Original Article

Evaluation of Preemptive Valdecoxib Therapy on Initial Archwire Placement Discomfort in Adults

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ABSTRACT

The purpose of this randomized, double-blinded, placebo-controlled prospective clinical trial was to compare the efficacy of preemptive and postoperative administration of valdecoxib in reducing discomfort caused by initial archwire placement in adults. A total of 56 orthodontic patients aged 18–54 years who were to begin treatment were randomly assigned to one of three groups: (1) placebo, (2) those who received preemptive valdecoxib 40 mg at least 30 minutes before initial archwire placement, or (3) those who received postoperative valdecoxib 40 mg two hours after initial archwire placement. Patients in the active treatment groups also received continuous valdecoxib therapy for an additional 48 hours. Discomfort levels were recorded on a visual analog scale at zero, two, six, 24, and 48 hours after initial archwire placement. At baseline, no significant differences were detected between the three groups. In the preemptive valdecoxib group, there was no significant increase ($P > .05$) in discomfort from baseline at any time point. The placebo and postoperative valdecoxib groups showed significant ($P < .05$) increases in discomfort after six hours, with the peak discomfort at 24 hours. The postoperative group showed a tendency toward decreased discomfort over time, but the changes were not significantly different from the placebo or the preemptive group. Preemptive analgesia with nonsteroidal anti-inflammatory drugs may be an approach to prevent discomfort associated with initial archwire placement in healthy adults. (*Angle Orthod* 2006;76:251–259.)

KEY WORDS: Valdecoxib; Archwire placement; Discomfort; Adults

INTRODUCTION

Approximately 95% of orthodontic patients report pain.[1] Pain is the most commonly reported detrimental effect of orthodontic treatment and the greatest reason for wanting to discontinue or avoid orthodontic care.[2] A survey of adult orthodontic patients showed discomfort to be the most discouraging aspect of orthodontia.[3] Patients who have received both premolar extraction and orthodontic tooth movement have perceived more pain 24 hours after initial archwire placement than 24 hours after tooth extraction.[4] Patients usually report the most pain within the first day of orthodontic treatment, with pain levels approaching pretreatment values approximately one week later.[1,4–10]

Despite numerous studies detailing the discomfort associated with orthodontic treatment, readily available and effective pain relievers are not commonly used by patients. It has been noted that analgesic consumption among patients in active orthodontic treatment ranges from 16% to 27%,[1,11] with both discomfort and analgesic demand decreasing after day 3.[1,6]

Although orthodontic pain is not fully understood, it is believed to be partly due to blood flow alterations in the periodontal ligament (PDL).[12] Chemical mediators, such as prostaglandins, play a major role in the genesis of the pain.[5,12] Pain is multifactorial in origin and has been linked to sex,[1,11] age,[1,4,6,7,11,13] internal locus

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of control, psychological state, ethnicity, and dental arch under treatment.[7]

There have been few clinical studies evaluating analgesic protocols to alleviate pain. White[12] found that 63% of patients reported less discomfort after chewing analgesic gum. Ngan et al[5] showed that patients receiving 400 mg ibuprofen experienced significantly less pain than those receiving either 650 mg aspirin or placebo after placement of archwires or separators. More recently, it has been reported that preemptive administration of 400 mg ibuprofen after separator placement in adolescents produces significantly less discomfort than a placebo.[9,10]

Preemptive analgesia blocks the sensory input that induces central sensitization.[14] Surgical studies have shown promise with preemptive administration of ibuprofen before third molar extraction.[15,16] Preemptive analgesia in orthodontia was initially suggested by Simmons and Brandt,[17] who recommended giving an analgesic to the patient 30 minutes before the procedure and then maintaining therapeutic doses for the next 24 hours.

Cyclooxygenase-2 (Cox-2) inhibitors provide an alternative to the short-term use of conventional nonsteroidal anti-inflammatory drugs (NSAIDs). In comparison with conventional NSAIDs, Cox-2 inhibitors have longer dosing intervals, different side effect profile (less alteration of platelet function and less gastric irritation), similar onset of action, and similar analgesic efficacy. Although these drugs are currently Food and Drug Administration (FDA)-approved only for adults and not for adolescents, both may benefit from preemptive analgesia during orthodontic treatment.

The drug valdecoxib (Bextra®, Pfizer Inc, New York, NY) has shown promise in the dental arena. A study on impacted third molar extractions revealed that patients receiving 40 mg valdecoxib postoperatively had a rapid onset of analgesia and pain relief similar to those who received oxycodone 10 mg/acetaminophen 1000 mg.[18] A similar study[19] found that all doses of preemptive valdecoxib (10, 20, 40, and 80 mg) produced analgesia with a duration and magnitude that was significantly greater than a placebo, with dose-dependent levels shown up to 40 mg. Recently, however, valdecoxib along with other Cox-2 inhibitors has been removed from the market.

The purpose of this clinical trial was to evaluate the effects of preemptive and postoperative valdecoxib on adult orthodontic patients after initial archwire placement. This study is important because (1) few studies have been published with preemptive analgesia to control discomfort associated with initial archwire placement,[20,21] (2) no orthodontic studies have studied control of discomfort with a Cox-2 inhibitor, (3) there is a growing demand for orthodontic treatment among adults,[22] and (4) adults undergoing archwire changes often report more pain than children.[1,4,6,7,11,13]

TABLE 1. Distribution of Patients Participating in the Initial Archwire Placement Study Based on Sex, Arch Bonding, and Wire Used

	Placebo (n = 18)	Preemptive Valdecoxib (n = 21)	Postoperative Valdecoxib (n = 17)
	n (%)	n (%)	n (%)
Female	10 (17.9)	10 (17.9)	9 (16.1)
Male	8 (14.3)	11 (19.6)	8 (14.3)
Maxillary arch	5 (8.9)	4 (7.1)	6 (10.7)
Mandibular arch	2 (3.6)	0 (0)	0 (0)
Both arches	11 (19.6)	17 (30.4)	11 (19.6)
0.014 inch Niti	10 (17.9)	12 (21.4)	10 (17.9)
0.016 inch Niti	7 (12.5)	8 (14.3)	4 (7.1)
0.018 CuNiti	1 (1.8)	1 (1.8)	3 (5.4)

MATERIALS AND METHODS

Seventy adult patients about to begin comprehensive orthodontic treatment at Baylor Orthodontic Department or at Dallas private practices were recruited to participate in this randomized, double-blinded, placebo-controlled prospective clinical trial. Sample size was determined using a power analysis based on variances of similar studies reported previously.[9,10,23] Patients were selected on the basis of the following criteria: (1) bracket placement to begin in the maxillary or mandibular arches (or both), (2) 18 years of age or older, (3) no antibiotic prophylaxis needed, (4) no chronic systemic diseases or clotting disorders, (5) not currently taking antibiotics or analgesics for any reason, (6) not lactose intolerant, (7) not pregnant or nursing, and (8) having no contraindications for the use of valdecoxib. A total of 56 patients aged 18–54 years (mean female age 36.4 $\pm$ 6.1 years, mean male age 34.9 $\pm$ 5.8 years) completed the study. Patients with existing brackets on any teeth were excluded from the study, and no bands or separators were placed the day of initial bonding. The study was approved by Baylor College of Dentistry's Institutional Review Board for human studies.

Brackets were placed for the first time in the maxillary (26.8%), mandibular (3.6%), or both arches (69.6%) (Table 1). Initial archwires inserted were 0.014-inch nickel titanium, 0.016-inch nickel titanium, or 0.018-inch Copper nickel titanium wires, and various ligation methods were used. (No relationship has been established previously between the amount of pain experienced and the size of the archwire used.[4,7,13]) On meeting the inclusion criteria, patients were randomly assigned to the placebo or active treatment groups using a random numbers table.

The study drug or matching placebo was dosed at

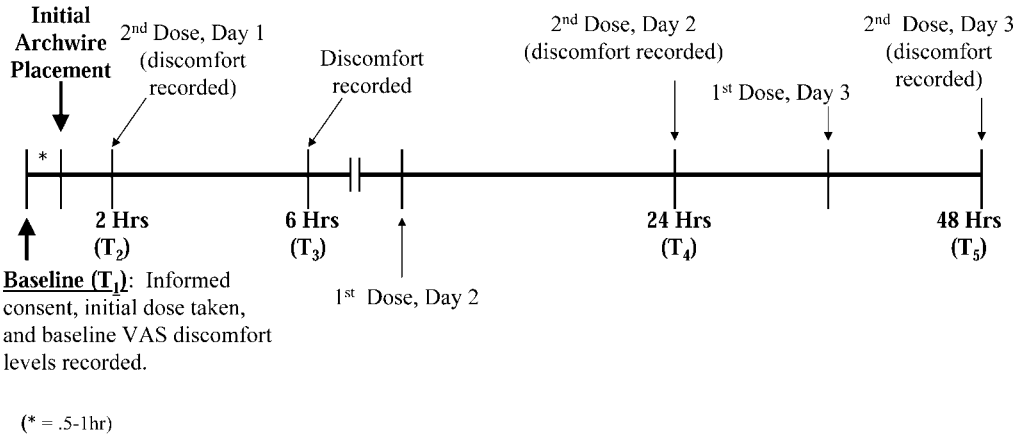

FIGURE 1. Study time line.

six time points: (1) at least 30 minutes before initial archwire placement, (2) two hours after archwire placement, and (3) every 12 hours starting the morning after bonding for the next 48 hours (Figure 1). The placebo group received a total of six doses. The preemptive valdecoxib group received a 40-mg valdecoxib loading dose before initial archwire placement and placebo two hours later. The postoperative valdecoxib group received a placebo at least 30 minutes before initial archwire placement and 40 mg valdecoxib two hours later. Beginning the morning after bonding, both treatment groups received 20 mg valdecoxib every 12 hours for four additional doses. Valdecoxib and matching placebo capsules were prepared by an unblinded licensed pharmacist. Patients were asked to avoid taking any other type of pain medication unless their pain was unbearable. If patients experienced additional pain, they had access to over-the-counter ibuprofen as a rescue medication. Use of rescue medication was recorded by the patients in their data diary. Data recorded after any rescue medication was taken were not included in the results analysis.

Data collection

Discomfort was measured at five time points (Figure 1). Patients were asked to record the amount of discomfort they experienced using a 10-cm visual analog scale (VAS) with ''No Discomfort'' to ''Worst Discomfort Ever'' as anchors at zero and 10 cm, respectively. The VAS produces significantly smaller session-to-session variation than those acquired with verbal descriptor scales (VDS).[24] Also, the VAS is significantly more sensitive than a VDS to small differences in perceived pain intensity and pain unpleasantness and does not exhibit some of the order effects present with a VDS.[24]

At each time point, patients rated their ''Worst pain ever'' on the VAS. This standardized each patient's pain threshold and helped to evaluate the consistency of the patients' response over time.[8,24] Patients then answered five previously validated questions[9] relating to dental discomfort and were instructed to mark a line on the VAS scale corresponding to their discomfort. Discomfort was evaluated during five activities important to orthodontic treatment (at rest, during chewing, with teeth apart, and when biting on back and front teeth).

Statistical analysis

VAS measurements were digitized using Dentofacial Planner® (Toronto, Canada), and the data were imported into SPSS® (SPSS Inc, Chicago, Ill) for statistical analysis.

Descriptive statistics were used to compare baseline characteristics and demographic information. Nonparametric statistics were used to evaluate group differences because the data were positively skewed. Pain measures are described using medians and interquartile ranges. Interrelations across the five time points of survey question 1 were evaluated using Spearman rank order correlations. Group differences at baseline were evaluated using Kruskal-Wallis tests. The Wilcoxon signed rank test was used to evaluate changes in discomfort from baseline. Group differences in changes in discomfort from baseline were compared using Mann-Whitney *U*-tests; post hoc comparisons were performed using the Wilcoxon signed rank test.

RESULTS

Of the 70 surveys distributed, 62 (88.6%) were returned. Of the 62 returned surveys, one (1.4%) patient used rescue medication, two (2.9%) patients did not complete the surveys, and three (4.3%) patients returned the surveys after the deadline and were not

TABLE 2. Median Baseline VAS Discomfort Levels Reported for Questions 2–6 (No Statistically Significant Differences for Any Question Were Noted Between Groups at Baseline)[a]

	Placebo	Preemptive Valdecoxib	Postoperative Valdecoxib
Discomfort currently experiencing	8.8	4.6	6.6
Discomfort last time you chewed	9.7	6.6	4.7
Discomfort with teeth apart	4.8	7	3.9
Discomfort when biting on BACK teeth	10.1	7.7	4
Discomfort when biting on FRONT teeth	11.9	5.9	5.5

[a] VAS indicates visual analog scale.

used. Thus, 56 (80%) completed surveys were included in the statistical analysis.

Spearman rank order correlations for question 1, ''Please remember the worst physical pain of your life and its intensity/unpleasantness,'' ranged between .70 and .97 ($P < .05$ for all measures) between the five time points indicating consistency of answers across all time points. Overall, 13 of 30 (43%) correlations were greater than 0.9, whereas 23 of 30 (77%) exceeded 0.8.

Baseline comparisons

No significant group differences in median baseline discomfort levels were noted for questions 2–6 (Table 2). Median discomfort values reported for each group were low (<12 mm on the VAS scale).

Discomfort within groups

The preemptive valdecoxib group showed no significant change in discomfort from baseline at any of the time points for any of the questions. With the exception of the second question, the placebo and postoperative valdecoxib groups showed significant increases in discomfort starting at six hours (Figures 2 through 6). The postoperative group also displayed a significant increase in discomfort at two hours to question 3. Both the placebo and postoperative valdecoxib groups generally attained peak discomfort approximately 24 hours after archwire placement; the maximum discomfort seen in the placebo group was reported with ''pain when biting on FRONT teeth'' at 48 hours.

Group comparisons

The placebo and postoperative groups showed significantly greater increases in discomfort than the preemptive valdecoxib group for questions 3–6 (Tables 3 and 4). There was a trend toward decreased discomfort for the postoperative group.

Between sexes

In a subgroup analysis, there was a tendency for greater discomfort among females than males. Significant sex differences were found in three of 30 (10%) time point/question combinations. Females reported significantly more discomfort compared with baseline than males at 48 hours when asked about ''Discomfort last time you chewed,'' ''Discomfort when biting on

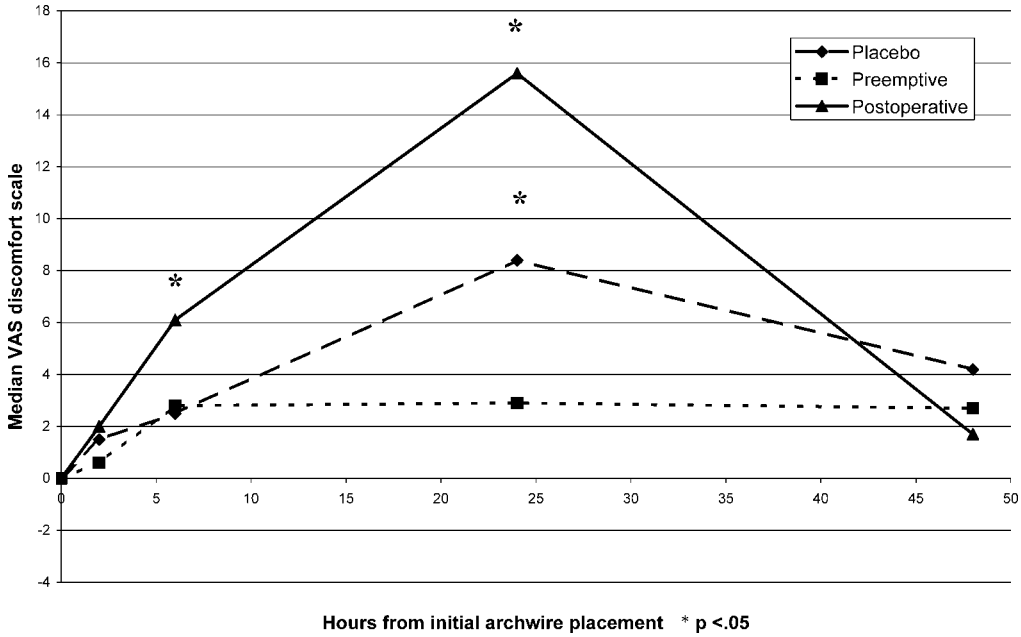

FIGURE 2. Median changes in discomfort from baseline when asked, ''How much discomfort are you currently experiencing?''

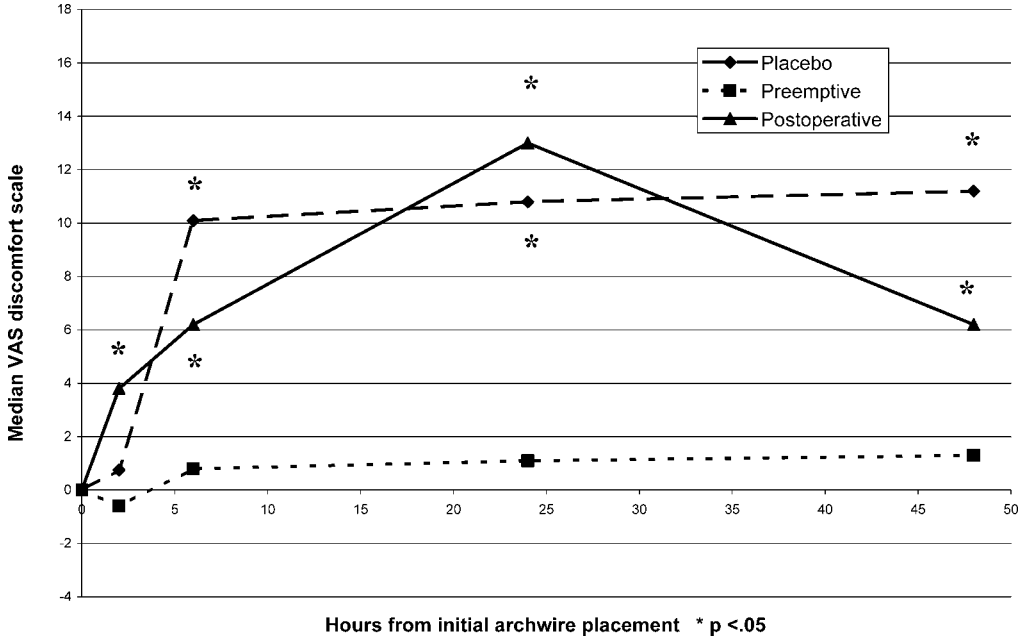

FIGURE 3. Median changes in discomfort from baseline when asked, ''How much discomfort did you experience the last time you chewed?''

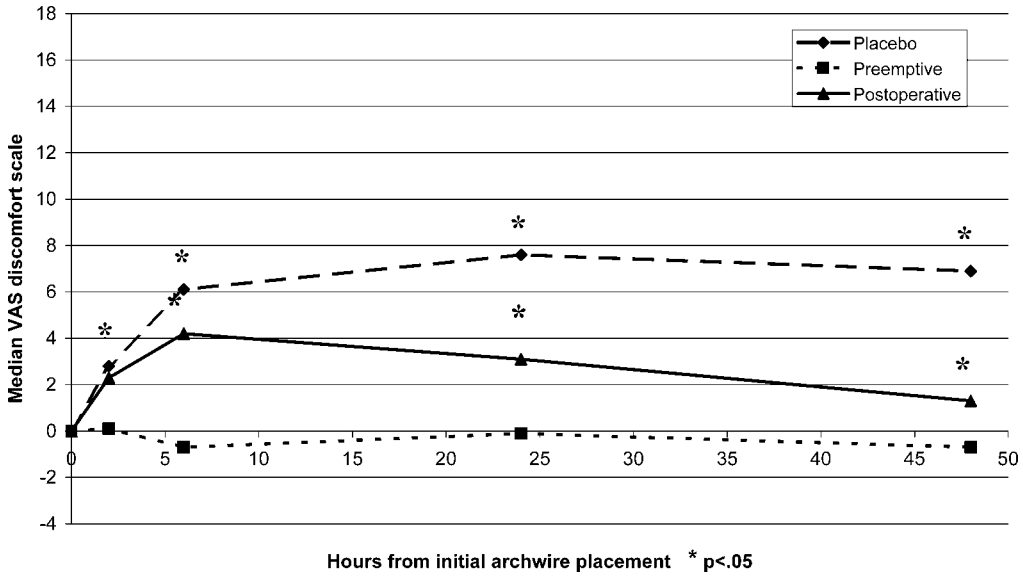

FIGURE 4. Median changes in discomfort from baseline when asked, ''How much discomfort are you experiencing when your teeth are apart?''

BACK teeth,'' and ''Discomfort when biting on FRONT teeth.''

DISCUSSION

Our placebo group showed peak levels of discomfort approximately 24 hours after placement of the initial archwire, which is consistent with previous studies.[1,4,8,25,26] In contrast, Fernandes et al[7] found peak levels of discomfort 11 hours after archwire insertion, whereas Jones and Chan[4] found peak levels at nine AM the morning after bonding. Orthodontic separators also produce peak pain between 17 and 24 hours.[8–10,12] Significant increases in discomfort were generally noted for the placebo and postoperative valdecoxib groups starting at two to six hours after archwire insertion. This was expected because the postoperative group received valdecoxib two hours after the procedure. Significant pain has been reported to start as early as four hours after insertion of archwires.[1,7,8,26]

Most importantly, the preemptive valdecoxib group showed no significant increases in discomfort from

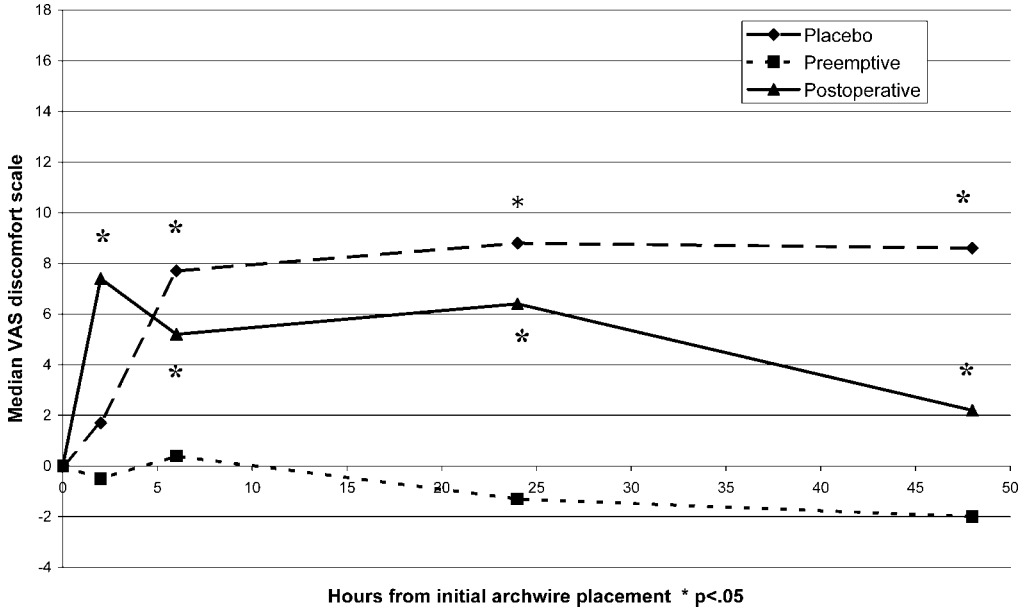

FIGURE 5. Median changes in discomfort from baseline when asked, ''How much discomfort are you experiencing when you bite down on your BACK teeth?''

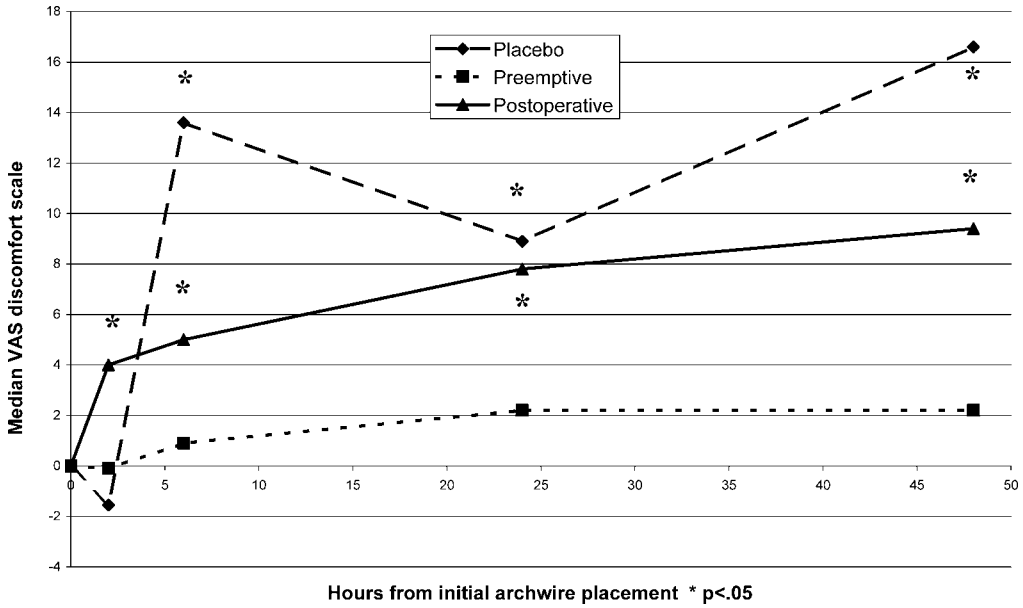

FIGURE 6. Median changes in discomfort from baseline when asked, ''How much discomfort are you experiencing when you bite down on your FRONT teeth?''

baseline. Law et al[9] showed that preemptive ibuprofen significantly reduced pain while chewing two hours after separator placement compared with placebo or postoperative ibuprofen. Bernhardt et al[10] noted that preemptive ibuprofen significantly lowered levels of ''pain to biting'' and ''pain to fitting front teeth together'' two hours after separator placement compared with postoperative ibuprofen. They also demonstrated that preemptive ibuprofen decreased ''pain to biting'' at bedtime on the day of separator placement when compared with postoperative ibuprofen. Preemptive NSAIDs have also produced delayed onset and decreased levels of pain after third molar extractions.[15,16,27] Third molar studies show that preoperative valdecoxib produced greater and more long-lasting analgesia than placebo.[19] Postoperatively, valdecoxib produced a more rapid onset of action, superior tolerability, and analgesia comparable with oxycodone/acetaminophen.[18] Although previous studies have shown significant reductions in pain with preemptive

TABLE 3. Group Differences in the Change of Discomfort From Baseline (T1) at Each Time Point for Each Question[a]

	Time Points							
	(T2) 2 Hours		(T3) 6 Hours		(T4) 24 Hours		(T5) 48 Hours	
Questions	*P*	Group Difference	*P*	Group Difference	*P*	Group Difference	*P*	Group Difference
2. Discomfort currently experiencing	.754	NS	.451	NS	.079	NS	.67	NS
3. Discomfort the last time you chewed	.267	NS	.076	NS	.021*	1>2, 3>2	.024*	1>2
4. Discomfort when teeth are apart	.059	NS	.016*	1>2, 3>2	.021*	1>2, 3>2	.051	1>2
5. Discomfort when biting on BACK teeth	.007*	3>2	.006*	1>2, 3>2	.034*	1>2, 3>2	.004*	1>2, 3>2
6. Discomfort when biting on FRONT teeth	.073	NS	.024*	1>2	.084	NS	.025*	1>2

[a] NS indicates not significant. * $P < .05$

TABLE 4. Interquartile Ranges for Questions 1–6: Changes in Discomfort from Baseline

		Time Points											
		(T2) 2 Hours			(T3) 6 Hours			(T4) 24 Hours			(T5) 48 Hours		
Questions	Interquartile Ranges	25	50	75	25	50	75	25	50	75	25	50	75
Discomfort currently experiencing	Placebo	8.5	1.5	−6.5	16.1	2.5	−4.1	22.9	8.4	−0.53	14.2	4.2	−8.6
	Preemptive	4.8	0.6	−1.4	8	2.8	−2.1	9	2.9	−2.65	6.3	2.7	−1.5
	Postoperative	9.2	2	−4.3	13.7	6.1	0.25	19.3	15.6	2.8	25	1.7	−1.65
Discomfort last time you chewed	Placebo	10.7	0.75	−4.5	20.1	10.1	−3.8	24.5	10.8	−1.4	35.2	11.2	4.9
	Preemptive	4.5	−0.6	−2.9	6	0.8	−6	7.3	1.1	−4.5	8.9	1.3	−4.2
	Postoperative	17.5	3.8	−2.3	17.8	6.2	1.5	28.1	13	3	25.3	6.2	−0.75
Discomfort with teeth apart	Placebo	7.9	2.8	−1.3	16.7	6.1	0.33	12.1	7.6	−1.1	13	6.9	0.1
	Preemptive	1.7	0.1	−3.1	2.8	−0.7	−3.4	2.2	0.1	−3.7	1.9	0.7	−2.7
	Postoperative	11.7	2.3	−1.7	9.5	4.2	1	20.8	3.1	−2.3	14	1.3	−0.7
Discomfort when you bite down on BACK teeth	Placebo	7.3	1.7	−4.1	20.4	7.7	−0.65	32	8.8	−4.3	14.5	8.6	−1.8
	Preemptive	1.6	−0.5	−7.5	4.3	0.4	−5.1	3.4	−1.3	−7.7	1.5	−2	−8.6
	Postoperative	20	7.4	0	18.4	5.2	3.3	22.7	6.4	−2	18.9	2.2	0.2
Discomfort when you bite down on FRONT teeth	Placebo	9.9	−1.6	−4.5	30	13.6	3.6	39.3	8.9	0	20	16.6	2
	Preemptive	3.4	−0.1	−8	6.2	0.9	−3.4	7.5	2.2	−1.3	6.9	2.2	−2.8
	Postoperative	6.4	4	0.45	19.5	5	−1.4	27	7.8	−2	22	9.4	−0.35

administration of analgesics, none have reported pain prevention.

Three factors may explain why preemptive valdecoxib prevented discomfort in this study. First, the valdecoxib loading dose likely produced maximal plasma concentrations within the therapeutic window after only one dose. A dose-dependent effect for valdecoxib, up to 40 mg, has been shown in third molar extraction studies.[19] The onset of action of valdecoxib may also have played a role. Maximum plasma concentrations of valdecoxib occur after three hours.[28] Patients in the preemptive valdecoxib group received valdecoxib at least 30 minutes before the procedure, allowing time for the valdecoxib to achieve therapeutic plasma concentrations and prevent much of the potential inflammation in the PDL.[18] Daniels et al showed a median time to onset of analgesia of 28 minutes for 40 mg valdecoxib in a third molar extraction study, which was significantly shorter than patients treated by placebo.[18]

In addition to using a loading dose and quick onset of action, the preemptive group continued to receive valdecoxib throughout the next 48 hours. Therapeutic levels were likely reached with the 40-mg loading dose and then sustained by administering 20 mg valdecoxib every 12 hours for two days after initial archwire placement. The mean elimination half-life of valdecoxib is 8.11 ± 1.32 hours.[28] The long half-life may also explain why therapeutic levels likely remained high and discomfort remained low. Our research supports the idea that an optimal schedule of pain treatment may be one that is applied both pre- and postoperatively to preempt the establishment of pain hypersensitivity during and after treatment.[14,17]

Postoperative valdecoxib revealed no pain relief presumably until therapeutic levels were reached (approximately six hours for most subjects on most questions). Minimal increases in discomfort occurred and were followed by decreases in discomfort over time. This trend toward relief from discomfort is similar to that seen with postoperative ibuprofen after separator placement.[9,10] The higher level of discomfort in the postoperative group might stem from the production of prostaglandins that occurred before the administration of valdecoxib in the postoperative group. The type of

discomfort seen in orthodontia may be because of changes in blood flow in the PDL and correlated with the presence of prostaglandins and the resulting hyperalgesia.[12,29]

Preemptive analgesia with NSAIDs or Cox-2 inhibitors attenuates the prostaglandin-induced inflammatory cascade and thereby decreases the likelihood that central sensitization will occur. Postoperative valdecoxib, which has its peak effect after the onset of inflammation and production of prostaglandins, might therefore be expected to be less effective.

Consistent with our findings, most orthodontic research shows pain to be greater while chewing and biting than at rest.[3,9,10,26] Greater pain is expected when chewing and biting because of the compression of the PDL during function. In this study, the highest VAS median discomfort scores for the placebo group were recorded for ''Discomfort when biting on Front teeth,'' which is in agreement with other fixed appliance studies.[1,18,26] In general, we noted peak discomfort at 24 hours after archwire insertion for most questions and time points; however, the highest single amount of discomfort recorded was at 48 hours in the placebo group.

Compared with other studies evaluating pain associated with archwire placement, our peak median placebo values (VAS = 28.5) are similar[7,11,13,30] or somewhat less than peak mean (VAS = 40–60) values reported previously.[1,30] Discomfort levels measured in this study were positively skewed, consistent with previous reports.[3,7,10,14] Pain is expected to be positively skewed because the left anchor on the VAS (ie, no discomfort) is an absolute state and is similar across individuals, whereas the right anchor (worst discomfort ever) is a relative, highly variable, state. Importantly, means exaggerate pain levels when distributions are positively skewed, which might explain some of the differences noted in the archwire and separator studies.

This study noted a trend toward more discomfort reported by women than men in three of 30 assessments. Several studies have found no differences in pain between males and females,[4,7,13,26] whereas others report significantly more orthodontic pain among females than males.[1,11] This finding was coincidental and was not a primary aim in this study. Further research aimed at detecting sex differences may be warranted.

Recently, rofecoxib (Vioxx®) and valdecoxib (Bextra®) were withdrawn from the US and European markets by their manufacturer because of reports of increased cardiovascular events and skin reactions, respectively. One other Cox-2 inhibitor, celecoxib (Celebrex®) is currently FDA approved for the treatment of several pain syndromes, although the FDA has requested product labeling to reflect potential increased risk of cardiovascular events. Previously, valdecoxib had been FDA approved for the treatment of osteoarthritis, adult rheumatoid arthritis, and primary dysmenorrhea but not for postoperative pain.[28] To date, no published data suggest that short-term valdecoxib use increases cardiovascular events in healthy adults. However, Valdecoxib® has been shown to increase cardiovascular events in patients immediately after coronary-artery bypass grafting[28] and has now been linked to rare but serious skin reactions.[31]

When used chronically, valdecoxib can cause other typical NSAID-associated adverse effects such as hypertension, peripheral edema, and kidney dysfunction.[28] In addition, valdecoxib is contraindicated in patients with a sulfonamide allergy and in rare cases can cause serious skin reactions including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis.[28] Overall, Cox-2 inhibitors may not be the drugs of choice for long-term pain relief in complicated patients and in those with active coronary heart disease. However, on the basis of the results of this study, short-term valdecoxib would have been a viable option to reduce acute orthodontic pain in healthy adults.

Because of its removal from the market, valdecoxib will no longer be available for short- or long-term pain relief. However, in light of the findings in this study, preemptive and postoperative administration of celecoxib (Celebrex®) or other NSAIDs will likely reduce discomfort associated with initial archwire placement in healthy adult orthodontic patients.

CONCLUSIONS

- This clinical trial showed no significant increases in discomfort from baseline with the use of preemptive valdecoxib.
- Lack of discomfort may be because of several reasons: the use of a 40-mg loading dose administered 30 minutes before initial archwire placement, Valdecoxib's® fast onset of action, its continued administration throughout the study, or its long elimination half-life (or all).
- The placebo group showed that discomfort started two to six hours after initial archwire placement, with peak discomfort generally occurring at 24 hours.
- Postoperative valdecoxib reduced discomfort to levels intermediate between the placebo group and the preemptive group, although no significant differences were noted.
- This study noted a trend toward slightly more discomfort reported by women than men, but this finding is incidental and further research is warranted.
- Preemptive with perioperative and postoperative an-

algesia with NSAIDs appears to an effective method for minimizing discomfort associated with initial archwire placement in healthy adults.

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