ORIGINAL ARTICLE

The effect of preemptive and/or postoperative ibuprofen therapy for orthodontic pain

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The control of pain during orthodontic treatment is of vital interest to both clinicians and patients. Surprisingly, there has been limited research into the control of orthodontic pain, and there is no standard of care for controlling this discomfort. The purpose of this study was to compare the effectiveness of preemptive ibuprofen therapy, postoperative ibuprofen therapy, and a combination of the 2 therapies. Forty-one orthodontic patients aged 9 years 3 months to 16 years 11 months who were to undergo separator placement were enrolled in this prospective study. Patients were randomly assigned to 1 of 3 experimental conditions: (1) 400 mg ibuprofen taken orally 1 hour before separator placement and 400 mg ibuprofen taken orally 6 hours after the initial dose, (2) 400 mg ibuprofen taken orally 1 hour before separator placement and a lactose capsule taken orally 6 hours after the initial dose, or (3) a lactose capsule taken orally 1 hour before separator placement and 400 mg ibuprofen taken 6 hours after the initial placebo. The results revealed that preemptive ibuprofen therapy significantly decreased pain that was experienced 2 hours after separator placement and at bedtime. Beginning on day 2, there was a trend for patients who had taken both preemptive and postoperative ibuprofen doses to have lower pain scores compared with the other 2 groups. In conclusion, these data indicate that ibuprofen taken 60 minutes before separator placement alleviates pain at 2 hours and at bedtime after treatment. Further study with the use of additional postoperative doses is warranted. (Am J Orthod Dentofacial Orthop 2001;120:20-7)

The control of pain during orthodontic treatment is of vital interest to both clinicians and patients. Research indicates that patients rank pain as the worst aspect of orthodontic treatment and the foremost reason for wanting to discontinue care.[1] When compared with the pain associated with extractions, both the incidence and severity of orthodontic pain is perceived to be greater.[2] Individual response varies widely and is believed to be a result of individualized pain thresholds[2-4]; the effects of age,[3-7] gender,[3,4,6-8] and magnitude of force[4,9] on orthodontic pain are not clear cut. With regard to the time course of pain that is associated with orthodontic treatment, it has been reported that peak pain occurs the day after the adjustment, with a decrease over the next 6 to 8 days.[3,4,7,10-11]

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Surprisingly, there is limited research into the control of orthodontic pain. White[12] reported that 63% of patients who chewed an analgesic chewing gum (Aspergum; Plough) immediately after archwire changes experienced less discomfort than usual. Ngan et al[13] compared the effectiveness of 650 mg aspirin, 400 mg ibuprofen, and placebo for the control of orthodontic pain caused by either separators or initial archwires. Seventy-seven subjects were given a single dose of either ibuprofen, aspirin, or placebo immediately after separator or wire placement. They evaluated the level of discomfort at 2, 6, and 24 hours and 2, 3, and 7 days after treatment. Their results demonstrated that the placebo group experienced significantly more discomfort than either the ibuprofen or the aspirin group and that the ibuprofen group had significantly less discomfort than the aspirin group. They concluded that ibuprofen was the preferred analgesic to decrease pain that is associated with orthodontic treatment.

In both medicine and dentistry, recent research has focused on the subject of preemptive (preoperative) analgesia to decrease postoperative pain. It has been hypothesized that the optimal method for treating acute pain is to abolish the immediate peripheral sensitization and prevent the subsequent central sensitization.[14] The goal of preemptive analgesia is to block the affer-

ent nerve impulses before they reach the central nervous system, causing central sensitization. This can be accomplished through the use of narcotics, local anesthetics, or nonsteroidal anti-inflammatory drugs (NSAIDs).[15] When NSAIDs are given before the procedure, the body has time to absorb and distribute the medication before tissue injury and the subsequent production of prostaglandins. This, in turn, will decrease the ensuing inflammatory response.[16]

Several authors have demonstrated the effectiveness of ibuprofen that is given prophylactically in controlling pain after dental treatment.[16-18] Dionne and colleagues[18] determined that ibuprofen given before third molar removal resulted in delayed onset and decreased severity of pain when compared with either acetaminophen or placebo. Similarly, Jackson et al[16] recommended prescribing ibuprofen 30 minutes before minor dental surgery to alleviate the painful sequelae that occur after surgery.

There is very little information in the literature about the control of orthodontic pain with the use of preemptive analgesics. Law et al[11] compared the effectiveness of preemptive ibuprofen, postoperative ibuprofen, and placebo therapy in controlling pain that is associated with separator placement in children and adolescents. They found that preemptive ibuprofen administered 1 hour before separator placement significantly decreased pain to chewing at 2 hours after the procedure, compared with the other 2 groups, with a trend for decreased pain scores during the week of orthodontic separation. They concluded that the preoperative administration of 400 mg ibuprofen could decrease the severity of pain perceived after orthodontic separation. However, they found that a significant amount of pain was still reported at 24 hours.

During orthodontic tooth movement, numerous system responses are believed to contribute to the resultant osseous changes. However, cytokines and prostaglandins, which are mediators of inflammation and have been found to be significantly elevated in gingival crevicular fluid during the early phases of tooth movement,[19] are implicated in the mediation of orthodontic pain.[20]

The purpose of this prospective clinical study was to compare the incidence and severity of pain after separator placement, specifically comparing the effectiveness of preemptive ibuprofen therapy, postoperative ibuprofen therapy, or a combination of preemptive and postoperative ibuprofen therapies.

MATERIAL AND METHODS

Subjects

One hundred fourteen orthodontic patients who were scheduled to receive comprehensive orthodontic treatment were identified from the College of Dentistry Department of Orthodontics clinical pool. All patients were to be treated by graduate students of the Department of Orthodontics. The following selection criteria were required for participation: (1) scheduled to begin comprehensive orthodontic treatment, (2) no prophylactic antibiotic coverage required, (3) no debilitating systemic diseases, (4) currently not using antibiotics or analgesics, (5) no contraindication to the use of ibuprofen, and (6) a maximum age of 16 years and a minimum weight requirement of 88 pounds (the weight requirement was based on Food and Drug Administration–approved over-the-counter pediatric dosage labeling guidelines).

Experimental conditions

Patients were randomly assigned to 1 of 3 experimental conditions: group A, 400 mg ibuprofen taken orally 1 hour before the appointment for routine separator placement and 400 mg ibuprofen taken orally 6 hours after the initial dose; group B, 400 mg ibuprofen taken orally 1 hour before the appointment for routine separator placement and a lactose capsule taken orally 6 hours after the initial dose; and group C, a lactose capsule taken orally 1 hour before appointment for routine separator placement and 400 mg ibuprofen taken orally 6 hours after the placebo dose.

The ibuprofen and placebo capsules were identical in appearance. The patient, research assistant, and investigator were blinded to each subject's experimental group.

Data collection

Subjects were given routine posttreatment instructions and were asked to complete a questionnaire at appropriate intervals during the week after the separator appointment. The questionnaire was in the format of a 9-page booklet that contained a series of 10-cm horizontal visual analog scales on which the patient marked the degree of discomfort (none to worst pain imaginable) at the indicated time periods.[21] The patients were instructed to make a check on the scale at each time interval to represent the perceived severity of pain during each of 4 activities: chewing, biting, fitting back teeth together, and fitting front teeth together. Incidence and severity of pain were recorded by the patient at 2 hours, at 6 hours, at bedtime on the day of appointment, on arising on the day after the appointment, and at 2 days, 3 days, and 7 days after separator placement. Patients were instructed to return the questionnaire in a stamped, self-addressed envelope 1 week later.

Patients were encouraged to not take any additional

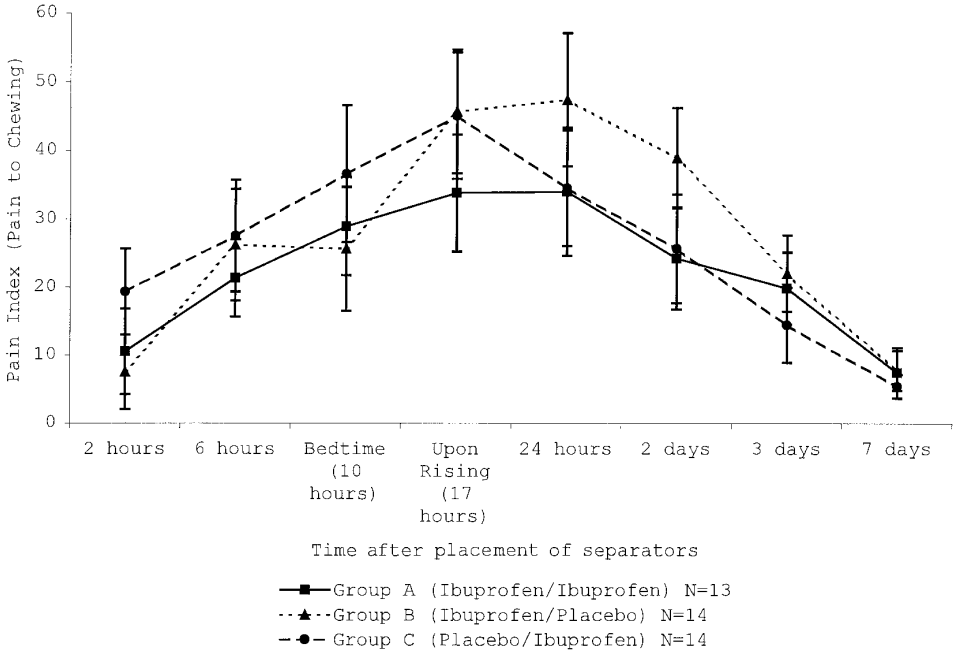

Fig 1. Mean pain scores (mean ± SEM) for "chewing," by condition and time.

Table I. Experimental groups defined by condition (preoperative medication/postoperative medication), age, gender

Group	*Mean age (y ± SD)*	*Gender (male/female)*
A (ibuprofen/ibuprofen)	12.1 ± 1.6	10/3
B (ibuprofen/placebo)	13.5 ± 1.9	4/10
C (placebo/ibuprofen)	12.8 ± 1.5	6/8

analgesics. If additional "rescue" medication was needed, they were advised to use acetaminophen. On the questionnaire they were instructed to indicate the date, time, dosage, and specific "rescue" medication taken.

Of the 114 patients who agreed to participate in the study, 63 patients returned the completed questionnaires, 22 of whom took additional medication and were excluded from the study. These 22 patients were evenly distributed among the 3 groups. Thus, data were collected from 41 subjects.

Statistics

Descriptive statistics were calculated for pain scores at each time interval for the experimental groups. An analysis of variance and Duncan's multiple range test were used to determine differences in mean pain scores between experimental conditions. A probability value of less than .05 was set for statistical significance.

RESULTS

The descriptive statistics for the 3 experimental groups are listed in Table I.

Time course of postoperative pain

Figures 1 through 4 show that, for all conditions, peak pain occurred on arising the day after separator placement, except for the pain that occurred at 24 hours for group A (pain to chewing, pain to biting, pain to fitting front teeth together) and for group B (pain to chewing). There was a gradual decrease in pain scores for all conditions from the peak pain period to 7 days after separator placement.

Differences in postoperative pain between experimental conditions

An analysis of variance and Duncan's multiple range test were used to identify a significant difference between group C (placebo/ibuprofen) and the other 2 groups (group A, ibuprofen/ibuprofen and group B, ibuprofen/placebo) with respect to postoperative "pain to biting" at 2 hours and "pain to fitting front teeth together" at 2 hours ($P < .05$). In other words, at 2 hours after separator placement, subjects who had taken preoperative ibuprofen doses reported significantly lower levels of "pain to biting" (group A, 4.3 ± 5.1; group B, 9.0 ± 14.8 [mean ± SD]) than those subjects who had no preemptive analgesic (group C, 30.1 ± 33.2). Similarly, at 2 hours after separator placement, subjects who had taken preopera-

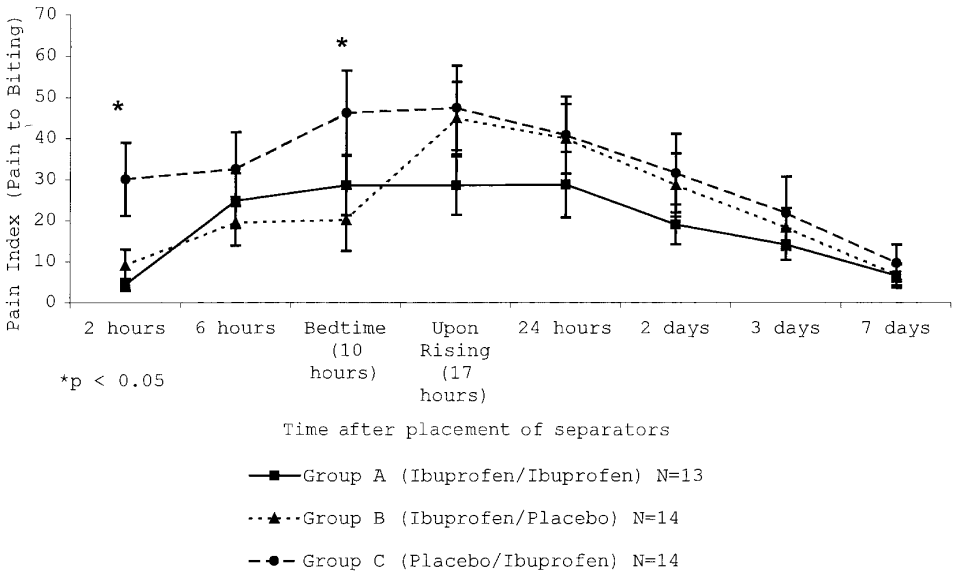

Fig 2. Mean pain scores (mean ± SEM) for "biting," by condition and time.

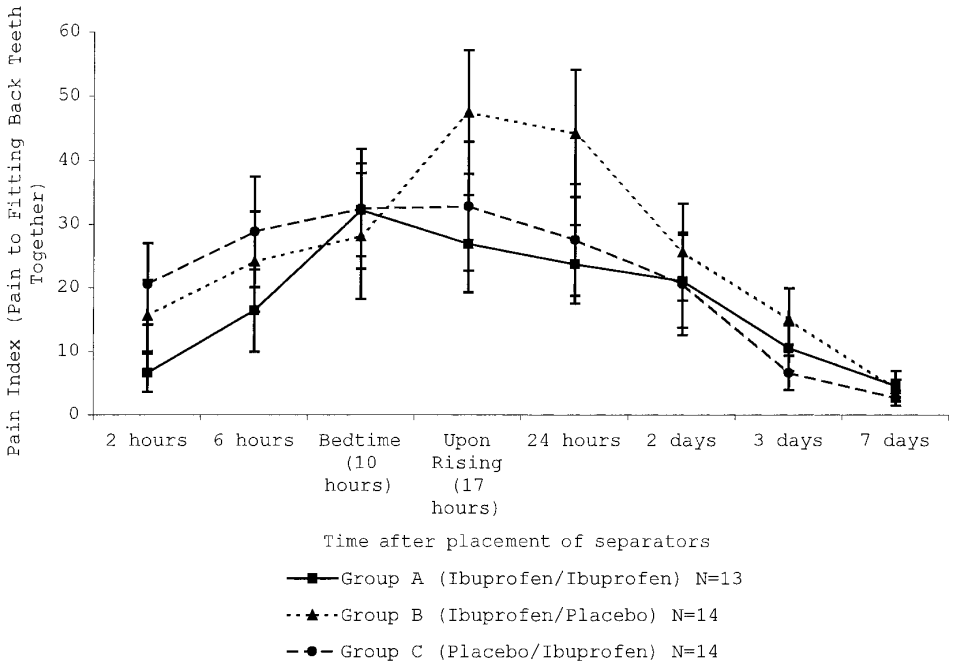

Fig 3. Mean pain scores (mean ± SEM) for "fitting back teeth together," by condition and time.

tive ibuprofen reported significantly lower levels of "pain to fitting front teeth together" (group A, 0.9 ± 1.5; group B, 1.9 ± 2.0) than those subjects who had no preemptive analgesic (group C, 10.5 ± 14.1).

Statistical analysis also demonstrated a significant difference between group C (placebo/ibuprofen) and group B (ibuprofen/placebo) with respect to postoperative "pain to biting" at bedtime the day of separator placement. At bedtime, subjects in group B who had taken preoperative ibuprofen reported significantly lower levels of pain (20.1 ± 28.3) than those who had no preemptive analgesic (group C, 46.2 ± 38.3). Group

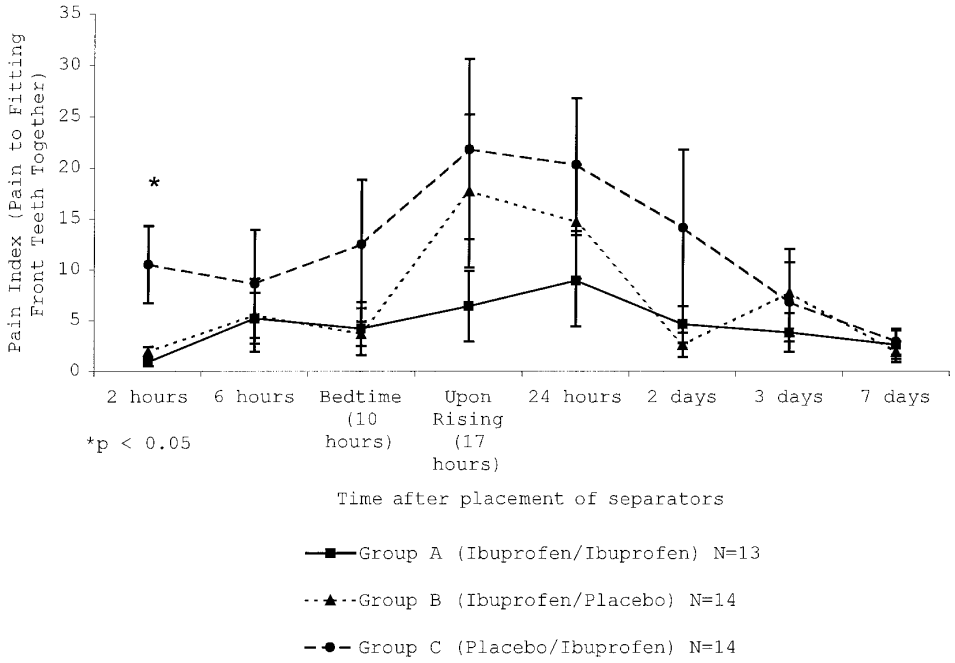

Fig 4. Mean pain scores (mean ± SEM) "fitting front teeth together," by condition and time.

A (ibuprofen/ibuprofen) did not differ significantly from either group B or group C.

There were no significant differences noted between experimental conditions at any of the subsequent postoperative time periods. However, beginning on day 2, there was an overall trend for patients in group A to have lower pain scores (Figs 1-4).

DISCUSSION

Time course of postoperative pain

In this study, it was found that there was an increase in pain from 2 hours after orthodontic separation to a peak level the day after separator placement. Peak pain scores were recorded most frequently on arising the day after separator placement. The second most frequent time for peak pain was at 24 hours after treatment. This is in agreement with the results of several other studies. Wilson et al[10] and Law et al[11] both reported peak discomfort at 24 hours after treatment with a gradual decrease in pain levels until 7 days after separator placement. Jones and Chan[4] found that the pain score was highest on the morning after treatment, with the discomfort gradually decreasing by day 6.

Differences in postoperative pain between experimental conditions

Patients who were given ibuprofen before treatment had significantly lower levels of "pain to biting" and "pain to fitting front teeth together" at 2 hours after separator placement compared with those patients who were given only postoperative ibuprofen. Preemptive ibuprofen was also shown to decrease "pain to biting" at bedtime the day of treatment compared with postoperative ibuprofen. These findings are similar to those of Law et al,[11] who found that preemptive ibuprofen significantly decreased "pain to chewing" at 2 hours compared with postoperative ibuprofen or placebo. These findings also concur with Dionne and Cooper[17] and Jackson et al,[16] who concluded that preemptive NSAIDs resulted in the delayed onset of pain and decreased levels of pain intensity after third molar extractions.

Although statistically significant findings were only recorded at 2 hours and at bedtime the day of separator placement, there was a trend for the group who were given ibuprofen both before and after treatment to have lower pain scores starting on day 2 compared with the other 2 groups. There are several possible explanations for this lack of statistical significance. First of all, the sample size was small. Although 114 subjects agreed to participate in the study, only 63 questionnaires were returned. Of those patients who returned questionnaires, 22 patients had taken additional analgesics and were excluded from the study. This left 41 subjects from whom to gather data. In addition, a wide range of individual variation was noted in the pain levels reported, which resulted in large standard deviations.

Another possible explanation is the uneven distribution of male and female patients among the groups (Table I). Although all subjects were randomly assigned to a treatment group, the gender distribution between groups was not evenly distributed. Numerous studies have found no differences in discomfort between the genders after orthodontic treatment[3,4,6,8]; however, differences related to gender have been noted.[7,22] Finally, because of the limited amount of ibuprofen taken, it is not surprising that there were no differences found between groups several days after the separators were placed.

Ibuprofen for control of orthodontic pain

Recent studies have focused on the establishment of an optimal analgesic protocol for controlling orthodontic pain. Comparing ibuprofen, aspirin, and placebo, Ngan et al[13] concluded that ibuprofen was the analgesic of choice to decrease pain during orthodontic treatment. Law et al[11] took the research 1 step further and found evidence to support the use of pretreatment ibuprofen for discomfort after the orthodontic appointment. On the basis of these findings, we hypothesized that a combination of preemptive and postoperative ibuprofen would significantly decrease the severity of pain that was perceived after separator placement compared with either dose alone. However, there were no significant differences noted between the patients who were given ibuprofen both before and after treatment and the patients who were given ibuprofen before and placebo after treatment. On the other hand, the patients who were given placebo before and ibuprofen after treatment did report significantly higher pain scores than the 2 groups who were given a dose of preemptive ibuprofen. From these results, we conclude that 400 mg ibuprofen taken 1 hour before separator placement can reduce the amount of discomfort experienced after treatment. Further study with the use of additional postoperative doses is warranted.

Factors affecting tooth movement

Although the mechanism of orthodontic tooth movement is not completely understood, current research suggests the following chain of events. Orthodontic mechanical stress causes disruption of the periodontal tissues, which leads to prostaglandin synthesis and intracellular cyclic adenosine monophosphate and calcium accumulation by monocytic cells. The resulting modulation and activation of osteoclastic activity leads to bone resorption and subsequent tooth movement.[23] An important link in this chain, the synthesis of prostaglandins as a result of mechanical deformation of the periodontal ligament, was confirmed in a study by Saito et al.[24] They found that the application of mechanical stress to the human periodontal ligament resulted in increased synthesis of prostaglandin E (PGE) and other inflammatory factors that enhance bone resorption. Grieve et al[19] demonstrated that PGE could be detected in gingival crevicular fluid during the early phases of orthodontic tooth movement.

A series of studies by Yamasaki et al[25-27] explored the role of prostaglandins in tooth movement. They found that PGE injected locally did cause the appearance of osteoclasts and subsequent bone resorption in rats.[25] They then determined that PGE administered locally in monkeys caused nearly twice the rate of tooth movement compared with controls.[26] In a human clinical study that followed, they concluded that the local administration of PGE resulted in a similar increase in the rate of tooth movement compared with that of control subjects.[27]

The important role that prostaglandins play in orthodontic tooth movement has led to recommendations that NSAIDs, such as ibuprofen, not be used to control orthodontic pain. Because these drugs inhibit the cyclooxygenase pathway and therefore the production of PGE, it is thought that they may inhibit the osteoclastic activity necessary for tooth movement. Likewise, it is well-established that the administration of NSAIDs can be used to slow periodontal bone loss.[28] Sandy and Harris[29] found that animals treated with prostaglandin inhibitors exhibited decreased osteoclastic activity. Similarly, Mohammed et al[30] found that treating animals with prostaglandin inhibitors caused a significant decrease in the rate of tooth movement. However, the dosage of the anti-inflammatory drugs used in these studies was much higher than over-the-counter therapeutic doses. In clinical orthodontics, lower doses are used for a short duration after orthodontic activation. To date, there is no evidence of the inhibition of tooth movement in humans because of prostaglandin inhibition.[31]

Kehoe et al[32] compared the effect of ibuprofen and acetaminophen on PGE synthesis and orthodontic tooth movement in guinea pigs. They found that ibuprofen significantly inhibited the production of PGE in the periodontal ligament and, subsequently, decreased the rate of tooth movement. On the other hand, although the acetaminophen had an inhibitory effect on peripheral PGE synthesis at the level of the periodontal ligament, the rate of tooth movement was not significantly different from the controls. They concluded that acetaminophen is the analgesic of choice for the relief of orthodontic discomfort. However, at the present time, there are no published studies that compare the effectiveness of ibuprofen and acetaminophen for the control of orthodontic pain.

Research in orthodontic pain control could proceed in many possible directions. It would be of interest to increase the number of doses of ibuprofen given to each patient so that the medication could remain in the bloodstream for a longer period of time in an effort to reduce the peak pain perceived the day after separator placement. Also, it would be interesting to use higher doses of ibuprofen. Another area to explore would be to compare the effectiveness of ibuprofen versus a longer acting NSAID to reduce the amount of pain perceived. Because of concerns regarding ibuprofen as an inhibitor of prostaglandin synthesis, it would be of particular interest to compare the effectiveness of acetaminophen versus ibuprofen for the control of orthodontic pain. It is clear that there is still a tremendous amount of research to be accomplished in this area.

CONCLUSIONS

Forty-one orthodontic patients aged 9 years 3 months to 16 years 11 months were enrolled in this prospective study to compare the incidence and severity of pain after separator placement, specifically comparing the effectiveness of preemptive ibuprofen therapy, postoperative ibuprofen therapy, or a combination of the 2 therapies.

The results demonstrate that:

1. Peak pain occurred between the time of arising the morning after separator placement and 24 hours after separator placement.
2. Ibuprofen (400 mg) taken 1 hour before orthodontic separator placement alone or in combination with 400 mg ibuprofen taken 6 hours after the initial dose significantly decreased the severity of pain perceived 2 hours after treatment when compared with placebo taken before separator placement and 400 mg ibuprofen taken 6 hours after the initial dose.
3. Ibuprofen (400 mg) taken 1 hour before treatment significantly decreased the severity of pain perceived at bedtime the day that the separators were placed, when compared with postoperative ibuprofen alone.
4. Beginning on day 2, there was a trend for the patients who had taken both preemptive and postoperative ibuprofen to have lower pain scores at most time intervals compared with the other 2 groups.

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