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Adjunctive techniques for enhancing mandibular growth in Class II malocclusion

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ABSTRACT

Class II malocclusions are generally characterized by mandible retrusion. For this reason, forward bite jumping appliances, also known as functional appliances were originally designed to enhance mandibular forward projection. However, there is still insufficient evidence to support the effectiveness, predictability and stability of functional appliances in modifying mandibular growth. This article was aimed at presenting evidences and hypotheses that mandibular growth may be enhanced through the use of adjunctive methods in conjunction with functional appliances. In formulating our hypothesis, we considered relevant data, mostly derived from animal studies, concerning alternative methods, such as low-intensity ultrasound and light-emitting diode, as well as their related cellular and molecular mechanisms. According to the evidences covered in this article, we suggest that both methods are potentially effective, and theoretically able to act in synergistic way to enhance functional appliances treatment on mandibular and condylar additional growth. The rationale for the use of these methods as adjunctive therapies for mandibular underdevelopment is attributed to their abilities on stimulating angiogenesis, cell differentiation, proliferation, and hypertrophy, as well as enhancing matrix production and endochondoral bone formation, especially on the condyle of growing animals. This article also proposed a study design which would be able to either prove or refute our hypothesis. If ratified, it would represent a significant scientific accomplishment which provides support for further investigations to be carried out on well-designed clinical trials.

Introduction

Class II malocclusion was originally described as having all the lower teeth occluding posterior to normal [1], and it is considered one of the most common orthodontic problems [2–4]. This type of malocclusion, especially when upper incisors are protruded, is likely to produce several consequences. Among these complications, for instance, there are significant esthetic [5] and social [6] impact on children, as well as on their dental health [7]; or it might even predispose them to upper front teeth trauma [8,9], or to upper airway complications, in severe cases [10].

Most of the Class II malocclusions are generally correlated to mandibular retrusion, rather than maxillary protrusion [11,12]. Besides, Class II dentoskeletal disharmony does not tend to self-correct with growth; rather it worsens [13]. Hence, in order to attempt stimulation of mandibular supplementary growth, a great variety of functional appliances were introduced [14–19]. Even though with diverse designs, such functional appliances are essentially based on the same principle on which the forward protruding position of the mandible would enhance condylar and mandibular bone growth, and, as a consequence, enable Class II malocclusion correction. However, according to several systematic reviews, there is still limited evidence to support a clinically significant change in mandibular length induced by functional appliances [20–22]; or to prove its predictability [23] and stability over time [24].

Therefore, many experimental studies on animal models have been carried out in order to investigate alternative methods of stimulating mandibular growth, such as pulsed electromagnetic field [25,26], low-intensity pulsed ultrasound (LIPUS) [27–33], light emitting diode (LED) [34], low-level laser (LLL) [34], growth hormone [32], and gene therapy [33,35,36].

Among these, pulsed electromagnetic field therapy is excessively time-consuming, growth hormone might still have its toxicity comprehensively investigated, and gene therapy still has some important questions to be answered regarding its safety, optimization, and mechanisms before human researches begin to be even considered [37]. Further, on recent study comparing the effects

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between LED and LLL methods on mandibular growth of rats, LED-treated animals demonstrated more mandibular growth than LLL groups [34].

Alternatively, LIPUS has been systematically investigated over the last years, with promising results concerning the enhancement of mandibular growth [27–33]. In addition, LIPUS, as well as LED, present little potential side effects, and relatively lower cost, which makes it suitable for implementation on clinical settings.

Hence, this theoretical article is intended to present key evidences capable of supporting our hypothesis that mandibular growth can be enhanced through simultaneous use of adjunctive methods, such as LIPUS and LED, in conjunction with functional appliances. In order to formulate our hypothesis and to suggest means to test it, we will objectively consider data concerning related treatment protocols, their effectiveness, and respective cellular and molecular mechanisms. Therefore, during the appraisal of the related literature, special attention will be paid to animal studies in which the sole or synergetic use of mandibular-protruding appliances and alternative methods were investigated.

Background

Therapeutic effects of bite-jumping appliances, LIPUS, and LED

Bite-jumping appliances are devices that are specially designed to continuously position the mandible forward further than regular bite in an attempt to improve patients' profiles. The use of such appliances has consistently demonstrated to induce replication and differentiation of cells, as well as new bone formation in the mandibular condyle and glenoid fossa [38–53]. There is a large body of evidence showing that mechanical manipulation of the condyle induces metabolic alterations, and changes in the expression of growth factors and other signaling molecules [54].

The suggested mechanisms through which forward mandibular positioning enhances mandibular growth are abundant [39,40,42–45,47,49,52,53]. It has been demonstrated, for instance, that anterior mandibular positioning increases VEGF (vascular endothelial growth factor) expression which is an important factor in angiogenesis, and subsequent bone formation in the condyle [39,44], and glenoid fossa [40,45] of growing rats. The close correlation between VEGF production and bone formation is inferred to be a result of the recruitment of required osteoprogenitor cells by new blood supply [55].

Mandibular protrusion also led to an up-regulation of the expression of the transcription factor Sox9 (sex determining-region Y-box 9) [42,52] and collagen, type II gene [42,43,47,49,50,52], involved in the chondrocytes differentiation, and in the collagenous matrix formation, respectively.

Another important mechanism was reported through which mandibular advancement elicits Runx2 (runt-related transcription factor 2) gene expression in condylar cartilage, which is responsible for mediating chondrocyte terminal maturation, and endochondral ossification, after osteoblast differentiation [47]. Forward mandibular positioning through bite-jumping appliances has also demonstrated to increase the expression of growth members, such as Ihh (Indian hedgehog: stimulates cellular proliferation in the condyle) and PTHrP (parathyroid hormone-related peptide: retards further maturation of chondroblasts, and thereby allows further replication of chondrogenic cells) [49].

Furthermore, mandibular advancement leads to the expression of Cyclin D1 (that accelerates the cell cycle), PCNA (proliferating cell nuclear antigen: indicates increased DNA replication of mesenchymal cells), and Wnt5a (wingless-type MMTV integration site family, member 5A: indicates an increase in chondrocyte proliferation and differentiation) [50]. In response to bite-jumping appliances, the increased expressions of BMP2 and BMP4 (bone morphogenetic proteins 2 and 4), which accelerates and enhances the differentiation of mesenchymal cells into bone-forming cells, has also been significantly observed [53].

Hence, the induced forward positioning of the mandible has demonstrated to evoke important mechanisms related to the stimulation of the differentiation and replication of chondrocytes, formation of blood vessels providing new mesenchymal cells, which are also stimulated to differentiate into bone-forming cells. In addition, anterior posture of the mandible might also favor the production of collagenous matrix. The recognition of these cellular/molecular events that take place after mandibular induced forward positioning indicates the "field" where current efforts should operate in order to "boost" mandibular growth. Thus, in the next paragraphs, important mechanisms triggered by LIPUS and LED will be presented and discussed.

As previously stated, the use of LIPUS has been documented to present promising results in the growth of the mandible [27–33]. In a study of rabbits [27], LIPUS significantly stimulated the differential mandibular growth. Histologically, treated sites presented hyperplasia of the fibrocartilaginous layer, hypertrophy of the chondroblasts of the chondrogenic layers, marked endochondral ossification, excessive bony trabeculae, and dilated blood capillaries, which was posteriorly observed by other authors as well [31].

Oyonarte et al. [29] used experimental rats in which LIPUS stimulation also increased the cartilaginous layer thickness, but apparently to a lesser degree. In addition, chondrocytes were more hypertrophic, and there was an increase in the matrix secretion in the maturation zone. At the subchondral bone level, the stimulated groups demonstrated elongated, longitudinally oriented trabeculae, and significantly increased medullar area and trabecular perimeter.

In addition to the evident enhanced endochondral ossification, LIPUS seems to play an important role in some of the mechanisms also elicited by mandibular forward positioning, such as neo-vascularization and matrix production. An *in-vitro* study, has confirmed LIPUS ability to stimulate chondrocyte proliferation, as well as to increase the collagenous matrix production by chondrocytes in human cells [56].

In a preliminary report [28], this ability was confirmed, when baboons treated with LIPUS had better morphological and histological results than those treated only with bite-jumping appliances. While non-LIPUS group showed more thickening of condylar cartilage and less bone formation, it was observed more bone formation and highly matured and organized bony trabeculae with few marrow spaces in the group that used both appliance and LIPUS.

Thus, there appears to be plenty of evidences which support LIPUS as a potentially adjunctive therapy to enhance mandibular growth. Such effect was finally observed on a clinical pilot-study [57] in which five children with hemifacial microsomia were treated with a modified functional appliance associated with LIPUS application on the underdeveloped side. After one year of treatment, there were significant clinical and radiographic improvements.

Even though positive results were presented in this initial trial [57], they cannot be overestimated, since only a limited number of children was evaluated. Besides, LIPUS use to enhance mandibular growth in human still requires adaptations. In order to be effective, such therapeutic approach required one year of compliance. Such fact indicates a significant challenge for the clinical application of this technique which, if implemented, would demand extremely high cooperation from the patients.

On the other hand, the effect of LED on condylar growth still has not received due scientific attention. According to our knowledge, only one study, already referenced [34], has been performed so far. The results of this research indicated that LED has proved to effectively enhance mandibular growth in rats; and histologic data indi-

cated that it significantly increased all condylar surface layers. Another study has indicated that LED application might increase new bone formation area, number of osteoblasts/osteoclasts, and vessels on rats subjected to orthopedic maxillary expansion [58]. Further researches have also demonstrated LED ability on promoting angiogenesis [59–60], and as an important adjunctive factor involved in the improvement of dentoalveolar osteogenesis [61].

It thus seems likely that the beneficial effects of LED are the same as reported to LLL, which include increased osteoblastic proliferation, collagen deposition, and bone neoformation [62]. Even though the LED effects and mechanisms on bone formation are not fully understood, and its molecular effects on mandibular condylar development are unclear, it still might be considered an alternative therapeutic approach to be comprehensively tested, since positive cellular events are observed after its application.

Since the associated use of functional appliances and LIPUS may be clinically unsuitable [37,57], the addition of LED, as an adjunctive therapy in addition to LIPUS might be beneficial to improve the effectiveness of functional appliance therapy in enhancing mandibular forward growth.

In the following paragraphs, we will roughly propose a study design in animals with the objective of testing our hypotheses. In our opinion, for the time being, larger human clinical trials should be postponed until well-designed animal studies obtain clearer results on the efficacy/effectiveness, stability, mechanisms, and eventual synergistic effects involved with the treatment modalities we addressed here (functional appliances, LIPUS, and LED).

Evaluation of the hypothesis

Proposal of an experiment

The authors would like to suggest an animal study in young rats, which will be divided in groups as follows: negative control (no therapy); positive control (functional appliance); treatment group 1 (functional appliance + LIPUS); treatment group 2 (functional appliance + LED); and treatment group 3 (functional appliance + LIPUS + LED). The functional appliances will be kept in position for 30 days and the LIPUS or LED applications will be performed during 20 minutes per day on the right condyle. In treatment group 3, LIPUS and LED will be applied in alternate days to the right condyle during the same treatment period performed in the other experimental groups. The positive control, as well as all of the treatment groups will have half of their animals sacrificed on day 30 (when treatment will be concluded), and the remaining will be euthanized on day 60 (30 days after treatment conclusion). After dissection, hemimandibles will be subjected to morphologic and histomorphometric analysis; and part of the samples will be used to measure the levels of expression of Sox9, Runx2, type II collagen and VEGF genes.

This study design aims at evaluating the synergetic effect of adjunct therapies in the mandibular growth enhancement. A secondary intent of this future study would be to investigate the long-term effect of the different treatment protocols, which is also under-appreciated by scientific literature. Another important objective of this proposed study would be to comprehensively understand the mechanisms involved in the eventual additive effects of therapies. The eventual acceptance or rejection of our hypothesis would represent an important step toward the investigation of such potential therapeutic approaches in well-designed clinical trials in patients.

Conflict of interest statement

All authors disclose that there was no conflict of interests that could inappropriately influence (bias) our work.

References

[1] Angle EH. Classification of malocclusion. Dental Cosmos 1899;41(2):248–64.
[2] Karaiskos N, Wiltshire WA, Odlum O, Brothwell D, Hassard TH. Preventive and interceptive orthodontic treatment needs of an inner-city group of 6- and 9-year-old Canadian children. J Can Dent Assoc 2005;71(9):649.
[3] Urrego-Burbano PA, Jiménez-Arroyave LP, Londoño-Bolívar MÁ, Zapata-Tamayo M, Botero-Mariaca P. Epidemiological profile of dental occlusion in children attending school in Envigado, Colombia. Rev Salud Publica (Bogota) 2011;13(6):1010–21.
[4] Reddy ER, Manjula M, Sreelakshmi N, Rani ST, Aduri R, Patil BD. Prevalence of malocclusion among 6 to 10 year old Nalgonda school children. J Int Oral Health 2013;5(6):49–54.
[5] Kiekens RM, Maltha JC, van't Hof MA, Kuijpers-Jagtman AM. Objective measures as indicators for facial esthetics in white adolescents. Angle Orthod 2006;76(4):551–6.
[6] Seehra J, Fleming PS, Newton T, DiBiase AT. Bullying in orthodontic patients and its relationship to malocclusion, self-esteem and oral health-related quality of life. J Orthod 2011;38(4):247–56.
[7] Almeida AB, Leite IC. Orthodontic treatment need for Brazilian school children: a study using the Dental Aesthetic Index. Dental Press J Orthod 2013;18(1):103–9.
[8] Patel MC, Sujan SG. The prevalence of traumatic dental injuries to permanent anterior teeth and its relation with predisposing risk factors among 8–13 years school children of Vadodara city: an epidemiological study. J Indian Soc Pedod Prev Dent 2012;30(2):151–7.
[9] Kalha AS. Early orthodontic treatment reduced incisal trauma in children with class II malocclusions. Evid Based Dent 2014;15(1):18–20.
[10] Flores-Mir C, Korayem M, Heo G, Witmans M, Major MP, Major PW. Craniofacial morphological characteristics in children with obstructive sleep apnea syndrome: a systematic review and meta-analysis. J Am Dent Assoc 2013;144(3):269–77.
[11] McNamara Jr JA. Components of class II malocclusion in children 8–10 years of age. Angle Orthod 1981;51(3):177–202.
[12] Jacob HB, Buschang PH. Mandibular growth comparisons of class I and class II division 1 skeletofacial patterns. Angle Orthod 2014;84(5):755–61.
[13] Stahl F, Baccetti T, Franchi L, McNamara Jr JA. Longitudinal growth changes in untreated subjects with class II, division 1 malocclusion. Am J Orthod Dentofacial Orthop 2008;134(1):125–37.
[14] Balters W. Extrait de technique du Bionator. Rev Franc Odontostomat 1964;11(2):191–212.
[15] Frankel R. The treatment of class II, division 1 malocclusion with functional correctors. Am J Orthod Dentofacial Orthop 1969;55(3):265–75.
[16] Pancherz H. Treatment of class II malocclusions by jumping the bite with the Herbst appliance. A cephalometric investigation. Am J Orthod 1979;76(4):423–42.
[17] Clark WJ. The twin block technique. A functional orthopedic appliance system. Am J Orthod Dentofacial Orthop 1988;93(1):1–18.
[18] Vogt W. The Forsus fatigue resistant device. J Clin Orthod 2006;40(6):368–77.
[19] Flores-Mir C, Barnett G, Higgins DW, Heo G, Major PW. Short-term skeletal and dental effects of the Xbow appliance as measured on lateral cephalograms. Am J Orthod Dentofacial Orthop 2009;136(6):822–32.
[20] Chen JY, Will LA, Niederman R. Analysis of efficacy of functional appliances on mandibular growth. Am J Orthod Dentofacial Orthop 2002;122(5):470–6.
[21] Cozza P, Baccetti T, Franchi L, De Toffol L, McNamara Jr JA. Mandibular changes produced by functional appliances in class II malocclusion: a systematic review. Am J Orthod Dentofacial Orthop 2006;129(5). 599.e1–12.
[22] Marsico E, Gatto E, Burrascano M, Matarese G, Cordasco G. Effectiveness of orthodontic treatment with functional appliances on mandibular growth in the short term. Am J Orthod Dentofacial Orthop 2011;139(1):24–36.
[23] Perillo L, Cannavale R, Ferro F, et al. Meta-analysis of skeletal mandibular changes during Frankel appliance treatment. Eur J Orthod 2011;33(1):84–92.
[24] Flores-Mir C, Ayeh A, Goswani A, Charkhandeh S. Skeletal and dental changes in class II division 1 malocclusions treated with splint-type Herbst appliances. A systematic review. Angle Orthod 2007;77(2):376–81.
[25] Gerling JA, Sinclair PM, Roa RL. The effect of pulsating electromagnetic fields on condylar growth in guinea pigs. Am J Orthod 1985;87(3):211–23.
[26] Wilmot JJ, Chiego Jr DJ, Carlson DS, Hanks CT, Moskwa JJ. Autoradiographic study of the effects of pulsed electromagnetic fields on bone and cartilage growth in juvenile rats. Arch Oral Biol 1993;38(1):67–74.
[27] El-Bialy T, El-Shamy I, Graber TM. Growth modification of the rabbit mandible using therapeutic ultrasound: is it possible to enhance functional appliance results? Angle Orthod 2003;73(6):631–9.
[28] El-Bialy T, Hassan A, Albaghdadi T, Fouad HA, Maimani AR. Growth modification of the mandible with ultrasound in baboons: a preliminary report. Am J Orthod Dentofacial Orthop 2006;130(4). 435.e7–14.
[29] Oyonarte R, Zárate M, Rodriguez F. Low-intensity pulsed ultrasound stimulation of condylar growth in rats. Angle Orthod 2009;79(5):964–70.
[30] El-Bialy T, Uludag H, Jomha N, Badylak SF. In vivo ultrasound-assisted tissue-engineered mandibular condyle: a pilot study in rabbits. Tissue Eng C Methods 2010;16(6):1315–23.
[31] Oyonarte R, Becerra D, Díaz-Zúñiga J, Rojas V, Carrion F. Morphological effects of mesenchymal stem cells and pulsed ultrasound on condylar growth in rats: a pilot study. Aust Orthod J 2013;29(1):3–12.

[32] Khan I, El-Kadi AO, El-Bialy T. Effects of growth hormone and ultrasound on mandibular growth in rats: MicroCT and toxicity analyses. Arch Oral Biol 2013;58(9):1217–24.
[33] Kaur H, Uludağ H, El-Bialy T. Effect of nonviral plasmid delivered basic fibroblast growth factor and low intensity pulsed ultrasound on mandibular condylar growth: a preliminary study. Biomed Res Int 2014;2014:426710.
[34] El-Bialy T, Alhadlaq A, Felemban N, Yeung J, Ebrahim A, H Hassan A. The effect of light-emitting diode and laser on mandibular growth in rats. Angle Orthod [in press].
[35] Rabie AB, Dai J, Xu R. Recombinant AAV-mediated VEGF gene therapy induces mandibular condylar growth. Gene Ther 2007;14(12):972–80.
[36] Dai J, Rabie AB. Gene therapy to enhance condylar growth using rAAV-VEGF. Angle Orthod 2008;78(1):89–94.
[37] El-Bialy T, Alhadlaq A. New therapeutics in promoting and modulating mandibular growth in cases with mandibular hypoplasia. Biomed Res Int 2013;2013:789679.
[38] Rabie AB, Zhao Z, Shen G, Hägg EU, Dr O, Robinson W. Osteogenesis in the glenoid fossa in response to mandibular advancement. Am J Orthod Dentofacial Orthop 2001;119(4):390–400.
[39] Rabie AB, Leung FY, Chayanupatkul A, Hägg U. The correlation between neovascularization and bone formation in the condyle during forward mandibular positioning. Angle Orthod 2002;72(5):431–8.
[40] Rabie AB, Shum L, Chayanupatkul A. VEGF and bone formation in the glenoid fossa during forward mandibular positioning. Am J Orthod Dentofacial Orthop 2002;122(2):202–9.
[41] Chayanupatkul A, Rabie AB, Hägg U. Temporomandibular response to early and late removal of bite-jumping devices. Eur J Orthod 2003;25(5):465–70.
[42] Rabie AB, She TT, Harley VR. Forward mandibular positioning up-regulates SOX9 and type II collagen expression in the glenoid fossa. J Dent Res 2003;82(9):725–30.
[43] Rabie AB, Xiong H, Hägg U. Forward mandibular positioning enhances condylar adaptation in adult rats. Eur J Orthod 2004;26(4):353–8.
[44] Leung FY, Rabie AB, Hägg U. Neovascularization and bone formation in the condyle during stepwise mandibular advancement. Eur J Orthod 2004;26(2):137–41.
[45] Shum L, Rabie AB, Hägg U. Vascular endothelial growth factor expression and bone formation in posterior glenoid fossa during stepwise mandibular advancement. Am J Orthod Dentofacial Orthop 2004;125(2):185–90.
[46] Xiong H, Hägg U, Tang GH, Rabie AB, Robinson W. The effect of continuous bite-jumping in adult rats: a morphological study. Angle Orthod 2004;74(1):86–92.
[47] Tang GH, Rabie AB. Runx2 regulates endochondral ossification in condyle during mandibular advancement. J Dent Res 2005;84(2):166–71.
[48] Ishii T, Yamaguchi H. Influence of extraoral lateral force loading on the mandible in the mandibular development of growing rats. Am J Orthod Dentofacial Orthop 2008;134(6):782–91.
[49] Rabie AB, Al-Kalaly A. Does the degree of advancement during functional appliance therapy matter? Eur J Orthod 2008;30(3):274–82.
[50] Al-Kalaly A, Wu C, Wong R, Rabie AB. The assessment of cell cycle genes in the rat mandibular condyle. Arch Oral Biol 2009;54(5):470–8.
[51] Taira K, Iino S, Kubota T, Fukunaga T, Miyawaki S. Effects of mandibular advancement plus prohibition of lower incisor movement on mandibular growth in rats. Angle Orthod 2009;79(6):1095–101.
[52] Sobue T, Yeh WC, Chhibber A, et al. Murine TMJ loading causes increased proliferation and chondrocyte maturation. J Dent Res 2009;90(4):512–6.
[53] Barnouti ZP, Owtad P, Shen G, Petocz P, Darendeliler MA. The biological mechanisms of PCNA and BMP in TMJ adaptive remodeling. Angle Orthod 2011;81(1):91–9.
[54] Von den Hoff JW, Delatte M. Interplay of mechanical loading and growth factors in the mandibular condyle. Arch Oral Biol 2008;53(8):709–15.
[55] Carlevaro MF, Cermelli S, Cancedda R, Descalzi Cancedda F. Vascular endothelial growth factor (VEGF) in cartilage neovascularization and chondrocyte differentiation: auto-paracrine role during endochondral bone formation. J Cell Sci 2000;113(Pt 1):59–69.
[56] Korstjens CM, van der Rijt RH, Albers GH, Semeins CM, Klein-Nulend J. Low-intensity pulsed ultrasound affects human articular chondrocytes in vitro. Med Biol Eng Comput 2008;46(12):1263–70.
[57] El-Bialy T, Hasan A, Janadas A, Albaghdadi T. Nonsurgical treatment of hemifacial microsomia by therapeutic ultrasound and hybrid functional appliance. Open Access J Clin Trials 2010;2:29–36.
[58] Ekizer A, Uysal T, Güray E, Yüksel Y. Light-emitting diode photobiomodulation: effect on bone formation in orthopedically expanded suture in rats – early bone changes. Lasers Med Sci 2013;28(5):1263–70.
[59] Corazza AV, Jorge J, Kurachi C, Bagnato VS. Photobiomodulation on the angiogenesis of skin wounds in rats using different light sources. Photomed Laser Surg 2007;25(2):102–6.
[60] Sousa AP, Paraguassú GM, Silveira NT, et al. Laser and LED phototherapies on angiogenesis. Lasers Med Sci 2013;28(3):981–7.
[61] Soares LG, Marques AM, Aciole JM, et al. Do laser/LED phototherapies influence the outcome of the repair of surgical bone defects grafted with biphasic synthetic microgranular HA + β-tricalcium phosphate? A Raman spectroscopy study. Lasers Med Sci 2014;29(5):1575–84.
[62] Pinheiro AL, Gerbi ME. Photoengineering of bone repair processes. Photomed Laser Surg 2006;24(2):169–78.

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