*EDITORIAL* 

# ORTHOPEDIC JOINT STABILITY INFLUENCES GROWTH AND MAXILLARY DEVELOPMENT: CLINICAL ASPECTS

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Orthopedic temporomandibular joint (TMJ) instability is very common among children and adults. It is often associated with pain in the cervicofacial region, and muscle contraction. To investigate whether muscle contraction can cause permanent posterior rotation of the head and whether treatment with splint and kinetotherapy is efficient, a literature review was carried out of patients with pain in the cervicofacial area. Additionally, the case of a 15-year old patient presenting with permanent posterior rotation of cranium, with no movement between the first two vertebra and pain in the cervicofacial area was reported. Kinetotherapy followed by rapid maxillary expansion improved the function of cervical vertebrae and reduced the cervicofacial pain within the first two weeks. Kinetotherapy, rapid maxillary expansion, and orthodontic treatment with a stable joint position could be a good therapy to control occipital-atlas function.

The cranio-cervico-mandibular (CCM) system has been defined as a functionally based system; any dysfunction of the CCM system is a site for disease. Pain in the facial region is associated with temporomandibular disorder (TMD) in 70% of the cases (1). Although only one in four people are aware of TMD, 60-70% of the general population suffers from this disease (1).

TMD is a disease that affects the temporomandibular joint (TMJ), myofascial muscle, and cervical spine. Pain is the most common symptom of TMD but determining the etiology of pain can be challenging. Pain can be described by patients in multiple ways:

shooting, burning, throbbing, aching, stinging, cramping, and tingling. Different types of pain can provide clues for appropriate diagnosis. Sharp pain can be caused by primary neuralgia, whereas burning pain can be caused by mechanical nerve irritation. Muscle spasm can result in cramping pain. Aching pain is associated with inflammation. A complete clinical evaluation must differentiate the pain caused by a joint pathology from the pain caused by muscular disorders (2). The specific treatment plan is determined by the diagnosis; therefore, an accurate diagnosis is crucial.

TMD disorders are most commonly classified using the research diagnostic criteria (RDC) for

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DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

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temporo-mandibular disorders (RDC/TMD). TMJ pain and clicking, myofascial pain, reduced range of motion, and mandibular deviation during function are the principle signs and symptoms of TMJ disorders. These symptoms could be associated with ear-related problems, headache, cervical spine-dysfunction, and altered cervical posture (3). In case of facial pain due to TMD, patients often describe an increase in pain intensity during mastication. Schiffman et al. classified orofacial pain as physical (Axis 1) and psychological (Axis 2) (3).

Orthopedic joint problems are very common among pediatric and elderly patients. Patients with joint problems complain about pain in the joint and ear regions, whereas patients with muscular pain usually describe pain in a more generalized area (2).

For good health, the patient must have a stable orthopedic joint with the condyles in the uppermost position in the temporal fossa and the disc in a concave-convex relation and the teeth in maximum intercuspation. In this position, all muscles will be relaxed so that the masticatory system can function correctly. Some authors reported that disc displacement (DD) is very frequent in children aged between 6 and 15 years, and that it progresses with age (4). Disturbance of mandibular growth can occur because of mandibular dysfunction. When DD is present in one joint, growth will be impeded; growth can also be affected by nonfunctional masticatory muscles. TMD could be associated with cervical anomalies that could impediment growth. If posterior rotation of the cranium is diagnosed at an early age, could this influence mandibular growth? Could Atlas-occipital fusion (AOA) and permanent posterior rotation of the cranium present the same radiologic characteristic?

# MATERIALS AND METHODS

This systematic review was performed in accordance with the guidelines of the Cochrane Collaboration (5) and the Centre for Reviews and Dissemination (6). The review was processed in accordance with the Preferred Reporting items from the Systematic Reviews and Meta-Analyses Statement (7).

The authors identified 8,023 publications in electronic databases, using PubMed, Scopus, and Web of Science

to search all the articles. Inclusion criteria for this review consisted of clinical trials, case reports, and free full text articles published in the last 5 years that studied TMJ pain and myofascial pain. Literature reviews, meta-analyses, and research on treatment with laser therapy, alternative medicine treatment, medication therapy, general disease, ozone therapy, and platelet reach plasma (PRP) were all excluded. The included articles are summarized in Table I. Eight eligible studies were included in this review. The full-text articles were assessed by two independent reviewers for eligibility. The quality assessment (risk of bias) of the selected studies was evaluated by the same reviewers according to the Cochrane risk of bias tool.

A 15-year-old girl was referred to the orthodontic department for treatment. She demonstrated a posterior cross bite with 9-mm maxillary transverse deficiency resulting in bilateral ectopic canine, a severe Class II malocclusion, crowding in the upper and lower arch, and oral breathing. The lower midline was shifted to the right due to crowding, and the upper midline was in the correct position. Clinical examination revealed a convex profile with retrognathic and small mandible, obtuse naso-labial angle, labial incompetence, and facial asymmetry with menton deviated to the right. We used Rocabado's map of pain to palpate the TMJ. Both left and right TMJ were sensitive to palpation. In addition, the masticatory muscle was tender and sensitive to palpation. The upper and lower incisors were protruded, and the molar relationship was Class II on both sides. The patient had an anterior open bite of 6 mm and an overjet of 5 mm. She was complaining of cervicofacial pain. When the muscles were palpated, the patient experienced pain in the upper trapezius and temporalis. When we examined the Lateral Cephalometric radiograph, we found that the C1 vertebra was in contact with the occipital bone and suspected an atlanto-occipital fusion with a posterior rotation of the cranium. We took another X-ray with the head in flexion and saw no movement between the occipital bone and atlas (Fig. 1).

There are few existing studies on occipito-atlas fusion. We were unable to find one involving differential diagnoses between osseous fusion and muscle contraction on its own. Atlanto-occipital assimilation (AOA) of atlas, and assimilation of atlas are abnormalities that are rarely recorded in anatomical, morphological, and radiological studies. It is usually associated with reduction in dimensions of foramen magnum, leading to acute or chronic

neurovascular compression and clinical manifestations of varying severity. Although atlanto-occipital fusion is rare, it is important for the diagnostic and therapeutic approaches of physicians and surgeons (8-10). Research by Sonnesen et al. showed a correlation between craniofacial and upper cervical spine morphology (11). Neurological disorders in patients with AOA often occur in the 3rd and 4th decades of life and require surgical treatment. AOA diagnosis is of vital importance for radiologists, neurologists, orthopedists, and neurosurgeons.

The treatment plan included muscle relaxation with physiotherapy, correction of transverse discrepancy, resolving the upper crowding, aligning and leveling the upper canines while avoiding protrusion of the upper incisors, leveling and aligning the lower arch while avoiding protrusion of the lower incisors, leveling and aligning both arches, Spee and Wilson curve, and establishing a Class I canine relationship with normal and stable overbite and overjet. Extraction of the first upper premolar was necessary in order to align the upper canine. In the lower arch, we corrected crowding by removing the right second impacted premolars and the first left premolar. We explained to the patient that, because of bimaxillary retrusion and the significance of her open bite, she would need surgical intervention later, after her growth has finished. The risks and benefits of the treatment plan were discussed with the patient and her parents.

For correction of the transverse discrepancy, we decided to use a hybrid hyrax anchored at the level of the first premolars and first molars. Expansion began immediately with one turn per day and continued for one month. At the same time, the patient was instructed to start physiotherapy during her first week in the office and then continue at home. The patient continued to be treated with hybrid hyrax for five months. After this period, we removed the upper first premolars. We continued the premolar extraction and fixed appliance with upper and lower brackets. The treatment time for the fixed appliances was 20 months.

After treatment, the patient had a stable occlusion and acceptable overbite and overjet. Moreover, the examination of lateral cephalogram revealed correction of the atlanto-occipital fusion (Fig. 2). The correlation between upper spine and cranio-facial morphology was observed. The overbite was correlated with upper spine morphological deviations. In earlier studies, a correlation was shown between upper spine morphological deviations and

mandibular retrognathia, large inclination of the jaws and of the cranial base angle (12).

Cervical column morphology in adult patients with OSA was compared to the cervical morphology of adult patients with neutral occlusion and no history of sleep apnea. The results show that morphological deviation of upper cervical vertebrae was correlated with obstructive sleep apnea (13). The cephalometric analyses is shown in Table II.

Cephalometric analysis after the treatment showed a correction of the atlanto-occipital relation, which suggests that the original position was due to muscle contraction. Looking at the growth prediction (14), C2 was concave trapezoid, C3 was concave trapezoid, C4 was concave trapezoid. This indicates that the patient was in stage 4 according to Bacetti and her growth peak was 1 to 2 years prior to treatment. During the treatment period, she grew 5.4 mm at her anterior cranial base and her mandible grew 1.2 mm (13).

### **RESULTS**

In their study, Schiffman et al. compared four treatment strategies for TMD with and without disc displacement and limited mouth opening (15). The treatment options proposed in this study were: medical management, non-surgical rehabilitation, arthroscopic surgery, and arthroplasty. A further Schiffman's study followed his report from 2007, (16) in which the success of the treatment was evaluated using two measures. These included the Symptom Severity Index (SSI) to evaluate TMJ pain and the Craniomandibular Index (CMI) to evaluate jaw dysfunction. The International Association of Oral and Maxillofacial Surgery recommendations and treatment strategies were used for a closed lock disorder to evaluate the TMJ disc status at 24 months and the TMJ hard tissue status at 60 months post-treatment. The patients included in the study were divided into two groups and then randomly assigned into groups for four treatment strategies. The study group that demonstrated limited mouth opening for less than 6 months was defined as non-chronic and patients with limited mouth opening more than 6 months were defined as chronic (15).

The medical treatment strategy consisted of counseling and a treatment strategy: a 6-day regimen of oral methylprednisolone followed by prescription of

**Table I.** Articles included in the review

Author	Sample size	Primary outcome	Pain management	Clinical assessment	Follow-up
Schiffman et al. (2014)	106 patients	TMJ pain, limited mouth opening, disc displacement without reduction	Pharmaceutical administration, nonsurgical rehabilitation, arthroscopy surgery and arthroplasty	Mandibular range of motion, TMJ sounds, impairment of chewing	3,6,12,18,24, 60 months
Walczynska et al. (2014)	60 patients	TMJ pain, cervical spine pain, neck pain	Occlusal splint, self control parafunctional habits	Medical history and physical examination based on a survey card according to RDC/TMD	3 weeks, 3 months
Silveira et al. (2015)	40 patients	Neck pain, TMJ pain, jaw dysfunction, muscle tenderness	-	Neck disability index and the limitations of daily High level of muscle tenderness in upper trapezius and temporalis	-
Costa et al. (2015)	60 patients	Masticatory myofascial pain according to RDC/TMD, mild anxiety(25%), mild depression	Group 1 counseling(verbal and written information Group 2 counseling+ occlusal splints (only at night whilst sleeping)	Symptoms of anxiety and depression and pain catastrophizing Self reported questionnaire consisting of 9 statements related to pain	2 and 5 months
Conti et al. (2015)	60 patients	TMJ pain and disc displacement with reduction and arthralgia	Group 1-anterior reposition and occlusal splint, group 2 nociceptive Trigeminal Inhibition Clenching Suppression system devices, manufacturer is not specified, group 3 counseling for behavioral changes and self-care	Evaluated by means of visual analogue scale, pressure pain threshold of the TMJ, maximum range of motion and TMJ sounds Possible adverse effects were recorded (discomfort while using the device and occlusal changes)	2 and 6 weeks, 3 months
Calixtre et al. (2016)	12 patients	TMJ disorder, myofascial pain	Cervical mobilization and exercise on clinical signs and mandibular function	Self reported pain, jaw function according to Mandibular functional impairment Questionnaire (MFIQ), pain free maximum mouth opening and pressure pain thresholds of masseter and temporalis	3 times-twice before (baseline phase), once after intervention
Grootel et al. (2017)	72 patients	TMJ disorders, pain and restricted jaw movement, myofascial pain	Splint therapy and physiotherapy	Scoring of the intensity of predominant pain by Visual analogue scale The progress and ultimate effect of treatment –evaluated by index treatment duration control(TDC)	10-21 weeks or 12-30 weeks, 1 year follow-up
Ishiyama et al. (2017)	25 patients	Prevention of TMD pain in patients with OSA treated with oral appliance	jaw opening exercise	Two weeks before insertion of the appliance OA and two weeks after using VAS in the morning and daytime	2 weeks, 1, 3 month

non-steroidal anti-inflammatory drugs for up to 6 weeks (ibuprofen 800 mg, 3 per day) and a muscle relaxant, typically cyclobenzaprine 10 mg, at bedtime. The rehabilitation strategy included medical management, cognitive behavioral therapy, physical therapy with mobilization of the joint, and a flat splint for 6 months. Arthroscopy was performed using Moses and Poker method (17) of an injection in the superior joint space of bupivacaine and Ringer's lactate solution. A blunt trocar was used to remove all adhesions in the intracapsular space. Arthroplasty was performed using open joint surgery to remove the disc. All patients were followed-up once a month for 6 months.

The success rate was considered as corresponding to patient concerns, and was as follows: 87% had an improvement in their ability to eat most foods, 77% had an improvement in their ability to open their mouth more than 35 mm, and 54% had pain decreased. Joint noises changed little over time.

All the patients were investigated by MRI; in each case, disc displacement without reduction was confirmed. Changes in disc displacement were measured only at the 24-month follow-up visit. The results were:

out of 25 patients in medical management, only 3 showed disc changes. One patient's disc had normal

positioning and two patients were diagnosed with disc displacement with reduction;

out of 20 patients in rehabilitation, only 3 showed disc displacement with reduction;

out of 32 patients who underwent joint arthroscopy, two patients had non-reducing disc which were reported to have normal positioning and five patients had disc displacement with reduction.

In Walczynska-Dragon's study, they suggested a correlation between TMD, cervical spine pain, and mobility (18). The study included 30 patients with TMD, cervical spine pain, and limited cervical range of movements. Patients were included in the study if they had pain in the area between occiput and C7 for at least 12 months (18).

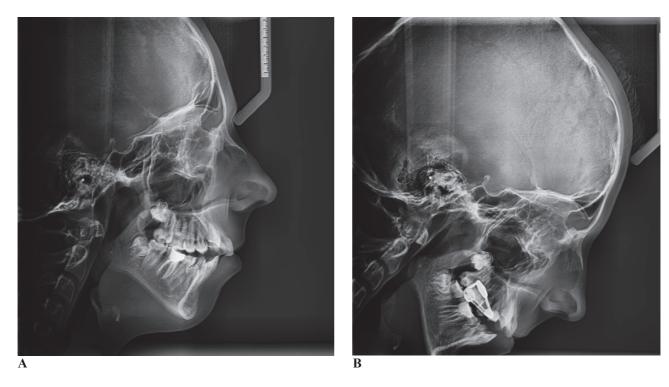
The examination protocol included:

- medical history and physical examination based on RDC/TMD;
- VAS scale for pain diagnosis;
- TMJ evaluation;
- Cervical spine motion and muscle palpation.

The treatment was performed with an anterior splint SVED (Sagittal Vertical Extrusion Device) to decrease muscle activity. The splint was worn for 8 to 10 hours a day during sleep. After 3 months of therapy, TMJ function improved considerably. Cervical pain

Table II. Cephalometric analysis

	Initial	Final
Anterior cranial base SN	58.6mm	64 mm
Mandibular length Go-Me	57.8mm	59 mm
SNA	76	76
SNB	68.5	70
ANB	7.6	5.9
IMPA	89.6	90.4
Upper incisors-SN	112	112
Ramus Height Ar-Go	36.1 mm	43
Posterior cranial base S-AR	27.5 mm	32



**Fig. 1.** Lateral cephalometric in normal position (A); Lateral cephalometric in flexion position with C1 in contact with occipital bone (B).

diminished after 3 weeks and only 8% of patients reported pain at 3 months.

Silveira's study revealed that TMD pathologies are often associated with neck disability in patients with and without chronic TMD (19). High levels of muscle tenderness were found in the upper trapeziums and temporalis. Patients also presented with high levels of jaw and neck dysfunction. This study showed that higher the tenderness in the muscle, the higher the level of jaw and neck disability.

Costa et al. demonstrated that an occlusal splint could provide an improvement in temporomandibular disorder subjects (20). Sixty patients with masticatory myofascial pain were divided into two groups; one received counseling while the other group received occlusal splints and counseling. The occlusal surface of the splint was flat, 2.5-mm thick in the posterior region, and was worn with anterior guidance for a 5-month period. The patients were instructed to wear their splint only at night, whilst sleeping. The patients were evaluated for symptoms of anxiety, depression and pain catastrophizing using nine statements related to pain

perception. The inclusion criteria were myofascial pain according to RDC/TMD with pain duration of at least 3 months. Exclusion criteria were occlusal risk factors for TMD, vascular disorders, trauma, and medication (anticonvulsants, muscle relaxant, antidepressants). The conclusions suggested that minimally invasive strategies could provide improvement and occlusal splint could add a plus value.

Conti et al. assessed the benefit of using intraoral devices in patients with disc displacement with reduction (DDWR) and arthralgia (21). Sixty patients with arthralgia were divided randomly into 3 groups. Inclusion criteria were patients with pain in the preauricular region for at least 30 days which increased during mastication and talking, and who also had disc displacement with reduction (II a) and arthralgia (IIIa.) Exclusion criteria were trauma, systemic diseases, disc displacement without reduction, dental pain, patients with full or partial dentures, and a history of TMJ surgery. They found that anterior repositioning appliances provided a significant effect in ameliorating pain at the TMJ

level and that joint sound decreased in frequency. The exact position of the disc was not recorded because no MRI imaging was used. The degree of protrusion was when joint clicking was eliminated, and splint was worn only at nighttime. The Nociceptive Trigeminal Inhibition Clenching Suppression System (NTI-tss) was also used. In this group, pain was reduced, but the TMJ sound increased.

According to the results of Calixtre et al., treatment of temporomandibular disorders with cervical spine joint mobilization and segmental stabilization decreased muscular pain and improved TMJ function (22). The interrelation between TMJ and cervical spine can be better understood by the neuroanatomical convergence of nociceptive neurons that received trigeminal and neck sensory inputs. There is a strong association between neck disability and TMD. The same study showed that sternocleidomastoid and anterior scalene muscles were increased. This study continued over 9 weeks. Patients had a primary diagnosis of myofascial pain with or without limited mouth opening. The distance between upper-lower central incisors was measured at the limit of pain-free mouth opening. The patients were also assessed for joint clicking. Exclusion criteria included arthritis without myofascial pain, trauma, systemic disease, and a history of any form of treatment. Patients had



**Fig. 2.** Final lateral cephalometric in normal position with correction of C1 fusion.

moderate or severe symptoms of TMD, according to Fonseca Anamnestic Index. Physiotherapy techniques involving manual therapy, active and passive stretching, strengthening of the involved muscles, and postural exercises were used for treatment (22). The protocol reported by La Touche was used, including 10 sessions of approximately 35 min each: 20 minof manual therapy, 10 min of muscle conditioning exercises, and 5 min of stretching (23).

Van Grootel compared the outcome of physiotherapy *versus* splint therapy using Treatment Duration Control (TDC) index for enabling a randomize clinical trial (RCT) (24). This study evaluated the number of visits and length of treatment needed to determine whether treatment was successful. A total of 72 patients were selected. They had solely myogenous TMD and were randomly divided into two groups, physiotherapy and splint therapy. Exclusion criteria were disc displacement, arthralgia, arthritis, arthrosis, or those who had undergone previous treatment with occlusal splint or occlusal adjustment.

Clinical and experimental studies of Solow showed that there was a possible role of occlusal interference in myogenous TMD (24). Patients with occlusal interference on the nonactive side which did not have contact with the active side and patients with forward sliding of at least 2 mm and lateral shift of at least 1 mm from centric occlusion were excluded from this study to reduce the influence of confounding factors. The patients were randomly assigned to two different therapy groups: the experimental group received physiotherapy of the masticatory system and occlusal therapy while the control group treatment was splint wear. The splint used in this study was the Michigan type and was used on the upper jaw, only at nighttime, with small adjustments. The patients were examined every 6 weeks. When the symptoms decreased, the splint was gradually withdrawn; during the first week, patients wore the splint for six nights, and only five nights in the second week (24). Physiotherapy used in this study involved learning techniques to avoid stress related to pain from the masticatory system, and relieving this pain with self-massage and relaxation. Recommended exercises included neck, head, shoulders, and tongue postures, controlling rotation and translation while opening the jaw, the

Jacobson method of relaxation, stretching the muscles that close the jaw, and resisting the urge to open the jaw. Techniques to reduce habits such as lip biting, clenching or grinding, and unilateral chewing were introduced. For 3 weeks, every 2 to 3 days, patients who were in the physiotherapy group participated in a program with a personal instructor and were then instructed to continue exercises at home for 6 weeks. Physiotherapy and occlusal therapy registered the same success rate and overall success rate of stepped care. There was no relationship of dependence between therapy sequences.

In their study, Ishiyama and coll. included how jaw-opening exercises affected prevention of TMD in patients with sleep apnea who wore an oral appliance (25). A number of 25 OSA (obstructive sleep apnea) patients were consecutively enrolled into a two-arm, randomized, double-blinded, placebo-controlled trial. They concluded that this exercise prior to OSA therapy reduced the risk of TMD pain in patients who were prescribed oral appliances.

### **DISCUSSION**

Although growth modification has been considered important from the beginning of orthodontics, the concepts underlying its use and the views of its clinical usefulness have varied greatly over time. To orthodontists in the late 19th and early 20th centuries, growth modification was easy because it was assumed that growth was largely controlled by environmental factors and was judged as successful because the dental occlusion improved. By midcentury, cephalometrics had shown that most of the changes produced by the treatment methods of that time were tooth movement, not modified growth.

Splint and physical therapy proved to be effective in treatment of TMD associated with pain. Permanent posterior rotation of the cranium or atlas occipital fusion could impede mandibular growth and a correct position of the maxilla. A more accurate diagnosis should be performed when AOA is suspected as it could just be a muscular problem that needs to be treated with physiotherapy and occlusal splint. An adaptive head position can be a factor in altering the direction of facial growth. Determination of head position

and mandible growth direction can be important indicators in patients with TMD treatment (26). The results may prove valuable for planning the treatment of children with Class II, during their growth period. The morphology of the upper spine was correlated with craniofacial morphology, maxillary transverse deficit, open bite, and cervical neck dysfunction.

Maxillary deficit and oral breathing can cause muscle contraction, TMJ instability, and cervical spine dysfunction. Treatment of maxillary transverse deficit should be started as early as possible together with kinetotherapy of the neck and TMJ which will have more significant improvement on growth. From a clinical point of view, orthodontists should recognize that the expected effects of joint stability on maxillary growth might differ between patients with short- and long-face. The greater counter-clockwise rotation of the maxilla would induce mandibular clockwise rotation and a subsequent increment of anterior facial height. There is no doubt that within certain limits, at least in the short term, some modification of growth of the different components of the midface can be obtained with intermaxillary traction. Furthermore, it is necessary to understand the crosslink with other oral or metabolic alterations before providing orthodontic treatment (27-34), according to the evidence based dentistry (35-43). In some cases, this may be sufficient to avoid orthognathic surgery, or at least reduce the severity of the surgical correction needed after completion of growth. Individual variations in treatment outcomes, however, are high. For all types of growth modification, and to prevent TMD/TMJ, specific clinical frameworks are needed to predict the outcome and to define guidelines and indications for an orthopedic approach.

# REFERENCES

- Dohan Ehrenfest DM, Del Corso M, Inchingolo F, Charrier JB. Selecting a relevant in vitro cell model for testing and comparing the effects of a Choukroun's platelet-rich fibrin (PRF) membrane and a platelet-rich plasma (PRP) gel: tricks and traps. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010; 110(4):409-11; author reply 411-3. doi: 10.1016/j.tripleo.2010.05.056.
- 2. Dohan Ehrenfest DM, Del Corso M, Inchingolo F,

- Sammartino G, Charrier JB. Platelet-rich plasma (PRP) and platelet-rich fibrin (PRF) in human cell cultures: growth factor release and contradictory results. Oral Surg Oral Med Oral Pathol Oral Radiol Endod.2010; 110(4):418-21; author reply 421-2. doi: 10.1016/j.tripleo.2010.05.059.
- Schiffman E, Ohrbach R, Truelove E, et al. Diagnostic Criteria for Temporomandibular Disorders (DC/ TMD) for Clinical and Research Applications: recommendations of the International RDC/TMD Consortium Network and Orofacial Pain Special Interest Group. J Oral Facial Pain Headache 2014; 28: 6-27.
- Ikeda K, Kawamura A, Ikeda R. Prevalence of disc displacement of various severities among young preorthodontic population: A magnetic resonance imaging study. J Prosthodont 2014; 35:397-401.
- Akers J, Aguiar-Ibáñez R, Sari AB, et al. Systematic reviews: CRD's guidance for undertaking reviews in healthcare. 3<sup>rd</sup> ed. York, UK: York Publishing Services Ltd; 2009.
- 6. Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0: updated March 2011.
- Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and metaanalysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015; 4:1.
- 8. Koç A, Karabıyık Ö, Tursem T, et al. Demonstration of craniocervical junction abnormalities for diagnosis of atlanto-occipital assimilation using MRI. Anatomy 2012; 7:76-82.
- Iizuka H, Sorimachi Y, Ara T, et al. Relationship between the morphology of the atlanto-occipital joint and the radiographic results in patients with atlantoaxial subluxation due to rheumatoid arthritis. Eur Spine J 2008; 17:826-30.
- Eunhye O, Sug-Joon A, Sonnesen L. Ethnic differences in craniofacial and upper spine morphology in children with skeletal Class II malocclusion. Angle Orthod 2018; 88:283-91.
- 11. Sonnesen L, Petri N, Kjaer I, et al. Cervical column morphology in adult patients with obstructive sleep apnoea. Eur J Orthod 2018; 30:521-36.
- 12. Arntsen T, Sonnesen L. Cervical vertebral column morphology related to craniofacial morphology and head posture in preorthodontic children with Class II

- malocclusion and horizontal maxillary overjet. Am J Orthod Dentofacial Orthop 2011; 140:e1-7.
- Cantore S, Ballini A, Farronato D, et al. Evaluation of an oral appliance in patients with mild to moderate obstructive sleep apnea syndrome intolerant to continuous positive airway pressure use: Preliminary results. Int J Immunopathol Pharmacol 2016; 29:267-73.
- Ballini A, Santacroce L, Cantore S, Saini R, Mastrangelo F, Desiate A, Scacco S. Orthodontic forces modulate insulin-like growth factor binding protein-5 changes in gingival crevicular fluid. J Biol Regul Homeost Agents 2016; 30:1235-40
- Schiffman EL, Velly AM, Look JO, et al. Effects of four treatment strategies for temporomandibular joint closed lock. Int J Oral Maxillofac Surg 2014; 43:217226.
- Schiffman EL, Look JO, Hodges JS, et al. Randomized effectiveness study of four therapeutic strategies for TMJ closed lock. J Dent Res 2007; 86:58-63.
- 17. Moses JJ. Poker ID. Temporomandibular joint arthroscopy: the endaural approach. Int J Oral Maxillofac Surg 1989; 18:347-51.
- Walczyńska-Dragon K, Baron S, Nitecka-Buchta A et al. Correlation between TMD and cervical spine pain and mobility: is the whole body balance TMJ related? Biomed Res Int 2014:582414.
- Silveira A, Gadotti IC, Armijo-Olivo S, et al. Jaw dysfunction is associated with neck disability and muscle tenderness in subjects with and without chronic temporomandibular disorders. Biomed Res Int 2015; 512792. doi: 10.1155/2015/512792
- Costa YM, Porporatti AL, Stuginski-Barbosa J, et al. Additional effect of occlusal splints on the improvement of psychological aspects in temporomandibular disorder subjects: A randomized controlled trial. Arch Oral Biol 2015; 60:738-44.
- 21. Conti PC, Corrêa ASDM, Lauris JRP, et al. Management of painful temporomandibular joint clicking with different intraoral devices and counseling: a controlled study. J Appl Oral Sci 2015; 23:529-35.
- 22. Calixtre LB, Grüninger BLDS, Haik MN, et al. Effects of cervical mobilization and exercise on pain, movement and function in subjects with temporomandibular disorders: a single group pre-post test. J Appl Oral Sci 2016; 24:188-97.
- 23. Van Grootel, RJ, Buchner R, Wismeijer D, et al.

Towards an optimal therapy strategy for myogenous TMD, physiotherapy compared with occlusal splint therapy in an RCT with therapy-and-patient-specific treatment durations. BMC Musculoskelet Disord 2017; 18:76.

- 24. Solow RA. The dental literature on occlusion and myogenous orofacial pain: Application of critical thinking. Cranio 2016; 34:323-31.
- 25. Ishiyama H, Inukai S, Nishiyama A, et al. Effect of jawopening exercise on prevention of temporomandibular disorders pain associated with oral appliance therapy in obstructive sleep apnea patients: A randomized, double-blind, placebo-controlled trial. J Prosthodont Res 2017; 61:259-67.
- Dubojska A, Smiech-Slomkowska G. Natural head position and growth of the facial part of the skull. Cranio 2013; 31:109-17.
- 27. Ballini A, Cantore S, Farronato D, et al. Periodontal disease and bone pathogenesis: the crosstalk between cytokines and porphyromonas gingivalis. J Biol Regul Homeost Agents 2015; 29:273-81.
- Grassi FR, Ciccolella F, D'Apolito G, et al. Effect of low-level laser irradiation on osteoblast proliferation and bone formation. J Biol Regul Homeost Agents 2011; 25:603-14.
- Ballini A, Tetè S, Scattarella A, et al. The role of anti-cyclic citrullinated peptide antibody in periodontal disease. Int J Immunopathol Pharmacol 2010; 23: 677-81.
- 30. Scattarella A, Ballini A, Grassi FR, et al. Treatment of oroantral fistula with autologous bone graft and application of a non-reabsorbable membrane. Int J Med Sci 2010; 7:267-71.
- 31. Foti C, Romita P, Rigano L, et al. Isobornyl acrylate: an impurity in alkyl glucosides. Cutan Ocul Toxicol 2016; 35:115-19
- 32. Grassi FR, Pappalettere C, Di Comite M, et al. Effect of different irrigating solutions and endodontic sealers on bond strength of the dentin-post interface with and without defects. Int J Med Sci 2012; 9:642-54.
- 33. Cicinelli E, Ballini A, Marinaccio M, Poliseno A, Coscia MF, Monno R, De Vito D. Microbiological findings in endometrial specimen: our experience. Arch Gynecol Obstet 2012; 285:1325-29.
- 34. Scattarella A, Ballini A, Grassi FR, et al. Treatment

- of oroantral fistula with autologous bone graft and application of a non-reabsorbable membrane. Int J Med Sci 2010; 7:267-71.
- 35. Ballini A, Capodiferro S, Toia M, Cantore S, Favia G, De Frenza G, Grassi FR. Evidence-based dentistry: what's new? Int J Med Sci 2007 6; 4:174-8.
- 36. Ballini A, Santacroce L, Cantore S, et al. Probiotics efficacy on oxidative stress values in inflammatory bowel disease: a randomized double-blinded placebocontrolled pilot study. Endocr Metab Immune Disord Drug Targets 2019; 19:373-81.
- 37. Inchingolo F, Dipalma G, Cirulli N, et al. Microbiological results of improvement in periodontal condition by administration of oral probiotics. J Biol Regul Homeost Agents 2018; 32:1323-28.
- 38. Cantore S, Ballini A, Mori G, et al. Anti-plaque and antimicrobial efficiency of different oral rinses in a 3-day plaque accumulation model. J Biol Regul Homeost Agents 2016; 30:1173-78.
- Di Comite M, Crincoli V, Fatone L, et al. Quantitative analysis of defects at the dentin-post space in endodontically treated teeth. Materials 2015; 8: 3268-3283.
- Ballini A, Scacco S, Coletti D, Pluchino S, Tatullo M. Mesenchymal stem cells as promoters, enhancers, and playmakers of the translational regenerative medicine. Stem Cells Int 2017; 2017: 3292810. doi: 10.1155/2018/6927401
- 41. Inchingolo F, Martelli FS, Gargiulo Isacco C, et al. Chronic periodontitis and immunity, towards the implementation of a personalized medicine: a translational research on gene single nucleotide polymorphisms (SNPs) linked to chronic oral dysbiosis in 96 Caucasian patients. Biomedicines 2020; 8: E115.
- 42. Pettini F, Savino M, Corsalini M, Cantore S, Ballini A. Cytogenetic genotoxic investigation in peripheral blood lymphocytes of subjects with dental composite restorative filling materials. J Biol Regul Homeost Agents 2015; 29: 229-33.
- Ballini A, Cantore S, Altini C, et al. 99mTcdiphosphonates bone scintigraphy for vitality evaluation in cleft palate. Eur Rev Med Pharmacol Sci 2018; 22:8497-501.