THE EFFICACY OF LASER THERAPY AND IBUPROFEN ON PAIN AFTER ELASTOMERIC SEPARATOR PLACEMENT: RAPID REVIEW

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ABSTRACT

Background: *Separator placement is the first step in orthodontic treatment, which aims to create space between teeth before molar band placement. This procedure can cause pain for the patient. Pain management after separator placement can be done through pharmacological and non-pharmacological approaches.*

Method: *The aim of this rapid review was to determine the efficacy of laser therapy and ibuprofen for pain management after elastomeric separator placement in orthodontic treatment.*

Result: *Ten articles were included in this review, four articles gave laser therapy interventions and six articles gave ibuprofen therapy interventions. The result of the quality assessment using Strength of Recommendation Taxonomy (SORT) was laser therapy intervention has one good quality articles and three limited-quality articles, while ibuprofen therapy has two good quality articles and four limited-quality articles.*

Conclusion*: The efficacy of laser therapy and the efficacy of ibuprofen on pain after separator placement is good, with the strength of the clinical recommendation of ibuprofen is better than laser therapy.*

INTRODUCTION

Separators are used to create space for placement of band that later anchors the fixed orthodontic appliance.[1] The use of elastic separators is widely spread in orthodontic treatment, not only for their convenience in handling, but also due to storage, and produced significantly more space compared to the spring separators.[1,2]

Placement of separator induces pain in patients. Pain usually begins at 4 hours after separator placement, increases to a peak level at 24 hours, remains bother for the next 3 days, and diminishes over the next 6-8 days. The pain experienced is due to the constant pressure, ischemia, inflammation, and edema in the periodontal ligaments of the teeth that are moved during orthodontic movements.[1,3–5]

Pain is a subjective response which shows large individual variation. It is affected by some factors such as age, gender, individual pain threshold, magnitude of force applied, present emotional state and stress, cultural differences and previous pain experiences.[3,6–9] Pain due to orthodontic treatment is defined as a moderate level of pain and a tolerable mild-to-moderate jaw discomfort.[10] Pain has been the prime reason for discontinuation of orthodontic treatment.[1,10]

Several methods have been invented to alleviate orthodontic pain in clinical practice,

including pharmacological approaches, mechanical approaches, laser irradiation therapy and behavioural approaches.[11,12] Ibuprofen is a nonsteroidal anti-inflammatory drug that has antinociception, anti-inflammatory, and antipyretic effects. It acts as a non-selective inhibitor of the cyclo-oxygenase 1 (COX-1) and COX-2.[13] Ibuprofen is significantly effective in reducing pain.[5,13–15] Laser, a highly popular technological application in recent times, is also being used as an alternative to reduce pain without affecting tooth movement.[8,16] Laser is thought to control pain by hyperpolarization of the nerve cell membrane, which increases the patient's pain threshold.[16]

The aim of this rapid review was to determine the efficacy of laser therapy and ibuprofen for pain management after elastomeric separator placement in orthodontic treatment.

LITERATURE REVIEW

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

Population: patients who used elastomeric separators in orthodontic treatment.

Intervention: article containing administration of laser therapy or ibuprofen to control pain after elastomeric separator placement.

Comparison: article containing administration of placebo or no treatment after elastomeric separator placement.

Outcome: efficacy of laser therapy and ibuprofen in reducing the pain scale based on the VAS score.

Specific search strategies per database were used to identify relevant articles using the AND and OR boolean operators and the limit function of each database if available. The search was carried out using keywords: VAS, pain, orthodontic, and separator by MeSH.

The inclusion criteria were articles in English and in Indonesian, articles containing clinical trials of administration of ibuprofen for pain management after elastomeric separator placement, articles containing clinical trial of laser therapy for pain management after elastomeric separator placement, and accessible full-text articles. The exclusion criteria were non-human trial articles, split-mouth design, absence of a control group, thesis, dissertation, scientific papers, and research that did not use VAS to measure pain.

The present review was done according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. A total of 361 articles were identified through a database search (PubMed = 48 articles, Google Scholar = 216 articles, ScienceDirect = 36 articles, Science.gov = 25 articles, Cochrane Library = 8 articles, and The Angle Orthodontist = 28 articles). The identified articles were exported to the Mendeley Desktop application (version 1.19.4) [17] to remove duplicates, and a total of 243 articles remained after the duplicates were removed. A total of 230 articles were excluded because they were irrelevant based on the title and abstract, while the other 13 articles were included in a full-text evaluation. A total of 10 articles met the eligibility criteria and were included in the review, the remaining 3 articles were excluded because 2 articles were split-mouth design and 1 article was an ongoing study. The flow diagram of the study selection process is presented in Figure 1.

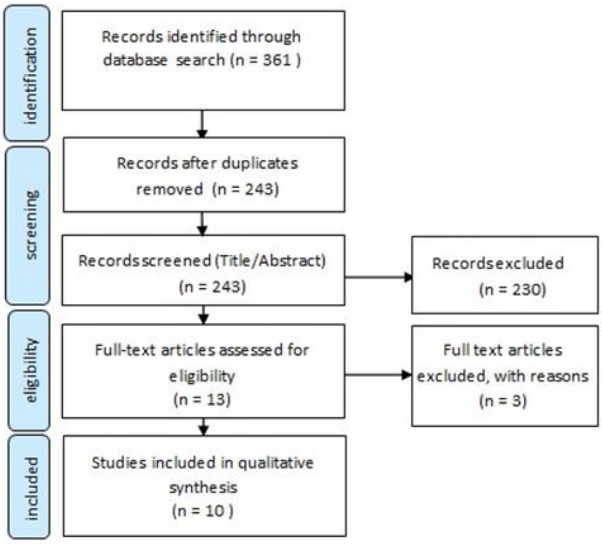

Figure 1. PRISMA Flow Diagram of The Study Selection Process

All included articles were a randomised control trial design, 3 articles[18–20] were a parallel study design, 3 articles[19,21,22] were a prospective design, 1 article[23] was a retrospective design, and 1 article[24] was a preliminary clinical study design. In total, 773 participants were included. A total of 4 included articles[23–26] comprised low level laser therapy interventions, while 6 articles[18–22,27] comprised ibuprofen interventions. One included article[26] reported laser irradiation was significantly effective in reducing pain compared to the placebo group. Three included articles[23–25] reported laser irradiation was significantly effective in reducing pain compared to the untreated control group, but 2 of them[24,25] reported that there was no significant difference in pain in the laser group compared to the placebo group. Six articles[18–22,27] reported ibuprofen was significantly effective in reducing pain compared to the placebo group. The characteristics of the included studies is presented in Table 1.

The risk of subjectivity of the included studies was made according to Cochrane Risk of Bias Tools for randomized control trial is presented in Figure 2.

Table 1. The characteristics of the included studies

Author's name	Study design	Participants	Intervention	Regiment	Evaluation period	Outcome
Kim et al (2013)[25]	RCT, single blind	**Baseline (final):** 88 (88) **Age:** 22,7 **F/M:** 65/23	AlGaInP diode laser, wavelength of 635 nm, energy of 10 mJ, output 6 mW LED as placebo No irradiation as control group	30 seconds on each area immediately then every 12 hours for 1 week with	5 minutes, 1 hour, 6 hours, 12 hours and then at days 1, 2, 3, 4, 5, 6, and 7 after the separators were applied.	The laser group showed a statistically significant decrease in pain scores compared with the control group (P = 0.003) The laser group showed significantly lower maximum pain level than those of the LED placebo and control groups 1 day after separator placement During the first 6 hours, the pain scores in the placebo group were not significantly different from those of the laser group At 12 and 24 hours after placement of separators, the pain scores of the placebo group were not significantly different

						from those of the control group.
Nobrega et al (2013)[26]	RCT, double-blind	**Baseline (final):**60(60) **Age:** 12-26 years **F/M:** ?	AlGalAr diode laser, 830 nm Placebo	25 sec per each 1 J/cm2 aplication along the root axis on the buccal side, with three spot	2, 6, and 24 hours and 3 and 5 days after orthodontic separator placement, in situations of relaxed and occluded mouth	There were significant differences in mean pain scores between the two groups favoring the group that received LLLT in all measures, for both spontaneous and in occlusion pain, except on day 5
Stein et al (2015)[23]	Retrospektif, Randomized fashion study	**Baseline (final):** 40 (40) **Age:** 6-9 years **F/M:** 19/21	Diode laser, 660nm, output power 100mW No irradiation as control group	20 seconds applied to the separated teeth at the root level perpendicular to the alveolar ridge in the mesial interproximal space, both distal interproximal spaces, and directly in the root centers	every day before bedtime, (day 1-5)	Pain level significantly ($p<0.05$) lower in the LLLT group than in the control group on day 1 There were no significant differences t demonstrable on days 2–5
Esper et al (2011)[24]	Preliminary clinical study	**Baseline (final):**55 (52) **Age:** 24,1±8,1 years **F/M:** 16/39	AlGaInP Laser 660nm, 0,03W, 25 detik LED GaAlAs 640 nm, 0,10 W, 70 detik Placebo group No irradiation as control group	touching the gum perpendicularly on two points of the vestibular side and on the lingual side of the separated molars, both points were in the cervical and radicular region.	2, 24, 48, 72, 96, and 120 h after therapy	A lowering in the pain sensitivity in the laser group could be observed when compared to the control group, however, there was no statistical significance between the groups during the 120-h study period. The placebo group was statistically significant compared to the laser group only 2 h after the orthodontic procedure and the placebo group had a lower sensitivity than the laser group.

Nik et al (2016)[27]	RCT, triple blind	**Baseline (final):** 101 (89) **Age:** 15,6 years **F/M:** ?	acetaminophen 650 mg, liquified ibuprofen 400 mg Placebo	one hour before separator placement and every six hours afterward (five doses in total)	immediately after separator placement, 2 hours, 6 hours , at bedtime, and 24 hours after separator placement	The mean pain scores in acetaminophen group and liquefied ibuprofen group were significantly lower than the placebo group
Law et al (2000)[21]	RCT prospective study, double blind	**Baseline (final):** 66 (63) **Age:** 13 years **F/M:** 38/25	ibuprofen 400 mg placebo	(1) ibuprofen taken orally 1 hour before separator placement and a lactose placebo taken orally immediately after the appointment (2) a lactose placebo taken orally 1 hour before separator placement and ibuprofen taken orally immediately after the appointment (3) a lactose placebo taken orally 1 hour before separator placement and again immediately after the appointment.	2, 6, and 24 hours, as well as at 2, 3, and 7 days after separator placement during chewing, biting, fitting back teeth together, fitting front teeth	Subjects who had taken ibuprofen before their appointment reported significantly decreased levels of pain (9.5 ± 11.6; mean ± SD) when compared with subjects who had taken preoperative placebo and postoperative ibuprofen (20.9 ± 21.7) or the placebo medication both preoperatively and postoperatively (25.2 ± 27.8). There was no significant difference in pain levels between groups at 2 hours after separator placement
Shetty et al (2013)[18]	RCT paralel, double blind	**Baseline (final):**68 (68) **Age:** 18 years **F/M:** 45/23	Piroxicam 20 mg Ibuprofen 400 mg Placebo	one hour prior to separator placement, 3 hours and 7 hours after separator placement.	2 hours, 4 hours, 6 hours, bedtime, on awakening the following day and 24 hours after administration during when biting,	piroxicam and ibuprofen group significantly showed less pain level (P<0,05) compared to those on the placebo group at 2 hours and 6 hours evaluation during bitting piroxicam and ibuprofen group significantly showed less pain level (P<0,05) compared to those on the placebo group at 2 hours, 6 hours ,

					chewing, fitting front teeth together, and fitting back teeth together	bedtime during fitting anterior teeth together piroxicam and ibuprofen group showed less pain level compared to those on the placebo group at 2 hours and 6 hours during fitting posterior teeth together, significance not stated.
Kohli et al (2011)[19]	Prospective study, parallel-arm, double blind	**Baseline (final):** 90 (90) **Age:** 13 years 9 months - 18 years 2 months **F/M:** 45/45	ibuprofen 400 mg, piroxicam 20 mg, Placebo	1 hour before separator placement	2 hours, 6 hours, nighttime on the day of appointment, 24 hours after the appointment, and 2 days, 3 days, and 7 days after separator placement during, chewing, biting, fitting front teeth, and fitting back teeth	The ibuprofen and piroxicam groups had significantly lower pain level (P <0.05) compared to the placebo group at 2 hours and 6 hours after separator placement during biting The ibuprofen and piroxicam groups had significantly lower pain perceptions (P <0.05) compared to the placebo group at 2 hours, 6 hours, and night time during fitting front teeth The ibuprofen and piroxicam groups had lower pain perceptions compared to the placebo group at the 2 h and 6 h during fitting posterior teeth, significance not stated.
Minor et al (2009)[20]	Parallel arm, double blind	**Baseline (final):** 51 (51) **Age:** 13-30 years **F/M:** ?	ibuprofen 400 mg placebo	one hour prior to separator placement, 3 hours and 7 hours after separator placement	Immediately after, 2 hours, 6 hours, bedtime, on awakening, and 24 hours after separator placement during biting, chewing, fitting front teeth to-gether, and fitting back teeth together	The group that received preemptive and posttreatment ibuprofen (group A) experienced less pain at 2 hours compared to the group that took ibuprofen only after separator placement (B) and the placebo group (C), but did not statistically significant. The group that received preemptive and posttreatment ibuprofen (group A) experienced significantly less pain at 6 hours and at bedtime on the night of separator placement. Group A also reported less pain on the morning after

						separator placement for biting only, significance not stated. there was no significant difference between the pain experienced by the group that took ibuprofen only after separator placement (B) and the placebo group (C) during the first 24 hours.
Sudhakar et al (2014)[22]	RCT prospective study, double blind	**Baseline (final):** 154 (138) **Age:** 14-21 years **F/M:** 72/66	paracetamol 650 mg ibuprofen 400 mg aspirin 300 mg placebo	1 hours before and 6 hours after separator placement	Over 7 days during teeth not touching, biting back teeth together, chewing food	The ibuprofen, paracetamol, aspirin group showed lower pain level than the placebo group during spontaneous pain, posterior occlusion, and chewing 2 hours after separator placement, significance not stated. The aspirin and ibuprofen groups showed lower pain level than the paracetamol and the placebo groups during chewing and posterior occlusion 6 hours after separator placement, significance not stated. The ibuprofen group showed lower pain level compared to the placebo group during all time evaluation, significance not stated

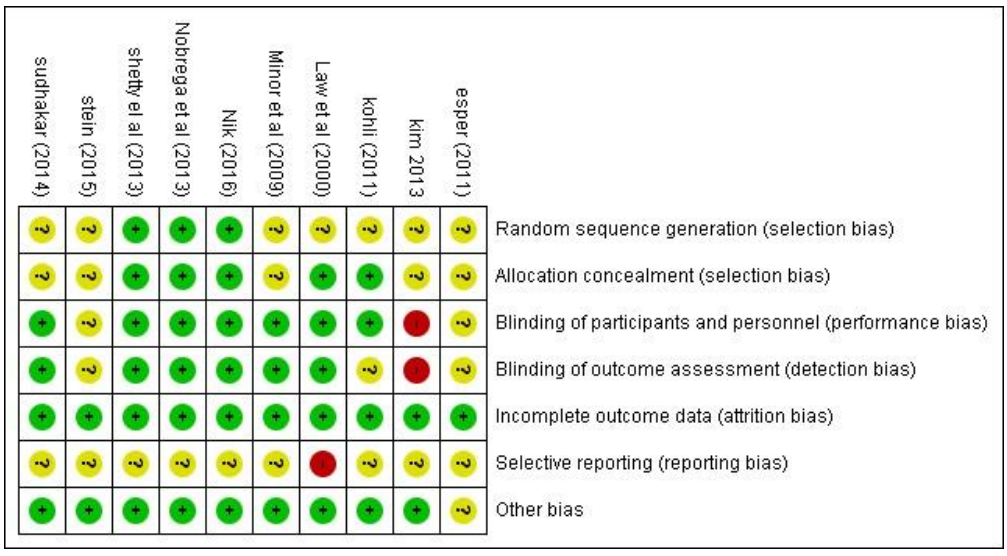

Figure 2 The risk of subjectivity of the included studies[28]
low risk, high risk, unclear risk

DISCUSSION

The heterogeneity of study designs such as differences in intervention components, study evaluation periods, comparison groups, and differences in the inclusion and exclusion criteria included in each article may lead to finding different results between studies. One article[23] included subjects aged 6-9 years with a mixed dentition period. Children's pain is very different from that which is experienced in adults. Different emotional and psychological factors can affect the children's pain comprehension and stimulate their response. Another difference is the nociceptive system, the number of nociceptors and neuromediators is higher in children, meaning a higher sensitivity to pain in childhood The number of nociceptors and neuromediators is higher in children, meaning a higher sensitivity to pain in childhood.[29]

Optimal penetration of lasers in humans seems to be in the range 690 nm and 860 nm.[30] Lasers in a range of 400nm-700nm can penetrate tissue for about 8mm, whereas the infrared lasers have approximately 2-3cm penetration depth. The receptors that produce orthodontic pain are located in deep areas, and thus the application of infrared wavelength is more suitable for pain management.[31]

The insignificant differences between laser and placebo group might be the result of placebo effect, such as emotional modulation and subjective stress reduction during pain stimulation.[25] The placebo effect can be defined as the improvement in the patient's symptoms after the administration of an inert substance in a context inducing positive expectations about its effects.[32] The placebo effect was affected by expectations and closely related to emotional factors.[33,34] The analgesic effect was obtained by suggestion through patient's expectations when taking a tablet that they believe was an analgesic.[18]

All articles containing ibuprofen for pain management after elastomeric separator placement gave it 1 hour prior to separator placement. Ibuprofen was rapidly and completely absorbed 1-2 hours after oral administration.[35,36] The aim of analgesics administration before treatment was to block the afferent nerve impulses before they reach to the central nervous system. The body has enough time to absorb and distribute the drug before tissue damage and prostaglandin sequence production, and consequently would reduce inflammation reactions.[13]

All included articles mentioned that the pain after separator placement peaked after 24 hours. This result is consistent with other studies evaluating pain after elastomeric separator placement.[4,5,37–39] Separators compressed the periodontal ligament and induced inflammatory reactions. The pain peaked 24 hours after separator placement was associated with increased production of inflammatory mediators such as interleukin-1β (IL-1β), substance P, and prostaglandin E2 at 24 hours after separator placement.[37] Therefore, orthodontists should provide information to patients about pain and its management prior to separator placement.[6,40–42]

All included articles did not mention any side effects from the use of either laser therapy or ibuprofen. Ibuprofen was contraindicated in patients with gastrointestinal disorders, allergies, and can adversely affect orthodontic tooth movement.[43] Ibuprofen inhibits prostaglandin production which was an important mediator of bone resorption

contributing to orthodontic tooth movement. However, Alqahtani, *et al* in their study found that patients prescribed ibuprofen did not report any problem with tooth movement along with a significant reduction in pain after separator placement.[14] The use of lasers for pain management in orthodontics, to date, has had no negative side effects.[44]

Quality of evidence of the included study was assessed using *Strength of Recommendation Taxonomy (SORT)* show that 3 articles have good quality evidence (level 1) and 7 articles have limited quality evidence (level 2). The strength of recommendation for clinical practice of low level laser therapy is moderate (B) based on a 1 article with good quality evidence and 3 articles with limited quality evidence. The strength of recommendations for clinical practice of ibuprofen therapy is strong (A) (based on 2 articles with good quality evidence and 4 articles with limited quality evidence.

Oshagh et al (2014) on their study compared the efficacy of ibuprofen and low level laser therapy on pain after separator placement concluded that laser therapy had no analgesic effect, whereas ibuprofen was most effective at 1 hour after administration. Laser therapy was a rather expensive treatment modality and harder to obtain, whereas ibuprofen seemed to be a cheaper, simpler and rather cost-effective treatment option.[43] The use of an analgesic drug should only be adopted for patients with less tolerant of pain, meanwhile a single application of low level laser therapy does not seem to provide a fully effective protocol for this purpose.[45] Therefore, ibuprofen could be used for pain management after elastomeric separator placement. While, low-level laser therapy can be used as an alternative to non-pharmacological pain management in patients who have contraindications to the use of ibuprofen.

CONCLUSION

The efficacy of laser therapy and the efficacy of ibuprofen on pain after separator placement is good, with the strength of the clinical recommendation of ibuprofen is better than laser therapy.

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CONFLICT OF INTEREST

No conflict of interest

REFERENCES

1. Al-Balbeesi H, Bin Huraib S, Alnahas N, Alkawari H, Abu-Amara A, Vellappally S, et al. Pain and distress induced by elastomeric and spring separators in patients undergoing orthodontic treatment. J Int Soc Prev Community Dent. 2016;6(6):549–53.
2. Mendes DF, Nascimento JE, Francisco A, Facholli DL, Casa MDA, Carvalho S, et al. Evaluation of plasticity and radiopacity of elastic separators by means of traction tests and radiography. Dental Press J Orthod. 2012;17(6):1–10.
3. Beck VJ, Farella M, Chandler NP, Kieser JA, Thomson WM. Factors associated with pain induced by orthodontic separators. J Oral Rehabil. 2014;41(4):282–8.
4. Goyal M, Khetwal D, Akshita, Amaan Ali S, Chawla R. Research article pain assessment after placing separators as well as initial archwire in orthodontic patients : A randomized clinical trial. Int J Curr Res. 2018;10(01):64631–4.
5. Aldrees A. Intensity of pain due to separators in adolescent orthodontic patients. J Orthod Sci. 2015;4(4):118.
6. Utomi IL, Odukoya OO. Pain and discomfort associated with orthodontic separator placement in patients attending the Lagos University Teaching Hospital, Lagos, Nigeria. Odontostomatol Trop. 2013;36(141):5–13.
7. Mahendra S, Reddy VP, M MC, Shetty B. Pain Control in Orthodontics—Causes and Management. Ann Essences Dent. 2011;3(3):102–6.
8. Kartal Y, Polat-Ozsoy O. Insight into orthodontic appliance induced pain: Mechanism, duration and management. World

J Anesthesiol. 2016;5(1):28.
9. Marini I, Bartolucci ML, Bortolotti F, Innocenti G, Gatto MR, Alessandri Bonetti G. The effect of diode superpulsed low-level laser therapy on experimental orthodontic pain caused by elastomeric separators: a randomized controlled clinical trial. Lasers Med Sci. 2015;30(1):35–41.
10. Zealaiy A, Sokhairi S, Rhbeini A, Alsaud B, Batwa W, Alzain I, et al. Differences in Self-Perceived Pain and Jaw Discomfort Between Adult and Adolescent Orthodontic Patients. EC Dent Sci. 2018;17:2167–74.
11. Iwata K, Takeda M, Oh SB, Shinoda M. Neurophysiology of Orofacial Pain. In: Contemporary Oral Medicine [Internet]. Cham: Springer International Publishing; 2017. p. 1–23. Available from: http://link.springer.com/10.1007/978-3-319-28100-1_8-3
12. Long H, Wang Y, Jian F, Liao LN, Yang X, Lai WL. Current advances in orthodontic pain. Int J Oral Sci. 2016;8(2):67–75.
13. Moradinejad M, Jafari S, Kazemi P, Jafari F. Effect of preoperative ibuprofen and acetaminophen on orthodontic pain. World J Dent. 2016;7(4):182–5.
14. Alqahtani N, Alwakeel A, Alzamil A, Alturki S, Aldawsari G, Aljabaa A, et al. Comparison of two analgesics used for pain relief after placement of orthodontic separators. Saudi Pharm J [Internet]. 2017 Dec;25(8):1169–74. Available from: http://dx.doi.org/10.1016/j.jsps.2017.07.010
15. Patel S, McGorray SP, Yezierski R, Fillingim R, Logan H, Wheeler TT. Effects of analgesics on orthodontic pain. Am J Orthod Dentofac Orthop [Internet]. 2011;139(1):e53–8. Available from: http://dx.doi.org/10.1016/j.ajodo.2010.07.017
16. Martins IP, Martins RP, Caldas SGFR, dos Santos-Pinto A, Buschang PH, Pretel H. Low-level laser therapy (830 nm) on orthodontic pain: blinded randomized clinical trial. Lasers Med Sci. 2019;34(2):281–6.
17. Mendeley Desktop [Internet]. Elsevier; Available from: https://www.mendeley.com/download-desktop-new/
18. Shetty S, Shenoy N, K AS, Unnikrishnan B, Mogra S. Comparison of effects of preoperative piroxicam and ibuprofen on pain after separator placement: A randomized controlled trial. J Orthod Res. 2013;1(2):57.
19. Kohli SS, Kohli VS. Effectiveness of piroxicam and ibuprofen premedication on orthodontic patients' pain experiences A randomized control trial. Angle Orthod. 2011;81(6):1097–102.
20. Minor V, Marris CK, McGorray SP, Yezierski R, Fillingim R, Logan H, et al. Effects of preoperative ibuprofen on pain after separator placement. Am J Orthod Dentofac Orthop [Internet]. 2009;136(4):510–7. Available from: http://dx.doi.org/10.1016/j.ajodo.2007.09.018
21. Law SLS, Southard KA, Law AS, Logan HL, Jakobsen JR. An evaluation of preoperative ibuprofen for treatment of pain associated with orthodontic separator placement. Am J Orthod Dentofac Orthop. 2000;118(6):629–35.
22. Sudhakar V, Vinodhini TS, Mathan Mohan A, Srinivasan B, Rajkumar BK. The efficacy of different pre-and post-operative analgesics in the management of pain after orthodontic separator placement: A randomized clinical trial. J Pharm Bioallied Sci. 2014;6(SUPPL. 1):80–5.
23. Stein S, Korbmacher-Steiner H, Popovic N, Braun A. Pain reduced by low-level laser therapy during use of orthodontic separators in early mixed dentition. J Orofac Orthop. 2015;76(5):431–9.
24. Esper MÂLR, Nicolau RA, Arisawa EÂLS. The effect of two phototherapy protocols on pain control in orthodontic procedure-a preliminary clinical study. Lasers Med Sci. 2011;26(5):657–63.
25. Kim WT, Bayome M, Park JB, Park JH, Baek SH, Kook YA. Effect of frequent laser irradiation on orthodontic pain a single-blind randomized clinical trial. Angle Orthod. 2013;83(4):611–6.
26. Nóbrega C, Da Silva EMK, De MacEdo CR. Low-level laser therapy for treatment of pain associated with orthodontic elastomeric separator placement: A placebo-controlled randomized double-blind clinical trial. Photomed Laser Surg. 2013;31(1):10–6.
27. Nik TH, Shahsavari N, Ghadirian H, Ostad SN. Acetaminophen versus liquefied ibuprofen for control of pain during separation in orthodontic patients: A randomized triple blinded clinical trial. Acta Med Iran. 2016;54(7):418–21.
28. Review Manager (RevMan) [Computer program] [Internet]. The Cochrane Collaboration; 2020. Available from: https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman/revman-5-download
29. Pancekauskaitė G, Jankauskaitė L. Paediatric Pain Medicine: Pain Differences, Recognition and Coping Acute Procedural Pain in Paediatric Emergency Room. Medicina (B Aires) [Internet]. 2018 Nov 27;54(6):94. Available from: http://www.mdpi.com/1010-660X/54/6/94
30. Hamblin MR, de Sousa MVP, Agrawal T. Handbook of Low-Level Laser Therapy

[Internet]. Hamblin MR, Agrawal T, de Sousa M, editors. Handbook of Low-Level Laser Therapy. Jenny Stanford; 2016. 35–49 p. Available from: https://www.taylorfrancis.com/books/9789814669610
31. Bayani S, Rostami S, Ahrari F, Saeedipouya I. A randomized clinical trial comparing the efficacy of bite wafer and low level laser therapy in reducing pain following initial arch wire placement. LASER Ther [Internet]. 2016;25(2):121–9. Available from: https://www.jstage.jst.go.jp/article/islsm/25/2/25_16-OR-10/_article
32. Castelnuovo G, Giusti EM, Manzoni GM, Saviola D, Gabrielli S, Lacerenza M, et al. What is the role of the placebo effect for pain relief in neurorehabilitation? Clinical implications from the Italian consensus conference on pain in neurorehabilitation. Front Neurol. 2018;9(MAY).
33. Klinger R, Stuhlreyer J, Schwartz M, Schmitz J, Colloca L. Clinical Use of Placebo Effects in Patients With Pain Disorders. Int Rev Neurobiol. 2018;139:107–28.
34. Blasini M, Movsas S, Colloca L. Placebo hypoalgesic effects in pain: Potential applications in dental and orofacial pain management. Physiol Behav. 2018;176(12):139–48.
35. Mazaleuskaya LL, Theken KN, Gong L, Thorn CF, FitzGerald GA, Altman RB, et al. PharmGKB summary: ibuprofen pathways. Pharmacogenet Genomics [Internet]. 2015 Feb;25(2):96–106. Available from: http://journals.lww.com/01213011-201502000-00006
36. Bushra R, Aslam N. An Overview of Clinical Pharmacology of Ibuprofen. Oman Med J [Internet]. 2010 Jul 15;25(3):155–61. Available from: http://omjournal.org/articleDetails.aspx?coType=2&aId=2171
37. Giannopoulou C, Dudic A, Kiliaridis S. Pain Discomfort and Crevicular Fluid Changes Induced by Orthodontic Elastic Separators in Children. J Pain. 2006;7(5):367–76.
38. Bruno MB, Bruno MAD, Krymchantowski A V., da Motta AFJ, Mucha JN. A double-blind, randomized clinical trial assessing the effects of a single dose of preemptive anti-inflammatory treatment in orthodontic pain. Prog Orthod [Internet]. 2011;12(1):2–7. Available from: http://dx.doi.org/10.1016/j.pio.2011.02.002
39. AlSayed Hasan MMA, Sultan K, Hamadah O. Evaluating low-level laser therapy effect on reducing orthodontic pain using two laser energy values: a split-mouth randomized placebo-controlled trial. Eur J Orthod. 2018;40(1):23–8.
40. Johal A, Ashari AB, Alamiri N, Fleming PS, Qureshi U, Cox S, et al. Pain experience in adults undergoing treatment: A longitudinal evaluation. Angle Orthod. 2018;88(3):292–8.
41. Asiry MA, Albarakati SF, Al-Marwan MS, Al-Shammari RR. Perception of pain and discomfort from elastomeric separators in Saudi adolescents. Saudi Med J. 2014;35(5):504–7.
42. Khan shakeel qutub, Dsouza J, Ashraf B, Talat M. Pain Anticipated & Pain Experienced During Orthodontic Procedures. Pakistan Oral Dent J. 2017;37(3):434–8.
43. Oshagh M, Najafi HZ, Bahramnia F. Comparison of the analgesic effect of Ibuprofen and pulsed low‐level laser in reducing pain after orthodontic separator placement and evaluation of the changes in the sulcular pain especially prostaglandin E2 level. J Dent Lasers. 2014;8(2):44–9.
44. Freitas PM, Simões A. Lasers in Dentistry: Guide for Clinical Practice. Iowa: John Wiley & Sons; 2015. 230–233 p.
45. Furquim RD, Pascotto RC, Neto JR, Cardoso JR, Ramos AL. Low-level laser therapy effects on pain perception related to the use of orthodontic elastomeric separators. Dental Press J Orthod. 2015;20(3):37–42.