ORTHODONTICS

Non-Invasive Adjunctive Modalities in Accelerating Orthodontic Tooth Movement: A Review

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ABSTRACT

Objective: **Clinical orthodontists tend to emphasize on reducing the orthodontic treatment duration as the treatment is a time consuming and the demand for it is increasing. The aim to shorten treatment duration is desirable to minimise the iatrogenic effects of fixed appliances treatment. The objective of this review was to assess the scientific evidence on the effectiveness of different non-surgical adjunctive procedures in accelerating orthodontic tooth movement (OTM), aim to shorten the total duration.**

Method: **An electronic search through Web of Sci, Scopus, Google Scholar and PubMed was performed, looking for original studies that test non-invasive supplemental therapy to accelerate OTM. The MeSH heading words, and free text words were, "orthodontic," "malocclusion", "accelerate", "facilitate", "tooth movement", "non-invasive".**

Results: **Pharmacological approach, and device-assisted therapies seem to have little evidence that able to accelerate the velocity of OTM. Photobiostimulation could accelerate OTM however further high quality of trials is encouraged focussing on optimal density and frequency of exposure to be more clinically practical.**

Conclusion: **This review provides additional overview about the existing methods with their existence advantages and drawbacks.**

KEY WORDS

accelerating tooth movement, non-invasive procedures orthodontic, adjunctive treatment

INTRODUCTION

Nowadays, in the contemporary world, increased awareness towards dental aesthetics boosts the demand for orthodontic treatment, especially among adults. Attractiveness has been the major motivation to undergo such treatment. There are many benefits such as oral health, including periodontal health and dental prosthesis outcomes, which could be improved by rectifying malocclusion through fixed orthodontic means. Besides that, self-confidence, and self-esteem with better teeth alignment are also the primary determinants of orthodontic treatment.

Orthodontic treatment is a time-consuming procedure, where generally requires less than 2 years (19.9 months) to complete, however a wide range of treatment durations from 14- 33 months were reported[1]. Thus, to shorten the treatment duration is of great interest to orthodontists[2]. Lengthy orthodontic treatment duration may expose to several unintended iatrogenic risks[1]. Minimising patient treatment length required a thorough review of the most effective method that can accelerate tooth movement, has high acceptance by patients as it is a less invasive procedure, is less traumatic, and passes the analysis of the risk-benefit ratio with no adverse effects.

Patient's keenness and adherence toward treatment can be worn when treatment period and frequency of visit go beyond a stage where they recognise significant improvement in their malocclusion. Additionally, compliance toward treatment and oral health-related quality of life may be impaired by lengthier therapy duration, predominantly in adults. Shortening the overall treatment time would benefit not only the patient but the oral health service as well. Many researchers tend to emphasise on accelerating orthodontic tooth movement (OTM) as the demand for quicker length of orthodontic treatment among adults is rising. Decreasing the treatment time now could be a reality with the advent of present innovative technology; however, it must be supported by robust evidence.

Animal studies suggested that Low-level laser therapy (LLLT) and flapless corticotomy have some evidence to facilitate tooth movement in orthodontics; nevertheless, an applicable and standard protocol has yet to be explored and decided[3]. In humans, various techniques have been implemented and reported to expedite OTM and can be divided to non-invasive and invasive method. Non-surgical adjunctive modalities including drug injection and physical/mechanical stimulation have been developed over the last few decades[4] and various surgical procedures have been reported to accelerate orthodontic tooth movement (OTM) with different degrees of invasiveness, ranging from total block osteotomies to flapless partial corticotomy[5]. Each technique has advantages and disadvantages. A clinical study compared the rate of maxillary canine retraction supplemented with corticotomy, which reported that the trial group recorded significantly higher in canine velocity than the control group, with a mean difference of 0.216 mm/ month[6]. Due to high morbidity effects, corticotomy has a low acceptance by the patients, and the cost/ benefit remains unclear; thus could not be recommended as a routine procedure[7]. Minimally invasive periodontal accelerated OTM, which is piezocision has proven to increase the rate; however, it has the possibility of root damage, as the incisions and corticotomies are 'blindly' performed and was associated with the presence of minimal scars in 66% of cases[8].

A meta-analysis disclosed that micro-osteoperforation (MOP) were statistically significant in facilitating the rate of canine retraction; nevertheless, from the clinical point of view, it was not exceptionally significant with an increase of only 0.45 mm per month. Additionally, results from this meta-analysis should be taken with caution because of the

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Table 1: Literature survey on non-invasive methods in accelerating OTM

Study	Study type	Treatment modality	Sample size	Study duration	Primary outcome	Findings
Collins and Sinclair[12]	In vivo	Intraligamentary injections of vitamin D metabolite	10 cats	21 days	Rate of canine retraction	Tooth movement increased by 60%and increased rate of recruitment and activation of osteoclasts caused greater bone resorption on the pressure side.
Kale *et al*[13]	In vivo	Local application of prostaglandin 2 (PGE_2) and 1,25-dihydroxycholecalciferol (1,25-DHCC)	37 rats	9 days	To compare the effects of PGE_2 and 1,25-DHCC on OTM	Both PGE_2 and 1,25-DHCC increased the amount of tooth movement 1,25-DHCC is more effective in modulating bone turnover during OTM
Cruz *et al*[30]	Clinical trial	Low-level laser therapy (LLLT). 780 nm continuous wave mode, 20 mW, 5J/cm^2	11 patients	2 months	Rate of canine retraction	Canine retraction is significantly faster in the trial side.
Limpanichkul *et al*[31]	Clinical trial	Low-level laser therapy (LLLT). 860 nm continuous wave mode, 100 mW, 5J/cm^2	12 patients	3 months	Rate of canine retraction	No significant mean difference of canine distalisation between the LLLT and the control side
Hazan-Molina *et al*[36]	In Vitro	Extracorporeal shock wave therapy (ESWT)	20 rats	3 days	PDL's cytokine concentration (expression of IL-1β and VEGF)	Significant increase of VEGF and interleukin-1β, which have important function in OTM
Falkensammer *et al*[35]	Clinical trial	Extracorporeal shock wave therapy (ESWT)	26 patients	4 months	Amount of OTM-mesialisation of lower second molar	ESWT did not significantly accelerate tooth movement
Woodhouse *et al*[37]	Clinical trial	Vibrational device AcceleDent (20 minutes per day)	81 patients	Until complete alignment	Rate of OTM during alignment	AcceleDent does not significantly accelerate the initial speed of tooth movement nor lessen the treatment duration to accomplish final alignment
Miles *et al*[50]	Clinical trial	Vibrational device Tooth Masseuse (20 minutes per day)	66 patients	10 weeks	Rate of OTM	No clinical advantage for initial alignment of crowding on mandibular six anterior teeth
Pavlin *et al*[38]	Clinical trial	Vibrational device OrthoAccel	45 patients	Until complete space closure	Rate of canine retraction	Significantly increase the tooth movement rate with the mean difference of 0.37 mm/month
Dogru *et al*[50]	In vivo	Shallow frequency electromagnetic fields (ELF-EMFs),	18 rats	8 days	Rate of OTM	ELF-EMF therapy can accelerate orthodontic tooth movement
Showkatbakhsh, *et al*[44]	Clinical trial	Pulsed electromagnetic fields (PEMFs)	10 patients	Until Class I canine relation-ship	Rate of canine retraction	Significantly faster rate of canine retraction with the PEMF compared to the control group (1.57 ± 0.83 mm more in the trial sides
Ekizer *et al*[46]	Clinical trial	Photobiomodulation therapy (PBM). 20 mW/ cm^2 energy density	20 patients	3 months	Rate of OTM	Significantly faster OTM with respect to the control side during the first month ($p < 0.001$; 1.58-fold), second month ($p < 0.05$; 1.21- fold), and third month ($p < 0.001$; 1.31- fold) of orthodontic treatment.
Samara *et al*[47]	Clinical trial	Photobiomodulation therapy (PBM). 33 mW/cm^2 energy density	60 patients	Completion of space closure	Rate of space closure during en masse retraction	Significant higher velocity of space closure by 0.22 mm/month ($p < 0.01$)
Shaughnessy *et al*[45]	Clinical trial	Photobiomodulation therapy (PBM). 42 mW/cm2 energy density	19 patients	Completion of initial alignment	Rate of tooth alignment	Significantly higher tooth alignment rate, and reduces the time it takes to resolve anterior dental crowding

variations in the study design and the different measurement methods of the primary outcome in those included RCTs. The heterogeneity could affect the analysis interpretation. The latest evidence suggests that there is inadequate evidence to conclude whether a single use of MOP be able to expedite OTM[9].

A synergistic series of the physical phenomenon of orthodontic forces and biological tissue remodelling is involved in tooth movement through the dentoalveolar complex. The biological system reacts directionally through receptor cells and signalling cascades, which generate bone remodelling and OTM. As the surgical procedures are associated with unintended side effects, the focuses of this review are within the non-surgical domain modification of the biological process of OTM and aim to assess the scientific evidence on its effectiveness in accelerating OTM.

METHODOLOGY

An electronic search through Web of Sci, Scopus, Google Scholar and PubMed was performed, looking for original research papers that perform non-invasive supplemental therapy to accelerate orthodontic treatment. The MeSH heading words, and free text words were, "orthodontic", "malocclusion", "accelerate", "facilitate", "tooth movement", "non-invasive", The general characteristics of the literature search were display in Table 1.

NON- INVASIVE ORTHODONTIC ADJUNCTIVE PROCEDURES

Pharmacological Approach

In the last decades, there has been notable experimental evidence, mainly in vitro and animal studies; however, to date, the evidence from case-control clinical studies is still lacking[10]. Several apparent problems in ethics and clinical matters arise related to this approach when used in human clinical studies. There are issues related to the enrolment of adequate participants, evaluation of the individual effect variation, and the initial dose-response required to evaluate the proper dose of the therapeutic agent and to measure the tissue-level outcomes[10]. Some of the pharmacological agents reported in animal studies that can enhance tooth movement included Prostaglandin, Leukotrienes, Cytokines, Vitamin D, and Osteocalcin[11].

Intraligamentary injections of vitamin D metabolite tested on canine retraction in cats by the study of Collins and Sinclair exhibited an increase in the presence of osteoclasts, and tooth movement increased by 60%[12]. Kale, Kocadereli[13] investigated the local application of prostaglandin 2 and 1,25-dihydroxycholecalciferol in rats on the rate of tooth movement and found that the latter is more effective in modulating bone turnover. Moreover, vitamin D receptors are not only present in osteoclasts but also in osteoblasts. It is suggested that vitamin D3 increases bone mass in several clinical trials and is used for the treatment of osteoporosis[14]. A preliminary study of local infiltration of vitamin D3 in humans with split-mouth clinical trial reported a significantly decreased rate and amount of tooth movement[15]. This beneficial effect on bone tissue suggested that this pharmacological agent is capable of impeding OTM.

Low-level Laser Therapy

Low-level laser therapy (LLLT) is a harmless, non-intrusive, and inexpensive procedure performed using a laser device. A laser is emitted to mucous areas of the moving tooth. Such therapy could be applied to accelerate orthodontic tooth movement in daily practice and to date, no associated undesirable systemic outcomes in patients undergoing LLLT have been reported[16]. Because of its bio-stimulatory effect, LLLT has been used for several different purposes, such as managing orthodontics pain, including following separators placement[17-21], the enhancement of wound healing[22,23] and nerve regeneration[24] and to stimulate tooth movement[25].

The bio-stimulation effects of LLLT have been investigated by many researchers since 1966 and it was suggested that clinical outcomes of LLLT would be determined by wavelength, energy intensity (J/cm^2), treatment interval, and frequency of repetition[25]. In vitro and in vivo studies proposed that the LLLT has an effect on bone formation consequently expedite the velocity of OTM by stimulating osteoblast cells proliferation, upregulate tissue gene expressions, and improve bone remodelling[26-28]. Most of the past studies were performed on maxillary canine retraction by using identical modality of laser therapy gallium-aluminium-arsenide (GaAlAs). There was a slight variation of the anatomic region for laser application, but all clinical trials approached buccal and palatal/lingual aspects of canine to be retracted at 5 points respectively. Two laser applications on cervical one third, one application on the middle, and two applications in the apical third of the canine root on both sides were finished. Most of the studies were conducted in a short duration, performed the evaluation from one to three months.

LLLT intervention does not associate with the damage to any tooth-supporting structures, as there is no evidence exhibiting any unfavourable impacts of LLLT[16]. The main concern of this therapy was the potential risk of retinal damage[29]. It was suggested to cover the laser probe with a sheath or a filter plate while wearing protective goggles as per the recommendation of the manufacturer to protect the operator as well as the subjects.

The first-ever clinical trial done by Cruz, Kohara[30] on human subjects investigated the biomodulation of LLLT to accelerate tooth movement involved in 11 participants in the age range of 12- to 18 years old. One half of the arch was considered for the control group and canine mechanical reactivation for every 30 days. The other half received the same clinical activation, while being radiated with a diode laser emitting light at a 780 nm continuous wave mode, 20 mW, 5 J/cm^2 for 10 seconds at each point. They suggested that LLLT does accelerate tooth movement, as suggested by previous experiments on animals. In accordance with the initial study, subsequent split-mouth clinical trial on human subjects by Limpanichkul, Godfrey[31] stated that there was no significant mean difference of canine distalisation between the LLLT and the control side. The laser parameters being used were 860 nm continuous wave mode, 100 mW, 25 J/cm^2.

Device - Assisted Treatment Mechanic
Extracorporeal Shock Wave Therapy

In medicine, Extracorporeal Shock Wave Therapy (ESWT) is used as a therapy for kidney and urethral stones, as well as for pseudoarthrosis recovery after long- bone fractures, the management of tendinopathies, and wound healing[32,33]. Its efficacy has also been investigated in the dental field, and it has been suggested that ESWT has a microbicidal effect on *Streptococcus mutans* and P*orphyromonas gingivalis* as well as having bone and muscular regenerative effects[34].

It is non-invasive, and its application might enhance OTM[35]. An in vitro study that investigated the effect of ESWT on tooth movement reported a significant increase of VEGF and interleukin-1β, which have important function in OTM[36]. Falkensammer, Arnhart[35] in their clinical trial, which investigated the impact of a single shock wave of ESWT with 1,000 impulses in the region of tooth movement, concluded that a single application of shock wave treatment did not significantly accelerate tooth movement. However, ESWT displayed no detrimental effects in the region under investigation.

Vibrational Devices

Vibrational forces have been proposed to enhance the speed of OTM by promoting periodontal and alveolar bone remodelling. For the few past decades, there has been increasing interest in the use of vibratory incitements. Hence, a number of marketable devices such as AcceleDent appliances and Tooth Masseuse have been commercialised to deliver cyclic forces directly on the tooth as an adjunctive therapy to orthodontic treatment. AcceleDent is comprised of two components, an activator unit and a removable mouthpiece with hands-free handling, providing a force of 0.2 N and a vibration frequency of 30 Hz. On the other hand, Tooth Masseuse is a one-component device that delivers a force of 0.06 N and a vibration frequency of 111 Hz. Patients need to bite down tenderly onto the thermoplastic wafer, allowing contact with both maxillary and mandibular occlusal surfaces[37].

Woodhouse, DiBiase[37] performed a prospective RCT comparing the regular use of a fully functional vibrational device AcceleDent for 20 minutes per day with placebo and control group in conjunction with straight wire appliance. A conclusion derived that the supplemental vibrational device does not significantly expediate the initial speed of tooth movement nor lessen the duration to accomplish final alignment. Another study by Miles, Smith[17] demonstrated no clinical advantage for initial alignment of crowding on mandibular six anterior teeth with 20 minutes use of Tooth Masseuse per day at a frequency of 111 Hz and

0.06 N. The velocity of tooth movement was assessed by using LII, as well as to verify the alignment rate. The reduction in irregularity showed a very minimal difference of 65% and 69% between the trial and control groups, respectively, at 10 weeks. In the same study, Tooth Masseuse also did not significantly have an advantage in alleviating pain among orthodontic patients[17].

Pavlin, Anthony[38] studied the use of OrthoAccel Device, with a frequency of 30 Hz and 0.02 N, to accelerate the extraction space of maxillary first premolar closure. This was achieved either by en masse retraction, or two-step retraction, with temporary anchorage device reinforcement. The results showed that the low-level cyclic vibrational forces significantly increase the tooth movement rate with the mean difference of 0.37 mm/month[38]. However, the concise Cochrane systematic review by El-Angbawi, McIntyre[4] concluded that the results from Pavlin's trial did not meet the statistically significant data between two groups based on the confidence intervals calculated from the mean differences. On top of that, the mentioned mean difference was reflected to be clinically not significant.

Pulsed Electromagnetic Fields

Pulsed electromagnetic fields (PEMFs) have been used widely in the treatment of bone fractures, bone grafts, osteotomies, osteonecrosis, and osteoporosis[39,40]. Besides that, its use also has been recognised to enhance the rapidity of OTM in animal studies[39,41]. The PEMF can stimulate osteoblast proliferation and differentiation, which may lead to a reduction in bone mass loss and accelerate bone formation. A study reported that PEMF was effective in reducing orthodontic pain caused by initial archwire placement[42]. Dogru, Akpolat[43] studied the use of 50 Hz, shallow frequency electromagnetic fields (ELF-EMFs), on the effect of OTM in 18 rats. The exposure was for eight hours per day for eight days. Several holes were drilled on the left and right maxillary central incisors in order to acquire tooth movement at a distance of 1.5- 2 mm from the gingiva, and 20 g orthodontic forces were applied to the teeth. They concluded that ELF-EMF therapy could accelerate OTM in rats.

Showkatbakhsh, Jamilian[44] performed a split-mouth clinical trial on the rate of canine retraction in ten patients by using coil springs in a process that included the extraction of first premolars. A generator consisting of a circuit and a watch battery that produced a PEMF at 1Hz was embedded in a removable appliance. The retraction was accomplished once a Class I canine relationship had been achieved. They found a significantly faster rate of canine retraction with the PEMF compared to the control group (1.57 ± 0.83 mm more in the trial sides), which suggested that PEMF can accelerate OTM[44].

Photobiomodulation

Photobiomodulation (PBM) is a technique that uses low- energy lasers or light-emitting diodes (LED) to manipulate light in the red to near-infrared (NIR) range (600- 1000 nm)[45]. It attempts to modify cellular biology, and it has been demonstrated to generate favourable outcomes on enhanced tissue regeneration and remodelling, including beneficial outcomes on fibroblastic and chondral proliferation[46].

A split-mouth clinical study by Ekizer, T ker[46] investigated the use of light-emitting diode-mediated photobiomodulation therapy (LPT) with 20 mW/ cm2 energy density over 21 successive days (20 minutes per day) on the movement of canine teeth. They assessed the effect of LPT on the stability of the miniscrews, canine retraction rate, and interleukin-1b levels in gingival and peri-implant crevicular fluid. They concluded that PBM had the potential to accelerate OTM with respect to the control side during the first month ($p < 0.001$; 1.58- fold), second month ($p < 0.05$; 1.21- fold), and third month ($p < 0.001$; 1.31- fold) of orthodontic treatment. They also determined that LPT had a positive outcome on stability of the miniscrews They evaluated the stability of the miniscrews throughout canine distalisation through resonance frequency analysis (RFA) using the Osstell ISQ RFA device (Osstell, Gothenburg, Sweden). However, LPT did not affect peri-implant crevicular fluid or IL-1b level in the gingival.

Samara, Nahas[47] investigated the effectiveness of low-level PBM therapy in accelerating premolar extraction space closure with en-masse retraction using NiTi closed springs with 150 g of force. Light therapy was conveyed for 3 minutes per arch per day using an intraoral OrthoPulse™ device from Biolux Research, producing near-infrared light with a continuous 850-nm wavelength and a power density of 33 mW/cm^2 to achieve a total energy density of approximately 6 J/cm^2 at the surface of the device. This study suggested that PBM therapy for 3 minutes per day accelerated the rate of orthodontic space closure.

These findings are also supported by another study by Shaughnessy, Kantarci[45]. They reported that the use of intraoral PBM, which produces near-infrared light with a continuous 850-nm peak wavelength, increases the tooth alignment rate, and reduces the time it takes to resolve anterior dental crowding. The therapy involved an average of 3.8 minutes' exposure per arch per day, on buccal side only, using an average power density of 42 mW/ cm^2 to attain a mean energy density of approximately 9.3 J/ cm^2 at the area of the LED array.

RESULT

Some results have suggested a potential acceleration of tooth movement by applying prostaglandin in human trials[48,49]. The disadvantages are a painful injection mode during administration and localised leakage of the drug[49]. Alternative methods via oral administration and intravenous administration positively enhance OTM, but demonstrated some unwanted systemic consequences, such as phlebitis and local irritation[48]. Currently, due to the necessity of weekly administration and the severe pain associated with the injection, the use of these drugs is limited[50].

Systemic side effects of each procedure of local substance infiltration must be prudently monitored. Hence, to date, no pharmacological agent subsists that will be able to accelerate OTM due to the risks and limitations identified safely. Further research is essential, involving refining methods of application before prostaglandin could be contemplated in daily clinical practice.

There are contradictory findings related to LLLT. Ge, He[16] support the use of LLLT to enhance OTM in their meta-analysis on the efficacy of LLLT in accelerating OTM. In contrast, another meta-analysis demonstrated there was no evidence to support LLLT in accelerating OTM[51]. Studies on both animals and humans displayed a variety of results, which are still controversial; however it can be concluded that the LLLT is convenient apparatuses in clinical orthodontics if practised appropriately[52]. One of the key issues of LLLT in routine practice is how to define the optimal dose or energy density to reach the desirable outcomes[16].

There is limited evidence pertaining to ESWT in humans study. Despite the effects on increased osteogenesis, angiogenesis, and revascularisation, however, its local and systemic remain unclear. A systematic review concluded that light vibrational forces might have a positive effect on OTM, but findings from current literature do not reach a consensus with either statistical or clinical significance[4]. This was supported by later studies, which recognised weak pieces of evidence that vibrational therapy is effective neither for the acceleration of canine distalisation nor for its alignment. Furthermore, influences of vibration on pain intensity and root resorption in the course of fixed appliance treatment are inconclusive[53]. Adjunctive therapy of vibratory force during the orthodontic treatment does not influence space closure rate, length of the treatment, number of overall visits, or final occlusion obtained[54].

Evidence pertain to the effect of PEMF on OTM is minimal[7]. Thus, its application as a daily routine in orthodontic clinical practice cannot be recommended at present. The efficacy and reliability of these adjunctive techniques require further clinical trials, and the results should be interpreted cautiously. Furthermore, the bulkiness of the devices, the carry-across effect and patient-related outcomes were not considered in any of the studies, which makes clinical recommendation even weaker[5].

To date, a consensus concerning the effective dose of PBM in orthodontics has not been achieved. The literature contemplates a broad range of PBM light sources and methods. The specific deed fields of cellular responses resulting from different variations of light wavelength and dose have yet to be revealed. There was some evidence of an effect; however, the effect size was not clinically significant[5]. Gkantidis, Mistakidis[7] appraised eighteen studies and acknowledged that some evidence displayed the effectiveness of LLLT, but the evidence for PBM was "very weak". Future trials are recommended to determine a standardised guideline for the use of PBM in orthodontics principally concentrating on wavelength, treatment duration, and power density.

CONCLUSION

Generally, many researchers favoured non-invasive methods to accelerate the rate of OTM. A reliable accelerating treatment modality should be affordable and cost-effective, repeatable, practical, efficient, and it should have no detrimental effects on the periodontium, including roots and alveolar bone. Any innovation or appliance by manufacturers should be tested before being released into the market, advertising and claiming something unsubstantiated.

Clinicians should be critical of a new intervention and evaluate its evidence before applying it clinically. Therefore, clinicians should demand a high level of evidence before routinely embarking with any adjunctive procedures to expedite orthodontic tooth movement. Findings in this review should to be taken with caution and it is recommended to improve the evidence of the methodologies described.

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