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Tenoxicam controls pain without altering orthodontic movement of maxillary canines

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Structured Abstract

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Objectives – To study the efficacy of tenoxicam for pain control, its potential for preemptive analgesia, and its influence on the orthodontic movement of upper canine teeth.

Design – This was a randomized controlled double-blind cross-over study. The patients were divided into three groups. Two groups received tenoxicam in daily doses of 20 mg orally for 3 days. Group A received the first dose of the drug before orthodontic activation and group B, just afterwards. Group C (control) received a placebo for 3 days. All groups had access to 750 mg of paracetamol up to four times a day. Three orthodontic activations were performed at 30-day intervals. Each patient belonged to two different groups. Pain intensity was assessed using a descriptive Pain Scale and a Visual Analog Scale.

Setting and Sample Population – Private clinic; 36 patients undergoing bilateral canine tooth retraction.

Results – The statistical analysis did not show any difference in movement between the active groups and the control at any time. There was no statistical difference between the groups that received tenoxicam. Pain intensity in these groups was lower than in the placebo group. The difference in pain intensity between the active groups and the control was greatest at the assessment made 12 h after activation and it tended to zero, 72 h after activation.

Conclusions – Tenoxicam did not influence orthodontic movement of the upper canines. It was effective for pain control and did not present any preemptive analgesic effect.

Key words: anti-inflammatory agents; drug administration schedule; non-steroidal; orthodontic space closure; pain measurement; tooth movement

Introduction

Pain caused by orthodontic treatment is mostly underestimated by orthodontists even if it is recurrent and lasts for more than 72 h on average after each activation (1). Considering that patients feel pain of varying intensity at each activation and that the orthodontic treatment may take years, during which many activations are implemented, the painful discomfort over this period ought to be adequately treated.

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Non-steroidal anti-inflammatory drugs (NSAIDs) are little used in orthodontic treatment as clinical and experimental studies have demonstrated that they diminish the tooth movement (2, 3) through inhibition of the periodontal inflammatory response caused by the activation. This response is believed to be responsible for the movement (4) and thus its inhibition compromises the orthodontic treatment. Tenoxicam is a NSAID belonging to the oxicam chemical class, with a mean elimination half-life of 67 h (5). Its advantage is that it can be taken only once a day, making tenoxicam a drug easy easy to use. Its activity has not yet been evaluated in patients undergoing orthodontic procedures.

Preemptive analgesia has been studied in relation to controlling the pain caused by orthodontic treatment. This technique changed the drug administration schedule, which consists of administration of an analgesic before the painful stimulus may diminish the intensity of the pain and reduce the consumption of analgesics (6). The aims of this study are to assess the efficacy of tenoxicam administered before or after orthodontic activation with regard to pain control and its influence on the orthodontic movement of upper canine teeth.

Materials and methods

Approval for this study was obtained from the institution's Research Ethics Committee before any procedures were undertaken. Before entering the study and after receiving explanations regarding the procedures, all patients (or their legal guardians in the case of patients aged under 18 years) signed a free and informed consent statement.

This was a randomized controlled double-blind cross-over study. Thirty-six patients of both sexes aged 16 to 25 years who had an orthodontic indication for bilateral retraction of the upper canine teeth were studied. Seventy-two retraction procedures were carried out using the straight arch technique (7). The teeth were leveled until a steel arch, measuring 0.017 mm $\times$ 0.025 mm with omega loops, was achieved. The retraction was carried out using nickel–titanium springs. The retraction force was measured using a dynamometer (Dental *Morelli* Ltda., Sorocaba, Brazil) and the movement was measured using a pachymeter (Mitutoyo Inc., Hiroshima, Japan). Each retraction procedure consisted of three activations that were started on the right side and then alternated between the right and left sides at 14-day intervals thus totaling 216 activations.

For the activations, the patients were initially randomized into three groups (A, B, and C) using the program for randomization available at http://www.random.org. For the activations on the opposite side, the patients from each group were randomized again into one of the other two groups. The drugs and administration methods had been concealed before the procedures. When the patient entered the study, he received a code that defined to which group each of his canine teeth (right and left) should belong.

Group A (preemptive) patients received one tablet of 20 mg of tenoxicam 45 min before the orthodontic activation process and one tablet of placebo just after finishing the activation. Group B patients received one tablet of placebo 45 min before the procedure and one tablet of 20 mg of tenoxicam just afterwards. Group C (control) patients received one tablet of placebo 45 min before the procedure and one tablet of placebo just afterwards. Subsequently, groups A and B both received one tablet of 20 mg of tenoxicam 24 and 48 h after the activation and group C received one tablet of placebo 24 and 48 h after the activation. The rescue analgesic offered to the patients in all three groups was paracetamol, at a dose of 750 mg, up to four times a day.

The intensity of the pain caused by the activations was measured 12, 24, 48, and 72 h after each activation by means of a Verbal Descriptive Scale (VDS) and a Visual Analog Scale (VAS). The consumption of rescue medication was also assessed. The VDS consisted of a group of words that describe pain intensity. The patients should mark the word that best described what they were feeling (8, 9). VAS measured the pain intensity by a gradual scale from 0 to 10 and the patients should mark the intensity of pain, considering 0 as no pain and 10 as unbearable pain intensity (10–13).

The tooth movement was determined by measuring the distance between the canine and second premolar teeth with a caliper, prior to activation and 4 weeks later. The movement was obtained by calculating the difference of these measures. ANOVA (14) was used to analyze the data using Bonferroni's *post hoc* test. The Friedman and Student's *t*-tests were used for

longitudinal analysis of paired data, comparing time intervals in relation to the variables of traction and pain intensity.

Results

The orthodontic movement was statistically similar between the placebo group and the groups that received tenoxicam (Fig. 1). Pain assessments using the VAS and VDS showed that the peak pain intensity occurred at the evaluation performed 12 h after activation. Notable decreases were observed thereafter, particularly in groups A and B at the first two activations. For all the groups, the evaluation performed 72 h after activation showed pain intensity close to zero (Figs 2 and 3).

The pain intensity values were statistically significantly higher in group C than in groups A and B. It was only at the evaluation performed 72 h after activation that there were no statistically significant differences in pain intensity among the three groups. Pain control in group A was 56.93% better according to the VAS and 73.57% better according to the VDS, in comparison with group C. In group B, it was 58.26% better according to the VAS and 54.64% better according to

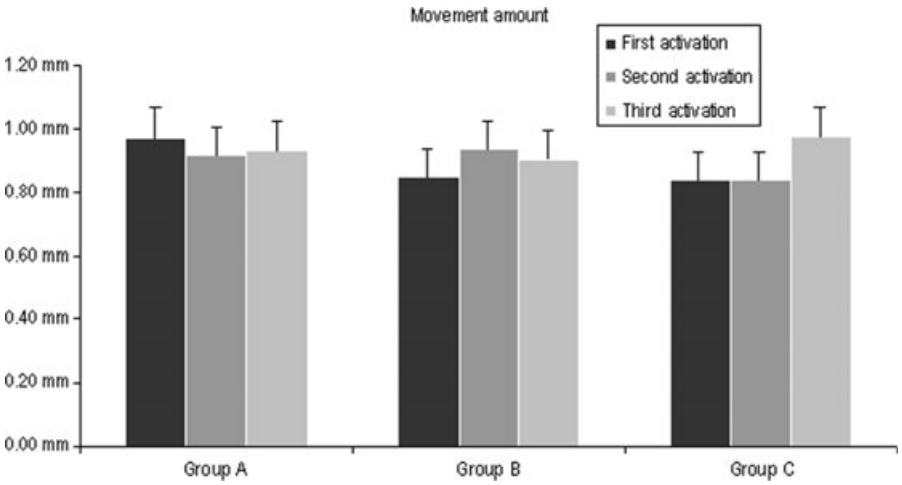

Fig. 1. Amount of tooth movement 4 weeks after each orthodontic activation (mm).

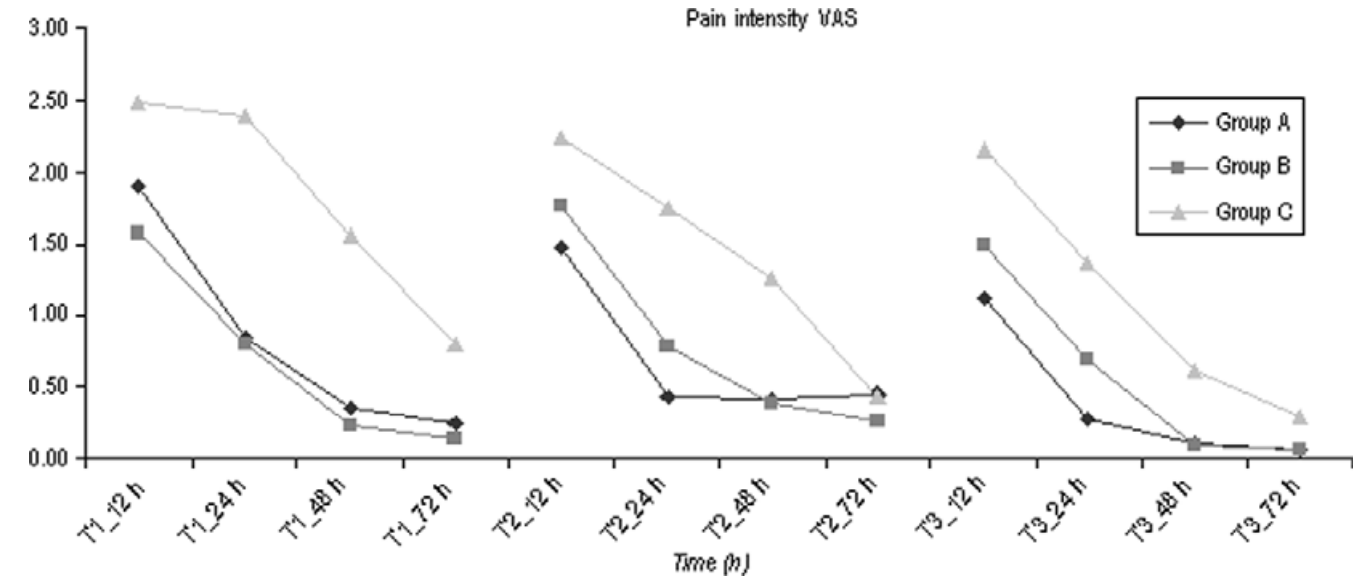

Fig. 2. Comparison of pain intensity using Visual Analog Scale (VAS) for groups A, B, and C at four different time points after each orthodontic activation (T1, T2, and T3).

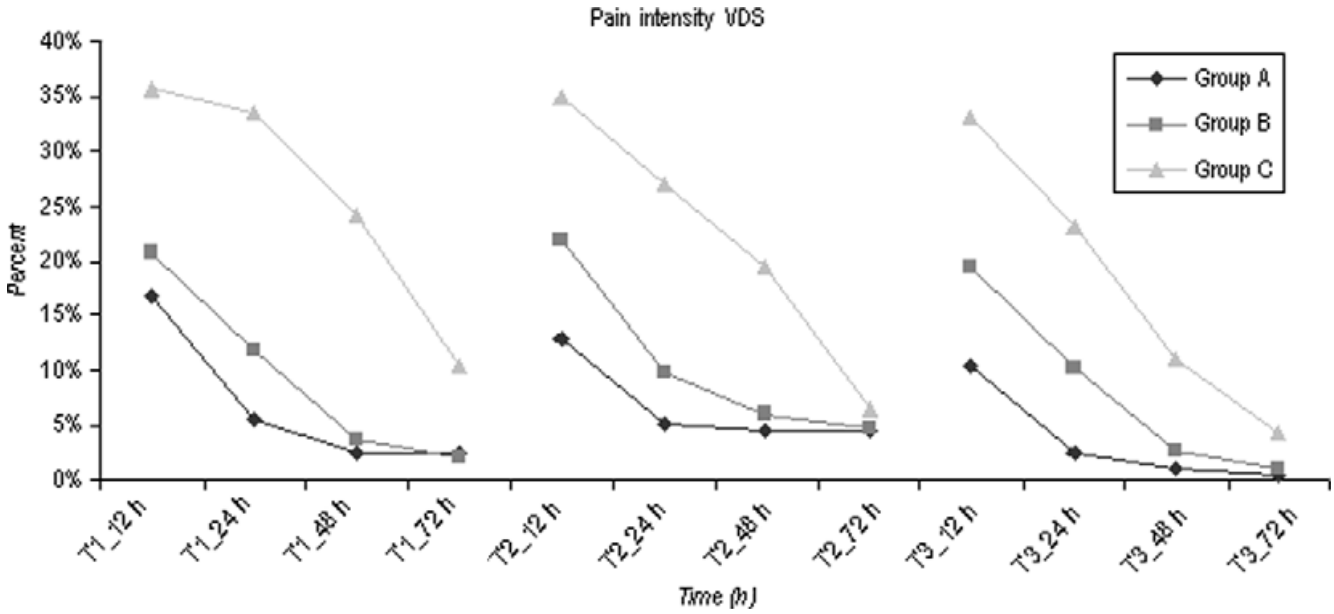

Fig. 3. Comparison of pain intensity using Visual Descriptive Scale (VDS) for groups A, B, and C at four different time points after each orthodontic activation (T1, T2, and T3).

Table 1. **Results of the Bonferroni *post hoc* test for differences among groups using a Visual Analog Scale (VAS)**

		Significance (*p*-value)		
Activations	Hours after activation (h)	Group A vs. B	Group A vs. C	Group B vs. C
Activation 1	12	1	0.713	0.22
	24	1	0.001	0.001
	48	1	0.002	0.001
	72	1	0.123	0.044
Activation 2	12	1	0.302	0.902
	24	0.831	< 0.001	0.008
	48	1	0.023	0.019
	72	1	1	1
Activation 3	12	1	0.046	0.385
	24	0.47	0.001	0.059
	48	1	0.005	0.004
	72	1	0.13	0.145

Table 2. **Results of the Bonferroni *post hoc* test for differences among groups using a Verbal Descriptive Scale (VDS)**

		Significance (*p*-value)		
Activations	Hours after activation (h)	Group A vs. B	Group A vs. C	Group B vs. C
Activation 1	12	1	0.002	0.02
	24	0.421	< 0.001	< 0.001
	48	1	< 0.001	< 0.001
	72	1	0.046	0.035
Activation 2	12	0.242	< 0.001	0.025
	24	0.663	< 0.001	< 0.001
	48	1	< 0.001	0.001
	72	1	1	1
Activation 3	12	0.143	< 0.001	0.012
	24	0.145	< 0.001	0.004
	48	1	< 0.001	0.002
	72	1	0.033	0.09

the VDS, in comparison with group C. Comparing groups A and B, there was no statistically significant difference regarding pain intensity. Tables 1 and 2 show that at many time intervals after activation there are statistically significant differences, when group C is compared with groups A and B. This is not the case comparing groups A and B.

Discussion

As seen in several orthodontic procedures and that reported in literature, retraction of the canine teeth causes slight to moderate pain intensity (15). In the same way as carried out by other authors, pain intensity was evaluated using the VAS (10–13) and VDS (8, 9)

methods that are recommended in the specialized literature.

Tenoxicam was the analgesic chosen for this study because it has been in use for a long time and its dosage is very convenient. It only needs to be used once a day because of its long elimination half-life (5) with good results in controlling acute pain of mild or moderate intensity, such as the pain triggered by orthodontic activation, without presenting any significant adverse effects (16, 17). The patients in this study did not have the need to use the rescue medication as the pain caused by the activations was not of great intensity. Moreover, the placebo effect cannot be neglected. Analgesia induced by suggestion is a known phenomenon that occurs through patients' expectations when taking a tablet that they believe is an analgesic (18).

In other studies, pain was evaluated at time intervals differing from what was used in this study: every hour for the first 24 h and every 6 h for the next 7 days (19) or at time 0, 6, 12, 24, and 48 h after activation (20). In those studies, the pain started in the sixth hour after activation and the peak pain occurred 24 h after activation. In the present study, although the pain was evaluated at the time points of 12, 24, 48, and 72 h, the peak pain occurred at an earlier time, 12 h after activation, i.e., at the time of the first measurement. Then, pain gradually decreased close to zero at the evaluation performed 72 h after activation. This pain pattern occurred in all three studied groups. If the assessments of pain intensity had been carried out at shorter intervals from the time of the activation, the peak pain intensity might have been identified at an even earlier time. Earlier appearance of the peak pain could be due to the fact that retraction of the canine teeth generates a force that is more precise and localized on only one tooth. In this aspect, this study differs from others that evaluated changes in orthodontic arches or a variety of activations (19, 20), as in such cases, the forces are distributed throughout the dental arch and depend on the orthodontic problem presented.

Tenoxicam has shown good pain control following dental implantation surgery (12, 17), without any significant adverse effects reported by patients. In this study also, the patients of the groups that received tenoxicam did not report any significant adverse effects. Their pain intensity was lower than what was reported by the control group patients. Likewise, the NSAIDs, such as ibuprofen (6, 21, 22), paracetamol (22), naproxen (1), and aspirin (1) have also been reported to provide adequate pain control without significant adverse effects observed.

The preemptive effect has already been demonstrated (6, 23). However, using the preemptive technique (24) in this study with tenoxicam did not show better pain control than when it was administered after orthodontic activation. Preemptive action has been effective in procedures in which the tissue lesions are larger and consequently the inflammation is more intense (23). In models with lower pain intensity, the responses seem to be less apparent and are not always conclusive. As the model for moving upper canine teeth is one of low pain intensity, the inflammatory response may not have been sufficiently intense to demonstrate the preemptive action of tenoxicam.

The orthodontic movement was not influenced by using tenoxicam, thus showing that this drug does not change the tooth movement just like celecoxib (25) and paracetamol (22), and unlike aspirin, ibuprofen, naproxen, diclofenac, and rofecoxib (1–3, 22) which diminish the number of orthodontic movement.

Diminished movement may occur through inhibition of cyclooxygenase. This enzyme has importance in relation to inflammation which appears to be one of the factors responsible for orthodontic movement (3, 4). Different types of inflammatory responses in different areas of the same tooth subjected to orthodontic forces have been described. The forces that act on the periodontal fibers cause occurrences of microenvironments with different inflammatory responses around the same tooth, but on opposite sides of the root. Tension on the fibers promotes differences in bone remodeling between areas of compression and traction of the fibers. This has been demonstrated by differences in cytokine expression (26, 27).

Thus, tenoxicam used only once a day was shown to be effective for pain control, like other drugs in the same class. It did not influence the orthodontic movement, just like celecoxib (25) and paracetamol (22) which also control pain without interfering with the number of movement, possibly because of their limited anti-inflammatory activity.

Our results showed an interesting potential for the use of tenoxicam in orthodontic treatment, it was effective for pain control when used once a day, had no

influence on the orthodontic movement, and did not present preemptive effect.

Clinical relevance

Pain control is fundamentally important for achieving satisfactory patient recovery. In orthodontic therapy, it is customary not to administer NSAIDs for pain control as clinical and experimental studies have demonstrated that they diminish the orthodontic movement. This study shows that administration of tenoxicam to orthodontic patients not only controls pain but also does not interfere with orthodontic movement.

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