Original Article

Orthodontic pain: an interaction between age and sex in early and middle adolescence

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ABSTRACT

Objective: To investigate the age and sex interaction effect on orthodontic pain in adolescence during the initial phase of fixed orthodontic treatment.

Materials and Methods: Three hundred participants (mean age 13.85 $\pm$ 1.98 years; 152 female, 148 male) met all inclusion criteria and enrolled in the study designed as 2 $\times$ 2 factorial trial with two levels each for age (11–14 years; 14–17 years) and sex (male; female). A 0.16-inch superelastic NiTi wire was used in a 0.022-inch slot (Roth's prescription) preadjusted edgewise appliance for initial leveling and alignment of mandibular anterior dentition. The follow-up period was 7 days. Pain was assessed by using 100 mm visual analog scale for one baseline and nine follow-up repeated measurements at prespecified time points. Data were analyzed by using generalized linear mixed effect model analysis.

Results: Three participants were lost to follow-up, and 17 participants were not considered for analysis due to incomplete or improperly completed questionnaire. Therefore, 280 participants (mean age 13.96 $\pm$ 2.01 years; 138 female, 142 male) were analyzed for results. Results showed that age and sex interaction had statistically significant effect on pain ($F = 3.56$; $P = .0151$; *df* 3/218). In the 11–14 year age group, there was no significant difference for pain between male and female. In the 14–17 year age group, girls reported significantly greater pain compared to 14- to 17 year-old boys ($t = 2.76$; $P = .0209$). Pain reported by 14- to 17-year-old girls was also significantly greater compared to 11- to 14-year-old boys ($t = 2.91$; $P = .0206$).

Conclusions: Age and sex interaction has significant effect on orthodontic pain during adolescence, and 14- to 17-year-old girls experienced maximum pain. (*Angle Orthod.* 2013;83:966–972.)

KEY WORDS: Age and sex interaction; Orthodontic pain; Adolescence

INTRODUCTION

Orthodontic treatment during adolescence can bring many psychosocial benefits, including improvement in esthetic self-perception.[1] However, fear of pain and discomfort is a concern for many prospective orthodontic patients,[2] and pain has been reported to be the worst aspect of treatment and the highest-ranking reason for discontinuing the orthodontic treatment.[3]

Orthodontic pain, being a subjective response, can be influenced significantly by several factors, including age[4,5] and sex[6–8] of the individual. However, many other studies have concluded that there is no significant effect of age[7,9] or sex[5,7,10] on orthodontic pain. Therefore, at present, there is no consensus regarding the effect of age and/or sex on orthodontic pain. One possible reason for this, perhaps, is the fact that all of these previous studies have investigated the effect of age and sex on orthodontic pain from an independent perspective. There is growing evidence that age and sex interaction has significant contribution to pain response in adolescents because the sex difference in pain responses emerges especially after puberty.[11]

The only specific study that investigated orthodontic pain during adolescence (11–17 years) was published in 1991, more than 20 years ago.[4] But, even this study

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investigated the effect of age only and did not consider the effect of sex. Furthermore, a literature search shows no study was ever undertaken to examine the effect of age and sex interaction on orthodontic pain during adolescence.

Therefore, the present study was designed with an objective to investigate the age and sex interaction effect on mean average orthodontic pain over a period of 7 days after initial archwire placement. The follow-up period of 7 days was considered because previous studies have shown that the maximum pain occurs during the first few days after orthodontic force application, and pain decreases substantially after 7 days.[5–7] The two age groups considered in this study represented early adolescence (11–14 years) and middle adolescence (14–17 years), as per the criteria of early and middle adolescence laid down by the American Academy of Pediatrics.[12]

MATERIALS AND METHODS

The trial was designed as a 2 $\times$ 2 factorial design with two levels each for age (11–14 years and 14–17 years) and sex (male and female). The primary issue in this type of study design, in which the primary objective is to investigate the interaction effect, is the sample size of the trial.[13] We adopted the same strategy for sample size calculation as recommended by Montgomery et al.[13] for interaction effect in a factorial design. Assumptions for determining sample size, such as target effect size and correlation between follow-up repeated measurements, were based on the results from the pilot study. Sample size was calculated by doing power analysis (Stata 10.0, StataCorp, College Station, TX) for repeated measure design with one baseline and nine follow-up measurements (correlation coefficient $r = 0.18$). Calculations showed that to demonstrate a mean average difference of 10 mm (standard deviation 25 mm for each group; Cohen d effect size 0.4) on a 100 mm visual analog scale (VAS) for age and sex interaction effect at a significance level of .05 and 90% power; 72 participants per group (total 288) were required.[13]

Total sample size for this trial comprised 300 participants (mean age 13.85 $\pm$ 1.98 years; 152 female, 148 male). The participants were consecutive patients who visited the private office of the first and second authors for orthodontic treatment and were enrolled in the study if all the inclusion criteria were satisfied. The study protocol was approved by the local Ethical Review Committee (Indian Medical Association, Jalandhar, Punjab India; January 28, 2011).

Inclusion criteria were as follows: (1) 11- to 17-year-old boys and girls who required fixed orthodontic treatment; (2) moderate to severe crowding in the mandibular anterior segment; (3) eruption of all mandibular anterior teeth; (4) no history of medical problem/medication that may influence the pain perception; and (5) informed and witnessed consent from the participants and parents/guardians.

Exclusion criteria were as follows: (1) severe deep bite or severe crowding (eg, blocked out lateral incisors) that could affect bracket placement on mandibular anterior teeth; (2) malocclusion correction that required treatment procedures other than continuous archwire mechanics; (3) medical condition that precluded the use of fixed orthodontic appliance such as allergy to nickel; recent history of epileptic seizure and physicians' consent could not be obtained; and (4) any chronic pain or pain in dental or orofacial region.

Preadjusted edgewise 0.022 $\times$ 0.028-inch slot twin brackets (Roth prescription, Gemini Metal Brackets, 3M Unitek Corporation, Monrovia, Calif) were bonded directly to mandibular dentition using light cure composite resin (Transbond XT, 3M Unitek Corporation). A 0.016-inch superelastic NiTi (austenitic active, preformed ovoid, superelastic archwire, 3M Unitek Corporation) wire was used as initial archwire for leveling and alignment. Only the mandibular arch was bonded until the completion of the study. The severity of initial crowding[14] and the number of extraction/nonextraction cases in each group were recorded. Intervention and follow-up was done by both first and second authors, both qualified orthodontists. The follow-up period was 7 days.

The outcome was assessed by using 100 mm VAS, which is a valid and reliable scale for pain assessment.[15] Pain was assessed for one baseline (prewire placement) and nine follow-up (post wire placement) measurements at the following prespecified time points: 1 hour, 4 hours, 12 hours, 24 hours (day 1 morning), 36 hours (day 1 bedtime), 48 hours (day 2 morning), 72 hours (day 3 morning), 120 hours (day 5 morning), and 168 hours (day 7 morning). At each time point, outcome was assessed at rest position.

Participants marked a line across the scale corresponding to perceived pain. The mark was then measured from the left margin of the line to the nearest millimeter to quantify the pain, recorded as VAS scores in mm. The VAS score was measured by trained dental assistants (blinded to study) using a calibrated Vernier caliper (manual type) (Mitutoyo 530-316 Stainless Steel Vernier Caliper; Mitutoyo Corporation, Kanagawa 213-8533, Japan) with a least count of 0.1 mm. To examine the reproducibility and reliability, 40 randomly selected VAS scales were measured by the first and second authors independently, and intraclass correlation coefficient 0.93 showed excellent reproducibility and reliability.

For pain relief, participants were allowed to take an over-the-counter analgesic of their choice. However, participants were requested, if possible, to record pain before taking the medication in order to minimize the effect of the analgesic on the pain recording.

Statistical Analysis

Data were analyzed by using SAS 9.2 software (SAS Institute Inc, Cary, NC). Demographic and clinical characteristics, including frequency, the arithmetic mean, and standard deviation were calculated using descriptive statistics. Generalized linear mixed model analysis was used for analysis of longitudinal data. Null hypothesis were tested at a significance level of .05. Preliminary exploratory and graphical analysis revealed that the pain trend was nonlinear and followed a quadratic pattern. Therefore, quadratic random coefficient analysis was undertaken by using maximum likelihood method of estimation and unstructured variance/covariance structures. The quadratic model fit was evaluated as described by Littell et al.[16] Age (0 = 11–14 years; 1 = 14–17 years) and sex (0 = male; 1 = female) were dummy coded. Time was recorded in hours and coded as an orthogonal polynomial because the objective of the trial was to capture the mean average pain. Orthogonal polynomials are best suited for such an objective and also eliminate the problem of multicollinearity.[17]

Multiple pairwise comparisons (MPC) of simple effect was done for hypotheses testing because the *P* values adjusted via simulation methods eliminate the problem of multiplicity, and adjusted *P* values can be compared directly to the significance level of .05.[18] We used Shaffer step-down simulation method for *P* values adjustment because it has superior Type I error control and power to detect true pairwise differences for unbalanced repeated measure designs.[19]

RESULTS

During the trial, three participants (two male and one female) were lost to follow-up, and data obtained from 17 participants (4 male and 13 female) were not considered for analysis due to incomplete or improperly completed questionnaire. A total of 280 participants (mean age 13.96 $\pm$ 2.01 years; 138 female, 142 male) were analyzed for results (Table 1). Table 2 shows VAS score data for each time point.

The result of quadratic random coefficient regression analysis is shown in Table 3a. Orthogonal polynomial intercept, time[1] (linear) term and time[2] (quadratic) term represent the mean average pain across all time points, linear pain trend, and quadratic pain trend, respectively, for 14- to 17-year-old girls. The mean average pain for 14- to 17-year-old girls was significantly greater compared to 14- to 17-year-old boys and 11- to 14-year-old boys due to significant age and sex interaction effect (F = 3.56; P = .0151) as shown by overall F test statistic results (Table 3b). There was no significant effect of age and sex interaction on linear or quadratic pain trend (Tables 3a and 3b). Least square means (LS-means) plots of VAS scores for each group and age and sex interaction effect are shown in Figures 1 and 2, respectively.

Table 1. Demographic and Clinical Characteristics Data[a] (n = 280)

Age	Sex: Male	Sex: Female
11–14 years		
Number	72 (25.7%)	70 (25.0%)
Mean age, y	12.3 (1.2)	12.4 (1.2)
Menarche onset		34 (48.6%)
Initial crowding[b]	6.5 (1.3)	6.8 (1.4)
Extraction[c]	32 (44.4%)	38 (54.2%)
VAS score[d]	17.1 (20.8)	20.6 (23.0)
14–17 years		
Number	70 (25.0%)	68 (24.3%)
Mean age, y	15.3 (1.1)	15.9 (1.0)
Menarche onset		64 (94.1%)
Initial crowding[b]	6.7 (1.4)	6.4 (1.3)
Extraction[c]	36 (51.4%)	31 (45.5%)
VAS score[d]	17.5 (20.0)	28.1 (26.3)

[a] Mean (SD) or number (percentage).
[b] Little's irregularity index score in millimeters.
[c] Cases in which extraction was done.
[d] Mean average visual analog scale (VAS) score in millimeters.

The result of the MPC substantiates these findings based on more valid and reliable *P* values (Table 4). Therefore, null hypothesis were rejected; 14- to 17-year-old girls experienced significantly greater pain compared to 14- to 17-year-old boys (t = 2.76; P = .0209) and 11- to 14-year-old boys (t = 2.91; P = .0206), and there was no significant difference for pain between 11- to 14-year-old boys and 11- to 14-year-old girls.

DISCUSSION

This clinical trial was designed as a 2 $\times$ 2 factorial design with an objective to investigate the age and sex interaction effect on mean average orthodontic pain in adolescence over a period of 7 days after initial archwire placement. In factorial design, a statistical interaction shows that the effect of one independent variable on the dependent variable changes depending on the level of another independent variable.[16]

The results show that due to significant age and sex interaction effect, 14- to 17-year-old girls reported maximum pain. This finding is in agreement with the general epidemiology of pain prevalence and sensitivity during adolescence. Recent systematic review concluded that pain prevalence rates are generally

Table 2. Descriptive Statistics of the Visual Analog Scale Scores (in mm) of Pain at Each Time Point

		Sex			
		Male		Female	
Age	Time	Mean	Standard Deviation	Mean	Standard Deviation
11–14 years	Baseline	0	0	0	0
	1 h	9.1	13.9	10.8	14.2
	4 h	17.9	17.3	21.9	19.6
	12 h	29.2	24.7	35.0	27.8
	24 h (day 1 morning)	31.6	24.3	39.2	25.3
	36 h (day 1 bedtime)	30.4	21.9	33.9	23.9
	48 h (day 2 morning)	23.2	19.6	28.1	21.3
	72 h (day 3 morning)	16.5	18.2	20.3	19.4
	120 h (day 5 morning)	10.1	11.8	12.0	14.9
	168 h (day 7 morning)	2.5	4.3	4.6	7.8
14–17 years	Baseline	0.0	0.0	0.0	0.0
	1 h	8.7	10.3	16.7	17.7
	4 h	17.6	16.7	29.8	22.3
	12 h	30.4	22.9	49.2	24.4
	24 h (day 1 morning)	33.6	22.6	51.0	25.7
	36 h (day 1 bedtime)	30.8	21.8	44.3	25.3
	48 h (day 2 morning)	23.9	20.8	34.5	24.3
	72 h (day 3 morning)	17.3	16.9	26.6	23.0
	120 h (day 5 morning)	10.5	10.9	18.5	19.9
	168 h (day 7 morning)	2.6	2.4	10.3	12.0

higher in girls and increases with age, therefore, suggesting an age and sex interaction effect on pain during adolescence.[20]

Biophysiologic, psychosocial, and physical factors can contribute to the age and sex interaction effect on pain during adolescence.[11,21] Evidence shows that pain perception among boys and girls changes significantly after puberty, and girls experience greater pain because hormone level fluctuation during the menstrual cycle lowers pain thresholds,[11] and complex central/peripheral interactions between specific neurotransmitters (eg, serotonin and opiates) and ovarian steroids lead to exaggerated response to painful stimulus.[22] In the present study, the effect of the aforementioned factors might have played an important role in greater pain reported by 14- to 17-year-old girls because the number of girls with a positive history of menarche onset in the 14–17 year age group (94.1%) was twice as high compared to the 11–14 year age group (48.6%).

Psychosocial factors also contribute to pain sensitivity during adolescence.[20] Anxiety and depression are the most common form of psychologic problems experienced during adolescence,[23] and both anxiety[24] and depression[25] are associated with increased clinical pain response. A recent study that examined 13- to 18-year-old adolescents concluded that symptoms of anxiety and depression showed the strongest associations with pain, and odds were significantly higher for girls than for boys.[26] Another study[27] investigated the

Table 3a. The Result of Quadratic Random Coefficient Regression Analysis

								95% Confidence Interval	
Effect[a]	Age, y	Sex	Estimate	Standard Error	*df*	*t* Value	Pr > |*t*|	Lower	Upper
Intercept			28.0933	2.7201	218	10.33	<.0001	22.7322	33.4543
Age × sex	11–14	Male	−11.0369	3.793	218	−2.91	0.004	−18.5125	−3.5613
Age × sex	11–14	Female	−7.5012	3.8192	218	−1.96	0.0508	−15.0285	0.02608
Age × sex	14–17	Male	−10.5552	3.8192	218	−2.76	0.0062	−18.0825	−3.0279
Time[1] (linear)			−15.0705	1.7121	2240	−8.8	<.0001	−18.428	−11.713
Time[1] × age × sex	11–14	Male	2.9293	2.3874	2240	1.23	0.22	−1.7524	7.6111
Time[1] × age × sex	11–14	Female	1.6023	2.4039	2240	0.67	0.5051	−3.1119	6.3164
Time[1] × age × sex	14–17	Male	2.9532	2.4039	2240	1.23	0.2194	−1.7609	7.6673
Time[2] (quadratic)			−24.5448	2.7179	256.4	−9.03	<.0001	−29.8971	−19.1925
Time[2] × age × sex	11–14	Male	5.6263	3.79	256.4	1.48	0.1389	−1.8371	13.0897
Time[2] × age × sex	11–14	Female	2.9401	3.8162	256.4	0.77	0.4418	−4.5749	10.4551
Time[2] × age × sex	14–17	Male	4.5893	3.8162	256.4	1.2	0.2302	−2.9258	12.1043

[a] Dummy coding: age (0 = 11–14 years; 1 = 14–17 years); sex (0 = male; 1 = female).
[b] Kenward Roger degree of freedom.

Table 3b. Overall *F* Test Statistic Results of Quadratic Random Coefficient Analysis

Effect	Numerator *df*[a]	Denominator *df*[a]	*F* Value	Pr > F
Age × sex	3	218	3.56	0.0151
Time[1] (linear)	1	2240	244.64	<.0001
Time[1] × age × sex	3	2240	0.68	0.5653
Time[2] (quadratic)	1	256.4	251.74	<.0001
Time[2] × age × sex	3	256.4	0.83	0.4768

[a] Kenward Roger degree of freedom.

prevalence of depression and factors influencing depression in adolescence (11–18 years of age) and reported higher level of depressive symptoms in girls than in boys, and more importantly, influence of pubertal onset of depression was greater in girls than in boys. Furthermore, poor body image and low self-esteem are crucial components in the development of depression and intensity of these risk factors is stronger for postpubertal girls.[27]

Therefore, it seems that various psychologic factors such as depression, anxiety, poor body image, and low self-esteem, which were earlier thought to be associated with orthodontic pain during adolescence,[2,4,6,28] have significant and substantial influence primarily on postpubertal girls.

Another possible reason for higher pain reported by 14- to 17-year-old girls could be attributed to the lower physical activity level. According to a recent survey[29] of high school students in grades 9–12 (14–18 years of age), the percentage of girls who engaged in any kind of physical activity was half (18.5%) that of boys (38.3%). Physical activity plays an important role in reducing pain sensitivity by inducing exercise-related physiologic hypoalgesia[30] and through a positive impact an individuals' mental toughness.[31] Mental toughness, which helps in coping with stress and anxiety, has a greater role in boys than girls because boys engage more frequently in physical activities than girls.[31] Research has also shown that sedentary behavior and pain are associated primarily in adolescent girls.[26]

In summary, the effect of age and sex on orthodontic pain during adolescence does not seem to occur in isolation, but there seems to be a synergistic effect of biophysiologic, psychosocial, and physical activity factors.

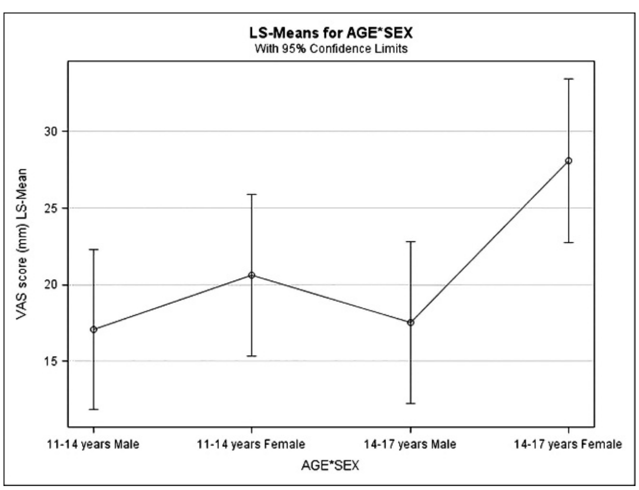

Figure 1. LS-means plot of VAS score for each group.

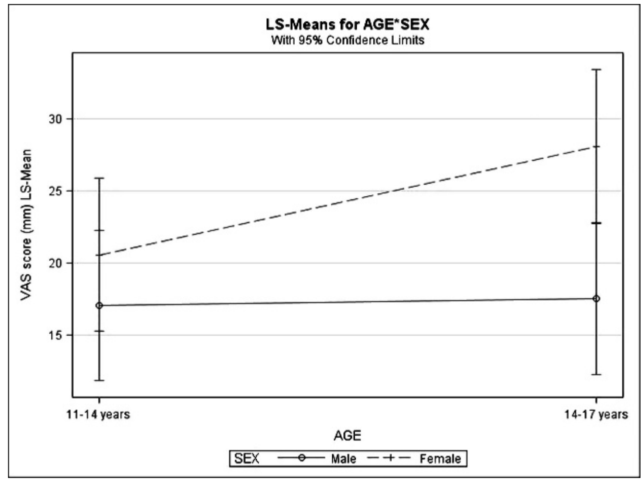

Figure 2. LS-means plot of VAS score for age and sex interaction effect.

Strength and Limitations of the Trial

The primary concern in clinical trials involving investigation of interaction effect is the adequacy of sample size. Results of this trial are conclusive in terms of power of statistical analysis because adequate sample size was included in the trial based on sound methodologic principles.[13] Furthermore, the minimum difference (10 mm) of VAS score used for sample size calculation and a hypothesis testing is a clinically significant difference for pain in children.[32]

However, the trial had limitations in terms of not including the various factors that could have influenced the outcome of the trial. Apart from biophysiologic, psychosocial, and physical activity factors, pain in adolescents can be influenced by many other factors such as the stage of biosocial development, parental education, and psychologic/mental health status, socioeconomic status, and sibling influence.[20] Therefore, more research investigating the correlates of pain in adolescent age is necessary.[20] We strongly recommend that the preliminary findings from this trial should be substantiated by future research in this direction to investigate the specific contribution of each of these aforementioned factors in orthodontic pain experienced by adolescents.

Table 4. Multiple Pairwise Comparisons of Simple Effects for Hypotheses Testing

Age, y	Sex	Age, y	Sex	Estimate	Standard Error	*df*[a]	*t* Value	Pr > |*t*|	Adjusted *P*[b]	95% Confidence Interval[b] Lower	Upper
11–14	Male	11–14	Female	−3.5357	3.765	218	−0.94	0.3487	.6163	−13.298	6.2265
11–14	Male	14–17	Male	−0.4817	3.765	218	−0.13	0.8983	.8983	−10.2439	9.2806
11–14	Male	14–17	Female	−11.037	3.793	218	−2.91	0.004	.0206	−20.8717	−1.2022
11–14	Female	14–17	Male	3.054	3.7914	218	0.81	0.4214	.6163	−6.7767	12.8848
11–14	Female	14–17	Female	−7.5012	3.8192	218	−1.96	0.0508	.0988	−17.404	2.4015
14–17	Male	14–17	Female	−10.555	3.8192	218	−2.76	0.0062	.0209	−20.458	−0.6525

[a] Kenward Roger degree of freedom.

[b] Shaffer-simulated step down adjustments of *P* values for pairwise comparisons.

Implications for Clinical Practice and Research

Management of orthodontic pain is of paramount clinical importance. Preliminary findings of this trial show that during the initial phase of fixed orthodontic treatment, 14- to 17-year-old girls are experiencing the maximum pain. This understanding can help in better management of resources such as patient education, motivation, and utilization of various pharmacologic and nonpharmacologic modalities for better pain management.

Findings of our study imply that imbalance for age and sex proportion in the sample size of interventional studies involving adolescents will severely affect the true outcome of the trial. The implications of imbalance in the baseline demographic characteristics, especially for the sex, are already widely recognized by the mainstream pain research.[21]

CONCLUSIONS

- Age and sex interaction has a significant effect on orthodontic pain.
- In the 11–14 year age group, there was no significant difference for pain between boys and girls, but in the 14–17 year age group, girls reported significantly greater pain compared to boys.

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