Research Article

Effects of various analgesics on pain perception and rate of tooth movement: a randomized controlled clinical study

Asem A M Abdaljawwad[1], Dheaa H Al-Groosh[2]

1Department of Orthodontics, College of Dentistry, University of Anbar, Iraq.
2Department of Orthodontics, College of Dentistry, University of Baghdad, Iraq.
* Correspondence: dheaaha73@yahoo.com

Received date: 12-12-2021
Accepted date: 20-1-2022
Published date: 15-6-2022

Copyright: © 2022 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

https://doi.org/10.26477/jbcd.v34i2.3144

Abstract: Background: Pain is one of the most reported side effects of orthodontic treatment despite the advanced technology in orthodontics. Many analgesics have been introduced to control orthodontic pain including acetaminophen and selective and nonselective nonsteroidal anti-inflammatory drugs. The great concern about these drugs is their adverse effect on rate of teeth movement. Aims: The purpose of this study was to evaluate and compare the effect of acetaminophen, ibuprofen and etoricoxib on pain perception and their influence on the rate of teeth movement during leveling and alignment stage. Methods: Forty patients were evenly and randomly distributed in a blinded way to one of four groups: placebo (starch capsules), acetaminophen 500mg thrice daily, ibuprofen 400mg thrice daily, and etoricoxib 60mg once daily. The drugs were given one hour before bonding and archwire placement and continued for three days. A visual analogue scale was used to express pain levels before and after archwire placement, on the first, second, third, and seventh day. Little's irregularity index was measured before bonding and at every activation visit until the end of the alignment and leveling stage. Results: All three drugs showed a lower pain level than placebo at the bonding and first activation visits. Etoricoxib showed the least pain level among other drugs followed by ibuprofen. No statistically significant differences were found between the drug groups and the placebo at the second and third activation visits. No statistically significant differences were detected between the 4 experimental groups concerning the rate of teeth movement. Conclusions: The three drugs were only effective in controlling pain during the first two visits of orthodontic treatment; and etoricoxib 60mg/day was the best. All three drugs had no influence on rate of teeth movement when used in their least recommended dose.

Keywords: *Orthodontic pain, pain perception, etoricoxib, analgesics.*

Introduction

Orthodontic pain was reported to be one of the most negative effects of orthodontic treatment, it has been rated as a major reason for discontinuing treatment [1-3].

Previous studies have well documented that orthodontic pain begins between 4h - 12h after orthodontic force application, peaks after 1 day, gradually subsides 3–7 days thereafter and returns to baseline levels after 1 month [4-6].

Non-steroidal anti-inflammatory drugs (NSAIDs) have been used for the relief of orthodontic pain for decades. Their effectiveness in orthodontic pain relief has been validated, but their side effect of reducing the rate of tooth movement is still being debated (7-9), making NSAIDs not routinely used for pain control in orthodontic practice.

Traditional NSAID are nonselective for two isoforms of cyclooxygenase (COX), COX-1 and COX-2. COX-1 is related to the synthesis of prostaglandins involved in the protection mechanism of the gastric mucosa, while COX-2 is induced after the inflammatory cells have been activated and participate in the synthesis of inflammation and pain mediators [10]. In this context, NSAIDs selective for COX-2 were newly developed, to overcome COX-1 inhibition side effects [11].

Acetaminophen was suggested to be the most effective drug that corroborates its pharmacological use in orthodontic movement disturbances, it seems to have no role in the synthesis of prostaglandins(12,13). However, there is still no precise recommendation regarding the most adequate drug for pain control in orthodontic treatment. In this context, determining the NSAID that reduces pain the most without influencing the rate of tooth movement becomes essential to optimize the orthodontic treatment [7,13,14].

The aims of the present study were to compare the analgesic effect of etoricoxib (a selective NSAID), Ibuprofen (a nonselective NSAID), and acetaminophen on the orthodontic pain generated after archwire placement and/or activation during the alignment and leveling stage, and to find if there is any effect of these analgesics on the rate of teeth movement.

Materials and Methods

Ethical approval and subjects

This randomized, double-blinded, placebo-controlled, prospective study was approved by the Ethical Committee of the College of Dentistry/ University of Baghdad on the 24th February 2020 with Ref. Number 186420. A total of forty patients (age ranged between 18 and 24 years old) who were about to receive fixed orthodontic appliance treatment agreed to enroll in this study. The patients were informed about the procedure through a detailed information sheet, and written informed consent was obtained. Sample size was measured according to a predetermined 80% power of study and 5% significance alpha level.

Selection criteria

Patients must have a full set of permanent dentitions excluding the third molars. No antibiotic treatment for at least four weeks before bonding. No history of systemic diseases or allergies. No current use of steroids or analgesics. Not contraindicated to NSAID. Must not extract teeth at least 4 weeks before bonding. No history of previous orthodontic treatment. Moderate crowding of a maximum of 10mm according to Little's irregularity index (LII) [15].

This study was done in the Orthodontic Clinic at the College of Dentistry/ University of Baghdad in addition to a private specialized dental center in Baghdad city.

Blinding and Randomization

Forty-four patients (age ranged between 18 and 24 years old) were recruited; however, three patients did not meet the oral hygiene requirement (GI or PLI >1). The remaining forty-one patients were randomly

assigned to one of four study groups. A simple non-stratified randomization was done using randomly assign subjects to treatment groups website (https://www.graphpad.com/quickcalcs/randomize1/) with an equal allocation ratio (10 participants per group except group B contained 11patients). The allocation was performed by an independent person. The groups were named as A, B, C, and D and both the patient and the investigator (A.A.M.A), who was responsible for the clinical part of the study, were blinded to the type of analgesic that were given to each group as well as to the grouping itself, which was kept sealed until the completion of data analysis.

The drug tablets did not have any markings or labels that represent brand name, and were put in small opaque pill boxes with a sticker containing the name of the group. The pills were put in the boxes by the independent person.

Study groups

Four experimental groups were predetermined: group A, were given a placebo (starch capsule) once daily (considered as the control group); group B, were given 500 mg acetaminophen (Paracetamol, Pristol House, Unit 3, Canalside, Northbridge Road, Berkhamsted Hertfordshire, United Kingdom) three times daily; group C, were given 400 mg ibuprofen (Denk Pharma, GmbH & Co. KG, Prinzregentenstr., München, Germany) three times daily; and group D, were given 60 mg etoricoxib (Arcoxia, Merck Sharp & Dohme B.V., Waarderweg Haarlem, Netherlands) once daily.

The lowest recommended dose for each medication was used according to the National Health Service, UK. Drug administration began 1 hour before commencing the bonding procedure and/or archwire change, and were given for three days including the bonding day. Patients were instructed not to take any additional analgesics. A standardized treatment protocol was followed for all participants. The same day after placing the fixed orthodontic appliance, a 0.012-inch archwire was placed for alignment as a starting arch wire and the usual wire consequence was followed (0.014-inch NiTi followed by 0.016-inch NiTi, then 18-inch NiTi) at 6 weeks visit intervals. Archwires were fully tied to the brackets by either ligature wires or elastomeric modules (rotated teeth were ligated with ligature wires). To ensure standardization, any debond happened during the treatment was rebonded within 24 hours, otherwise the case will be excluded. Patients were all reminded about their upcoming visits via cell phone call one day before appointment.

Pain assessment

Patients recorded the pain perceived on a graded linear visual analogue scale (VAS). Subjects were given routine post-bonding instructions and were thoroughly trained on how to deal with the VAS. Then patients were asked to complete a questionnaire at appropriate intervals during the week after the bonding appointment.

The questionnaire was in the format of a printed six-page booklet that contained 100 mm horizontal VAS on which patients were asked to mark the degree of discomfort at the indicated time periods. 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 the three activities:

Chewing, fitting or occluding on the front teeth, and fitting the back teeth. Incidence and severity of pain were recorded by the patient prior to bonding and drug administration, immediately after bonding, and on the first, second, third and seventh day after bonding. Patients were asked to return the questionnaire on the seventh day.

This questionnaire was repeated for all activation visits until the end of the alignment stage. A text message reminder was sent to every patient to remind them to mark the questionnaire on the scheduled day. All of the forty patients who enrolled in this study returned their questionnaires, and none of them were recorded to use additional medication.

Rate of tooth movement

The rate of tooth movement was estimated by measuring the LII for the lower arch before appliance bonding and at each archwire changing visit which was made every 6 weeks till the end of alignment stage directly in patients' mouth using a four-digit caliper with tenth of a millimeter.

The difference between each measurement and its previous one determined the amount of teeth movement for that visit. In the present study we have calculated the rate of teeth movement four times before it reached zero crowding.

LII is a quantitative method of assessing the anterior teeth irregularity. The technique involves measurement of teeth irregularities directly from the patient's mouth or from the dental cast with a caliper (four-digit caliber with a tenth of a millimeter) held parallel to the occlusal plane. The linear displacement of the adjacent anatomic contact points of the incisors is determined, and the sum of the five measurements represents the Irregularity Index value of a case [15].

Statistical analysis

The statistical analysis was performed using SPSS 22 on windows 10 software (SPSS Inc., Chicago, Illinois, USA). Data distribution of the VAS scores for pain levels was checked using Shapiro-Wilk test.

Descriptive statistics were done for all data. Age differences between groups were evaluated using one-way ANOVA (analysis of variance). All statistical comparisons done included all the three different actions (chewing, fitting anterior teeth and fitting posterior teeth) at each time interval, and were repeated for each archwire changing visit.

Comparisons within each drug group over time by means of pain were done using Wilcoxon test with Bonferroni correction, and since 45 multiple comparisons were made for each group, a significance value of $P < 0.0011$ was considered significant.

Differences between the drug groups to compare pain over time were evaluated using Kruskal Wallis test. In the first and third orthodontic visits, ten actions were found to be statistically significant, so Mann Whitney test with Bonferroni correction was done. As sixty multiple comparisons were made, a significant value of $P < 0.00083$ was considered to be significant. In the second orthodontic visit, 14 actions were found

statistically significant, the Bonferroni correction of Mann Whitney test indicated considering a significance value of $P < 0.0006$ to be significant because 84 multiple comparisons were made. In the fourth orthodontic visit, only 6 actions were found statistically significant, so Mann Whitney test with Bonferroni correction was done, and a significance value of $P < 0.0014$ was considered significant, since 36 multiple comparisons were made.

Intraclass correlation coefficient (ICC) was used to test the inter-examiner reliability of the LII of a twelve randomly selected patients, LII was remeasured by another investigator at the same visit. The rate of teeth movement was compared between the drug groups using one-way ANOVA test.

Results

One patient from group B missed to record the pain assessment form and, therefore, were dropped out of the study. The remaining 40 patients who participated in our study completed the whole procedures until the end of their alignment and leveling stage and returned all their pain assessment forms. The CONSORT flowchart of the current trial is shown in Figure 1. Patient recruitment started in November 2020 and completed in May 2021.

Descriptive statistics of the patients' age for the four groups was calculated as shown in Table 1. The average age for the four groups was not significantly different from each other ($P < 0.05$). Gender differences were not taken into consideration.

Pain levels of the drug groups

In all the study groups, the pain level reached its peak after 24 hours of archwire placement and/or activation, this was true through all different actions and in all activation visits. Interestingly, no statistically significant differences ($P < 0.0011$) were detected between different time intervals for all activities within the same group.

Table 1 Descriptive statistics and distribution of age in the study groups.

Group	Drug	N	Mean	Std. Deviation	Min.	Max.	F	P
A	**Placebo**	10	21	2.055	18	24	0.139	0.936
B	**Acetaminophen**	10	20.9	1.792	19	24		
C	**Ibuprofen**	10	21.4	1.506	19	23		
D	**Etoricoxib**	10	21.2	2.098	19	24		
Total		40	21.13	1.814	18	24		

All the data are presented as mean (95% confidence interval).

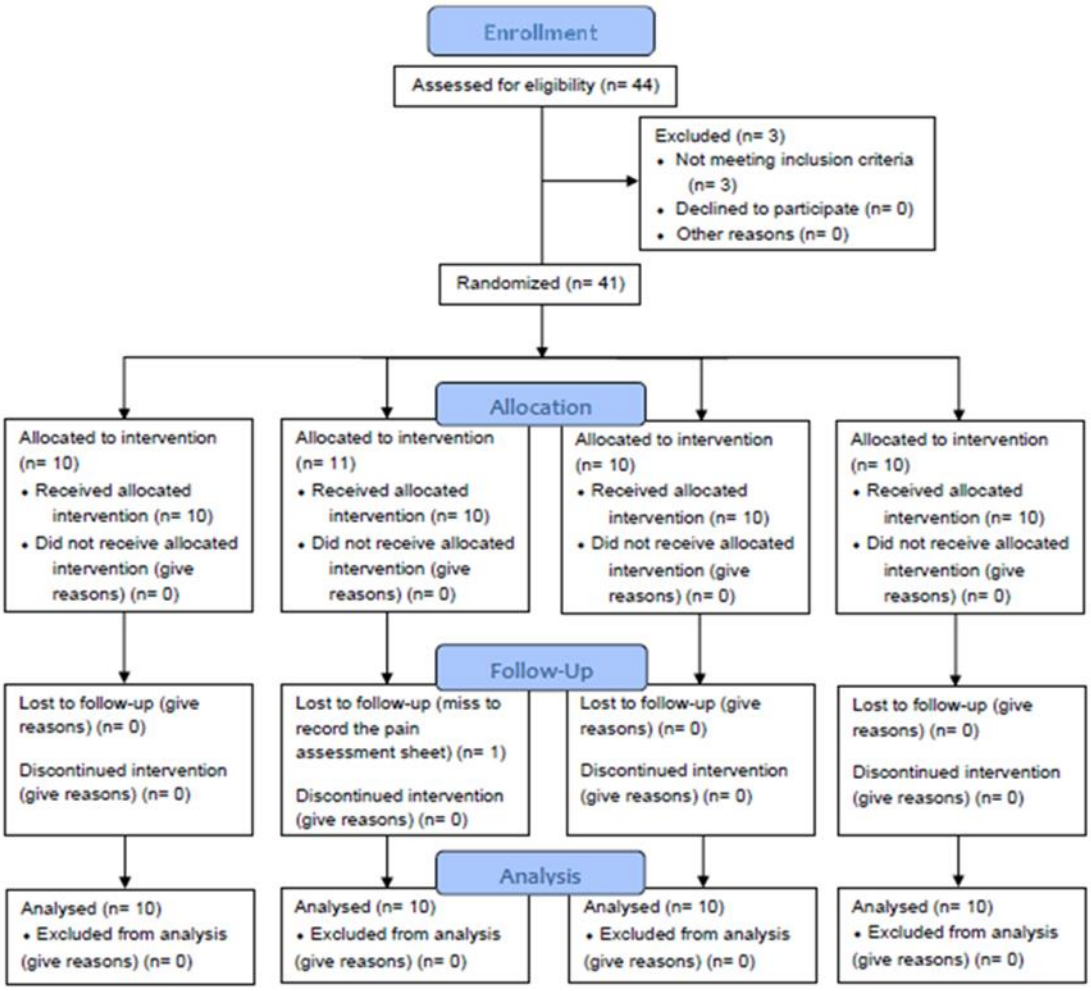

Figure 1. CONSORT flowchart of participants through each stage of the study.

Pain levels between the drug groups

After the bonding visit and at 24 and 72 hours; ibuprofen, acetaminophen and placebo groups had a comparable pain levels, while etoricoxib group showed a superior analgesic effect over them at chewing and fitting on anterior teeth and the differences were statistically significant ($P < 0.00083$) (Table 2).

After 48 hours etoricoxib, ibuprofen and acetaminophen groups had a comparable analgesic effect during chewing, but all showed significantly ($P < 0.00083$) higher analgesic effect than placebo group. However, etoricoxib group showed significantly ($P < 0.00083$) less pain levels than ibuprofen and acetaminophen groups during fitting on anterior teeth (Table 2).

Results after the first activation visit showed significant higher pain levels in the placebo group over other drug groups ($P < 0.0006$) in all actions. At the first day, Etoricoxib group presented with significantly lower pain levels ($P < 0.0006$) than ibuprofen group during fitting on anterior teeth, and lower than acetaminophen group during chewing and fitting on posterior teeth. Ibuprofen group was better in controlling pain than acetaminophen group only during fitting on posterior teeth, the difference was significant ($P < 0.0006$) (Table 2).

At the second and third days, etoricoxib and ibuprofen groups had a comparable pain levels, however, these were lower than that of acetaminophen group during fitting on posterior teeth ($P < 0.0006$), in addition, ibuprofen group showed significantly lower pain levels than acetaminophen group chewing ($P < 0.0006$) (Table 2).

No statistically significant differences were found between the drug groups After the second and third activation visits, except that etoricoxib showed a significantly ($P < 0.00083$) better analgesic effect than acetaminophen group during fitting on anterior teeth at day 3 (Table 2).

Table 2 Pain levels of the four groups at measured functions and time intervals.

Action	Time	Placebo	Acetaminophen	Ibuprofen	Etoricoxib
Chewing	**Day 1**	33 (15-55)[a] 56 (30-75)[b]	29 (15-40)[b]	33 (20-45)[a] 19 (10-25)[b]	7.2 (0-13)[a] 9.4 (3-18)[b]
	Day 2	58 (50-70)[a] 66 (25-100)[b]	28 (15-50)[a] 20 (10-35)[b]	24 (5-35)[a] 3 (0-5)[b]	14.2 (8-20)[a] 7.2 (0-18)[b]
	Day 3	40 (15-55)[b]	23 (15-35)[a] 15 (5-25)[b]	2 (0-5)[b]	4.6 (0-10)[a] 5.2 (0-13)[b]
	Day 7	22 (5-40)[b]	15 (5-25)[b]	2 (0-5)[b]	
Fitting on Front teeth	**Day 1**	56 (45-70)[b]	54 (45-70)[a]	22 (20-25)[b]	21.6 (13-35)[a] 9.4 (3-18)[b]
	Day 2	54 (40-80)[a] 65 (40-85)[b]	39 (20-55)[a]	31 (20-60)[a] 19 (15-25)[b]	15.6 (13-20)[a] 7.2 (0-18)[b]
	Day 3	37 (20-80)[a] 32 (20-55)[b]	26 (15-60)[c]	45 (30-60)[a]	5 (0-10)[a] 6 (0-15)[b] 11.2 (8-15)[c]
	Day 7	29 (10-60)[b]	20 (10-30)[a] 16 (10-20)[b]	2 (0-5)[b]	4.6 (0-10)[a] 4 (0-10)[b]
Fitting on back teeth	**After bonding/ archwire replacement**	21 (10-40)[b]			2.2 (0-5)[b]
	Day 1	59 (25-85)[b]	21 (20-25)[b]	9 (0-15)[b]	7.4 (3-13)[b]
	Day 2	64 (50-75)[a] 64 (20-100)[b]	11 (0-35)[a] 19 (15-25)[b]	2 (0-5)[b]	13.2 (3-20)[a] 5.2 (0-13)[b]
	Day 3	42 (10-65)[b]	22 (15-35)[b]	3 (0-10)[b]	4 (0-10)[b]
	Day 7	27 (10-50)[b]		2 (0-5)[b]	3.2 (0-8)[b]

A: Significant differences were found at bonding visit ($P < 0.00083$), b: Significant differences were found at the first activation visit ($P < 0.0006$), c: Significant differences were found at the second activation visit ($P < 0.00083$).

Rate of teeth movement of the drug groups

The mean rate of teeth movement measured at the first visit after 6 weeks of bonding and loading the initial arch wire (first activation) were 2.192 ± 0.735 mm for placebo group, 3.972 ± 1.929 mm for acetaminophen group, 2.468 ± 1.95 mm for ibuprofen group, and 3.4 ± 1.158 mm for etoricoxib group (Table 3).

After the second activation (12 weeks after bonding), the mean rate of teeth movement calculated were 2.09 ± 1.07 mm for placebo group, 2.748 ± 1.3 mm for acetaminophen group, 3.252 ± 0.904 mm for ibuprofen group, and 2.414 ± 0.519 mm for etoricoxib group (Table 3).

The mean rate of teeth movement estimated after the third activation (18 weeks of starting alignment and leveling) were 1.92 ± 2.138 mm for placebo group, 1 ± 1.302 mm for acetaminophen group, 1.16 ± 1.055 for ibuprofen group, and 2.266 ± 2.352 mm for etoricoxib group (Table 3).

The calculated means of teeth movement after the fourth activation (24 weeks after bonding) were 1.3 ± 0.544 mm for placebo group, 1 ± 0.289 mm for acetaminophen group, 0.9 ± 0.155 mm for ibuprofen group, and 1.25 ± 0.866 mm for etoricoxib group (Table 3).

Table 3 Descriptive statistics of the rate of teeth movement in drug groups.

Time	Groups	N	Mean	Std. Deviation	Min.	Max.
First activation (after 6 weeks)	**Placebo**	10	2.192	0.73525	1.29	3.02
	Acetaminophen	10	3.972	1.92894	1.26	6.6
	Ibuprofen	10	2.468	1.95013	0.19	5.85
	Etoricoxib	10	3.402	1.15817	1.96	5
	Total	40	3.0085	1.64139	0.19	6.6
Second activation (after 12 weeks)	**Placebo**	10	2.09	1.06531	1.15	4.05
	Acetaminophen	10	2.748	1.30043	1.6	4.7
	Ibuprofen	10	3.252	0.90444	2.5	4.9
	Etoricoxib	10	2.414	0.51938	1.72	3.25
	Total	40	2.626	1.04531	1.15	4.9
Third activation (after 18 weeks)	**Placebo**	10	1.92	2.13817	0	4.4
	Acetaminophen	10	1	1.30171	0	2.75
	Ibuprofen	10	1.16	1.05536	0	2.5
	Etoricoxib	10	2.266	3.92046	0	9.58
	Total	40	1.5865	2.35197	0	9.58
Fourth activation (after 24 weeks)	**Placebo**	6	1.3	0.54406	0.9	2
	Acetaminophen	4	1	0.28868	0.75	1.25
	Ibuprofen	6	0.9	0.15492	0.7	1
	Etoricoxib	4	1.25	0.86603	0.5	2
	Total	20	1.11	0.49778	0.5	2

All the data are presented as mean (95% confidence interval).

Rate of teeth movement between the drug groups

Intra class correlation coefficient revealed a high reliability level [ICC = 0.976 (95% CI 0.917–0.993)] for LII (Table 4).

Table 4 Intraclass Correlation Coefficient.

	Intraclass Correlation	95% Confidence Interval		F Test with True Value			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	0.953	0.847	0.986	38.578	11	11	0.000
Average Measures	0.976	0.917	0.993	38.578	11	11	0.000

No statistically significant difference (P < 0.05) was detected by ANOVA test between the different experimental groups through the whole alignment and leveling period (after the first, second, third and fourth activations after bonding) (Table 5).

Table 5 ANOVA test for comparisons of rate of teeth movement between drug groups after different activation times.

Activation		Sum of Squares	df	Mean Square	F	Sig.
First activation	**Between Groups**	20.42	3	6.807	2.895	0.058
	Within Groups	84.652	36	2.351		
	Total	105.072	39			
Second activation	**Between Groups**	7.39	3	2.463	2.518	0.074
	Within Groups	35.224	36	0.978		
	Total	42.614	39			
Third activation	**Between Groups**	10.988	3	3.663	0.644	0.592
	Within Groups	204.75	36	5.688		
	Total	215.739	39			
Fourth activation	**Between Groups**	0.608	3	.0203	0.791	0.517
	Within Groups	4.1	16	0.256		
	Total	4.708	19			

Discussion

One of the most common complaints among orthodontic patients is pain, especially during the first week of fixed appliance placement and the ongoing activation and archwire changing visits. Many factors have been reported to affect the severity of orthodontic pain such as age, force type, and type of personality (16), moreover, the amount of patients' discomfort and attitude toward treatment found to effect on appliance acceptance [17]. Because of such important effect on patients' compliance, pain management is a priority to ensure a successful orthodontic treatment.

Pain is a subjective feeling caused and affected by many factors. Several methods were suggested to assess pain in the literature and nearly all of them depends on subjective methods. Like most of the orthodontic studies in the literature, VAS was used in the current study to assess pain. It is found to be the most accepted and appropriate over other pain scales because of its ease of measurement and reproducibility [18,19].

The current randomized controlled study was conducted on a total of 40 patients who scheduled to have fixed orthodontic appliance therapy. Patients were randomly distributed into one of four experimental groups: patients in group A were given placebo (starch capsules), patients in group B administered 500 mg acetaminophen, patients in group C took 400 mg ibuprofen, and patients in group D administered 60 mg etoricoxib; in all four groups, medication was started 1 hour before the bonding/archwire activation procedure and continued for 3 days. All the patients completed the study without using any additional medications. The lowest recommended doses of acetaminophen, ibuprofen and etoricoxib were used to control pain (as suggested by National Health Service, UK). Pain level scores were obtained using VAS at the particular time intervals. The aims of this randomized placebo-controlled study were to assess the efficacy of acetaminophen, ibuprofen (non-selective NSAID), and etoricoxib (highly selective NSAID) administration on controlling orthodontic pain and their possible effect on the rate of orthodontic tooth movement.

The uniqueness of the current study is that pain evaluation was conducted through the whole leveling and alignment period over about 6 months of orthodontic treatment, with repeating the pain control drugs and scoring process during the first week of each visit interval. Rate of teeth movement was also measured through the same leveling and alignment period by measuring the amount of teeth movement at each visit interval.

In the present study and through all activation visits, pain started immediately after archwire placement or activation and reached its peak after 24 hours in all study groups and all different activities, which markedly reduced at day 7. These findings were similar to previous studies [16,20-24].

The average pain score on VAS through the entire study did not exceed 67 on 100 mm scale in placebo group, indicating a moderate pain, which was in agreement with Gupta et al (2014) (24), while in other drug groups the scores were below 44 mm, indicating a mild pain, these results were similar to what found by Salmassian et al (2009) [16].

Analgesic effect within the same group of different activities at different time intervals showed no statistically significant difference in all experimental groups. For drug groups pain scores were all mild which made it difficult for the patients to detect a significant reduction in pain, besides, administration timing plays a significant role in the effectiveness of analgesics used for orthodontic pain management due to the differences in their plasma half-life [25]. In the current study analgesics were given 1 hour preoperatively which allow enough time for them to reach a high plasma concentration before pain reached its peak levels.

In the placebo group, even though patients didn't take analgesic medications, no significant difference in pain levels were detected in response to different time intervals through different actions. This is mainly

due to the psychological effect of placebo drugs which could reach 30-40 % in medical and dental studies [26].

Pain evaluation at the bonding visit and at the first visit after bonding revealed that etoricoxib was the most effective drug in pain reduction among other groups, these results were statistically significant for all different actions after 24, 48, and 72 hours, where pain reached its peak levels. This was in agreement with (24) which was the only study in the literature comparing etoricoxib analgesic efficacy in controlling orthodontic pain to other drugs. A systematic review and meta-analysis which published recently concluded that placebo is the least effective, while etoricoxib is the most effective analgesic in controlling orthodontic pain [25].

At the bonding visit ibuprofen and acetaminophen showed similar results in pain reduction with no statistically significant difference between them, but at the first visit after bonding (6 weeks after bonding) ibuprofen was significantly more effective than acetaminophen in reducing pain in fitting on posterior teeth and on chewing actions after 24, 48, and 72 hours. both drugs were significantly more effective than placebo in those time intervals. When these results compared to previous studies comparing ibuprofen to acetaminophen and placebo, conflicting results were found. Bernhardt et al. (2001) [20] and Bradley et al. (2007) [27] found that ibuprofen administration causes less pain than acetaminophen. Another study which done by Patel et al. (2011) [28] showed similar analgesic effect between acetaminophen and placebo, whereas ibuprofen revealed superior analgesic effect. However, Bird et al. (2007) [29], Salmassian et al. (2009) (16), and Tunçer et al. (2014) [30] have found no statistically significant difference between acetaminophen and ibuprofen. A systematic review done by Xiaoting et al. (2010) [31] concluded that there is no statistical difference detected between ibuprofen, acetaminophen or placebo. Another more recent systematic review and meta-analysis indicated that ibuprofen can be effective in reducing pain after separators or archwire placement only after 2 and 6 hours compared to placebo, but not at 24 hours. Ibuprofen and acetaminophen seem to be equally effective [32].

The current study showed similar effect in reducing orthodontic pain between the four experimental groups at the second and third visits after bonding (12 and 18 weeks after bonding).

It is widely known that teeth movement process happened by blood flow obstruction of the periodontal ligament (PDL) at the pressure site leading to the release of PE2 which activate bone resorption process [33]. NSAIDs are the most common drugs given to control pain in patients act by blocking the PGE2 production by inhibiting the COX enzyme and thus disrupting teeth movement as reported in many previous animal studies [34,35]. On the other hand, the highly selective COX 2 inhibitor NSAIDs such as etoricoxib suggested to reveal a very little effect on teeth movement in comparison to conventional non-selective NSAIDs [24]. Unlike NSAIDs, acetaminophen is not an active anti-inflammatory agent and does not prevent PGE2 production and teeth movement [30,36].

Previous studies have shown that acetaminophen consumption for orthodontic pain control has no significant effect on the rate of teeth movement [7,12,13,35,37,38], while ibuprofen administration negatively affect the rate of teeth movement [7,12,35,38]. However, other studies concluded that ibuprofen and loxoprofen administration longer than two weeks did not have any significant effect on the rate of teeth movement [39,40].

Recently, it has been demonstrated that only high doses of etoricoxib significantly decrease the rate of teeth movement [41].

In the current study, no statistically significant differences were found between the four experimental groups through all activation visits till the end of the leveling and alignment period, these findings indicate that etoricoxib, acetaminophen, and ibuprofen drugs have no negative effect on the rate of orthodontic teeth movement when prescribed with their recommended doses for three days after each archwire placement and/or activation.

The half-life period of the high selective COX-2 inhibitor etoricoxib is 22 hours and reaches its maximum concentration in blood plasma after one hour of oral intake, which is far longer than most of other non-selective NSAIDs [42]. This have been shown clearly in the current study, a daily single dose intake of etoricoxib is more effective in orthodontic pain control than ibuprofen or acetaminophen given thrice daily. Furthermore, etoricoxib have the least effect on the gastric mucosa and no inhibitory effect on teeth movement.

Based on the current randomized study, and for better pain control in patients undergoing orthodontic treatment, it is recommended to prescribe etoricoxib rather than acetaminophen or ibuprofen due to its excellent pain controlling ability without affecting the rate of teeth movement. It is also better to prescribe ibuprofen over acetaminophen because of its superior analgesic effect in the absence of decelerating teeth movement.

Conclusion

Pain resulting from routine orthodontic treatment is of moderate intensity, and in cases of analgesic prescriptions is of mild intensity.

Etoricoxib, ibuprofen and acetaminophen are significantly effective in reducing orthodontic pain in the first 3 months of treatment, but have the same effect as the placebo after that.

Etoricoxib was the best efficient analgesic in reducing orthodontic pain.

Ibuprofen is significantly better than acetaminophen in controlling orthodontic pain.

Etoricoxib, ibuprofen and acetaminophen when prescribed with their least recommended doses have no inhibitory effect on the rate of orthodontic teeth movement.

Conflict of interest: None.

References

1. Brown DF, Moerenhout RG The pain experience and psychological adjustments to orthodontic treatment of preadolescents, adolescents and adults. Am J Orthod Dentofacial Orthop 1991; 100:349–356.

2. Kluemper GT, Hiser DG, Rayens MK, Jay MJ Efficacy of a wax containing benzocaine in the relief of oral mucosal pain caused by orthodontic appliances. Am J Orthod Dentofacial Orthop 2002; 122:359–365.

3. Shenoy N, Shetty S, Ahmed J, Shenoy AK. 2013 The pain management in Orthodontics. J Clin Diagn Res 2013; 7(6): 1258–1260.

4. Krishnan Vinod, Orthodontic pain: from causes to management — a review, Eur J Orthod. 2007; 29: 170–179.

5. Wang J, Jian F, Chen J et al. Cognitive behavioral therapy for orthodontic pain control: a randomized trial. J Dent Res 2012; 91(6): 580–585.

6. Marković E, Fercec J, Šćepan I et al. The correlation between pain perception among patients with six different orthodontic archwires and the degree of dental crowding. Srp Arh Celok Lek 2015; 143(3/4): 134–140.

7. Arias OR, Marquez-Orozco MC. Aspirin, acetaminophen, and ibuprofen: their effects on orthodontic tooth movement. Am J Orthod Dentofacial Orthop 2006; 130(3): 364–370.

8. Arantes GM, Arantes VM, Ashmawi HA et al. Tenoxicam controls pain without altering orthodontic movement of maxillary canines. Orthod Craniofac Res 2009; 12(1): 14–19.

9. Krasny M, Zadurska M, Cessak Get al. Analysis of effect of non-steroidal antiinflammatory drugs on teeth and oral tissues during orthodontic treatment. Report based on literature review. Acta Pol Pharm 2013; 70(3): 573–577.

10. LAUDANNO OM, CESOLARI JA, ESNARRIAGA J, RISTA M, PIOMBO G, MAGLIONE C, ARAMBERRY L, SAMBRANO J, GODOY A, ROCASPANA A Gastrointestinal damage induced by celecoxib and rofecoxib in rats. Dig Dis Sci 2001; 46: 779-784.

11. BOMBARDIER C ET AL Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis – VIGOR Study Group. N Engl J Med 2000; 343: 1520-1528.

12. SHETTY N, PATIL AK, GANESHKAR SV, HEGDE S Comparison of the effects of ibuprofen and acetaminophen on PGE2 levels in the GCF during orthodontic tooth movement: a human study. Prog Orthod 2013; 14: 6-6.

13. Correa AS, Almeida VL, Lopes BMV, Franco A, Matos FR, Quintans-Junior LJ, et al. The influence of non-steroidal anti-inflammatory drugs and paracetamol used for pain control of orthodontic tooth movement: a systematic review. An Acad Bras Cienc. 2017; 89:2851–2863.

14. GONZALES C, HOTOKEZAKA H, MATSUO K, SHIBAZAKI T, YOZGATIAN JH, DARENDELILER MA AND YOSHIDA M. Effects of steroidal and nonsteroidal drugs on tooth movement and root resorption in the rat molar. Angle Orthod 2009; 79: 715-726.

15. Little, R.M. The irregularity index: a quantitative score of mandibular anterior alignment. Am. J. Orthod. 1975; 68, 554–563.

16. Salmassian Reza, Oesterle Larry J., Shellhart W. Craig, and Newman Sheldon M. Comparison of the efficacy of ibuprofen and acetaminophen in controlling pain after orthodontic tooth movement. Am J Orthod Dentofacial Orthop 2009; 135:516-521.

17. Doll G M, Zentner A, Klages U, Sergl H G. Relationship between patient discomfort, appliance acceptance and compliance in orthodontic therapy. J Orofac Orthop 2000; 61: 398–413.

18. Dubner R. Neurophysiology of pain. Dent. Clin. N. Am. 1978; 22: 11–30.

19. Seymour R A, Simpson J M, Charlton J E, Phillips M E. An evaluation of length and end-phrase of visual analogue scales in dental pain. Pain 1985; 21: 177–185.

20. Bernhardt MK, Southard KA, Batterson KD et al. The effect of preemptive and/or postoperative ibuprofen therapy for orthodontic pain. Am J Orthod Dentofacial Orthop 2001; 120:20–27.

21. Aslihan M, Erdinc E, Dincer B. Perception of pain during orthodontic treatment with fixed appliances. Eur J Orthod 2004; 26:79–85 2.

22. Omur P, Ihya AI. Pain control during fixed orthodontic appliance therapy. Angle Orthod 2005; 75:214–219.

23. Polat O, Karaman AL, Durmus E. Effects of pre-operative ibuprofen and naproxen sodium on orthodontic pain. Angle Orthod 2005; 75:791-6.

24. Gupta M, Kandula S, Laxmikanth SM, Vyavahare SS, Reddy SB, Ramachandra CS. Controlling pain during orthodontic fixed appliance therapy with non-steroidal anti-inflammatory drugs (NSAID): a randomized, double-blinded, placebo-controlled study. J Orofac Orthop. 2014; 75(6):471-6.

25. Sandhu SS, Piepho HP, Khehra HS. Comparing the effectiveness profile of pharmacological interventions used for orthodontic pain relief an arm-based multilevel network meta-analysis of longitudinal data. Eur J Orthod. 2017; 39(6):601–614.

26. Bouncher Y. Pharmacology and pain. Rev. orthop. dento-fac. 1999; 33: 123–141.

27. Bradley R L, Ellis P E, Thomas P, Bellis H, Ireland A J, Sandy J R. A randomized clinical trial comparing the efficacy of ibuprofen and paracetamol in the control of orthodontic pain. Am J Orthod Dentofacial Orthop 2007; 132: 511–517.

28. Patel S, McGorray S P, Yezierski R, Fillingim R, Logan H, Wheeler TT. Effects of analgesics on orthodontic pain. Am J Orthod Dentofacial Orthop 2011; 139: e53–e58.

29. Bird S E, Williams K, Kula K. Preoperative acetaminophen vs ibuprofen for control of pain after orthodontic separator placement. Am J Orthod Dentofacial Orthop 2007; 132: 504–510.

30. Tunçer Zeynep, Polat-Ozsoy Omur, Demirbilek Muge, Bostanoglu Ebru. Effects of various analgesics on the level of prostaglandin E2 during orthodontic tooth movement. Eur J Orthod 2014; 36: 268–274.

31. Xiaoting L, Yin T, Yangxi C. Interventions for pain during fixed orthodontic appliance therapy. A systematic review. Angle Orthod 2010; 80: 925–932.

32. Angelopoulou M. V., Vlachou V., Halazonetis D.J. Pharmacological management of pain during orthodontic treatment: a meta-analysis Orthod Craniofac Res 2012; 15: 71–83.

33. Reitan K, Rygh P 2007 Biomechanical principles and reactions. In: Proffit W R, Fields H W (eds). Contemporary Orthodontics, 2nd edn, Mosby Year Book, St Louis, pp. 122.

34. Chumbley AB, Tuncay OC. The effect of indomethacin (an aspirin-like drug) on the rate of orthodontic tooth movement. Am J Orthod. 1986; 89:312–14.

35. Kehoe MJ, Cohen SM, Zarrinnia K, Cowan A. The effect of acetaminophen, ibuprofen and misoprostol on prostaglandin E2 synthesis and the degree and rate of orthodontic tooth movement. Angle Orthod. 1996; 66(5):339–50.

36. Joint Formulary Committee British National Formulary 73. London: BMJ Publishing and RPharmS 2017.

37. Stabile AC, Stuani MB, Leite-Panissi CR, et al. Effects of shortterm acetaminophen and celexocib treatment on orthodontic tooth movement and neuronal activation in rat. Brain Res. Bull. 2009; 79: 396–401.

38. Kaklamanos Eleftherios G., Makrygiannakis Miltiadis A., Athanasiou Athanasios E. Do analgesics used for the pain experienced after orthodontic procedures affect tooth movement rate? A systematic review based on animal studies. Orthod Craniofac Res. 2020; 23:143–150.

39. Brunson TD. (2008) Effect of cyclooxygenase inhibitors on rat root resorption and tooth movement. PhD Thesis, University of South California, USA.

40. Yamamoto T, Kaku M, Sumi H, et al. Effects of loxoprofen on the apical root resorption during orthodontic tooth movement in rats. PLoS One 2018; 13: e0194453.

41. Kirschneck C, Küchler EC, Wahlmann U, et al. Effects of the highly COX-2-selective analgesic NSAID etoricoxib on the rate of orthodontic tooth movement and cranial growth. Ann. Anat. 2018; 220: 21–28.

42. Patrignani, P., Capone, M.L., Tacconelli, S. Clinical pharmacology of etoricoxib: a novel selective COX2 inhibitor. Expert Opin. Pharmacother. 2003; 4, 265–284.

فعالية مسكنات الألم على إدراك الألم ومعدل حركة الأسنان تجربة سريرية عشوائية.

د.عاصم عباس عبد الجواد، ا.د. ضياء حسين الكروش

المستخلص:

الخلفية: يعتبر الألم احد اكثر الآثار الجانبية لعلاج تقويم الاسنان بالرغم من التطور العلمي في مجال تقويم الاسنان. تم تقديم العديد من الادوية المسكنة للسيطرة على الالم الناتج عن تقويم الاسنان وتشمل البراسيتامول و الادوية المضادة للالتهاب الغير ستيرويدية الانتقائية والغير انتقائية. الهم الاكبر فيما يخص هذه الادوية هو انها تؤثر سلبا على معدل حركة الاسنان.

الهدف: الهدف من هذه الدراسة هو لتقييم ومقارنة تأثير كل من البراسيتامول والبروفين والاتوريكوكسب على الاحساس بالالم ومعرفة مدى تأثيرهم على معدل حركة الاسنان في مرحلة تسوية وانتظام الاسنان.

المواد والطرق: اربعون مريضا تم اختيارهم وتوزيعهم بصورة عشوائية وبطريقة عمياء على احد اربع مجموعات: علاج وهمي (كبسولات النشاء)، البراسيتامول ٥٠٠ ملغم ثلاث مرات في يوم، البروفين ٤٠٠ ملغم ثلاث مرات في يوم، الإتوريكوكسب ٦٠ ملغم مرة واحدة في اليوم. تم اعطاء الادوية قبل ساعة من وضع جهاز التقويم واستمرت لمدة ثلاثة ايام. تم استخدام مقياس التناظرية البصرية للتعبير عن مستوى الالم بعد وضع سلك التقويم ، وفي اليوم الاول والثاني والثالث والسابع. تم قياس مقدار فهرس ليتل لقياس تراكب الاسنان قبل وضع جهاز تقويم الاسنان وعند كل زيارة لتفعيل الجهاز حتى نهاية مرحلة تسوية وانتظام الاسنان.

النتائج: جميع مجاميع الادوية الثلاث اظهرت مستوى الم اقل من مجموعة العلاج الوهمي بعد وضع جهاز التقويم وعند زيارة التفعيل الاولى. الإتوريكوكسب اظهر اقل مستوى للالم من بين جميع الادوية يأتي من بعده البروفين. لا وجود لاختلاف احصائي بارز بين مجموعات الادوية ومجموعة العلاج الوهمي عند زيارات التفعيل الثانية والثالثة. لا وجود لاختلاف احصائي بارز بين جميع المجموعات الاربع فيما يخص معدل تحرك الاسنان.

الإستنتاج: جميع الادوية الثلاث فعالة فقط في السيطرة على الالم الناتج من علاج تقويم الاسنان في الزيارتين الاولى والثانية، وان الاتوريكوكسب ٦٠ ملغم مرة واحدة في اليوم هو الافضل. جميع الادوية الثلاث ليس لها تأثير على معدل حركة الاسنان عند استعمالها ضمن الحد الادنى الموصى به.