

Pharmacological Means of Pain Control during Separator Placement: A Systematic Review

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ABSTRACT

Aim: To assess the effectiveness of adjuvant analgesics/anesthetics in pain control after separator placement compared with no medication.

Background: Separator placement to create space for cementing bands is the first clinical procedure done in orthodontics. Pain in this stage can negatively affect patient compliance and trust in the clinician. To date, there is no universally accepted regimen for pain control.

Materials and methods: Electronic databases of PubMed, Scopus, and Web of Science were searched. One hundred and thirty-two potentially relevant studies were found. A total of eight randomized clinical trials including 642 subjects were selected. Data were extracted into customized forms, and selected studies were assessed for risk of bias using the Joanna Briggs Institute.

Results: Results showed the use of analgesics led to lower reported pain scores at almost all time intervals. NSAIDs resulted in a statistically significant reduction in pain compared to a control group.

Conclusion: According to the available literature, the use of analgesics is effective in controlling orthodontic pain due to separators. Acetaminophen and ibuprofen show a stable analgesic effect.

Clinical implication: Acetaminophen 650 mg or ibuprofen 400 mg taken 1 hour prior to separator placement can reduce pain associated with the procedure.

Keywords: Analgesics, Pain management, Separator.

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INTRODUCTION

Pain and discomfort during orthodontic treatment are inevitable. Of the various factors that deter a patient from seeking or completing orthodontic treatment, pain ranks highest in the patient's mind.¹ Fixed and removable appliances apply force on the crown to bring about required tooth movement. In contrast to other dental procedures such as extraction or subgingival scaling, pain during orthodontic treatment seems to continue increasing in intensity postappointment till finally plateauing. Pain arises as a result of interconnected cascading events that begin with the application of force resulting in local ischemia, recruitment of inflammatory mediators, and changes to the periodontal ligament. The release and expression of these biochemical mediators occur over a period of hours to days, accounting for the increase in perception of pain over time.² There is a great individual variation on a patient's perception of pain based on age, gender, sex, etc.³ The nature of the pain differs based on the tooth movement.

The first clinical procedure carried out is the placement of elastic separators between molars to create space for seating of bands. Elastic separators apply pressure on the periodontal ligament and rapidly create space in 24 hours.⁴ An orthodontic patient experiences pain during various stages of treatment such as archwire change and activation of the appliance.⁵ Yet, the severity of pain associated with the initial procedure of separator placement is a major factor in noncompliance and dampens the patient's resolve.⁶

Pain control methods include pharmacological, such as the use of NSAIDs and anesthetic gels, and mechanical through the use of medicated chewable gums and transcutaneous nerve stimulation.⁷ Recently, low-level laser therapy also has emerged

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as another pain management technique.⁸ There are no universal policies or guidelines for pain management during orthodontic treatment. Research and consensus in this regard remain elusive. Pharmacological means using over-the-counter drugs is straightforward and presents few complications. Preoperative

doses of acetaminophen or ibuprofen can minimize pain and improve quality of life. Each analgesic also has its own drawbacks.⁹

Pretreatment doses of NSAIDs may reduce pain and inflammation through interfering in prostaglandin synthesis. This can negatively affect the rate of tooth movement and lead to longer treatment time.¹⁰ NSAIDs can also have gastrointestinal side effects.^{11,12}

Pain is the most significant factor for adolescents and adults to eschew orthodontic treatment. The purpose of the present systematic review is to analyze data regarding various pharmacological means used for pain control during initial separator placement and provide recommendations for their use in patients undergoing orthodontic treatment.

MATERIALS AND METHODS

The present systematic review was performed based on PRISMA guidelines.

Focused Question

“Does the use of adjuvant analgesics/anesthetic medication help improve pain control after placement of separators?”

Search Strategy

An electronic search of PubMed, Scopus, and Web of Science databases was done up to November 1, 2020. There were no restrictions placed on the starting date. The keywords used for the search were “separator, orthodontics, and drugs.” A single keyword was not used. Electronic search was supplemented using manual search of references of identified articles.

Inclusion Criteria

The following criteria were used in the selection of the articles:

- P—patients who are undergoing orthodontic treatment
- I—administration of analgesics/anesthetic
- C—placebo, or no analgesic administered
- O—at intervals, the patient’s pain perception is evaluated based on visual analog scale (VAS)
- S—randomized control trial

Randomized controlled trials that compared the efficacy of analgesics to placebo.

Randomized controlled trials that compared the efficacy of analgesics to control group with no analgesics given.

Randomized controlled trials that compared the efficacy of anesthetic agent to control group with no medication given.

VAS was used to report the patient’s perception of pain.

Pain level measured at intervals.

Participants underwent separator placement.

Exclusion Criteria

Trials concerned with pain due to orthodontic procedures other than separator placement.

Trials that used nonpharmacological means for pain control.

Trials concerned with pain due to TMD.

Trials without a control/placebo group.

Study Selection and Data Extraction

Two authors independently examined titles and abstracts of all identified studies. Duplicates and studies that did not meet the eligibility criteria were discarded. In cases where title and abstract

provided insufficient information to make a decision regarding eligibility, the full-text article was obtained. Complete articles of all studies included in this review were appraised.

We excluded studies that had split-mouth design and trials that did not have a placebo or a control group. Studies that had a nonpharmacological intervention were also excluded. Data were extracted independently by two researchers. Data were collected in a customized form that included the name of first author, year and country of publication, methods, study design, sample characteristics, details of pharmacological intervention, method of detection, results, and inferences. The extracted data are presented in [Table 1](#).

Risk of Bias Assessment

Both review authors independently assessed the included studies for bias. The Joanna Briggs Institute critical appraisal tools were used to consider 13 domains.

Risk of Bias was Categorized into Three Tranches

Low risk of bias—percentage of “yes” score was more than 70%

Moderate risk of bias—percentage of “yes” score was 50 to 69%

High risk of bias—percentage of “yes” score was less than 49%

Risk of bias judgment is presented in [Table 2](#).

Statistical Analysis

Cohen’s kappa coefficient (κ) was used to evaluate observer bias. Kappa coefficient for Step 1 and Step 2 was 0.98 and 0.96, respectively.

RESULTS

Study Selection

A search of electronic databases revealed 141 potentially relevant studies ranging from 1989 to 2020. Titles and abstracts of these studies were examined. One hundred and five studies were discarded for not meeting eligibility criteria. Thirty-six articles were selected for further scrutiny. Full-text articles of these studies were obtained. After assessment, 28 articles were excluded. Most of these studies were excluded as they did not have a clear control/placebo group. Some had interventions that were measured against nonpharmacological interventions. In the end, eight randomized controlled trials were selected for this review.¹³⁻²⁰ The selection process is represented graphically using a flowchart in [Flowchart 1](#).

Study Characteristics

Countries

Of the eight included trials, three were conducted in the USA¹³⁻¹⁵; two in India^{17,18}; and one in Brazil,¹⁶ Iran,¹⁹ and Kuwait.²⁰

Design

Seven studies selected had the following characteristics:

- Had three arms
- Were single-center studies
- Had parallel design

One study had four parallel arms.¹⁸ In all eight studies, the participants had separators placed on their lower molars.

Characteristics of the Intervention

In six of the eight studies, the analgesia/anesthetic was given both preemptively and after separator placement.^{14,15,17-20} One study evaluated only preemptive analgesic medication.¹⁶ One study

Table 1: Summary of data extracted from the included studies

Sl. No.	Author/year/ country	Type of study	Sample size		Matching	Method of detection	Pain report time intervals	Results	Inference
			Group 1 experiment	Group 2 control/placebo					
1	Ngan 1994, USA ¹³	RCT	Grp1a n = 28 pts, ibuprofen 400 mg, immediately after placement Grp1b n = 28 pts, aspirin 650 mg, immediately after placement	n = 28, placebo—beta lactose, immediately after placement	Age/sex unclear	VAS (1–10), Questionnaire, Discomfort Index Card	2, 6, 24 hr, 2, 3, 7 days	Experimental group reported significantly less pain at 2, 6 hr intervals. Grp1a reported significantly less pain than Grp1a or control group	Ibuprofen showed better pain control than aspirin
2	Steen Law 2000, USA ¹⁴	RCT	Grp1a n = 22, ibuprofen 400 mg, 1 hr before, lactose taken immediately after Grp1b n = 19, lactose placebo taken 1 hr before, ibuprofen 400 mg taken immediately after	n = 19, lactose placebo taken 1 hr before procedure and immediately after	Age/sex unclear	VAS (1–10), Questionnaire	2, 6, 24 hr, 2, 3, 7 days	Grp1a reported significantly less pain	Administration of ibuprofen preoperatively showed better pain control
3	Minor 2009, USA ¹⁵	RCT	Grp1a n = 16, ibuprofen 400 mg, 1 hr before, 3 hr after, 7 hr after Grp1b n = 17, placebo 1 hr before, ibuprofen 400 mg 3 hr after and 7 hr after	n = 18, placebo 1 hr before, 3 hr after, 7 hr after	Age/sex unclear	VAS (1–10), Questionnaire	2, 6hr, bedtime, awakening, 24 hr	Experimental group reported significantly less pain at two intervals. p <0.05	Administration of ibuprofen pre- and postop showed better pain control
4	Bruno 2011, Brazil ¹⁶	RCT	17, 4 male, 13 female, 400 mg lumiracoxib 1 hr prior	17, 5 male, 12 female, placebo one hour prior 17, 5 male, 12 female, control, no analgesic	Age/sex unclear	VAS (1–10), Questionnaire	2, 6, 24 hr, 2, 4 days	VAS values are lower in group receiving drug. Statistically significant. p ≤ 0.005 value	All groups reported pain and discomfort at all time intervals. Patients taking analgesics reported less pain
5	Kohli 2011, India ¹⁷	RCT	Grp1a n = 30, ibuprofen 400 mg, 1 hr prior Grp1b n = 30, piroxicam 20 mg, 1 hr prior	n = 20, placebo—lactose	Age/sex unclear	VAS (1–10), Questionnaire	2, 6, 24 hr, 2, 3, 7 days	Experimental group reported significantly less pain at 2, 6 hr intervals. Grp1b reported significantly less pain than Grp1a. p <0.05	Piroxicam showed better pain control than ibuprofen
6	Sudhakar 2014, India ¹⁸	RCT	Grp1a n = 38, acetaminophen 650 mg, 1 hr prior, 6 hr after Grp1b n = 39, ibuprofen 400 mg, 1 hr prior, 6 hr after Grp1c n = 36, aspirin 300 mg, 1 hr prior, 6 hr after	n = 41, placebo	Age/sex unclear	VAS (1–10), Questionnaire	2, 6 hr, bedtime, morning, 2, 3, 7 days	Experimental group taking aspirin reported least amount of pain felt, followed by groups taking ibuprofen and acetaminophen	Preemptive and postop administration of aspirin can effectively control pain

Contd...



Contd...

Sl. No.	Author/year/ country	Type of study	Sample size		Method of detection	Pain report time intervals	Results	Inference
			Group 1 experiment	Group 2 control/placebo				
7	Nik 2016, Iran ¹⁹	RCT	Grp 1a n = 32, acetaminophen 650 mg, before separator placement and at 6, 24 hr Grp 1b n = 29, liquefied ibuprofen 400 mg, before separator placement and at 6, 24 hr	n = 28, placebo, before separator placement and at 6, 24 hr	VAS (1–10), Questionnaire	2, 6, 24 hr	Statistically significant difference in pain scores between experimental and placebo scores. p < 0.001	Experimental group reported less pain and discomfort. No difference in both experimental groups. Imperfect pain control with analgesics.
8	Al-Melh 2019, Kuwait ²⁰	RCT	Grp 1a n = 20, anesthetic chewing gum—lidocaine 2 mg + prilocaine 2 mg, every 25 min Grp 1b n = 20, unmedicated chewing gum, every 25 min	n = 20, no medication	VAS (1–10), Questionnaire	0, 1, 4, 8 hr	Grp 1a reported almost no pain compared to Grp 1b and control group. Highly significant difference in pain scores between experimental group and control group. p < 0.0001	Anesthetic gum provided almost complete pain control

evaluated the effects of postprocedural analgesic medication.¹³ All eight studies had an experimental group, a placebo group, and/or a control group.

NSAIDs

Six studies compared ibuprofen 400 mg with a control group that received a placebo or no medication.^{13,14,15,18} One study compared the efficacy of piroxicam, an NSAID of the oxicam class, with ibuprofen and a placebo.¹⁷ One study compared lumiracoxib 400 mg, a COX-2 selective inhibitor, with a placebo of beta lactose and a control of no medication.¹⁶ Two studies compared aspirin with ibuprofen 400 mg with a placebo of beta lactose.^{13,18}

Acetaminophen

Two studies compared the efficacy of acetaminophen 650 mg with aspirin 300 mg and/or ibuprofen 400 mg and a control of no medication.^{18,19}

Anesthetic

One study compared the efficacy of chewing gum with prilocaine and lidocaine anesthetic with a placebo group who were given conventional chewing gum and a control group to whom no medication was administered.²⁰

Control/Placebo

Six out of the eight studies reported using a placebo. Only three studies mentioned the content of the placebo administered—beta lactose.^{13,14,17} Two studies had a control group that was not administered any medication.^{16,20}

Visual Analog Scale

All eight studies used VAS to measure pain outcomes. Registration of pain was done after placement of separators at distinct time intervals.

Duration of Study

Duration of the studies showed a wide variation. One study lasted only 8 hours.²⁰ Three studies took pain measurements at set intervals over a period of 7 days.^{13,14,18} Four studies spanned a period of 2 to 4 days posttreatment.^{15-17,19}

Characteristics of the Participants

A total of 642 participants were randomized. Generally, all participants ranged in age from 14 to 21. Only one study had participants who were in the age-group of 23 to 41 years.²⁰

Results of the Studies

All patients who had a separator placed gave testimonies of pain and discomfort that increased over a period of time. All eight studies described an association of analgesics/anesthetic administered and lower reported pain scores; that is, the experimental group that were given medication consistently reported less pain. The pain scores recorded within the experimental group varied based on the analgesic administered. There was a correlation of preemptive administration of medication with better pain control.

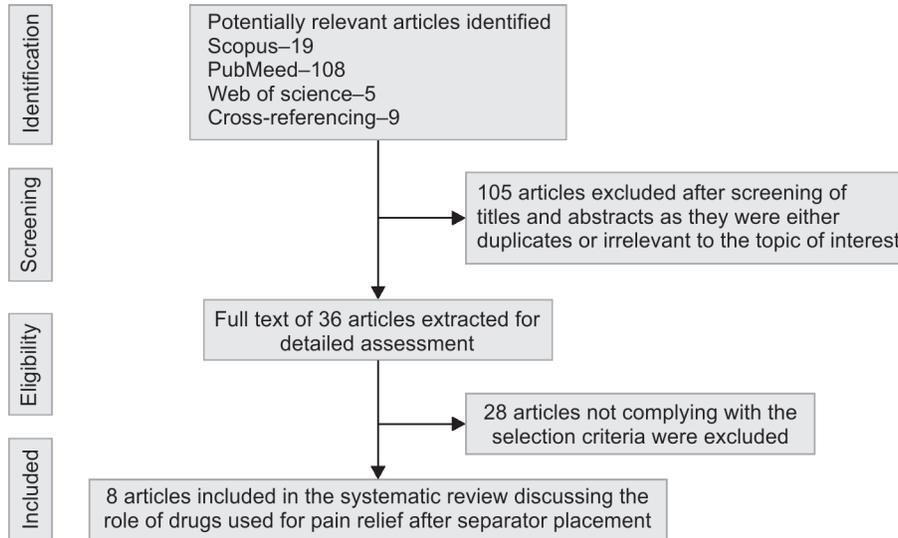
DISCUSSION

One of the most frequent questions an orthodontist is asked at the beginning of treatment is “Will it hurt?” Unfortunately, oftentimes, the answer is yes. Orthodontic tooth movement is a result of mechanical forces directed against the tooth. Pain and

Table 2: The Joanna Briggs Institute critical appraisal checklist for randomized controlled trials to assess the risk of bias for the included studies

First author name/ country/ year of publication/ reference number	1. Was true randomization used for the assignment of participants to treatment groups?	2. Was allocation to treatment groups concealed?	3. Were treatment groups similar at the baseline?	4. Were participants blind to treatment assignments?	5. Were those delivering treatment blind to treatment assignment?	6. Were outcome assessors blind to treatment assignment?	7. Were treatment groups treated identically other than the intervention of interest?	8. Was follow-up complete, and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	9. Were participants analyzed in the way for treatment groups?	10. Were outcomes measured reliably?	11. Were appropriate statistical analysis used?	12. Was appropriate statistical analysis used?	13. Was the trial design appropriate, and any deviation from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?	The overall risk of bias
Ngan 1994, USA ¹³	Unclear	Unclear	No	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Steen Law 2000, USA ¹⁴	Unclear	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Minor 2009, USA ¹⁵	Unclear	Unclear	Unclear	Unclear	Unclear	No	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate
Bruno 2011, Brazil ¹⁶	Yes	Unclear	Yes	No	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Low
Kohli 2011, India ¹⁷	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Moderate
Sudhakar, 2014, India ¹⁸	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Low
Nik 2016, Iran ¹⁹	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Low
Al-Melh 2019, Kuwait ²⁰	Unclear	Unclear	No	Unclear	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Moderate

Risk of bias categorized as high when the study reached up to 49% score, yes; moderate when the study reached 50 to 69% score, yes; and low when the study reached more than 70% score, yes



Flowchart 1: Workflow of the systematic review

discomfort are undesirable byproducts of this force application. All orthodontic procedures cause pain to a certain extent. This pain is a subjective response.² Separator placement is widely seen as one of the most painful phases in orthodontic therapy.²¹ Practitioners generally recommend analgesics if the patient feels any discomfort. There is no universally recognized pain control regimen till date.

Discomfort that initially arises from separator placement is minor. The patient’s perception of pain increases after 4 hours and tends to peak at 24 to 48 hours. This pain and discomfort gradually decrease over a period of 7 days.² Clinically, in practice, most patients could be expected to take pain medication every 6 to 8 hours initially.²² Only four studies evaluated administration of multiple doses of analgesic or anesthetic.^{15,18-20} Four studies^{13,14,16,17} investigated the use of a single-dose analgesic to assess pain control.

Analgesics/Anesthetic vs No Medication

There is moderate-quality evidence that analgesics could reduce pain over a period of 24 hours. All eight studies found that subjects who were on pain relief medication (analgesics or anesthetic) reported lower scores of pain at all points of time. However, none of the analgesics examined in this review provided complete and total pain control.

Aspirin vs Ibuprofen

Two studies examined the efficacy of ibuprofen and aspirin in relief of pain due to separator placement.^{13,18} In both studies, ibuprofen 400 mg and aspirin 300 mg/650 mg elicited good pain control. This is in agreement with a previous study by Xiaoting.²³ When two drugs have the same level of efficacy, the drug with lesser known side effects should be the obvious choice. Ibuprofen reportedly has fewer side effects compared to aspirin.

Other NSAIDs

Piroxicam is a long-acting NSAID. Kohli found that a single dose of piroxicam 20 mg resulted in a significantly decreased pain score at time intervals up to 3 days postprocedure.

Bruno et al. examined the efficacy of using a NSAID with less incidence of gastric side effects.¹⁶ Lumiracoxib is an NSAID that selectively inhibits the COX-2 enzyme in prostaglandin synthesis. They are thought to have fewer adverse effects and interference with tooth movement than conventional NSAIDs.²⁴ Data regarding their cardiovascular safety are still inconclusive and thus preclude their widespread use.²⁵

Ibuprofen vs Acetaminophen

Acetaminophen is a para-amino phenol derivative that has poor anti-inflammatory action. It is a nonopioid, non-NSAID analgesic.²⁶ Two studies examined the efficacy of ibuprofen and acetaminophen against a control group.^{18,19} Nik et al. found no difference in the analgesic efficacy of ibuprofen compared to acetaminophen. This is in agreement with previous studies by Xiaoting²³ and Angelopoulou²⁷.

Selection of Analgesic

Oftentimes, it is not only the analgesic effect but also the possible side effects that must be considered before prescribing a medication for pain relief.

Animal studies have previously shown that NSAIDs can affect the rate of tooth movement.¹⁰ NSAIDs suppress the synthesis of prostaglandins. Prostaglandins are biochemical mediators of inflammation and bone resorption. Prostaglandin activity can alter the number of osteoclasts that are important for bone remodeling. It is hypothesized that NSAIDs that exert an anti-inflammatory action through the suppression of PG synthesis may interfere with tooth movement.²⁸ This interference could slow down the velocity of orthodontic tooth movement and increase the duration of treatment.²⁹

Newer NSAIDs, such as piroxicam and lumiracoxib, offer no substantial advantage in preventing interference to tooth movement.

Acetaminophen is a weak anti-inflammatory and does not affect PG synthesis significantly.³⁰ In agreement with studies by Arias²⁸ and Angelopoulou,²⁷ there is moderate evidence for acetaminophen to be recommended as an analgesic to relieve minor discomfort.

Anesthetics

Both prilocaine and lidocaine are amide group anesthetics that act by a combination of receptor and receptor-independent mechanism. This topical anesthetic mix is potent and has a quick onset of action.³¹

Only one study evaluated the use of topical anesthetics.³⁰ The experimental group was directed to use anesthetic chewing gum over a period of 8 hours. Subjects reported a rapid onset of the anesthetic effect. The effect diminished after half an hour. The subjects were asked to chew gum every half hour. Subjects in the experimental group had low pain scores, approaching zero. Complaints of muscle soreness and gum sticking to the separator were reported.²⁰ A striking feature of this study was that it lasted for only 8 hours, whereas pain and discomfort due to a separator can increase gradually and reach peak levels at 24 hours. It may be implausible for an adult to continuously apply topical anesthetic over that period of time. When prescribing topical anesthetics, it is important to consider the potential negative effects that may result from high doses.³²

Preemptive Analgesic vs Postprocedure

Three studies investigated the effect of preemptive administration of analgesics before separator placement.^{15,18,19}

In all three studies, preoperative doses of NSAIDs resulted in lower reported pain scores over all time periods. NSAIDs reach peak plasma concentration about 2 hours. This could explain why subjects in the experimental groups had little discomfort even at initial time intervals.^{15,18,19} Administration of ibuprofen 400 mg 1 hour before delayed the onset of pain. This is in agreement with previous studies by Bernhardt et al.³³

There is moderate-quality evidence that preemptive dosing of analgesics provided better pain control.

Further Research Required Examining

Design of future studies should include larger sample sizes to reduce risk of them being underpowered. The effect of multiple doses of analgesic along with reports of adverse effects needs to be further investigated. Supplementary studies examining the role of nonpharmacological means for pain relief may put forth an alternative to analgesics.

CONCLUSION

Based on available data, the use of adjuvant analgesics is effective in controlling pain due to separator placement. There is moderate-quality evidence that supports the use of acetaminophen as the first choice for pain control. Ibuprofen may be an equally effective secondary choice as both show stable analgesic effect.

Implication for Clinical Practice

There is moderate-quality evidence that acetaminophen 650 mg or ibuprofen 400 mg taken 1 hour prior to separator placement can reduce pain associated with the procedure.

Compliance with Ethical Standards

Ethical Approval: This article does not contain any studies with human participants or animals performed by any of the authors.

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