

Orthodontic pain – the state of the evidence

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Abstract

Pain is a common side effect of orthodontic treatment. An understanding of its mechanism, implications and subsequent management is essential for any orthodontist to improve patient compliance and satisfaction with treatment. This paper provides a comprehensive review and state of the evidence on orthodontic pain from the viewpoint of clinicians and patients – clinical features, its pathways, factors influencing pain perception, and finally the pharmacological and non-pharmacological management of orthodontic pain.

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Introduction

Pain is an unpleasant sensory and emotional subjective experience associated with actual or potential tissue damage (Treede, 2018) and is a common phenomenon reported by patients undergoing any form of dental treatment, including orthodontic treatment. 90% of orthodontic patients complained of pain and discomfort especially after placement and activation of fixed, functional or removable appliances (Sawada *et al.*, 2015; Antonio-Zancajo *et al.*, 2020). This subjective feeling is often expressed as sensation of pressure, tension and soreness by patients. Previous research has indicated

that the type of pain is usually mild to moderate in nature, starts two hours after orthodontic appliance placement, peaks at 24 hours after appliance activation and lasts for about five to seven days, with the pain occurring on exertion such as during mastication (Johal *et al.*, 2018; Costa *et al.*, 2020).

Pain can have a negative impact on oral health-related quality of life (Antonio-Zancajo *et al.*, 2020). High pain level affects compliance (Jawaid *et al.*, 2020) which may affect the patient's relationship with the practice and lead to early termination of orthodontic treatment (Brown & Moerenhout, 1991). Furthermore,

orthodontic pain can result in anxiety among patients, and this would in turn exacerbate the pain among them. A survey data collected from orthodontic providers revealed that most orthodontists were not aware that their patients had taken pain medication to ameliorate pain caused during treatment, and unsurprisingly underestimated their patients' pain level (Seers *et al.*, 2018). It is therefore crucial for clinicians to understand mechanism of orthodontic pain, factors influencing pain perception and finally appropriate pain management for their patients.

Pain Pathways

Nociceptors in the peripheral tissues respond to noxious stimuli (mechanical, heat, chemical) and produce nerve impulses. The messages initiated are transmitted by primary afferent nociceptor of trigeminal nerve origin (A δ and C nerve fibres), which are then conducted to second-order pain transmission neurons in the spinal cord through dorsal root ganglion (Yam *et al.*, 2018). A δ fibres are myelinated primary

afferent fibres which respond to mechanical and thermal stimuli and are associated with acute pain. C fibres, on the other hand, are unmyelinated and are associated with slower, persistent pain.

Second-order neurons ascend in the anterolateral tract and relay the message to third-order neurons in the thalamic nuclei, either directly via the spinothalamic tract or indirectly via the reticular formation and the reticulothalamic pathway. From the thalamus, the message is relayed to the cerebral cortex (Figure 1).

Apart from the direct stimulation of nociceptive nerve fibres described above, pain sensation can also be initiated indirectly via the release of inflammatory mediators such as histamine, serotonin, bradykinin, prostaglandins (PG) and leukotrienes (Baral *et al.*, 2019). These pain-producing chemicals may be released by damaged tissue cells, or are synthesized by enzymes activated by tissue damage, and are found in areas of pain and inflammation.

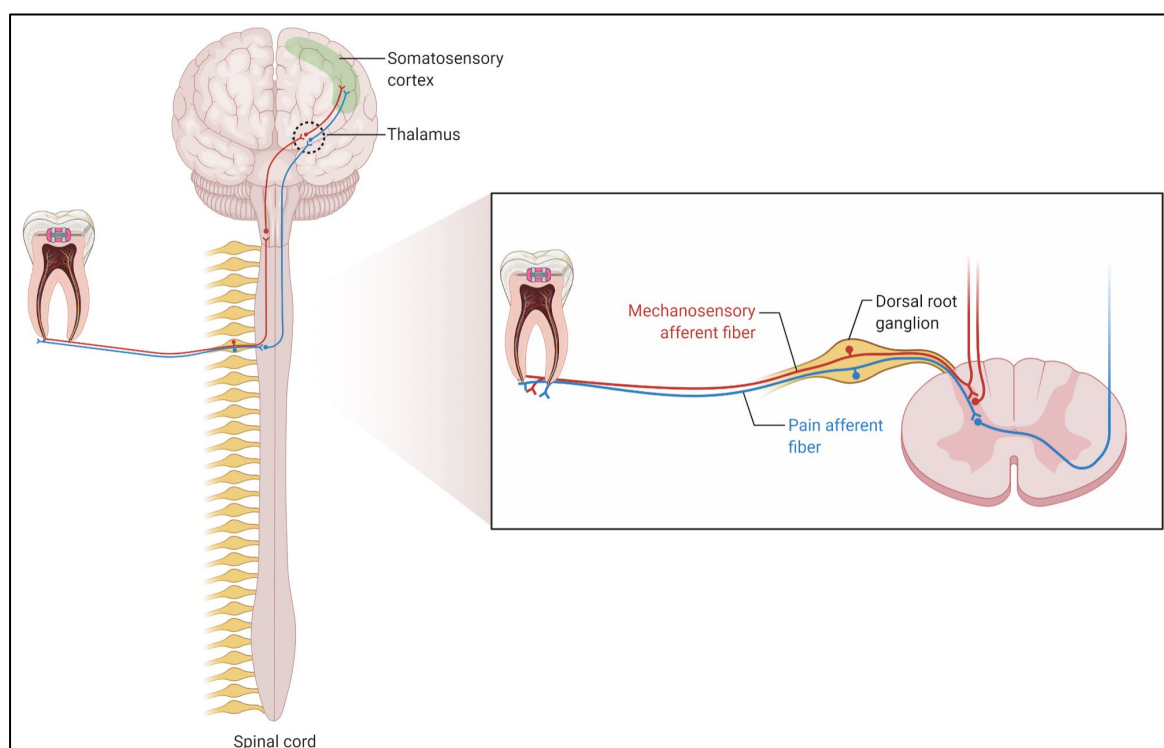


Figure 1. Somatosensory afferents convey information from periphery to central cortex.

Factors influencing pain perception

There is a wide variability of individual pain responses when similar orthodontic forces are applied to the teeth (Bucci *et al.*, 2021). Since pain is a subjective event, its perception can be influenced by psychological, physiological, cultural and social factors (Lamarca *et al.*, 2018). According to gate control theory, nociceptive impulses that arise from the brain stem can be altered at the dorsal horn of spinal cord resulting in less or no pain sensation (Melzack & Wall, 1965). Nociceptive impulses entering a calm and normal functioning brainstem may never reach the higher centres to elicit a pain response. On the contrary, if the same impulse enters the brainstem of patient suffering from chronic pain, a significant pain response may be produced (Therkildsen & Sonnesen, 2022).

The emotional state and psychological factors influence the patient's adaptation to pain and discomfort. When the nociceptive impulses enter the thalamus, they are directed to the cortex and limbic structures where pain is evaluated at an emotional state. The limbic system consists of few structures such as amygdala (which is involved in emotions) and hippocampus (which is responsible for pain memory). The perception of pain by the amygdala can precipitate certain emotions such as fear and anxiety (Topolski *et al.*, 2018). These pain signals are then sent to the cortex in which pain is perceived and emotion associated with the pain is generated, for example anxiety. This information is further transmitted back to the amygdala and to the descending system that influences the final pain sensations (Ossipov *et al.*, 2010).

Stress can significantly perpetuate the degree of pain; the increase in sympathetic nervous activity occurs in spite of the absence of physical threat. Stress reduces the pain threshold levels, in which the perception of normally painless impulse would be perceived as painful (Ireland *et al.*, 2017). Psychological stress can exacerbate inflammatory process and have a negative impact on the regulatory process of

neuroendocrine pathway leading to neuroinflammation (Rivat *et al.*, 2010).

Previous pain experiences may influence clinical orthodontic pain (Costa *et al.*, 2020). Repetition of similar circumstances could generate clinical pain associated with former traumatic experiences, despite the fact that no noxious stimulation occurs. In this respect, memory of previous orthodontic pain experience may alter pain perception, and this could be attributed to the role of hippocampus (Ding *et al.*, 2016). When pain impulse reaches the cortex, the cortex searches pain memory and this information is then sent to the limbic system for processing after which it is returned to the cortex again. The present pain information and past memory pain information are then integrated, ultimately modifying the current pain perception.

There is a body of literature on the cultural influences on pain perceptions and behaviours (Bates *et al.*, 1993; Wang *et al.*, 2018; Craig & Mackenzie, 2021). In 1952, the pioneer work by Zborowski (1952) showed that different culture has its own language of distress when experiencing pain. Pain coping styles are different across different ethnicities, with one meta-analysis reported African Americans or black individuals experience higher pain intensity across clinical and experimental modalities compared with white individuals (Meints *et al.*, 2016). It has also been suggested patients from the Far East have higher pain tolerance than those from the West (Khalaf & Callister, 1997). Therefore, orthodontic practitioners should be sensitive towards patients' cultural beliefs, values, pain coping strategies and life experiences when managing pain arising during treatment.

Findings of the effect of age on pain perception has been inconsistent. A systematic review and meta-analysis conducted in 2017 reported that older patients had higher pain threshold and therefore experienced less pain than younger patients (Lautenbacher *et al.*, 2017). Interestingly, another systematic review and meta-analysis conducted in the same year concluded there was no difference

between the different age groups and pain perception (Monk *et al.*, 2017). The inconsistent evidence could be due to the difficulty in measuring age-related differences of pain since there are different treatment protocols for young and older patients. In the same vein, evidence surrounding the effect of gender on pain perception is also equivocal, with one meta-analysis revealed females displayed greater pain sensitivity than males (Mcdougall *et al.*, 2021), whilst Raak *et al.* (2022) argued that there was no gender differences following initial archwire placement.

Orthodontic procedures inducing pain

(A) Separator placement

Pain has been significantly associated with separator placement. A study in Switzerland assessed children's pain level following separator placement and found that tooth displacement with separators induced pain which resulted in the rapid release of biochemical mediators in gingival crevicular fluid. The pain experience peaked at day one and subsequently reduced one week after. The initial pain intensity was attributed by the presence of PGE₂ levels, whilst pain intensity one day later was due to the increase in interleukin (IL)-1 β levels (Giannopoulou *et al.*, 2006). In terms of the types of orthodontic separators, there was some evidence that elastomeric separator was considered to be more painful than spring separator although the difference was not significant (Tripathi *et al.*, 2019).

(B) Bond up and initial archwire placement

Orthodontic pain peaks at 24 hours following first archwire placement and reduces gradually subsequently (Raak *et al.*, 2022). A Cochrane review by Wang *et al.* (2018) found there was no evidence that the use of any archwire material / type for initial alignment has any effects on perceived pain. Similarly, neither types of brackets bonded (conventional / self-ligating brackets) nor bracket slot size (0.022" / 0.028" slot) has

any significant effects on pain perception (El-Anbawi *et al.*, 2019). However, placement of brackets at the lingual surface is associated with soft tissue discomfort especially with regards to tongue ulceration, as compared to brackets bonded labially (Papageorgiou *et al.*, 2016).

(C) Fixed versus removable appliance treatment

Previous studies have shown that fixed appliances produced greater intensity of pain compared to removable appliances (Diddige *et al.*, 2020), possibly due to the application of constant force used in fixed orthodontic appliance compared with intermittent force used with removable appliance. A recent randomized controlled trial (RCT) by Wiedel & Bondemark (2016) reported pain of low to moderate levels in both groups, albeit the difficulty with eating being more pronounced in the fixed group.

(D) Orthopaedic appliances

Rabah *et al.* (2022) have recently compared the pain and discomfort levels in patients treated with either slow or rapid maxillary expansion (RME) and concluded that RME resulted in higher levels of pain and more chewing difficulties, presumably due to the mechanical forces of increased magnitude being transmitted and absorbed by the craniofacial complex. Despite this, these difficulties slowly decreased over time as treatment progressed. Another extraoral orthopaedic appliance, headgear, which is commonly used for extraoral anchorage and traction purposes produces discomfort after 24 hours, after which the pain declines after three days (Cureton, 1994).

(E) Debonding

The action of applying rotational or torqueing forces to remove orthodontic brackets / bands and their residual adhesive from the enamel has been shown to induce pain as forces are transmitted to the teeth (Kilinc & Sayar, 2019). Pain varies according to the teeth being debonded, with upper and lower anterior segments experiencing greater pain than posterior segments. In

terms of bracket types, ceramic brackets removal caused significantly greater pain than either plastic or metal brackets (Nakada *et al.*, 2021). It has been suggested applying finger pressure onto the teeth (Bavbek *et al.*, 2016), or asking patient to bite onto a cotton roll could minimise the pain associated with bracket debonding (Gupta *et al.*, 2022), presumably due to the stabilising intrusive force.

Management of orthodontic pain

The control of pain during orthodontic treatment is of great interest to clinicians. Although it is not possible to remove pain completely despite the developments in understanding pain mechanism, it should be every orthodontist's objective to minimize pain as much as possible.

A) Pharmacological

Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit cyclooxygenase (COX) enzyme, which is the enzyme that converts arachidonic acid into prostaglandin (PG), subsequently inhibit the synthesis of PG, specifically PGE₂, the primary mediators of inflammatory response. Some commonly used NSAIDs include ibuprofen, aspirin, naproxen sodium, piroxicam and the recently introduced COX-2 inhibitor, rofecoxib (Sari *et al.*, 2004). These drugs are categorised as being non-opioid and peripherally acting analgesics. Different NSAIDs demonstrate different effects. Ngan *et al.* (1994) conducted a double-blind, RCT to compare the analgesic efficacy of ibuprofen, aspirin and placebo. The pain intensity in the three groups were recorded using visual analogue scale, and ibuprofen was found to relieve pain and discomfort associated with post-orthodontic adjustment better than aspirin and placebo. In the same vein, Monk *et al.* (2017) pointed out that analgesic use is more successful in reducing orthodontic pain than no treatment or placebo in a recent Cochrane systematic review.

Previous studies have reported the use of pre-emptive analgesic to control orthodontic pain (Alqahtani *et al.*, 2017; Eslamian *et al.*,

2017; Eslamian *et al.*, 2019). Polat *et al.* (2005) showed that analgesics administration one hour before archwire placement significantly reduced pain severity thereafter, and suggested additional postoperative dose for sufficient pain relief. It could be that afferent nerve impulses are blocked before they can reach the central nervous system. If NSAIDs are given preoperatively, the body absorbs the analgesics before tissue damage can occur, subsequently reducing the inflammatory damage.

There has been some evidence to suggest NSAIDs delay the rate of orthodontic tooth movement (Walker & Buring, 2001), thus prolonging overall duration of orthodontic treatment. The rationale behind this was that NSAIDs affect the synthesis and action of inflammatory mediators including PG and interleukins, which are the primary mediators of inflammatory response following mechanical force application to the teeth. Subsequently, the drugs may reduce the inflammatory and bone resorptive processes and thus orthodontic tooth movement, since tooth movement is closely associated with bone remodelling which involves a complex series of events that act synergistically and antagonistically (Iwasaki *et al.*, 2009). In a molecular study which was set out to determine the effects of NSAIDs on the COX-PG pathway, Kyrkanides *et al.* (2000) reported that there was an increase in the levels of collagenase activity along with matrix metalloproteinases (MMPs)-2 and -9, with concomitant decrease in procollagen synthesis as a result of NSAIDs administration, causing altered remodelling of bone and periodontal ligament and ultimately possible reduction in the speed of tooth movement.

Overall, there seems to be some evidence to indicate that NSAIDs administration could potentially affect the efficacy of orthodontic tooth movement. However, Grewal *et al.* (2020) pointed out that the use of NSAIDs during orthodontic treatment for pain control is transient, and any effect on tooth movement is probably clinically insignificant.

B) Non-pharmacological

Some non-pharmacological approaches that have been tested to alleviate pain arising from orthodontic procedures include low level laser therapy (LLLT), chewing gum/bite wafers, cognitive behavioural treatment, vibratory stimulation and Transcutaneous Electrical Nerve Stimulation (TENS).

(i) LLLT

LLLT have been used in medical and dental fields due to its non-invasiveness (Topolski *et al.*, 2018). It is believed that LLLT reduces pain by hyperpolarization of nerve cell membrane which results in the increase of pain threshold, inhibiting C-fibre activity and secretion of inflammatory substance such as bradykinin, and stimulation of endorphin release (Bakshi *et al.*, 2022). However, the efficacy result of LLLT in orthodontic pain management has been contradictory, with some studies found the procedure to be effective (Nobrega *et al.*, 2013; Almallah *et al.*, 2016; Deana *et al.*, 2017; Martins *et al.*, 2019), whilst others refuted its effectiveness (Furquim *et al.*, 2015; Farsaii & Al-Jewair, 2017). A recent systematic review demonstrated that the effective laser wavelength for orthodontic pain relief was in the range of 780 – 830 nm (Dominguez Camacho *et al.*, 2020) when applied immediately after orthodontic adjustment. However, as discussed earlier, it is the pre-emptive analgesic use, rather than post-treatment, which has been shown to be most effective for pain control.

(ii) Chewing gum

The use of chewing gum to reduce orthodontic pain was first proposed by Proffit (2000), in which the cycles of chewing, along with periodontal ligament compression and decompression helps loosen the tightly packed periodontal fibres, thus reducing the ischaemia, oedema and inflammation and therefore restoring the vascular and lymphatic circulation (Santos & Jr, 2021). In clinical orthodontic practice, clinicians tend to advise patients against gum chewing in fear of appliance breakages.

A recent RCT by Al Shaye'a (2020) found that there was no significant difference between chewing gum group and control group on the frequency of orthodontic appliance breakages. Ireland *et al.* (2016) in their multi-centre RCT study suggested chewing soft, sugar-free gum to reduce the amount of ibuprofen uptake by patients following initial bond up and first archwire change. Together these studies seem to provide promising result on the use of chewing gum in relieving orthodontic pain.

(iii) Cognitive behavioural treatment (CBT)

CBT interventions cited in the literature included relaxation training, guided imagery, activity pacing, problem solving and learning to deal with pain-related anxiety (Peters *et al.*, 2019). These techniques aim to improve pain-coping efficacy and reduce pain-related disability. The first RCT study of CBT on orthodontic pain management was undertaken by Wang *et al.* (2012), and showed CBT was as effective as ibuprofen in controlling pain suggesting its potential clinical usage.

(iv) TENS

Using a small battery-powered device with cutaneous electrodes placed adjacent to the painful area, this mode of non-pharmacological intervention delivers short, low amplitude electrical impulse to reduce pain. Following electrical stimulation, the impulse from β -fibres (large nerve fibres responsible for touch and pressure sensation) reaches the central nervous system before the impulse from the slower A and C nerve fibres (small nerve fibres responsible for pain sensation). In other words, the β impulse blocks the pain impulses. In addition, the electrical impulse stimulates the production of β endorphin and substance 'P' in the nerve cells, and serotonin in the brain, raising the patient's pain tolerance (Vance *et al.*, 2014). TENS has been demonstrated to effectively control acute and chronic pain in dentistry that affects the maxillofacial area (Devi *et al.*, 2021).

(v) *Vibratory stimulation*

This non-invasive pain reduction method employs the use of a patient-controlled apparatus that has a battery-powered vibrating motor attached to a soft acrylic mouthpiece, with vibration being transmitted to all the teeth. There is a consensus among earlier clinicians that the appliance need to be used before the onset of pain (Cochrane, 2019). This confirms the theory that blood supply to the teeth and surrounding tissues is re-established following vibration action and this effect intercepts the ischaemic phenomenon that induces pain (Bakdach & Hadad, 2020). However, once orthodontic pain manifests, the vibratory effect is not effective in ameliorating the pain, and most patients reported not being able to tolerate the vibratory stimulation once discomfort was present (Thammanichanon *et al.*, 2020).

Collectively, these studies provide important insights into the management of orthodontic pain in order to maximize patient's experience during treatment. Overall, there is very little high quality evidence for the use of non-pharmacological interventions for orthodontic pain control. Future studies should consider long term follow-up and patient-reported outcomes to evaluate the effectiveness of these non-pharmacological approaches.

Conclusion

In summary, although pain is unavoidable in every stage of orthodontic treatment and is impossible to eliminate it completely, it is important that orthodontists understand pain in order to improve pain management, patient compliance and ultimately treatment acceptance and overall patient satisfaction. Patient needs to be informed about each phase of treatment along with the pain associated with it. The evidence thus far suggests that pre-emptive analgesic with the least possible side effects can be prescribed, or soft, sugar-free chewing gum can be considered to reduce analgesic intake. Most importantly, patient's anxiety level should be reduced as much as possible to avoid pain

exacerbation associated with orthodontic treatment, since trusting relationships between orthodontist and patient can reduce anxiety and pain.

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References

Al Shayea, E. I. (2020). Comparative assessment between ibuprofen, chewing gum, and bite wafers in pain control following first archwire placement in orthodontic patients. *Journal of Contemporary Dental Practice*, 21(4), 416-420.

Almallah, M. M., Almahdi, W. H., Hajeer, M. Y. (2016). Evaluation of low level laser therapy on pain perception following orthodontic elastomeric separation: A randomized controlled trial. *Journal of Clinical and Diagnostic Research*, 10(11), ZC23-ZC28.

Alqahtani, N., Alwakeel, A., Alzamil, A., Alturki, S., Aldawsari, G., Aljabaa, A. *et al.* (2017). Comparison of two analgesics used for pain relief after placement of orthodontic separators. *Saudi Pharmaceutical Journal*, 25(8), 1169-1174.

Antonio-Zancajo, L., Montero, J., Albaladejo, A., Oteo-Calatayud, M. D., Alvarado-Lorenzo, A. (2020). Pain and oral-health-related quality of life in orthodontic patients during initial therapy with conventional, low-friction, and lingual brackets and aligners (invisalign): A prospective clinical study. *Journal of Clinical Medicine*, 9(7), 2088.

Bakdach, W. M. M., Hadad, R. (2020). Effectiveness of supplemental vibrational force in reducing pain associated with orthodontic treatment: A systematic review. *Quintessence International*, 51(9), 742-752.

Bakshi, P. V., Setty, S. B., Kulkarni, M. R. (2022). Photobiomodulation of human gingival fibroblasts with diode laser - a systematic review. *Journal of Indian Society of Periodontology*, 26(1), 5-12.

Baral, P., Udit, S., Chiu, I. M. (2019). Pain and immunity: Implications for host defence. *Nature Reviews: Immunology*, 19(7), 433-447.

Bates, M. S., Edwards, T. W., Anderson, K. O. (1993). Ethnocultural influences on variation in chronic pain perception. *Pain*, 52(1), 101-112.

Bavbek, N. C., Tuncer, B. B., Tortop, T., Celik, B. (2016). Efficacy of different methods to reduce pain during debonding of orthodontic brackets. *Angle Orthodontist*, 86(6), 917-924.

Brown, D. F., Moerenhout, R. G. (1991). The pain experience and psychological adjustment to orthodontic treatment of preadolescents, adolescents, and adults. *American Journal of Orthodontics and Dentofacial Orthopedics*, 100(4), 349-356.

Bucci, R., Koutris, M., Simeon, V., Lobbezoo, F., Michelotti, A. (2021). Effects of acute pain and strain of the periodontium due to orthodontic separation on the occlusal tactile acuity of healthy individuals. *Clinical Oral Investigations*, 25(12), 6833-6840.

Cochrane, D. J. (2019). The inclusion of vibration therapy in rehabilitating a gastrocnemius tear: A case study in master athlete. *The Journal of Physical Therapy Science*, 31(9), 738-742.

- Costa, E. O. D., Blagitz, M. N., Normando, D. (2020). Impact of catastrophizing on pain during orthodontic treatment. *Dental Press Journal of Orthodontics*, 25(1), 64-69.
- Craig, K. D., Mackenzie, N. E. (2021). What is pain: Are cognitive and social features core components? *Paediatric and Neonatal Pain*, 3(3), 106-118.
- Cureton, S. L. (1994). Headgear and pain. *Journal of Clinical Orthodontics*, 28(9), 525-530.
- Deana, N. F., Zaror, C., Sandoval, P., Alves, N. (2017). Effectiveness of low-level laser therapy in reducing orthodontic pain: A systematic review and meta-analysis. *Pain Research and Management*, 2017, 8560652.
- Devi, M. S., Ranjan, R., Devi, T. D., Sorokhaibam, B. J. I. O. F. M., Toxicology (2021). Application of transcutaneous electrical nerve stimulation in dentistry. 15(3).
- Diddige, R., Negi, G., Kiran, K. V. S., Chitra, P. (2020). Comparison of pain levels in patients treated with 3 different orthodontic appliances - a randomized trial. *Medicine and Pharmacy Reports*, 93(1), 81-88.
- Ding, T. T., Xu, X. X., Cao, Y., Liu, C. R., Gan, Y. H., Xie, Q. F. (2016). Inflammatory pain memory facilitates occlusal interference-induced masticatory muscle hyperalgesia in rats. *European Journal of Pain (London, England)*, 20(3), 353-364.
- Dominguez Camacho, A., Bravo Reyes, M., Velasquez Cujar, S. A. (2020). A systematic review of the effective laser wavelength range in delivering photobiomodulation for pain relief in active orthodontic treatment. *International Orthodontics*, 18(4), 684-695.
- El-Angbawi, A. M., Yassir, Y. A., McIntyre, G. T., Revie, G. F., Bearn, D. R. (2019). A randomized clinical trial of the effectiveness of 0.018-inch and 0.022-inch slot orthodontic bracket systems: Part 3-biological side-effects of treatment. *European Journal of Orthodontics*, 41(2), 154-164.
- Eslamian, L., Kianipour, A., Mortazavi, S. a. R. (2017). The analgesic efficacy of 5% naproxen gel for pain associated with orthodontic separator placement: A randomized double-blind controlled trial. *Anesthesia and Pain Medicine* 7(2), e42708.
- Eslamian, L., Torshabi, M., Motamedian, S. R., Hemmati, Y. B., Mortazavi, S. A. (2019). The effect of naproxen patches on relieving orthodontic pain by evaluation of vas and il-1 β inflammatory factor: A split-mouth study. *Dental Press Journal of Orthodontics*, 24(6), 27e21-27e27.
- Farsaii, A., Al-Jewair, T. (2017). Insufficient evidence supports the use of low-level laser therapy to accelerate tooth movement, prevent orthodontic relapse, and modulate acute pain during orthodontic treatment. *Journal of Evidence-Based Dental Practice*, 17(3), 262-264.
- Furquim, R. D., Pascotto, R. C., Rino Neto, J., Cardoso, J. R., Ramos, A. L. (2015). Low-level laser therapy effects on pain perception related to the use of orthodontic elastomeric separators. *Dental Press Journal of Orthodontics*, 20(3), 37-42.
- Giannopoulou, C., Dudic, A., Kiliaridis, S. (2006). Pain discomfort and crevicular fluid changes induced by orthodontic elastic separators in children. *Journal of Pain*, 7(5), 367-376.
- Grewal, S., Harris L. M. J., Ponduri, S., Naish, H., Ellis, P., Sandy, J. R. et al. (2020). Orthodontic pain. *Orthodontic Update*, 13, 50-56.
- Gupta, S. P., Rauniyar, S., Prasad, P., Pradhan, P. M. S. (2022). A randomized controlled trial to evaluate the effectiveness of different methods on pain management during orthodontic debonding. *Progress in Orthodontics*, 23(1), 7.
- Ireland, A. J., Ellis, P., Jordan, A., Bradley, R., Ewings, P., Atack, N. E. et al. (2016). Comparative assessment of chewing gum and ibuprofen in the management of orthodontic pain with fixed appliances: A pragmatic multicenter randomized controlled trial. *American Journal of Orthodontics and Dentofacial Orthopedics*, 150(2), 220-227.
- Ireland, A. J., Ellis, P., Jordan, A., Bradley, R., Ewings, P., Atack, N. E. et al. (2017). Chewing gum vs. Ibuprofen in the management of orthodontic pain, a multi-centre randomised controlled trial - the effect of anxiety. *Journal of Orthodontics*, 44(1), 3-7.
- Iwasaki, L. R., Chandler, J. R., Marx, D. B., Pandey, J. P., Nickel, J. C. (2009). Il-1 gene polymorphisms, secretion in gingival crevicular fluid, and speed of human orthodontic tooth movement. *Orthodontics & Craniofacial Research*, 12(2), 129-140.
- Jawaid, M., Qadeer, T. A., Fahim, M. F. (2020). Pain perception of orthodontic treatment - a cross-sectional study. *Pakistan Journal of Medical Sciences*, 36(2), 160-165.
- Johal, A., Ashari, A. B., Alamiri, N., Fleming, P. S., Qureshi, U., Cox, S. et al. (2018). Pain experience in adults undergoing treatment: A longitudinal evaluation. *Angle Orthodontist*, 88(3), 292-298.
- Khalaf, I., Callister, L. C. (1997). Cultural meanings of childbirth: Muslim women living in Jordan. *Journal of Holistic Nursing*, 15(4), 373-388.
- Kilinc, D. D., Sayar, G. (2019). Evaluation of pain perception during orthodontic debonding of metallic brackets with four different techniques. *Journal of Applied Oral Science*, 27, e20180003.
- Kyrkanides, S., O'banion, M. K., Subtelny, J. D. (2000). Nonsteroidal anti-inflammatory drugs in orthodontic tooth movement: Metalloproteinase activity and collagen synthesis by endothelial cells. *American Journal of Orthodontics and Dentofacial Orthopedics*, 118(2), 203-209.
- Lamarca, G. A., Vettore, M. V., Monteiro Da Silva, A. M. (2018). The influence of stress and anxiety on the expectation, perception and memory of dental pain in schoolchildren. *Dentistry Journal (Basel)*, 6(4).
- Lautenbacher, S., Peters, J. H., Heesen, M., Scheel, J., Kunz, M. (2017). Age changes in pain perception: A systematic-review and meta-analysis of age effects on pain and tolerance thresholds. *Neuroscience and Biobehavioral Reviews*, 75, 104-113.
- Martins, I. P., Martins, R. P., Caldas, S., Dos Santos-Pinto, A., Buschang, P. H., Pretel, H. (2019). Low-level laser therapy (830 nm) on orthodontic pain: Blinded randomized clinical trial. *Lasers in Medical Science*, 34(2), 281-286.
- Mcdougall, J. F., Bailey, N. G. N., Banga, R., Linde, L. D., Kramer, J. L. K. (2021). The influence of examiner gender on responses to tonic heat pain assessments: A preliminary investigation. *Frontiers in Pain Research (Lausanne)*, 2, 729860.
- Meints, S. M., Miller, M. M., Hirsh, A. T. (2016). Differences in pain coping between black and white americans: A meta-analysis. *Journal of Pain*, 17(6), 642-653.
- Melzack, R., Wall, P. D. (1965). Pain mechanisms: A new theory. *Science*, 150(3699), 971-979.
- Monk, A. B., Harrison, J. E., Worthington, H. V., Teague, A. (2017). Pharmacological interventions for pain relief during orthodontic treatment. *Cochrane Database of Systematic Reviews*, 11, CD003976.
- Nakada, N., Uchida, Y., Inaba, M., Kaetsu, R., Shimizu, N., Namura, Y. et al. (2021). Pain and removal force associated with bracket debonding: A clinical study. *Journal of Applied Oral Science*, 29, e20200879.
- Ngan, P., Wilson, S., Shanfeld, J., Amini, H. (1994). The effect of ibuprofen on the level of discomfort in patients undergoing orthodontic treatment. *American Journal of Orthodontics and Dentofacial Orthopedics*, 106(1), 88-95.
- Nobrega, C., Da Silva, E. M., De Macedo, C. R. (2013). Low-level laser therapy for treatment of pain associated with orthodontic elastomeric separator placement: A placebo-controlled randomized double-blind clinical trial. *Photomedicine and Laser Surgery*, 31(1), 10-16.
- Ossipov, M. H., Dussor, G. O., Porreca, F. (2010). Central modulation of pain. *Journal of Clinical Investigation*, 120(11), 3779-3787.

- Papageorgiou, S. N., Golz, L., Jager, A., Eliades, T., Bourauel, C. (2016). Lingual vs. Labial fixed orthodontic appliances: Systematic review and meta-analysis of treatment effects. *European Journal of Oral Sciences*, 124(2), 105-118.
- Peters, L., Romano, M., Byrow, Y., Gregory, B., Mcllellan, L. F., Brockveld, K. *et al.* (2019). Motivational interviewing prior to cognitive behavioural treatment for social anxiety disorder: A randomised controlled trial. *Journal of Affective Disorders*, 256, 70-78.
- Polat, O., Karaman, A. I., Durmus, E. (2005). Effects of preoperative ibuprofen and naproxen sodium on orthodontic pain. *Angle Orthodontist*, 75(5), 791-796.
- Proffit, W.R., Fields, H.W., Larson, B., Sarver, D.M. (2018). *Contemporary Orthodontics*, 6th ed. St Louis: Mosby Elsevier, pp. 268.
- Raak, C. K., Ostermann, T., Schöenberg-Tu, A. L., Fricke, O., Martin, D. D., Robens, S. *et al.* (2022). No gender differences in pain perception and medication after lumbar spine sequestrectomy-a reanalysis of a randomized controlled clinical trial. *Journal of Clinical Medicine*, 11(9).
- Rabah, N., Al-Ibrahim, H. M., Hajeer, M. Y., Ajaj, M. A., Mahmoud, G. (2022). Assessment of patient-centered outcomes when treating maxillary constriction using a slow removable versus a rapid fixed expansion appliance in the adolescence period: A randomized controlled trial. *Cureus*, 14(3), e22793.
- Rivat, C., Becker, C., Blugeot, A., Zeau, B., Mauborgne, A., Pohl, M. *et al.* (2010). Chronic stress induces transient spinal neuroinflammation, triggering sensory hypersensitivity and long-lasting anxiety-induced hyperalgesia. *Pain*, 150(2), 358-368.
- Santos, D., Jr, J. C. (2021). Chewing gum as a non-pharmacological alternative for orthodontic pain relief: A randomized clinical trial using an intention-to-treat analysis. *The Korean Journal of Orthodontics* 51(5), 346-354.
- Sari, E., Olmez, H., Gurton, A. U. (2004). Comparison of some effects of acetylsalicylic acid and rofecoxib during orthodontic tooth movement. *American Journal of Orthodontics and Dentofacial Orthopedics*, 125(3), 310-315.
- Sawada, A., Usui, N., Shimazaki, K., Taira, M., Ono, T. (2015). The effects of cognitive behavioral therapy on experimental orthodontic pain. *Orthodontic Waves*, 74(1), 10-14.
- Seers, T., Derry, S., Seers, K., Moore, R. A. (2018). Professionals underestimate patients' pain: A comprehensive review. *Pain*, 159(5), 811-818.
- Thammanichanon, P., Kaewpitak, A., Binlath, T., Leethanakul, C. (2020). Interval vibration reduces orthodontic pain via a mechanism involving down-regulation of trpv1 and cgrp. *In Vivo*, 34(5), 2389-2399.
- Therkildsen, N. M., Sonnesen, L. (2022). Bite force, occlusal contact and pain in orthodontic patients during fixed-appliance treatment. *Dentistry Journal (Basel)*, 10(2).
- Topolski, F., Moro, A., Correr, G. M., Schimim, S. C. (2018). Optimal management of orthodontic pain. *Journal of Pain Research*, 11, 589-598.
- Treede, R. D. (2018). The international association for the study of pain definition of pain: As valid in 2018 as in 1979, but in need of regularly updated footnotes. *Pain Reports*, 3(2), e643.
- Tripathi, T., Singh, N., Rai, P., Khanna, N. (2019). Separation and pain perception of elastomeric, kesling and kansal separators. *Dental Press Journal of Orthodontics*, 24(2), 42-48.
- Vance, C. G., Dailey, D. L., Rakel, B. A., Sluka, K. A. (2014). Using tens for pain control: The state of the evidence. *Pain Management*, 4(3), 197-209.
- Walker, J. B., Buring, S. M. (2001). Nsaid impairment of orthodontic tooth movement. *Annals of Pharmacotherapy*, 35(1), 113-115.
- Wang, J., Jian, F., Chen, J., Ye, N. S., Huang, Y. H., Wang, S. *et al.* (2012). Cognitive behavioral therapy for orthodontic pain control: A randomized trial. *Journal of Dental Research*, 91(6), 580-585.
- Wang, K., Kim, H. A., Felson, D. T., Xu, L., Kim, D. H., Nevitt, M. C. *et al.* (2018). Radiographic knee osteoarthritis and knee pain: Cross-sectional study from five different racial/ethnic populations. *Scientific Reports*, 8(1), 1364.
- Wang, Y., Liu, C., Jian, F., McIntyre, G. T., Millett, D. T., Hickman, J. *et al.* (2018). Initial arch wires used in orthodontic treatment with fixed appliances. *Cochrane Database of Systematic Reviews*, 7, CD007859.
- Wiedel, A. P., Bondemark, L. (2016). A randomized controlled trial of self-perceived pain, discomfort, and impairment of jaw function in children undergoing orthodontic treatment with fixed or removable appliances. *Angle Orthodontist*, 86(2), 324-330.
- Yam, M. F., Loh, Y. C., Tan, C. S., Khadijah Adam, S., Abdul Manan, N., Basir, R. (2018). General pathways of pain sensation and the major neurotransmitters involved in pain regulation. *International Journal of Molecular Sciences*, 19(8).
- Zborowski, M. (1952). Cultural components in responses to pain. *Pain*, 8(4), 16-30.