moderate; S, severe.
* $P < .05$, indicating a significant intergroup difference in the proportion.

calculated and compared from day 7 on, because the pain was reported to begin disappearing on day 7.[18] Our results showed that the proportion of subjects reporting no pain in S was significantly lower compared to that of the other groups until day 14, at which point the proportions of Mi and Mo reached a similarly high level, approximating 100%. This suggests that females with severe PD tend to suffer from a persistent orthodontic pain. Taken together, our data indicated that PD could potentially serve as an intuitive and simple reference to preliminarily predict orthodontic pain in females.

The relationship between the two types of pain could possibly be explained by the following aspects. From a molecular level, both PD and orthodontic pain share some vital pain-mediating substances that activate nociceptors to induce pain perception. Calcitonin gene-related peptide (CGRP) is one of those mediators. It in one way enhances pain perception by promoting release of substance P (SP), a common neurotransmitter released in response to nociceptive stimulus, and in another way prolongs pain perception by postponing degradation of SP.[19] The role of CGRP in inducing orthodontic pain has been widely acknowledged by researchers.[20,21] Recently it was found to be highly expressed in the dorsal root ganglia cultured with peritoneal fluids from patients with dysmenorrhea.[22] Taken altogether, CGRP is a possible pathway that to some extent explains why PD victims tend to react more intensely and more persistently to orthodontic pain. From a macroscopic perspective, both types of pain bear some resemblance in terms of their temporal features. To be specific, both PD and orthodontic pain generally occur on a monthly basis and peak during period onset. As severity and duration of pain are closely related with psychogenic processes, the negative pain memory and related anxiety associated with PD might induce heavier and more persistent nociception in response to a temporally similar type of pain. These assumptions about joint pathways of pain generation need to be further investigated step by step.

One limitation to this preliminary investigation is that only college students were studied, which restricted the extension of our findings to a broad majority of female orthodontic patients. Moreover, patients with minor crowding could be merely representative for a minority of the patient population. Additional studies with a larger panel of subjects should be carried out to validate these findings and provide more detailed insights into prediction of orthodontic pain using PD.

To summarize, PD is potentially predictive for orthodontic pain in female patients, after it has been confirmed on an independent panel of female patients. The present study renders orthodontists some implications to roughly predict the intensity and duration of orthodontic pain by referring to patients' experiences with menstrual pain, a possible method that might help in addressing a significant side-effect during orthodontic treatment.

CONCLUSIONS

- Females with a higher level of menstrual pain tended to perceive orthodontic pain with higher intensity and prolonged duration.
- PD could potentially serve as a reference to predict orthodontic pain in clinical settings.

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REFERENCES

1. Scheurer PA, Firestone AR, Bürgin WB. Perception of pain as a result of orthodontic treatment with fixed appliances. *Eur J Orthod*. 1996;18:349–357.
2. Bergius M, Berggren U, Kiliaridis S. Experience of pain during an orthodontic procedure. *Eur J Oral Sci*. 2002;110: 92–98.
3. Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. *Pain*. 1975;1:277–299.
4. Graber TM, Eliades T. *Risk Management in Orthodontics: Experts' Guide to Malpractice*. Hanover Park, Ill: Quintessence; 2004.
5. Bergius M, Broberg AG, Hakeberg M, Berggren U. Prediction of prolonged pain experiences during orthodontic treatment. *Am J Orthod Dentofacial Orthop*. 2008;133: 339.e1–339.e8.
6. Abu Alhaija ES, Aldaikki A, Al-Omairi MK, Al-Khateeb SN. The relationship between personality traits, pain perception and attitude toward orthodontic treatment. *Angle Orthod*. 2010;80:1141–1149.
7. Coco AS. Primary dysmenorrhea. *Am Fam Physician*. 1999; 60:489–496.
8. Roth-Brandel U, Wiqvist N, Bygdeman M. Effect of prostaglandins on the contractility of the non-pregnant human uterus in vivo. *Acta Obstet Gynecol Scand Suppl*. 1971;9(suppl 9):35.
9. Chan WY, Dawood MY, Fuchs F. Prostaglandins in primary dysmenorrhea. Comparison of prophylactic and nonprophylactic treatment with ibuprofen and use of oral contraceptives. *Am J Med*. 1981;70:535–541.
10. Giannopoulou C, Dudic A, Kiliaridis S. Pain discomfort and crevicular fluid changes induced by orthodontic elastic separators in children. *J Pain*. 2006;7:367–376.
11. Ren Y, Vissink A. Cytokines in crevicular fluid and orthodontic tooth movement. *Eur J Oral Sci*. 2008;116:89–97.
12. Kehoe MJ, Cohen SM, Zarrinnia K, Cowan A. The effect of acetaminophen, ibuprofen, and misoprostol on prostaglandin E2 synthesis and the degree and rate of orthodontic tooth movement. *Angle Orthod*. 1996;66:339–349.
13. Shek DT. The Chinese version of the State-Trait Anxiety Inventory: its relationship to different measures of psychological well-being. *J Clin Psychol*. 1993;49:349–358.
14. Johnson MH, Petrie SM. The effects of distraction on exercise and cold pressor tolerance for chronic low back pain sufferers. *Pain*. 1997;69:43–48.
15. McCaffery MB. *Pain: Clinical Manual of Nursing Practice*. Baltimore, Md: Mosby; 1993.
16. Smillie LD, Bhairo Y, Gray J, Gunasinghe C, Elkin A, McGuffin P, et al. Personality and the bipolar spectrum: normative and classification data for the Eysenck Personality Questionnaire-Revised. *Compr Psychiatry*. 2009;50: 48–53.
17. Yang Z, Luo W, Hou J, Zhao Z, Jian F, Wamalwa P, et al. Development of a behavior model of pain induced by experimental tooth movement in rats. *Eur J Oral Sci*. 2009;117:380–384.
18. Erdinc AM, Dincer B. Perception of pain during orthodontic treatment with fixed appliances. *Eur J Orthod*. 2004;26: 79–85.
19. McCulloch J, Uddman R, Kingman TA, Edvinsson L. Calcitonin gene-related peptide: functional role in cerebrovascular regulation. *Proc Natl Acad Sci U S A*. 1986;83: 5731–5735.
20. Hall M, Masella R, Meister M. PDL neuron-associated neurotransmitters in orthodontic tooth movement: identification and proposed mechanism of action. *Todays FDA*. 2001; 13:24–25.
21. Norevall LI, Forsgren S, Matsson L. Expression of neuropeptides (CGRP, substance P) during and after orthodontic tooth movement in the rat. *Eur J Orthod*. 1995;17:311–325.
22. Barcena de Arellano ML, Arnold J, Vercellino GF, Chiantera V, Ebert AD, Schneider A, et al. Influence of nerve growth factor in endometriosis-associated symptoms. *Reprod Sci*. 2011;18:1202–1210.