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Quantitative Analysis for Effect of Orthodontic Treatment on Body Posture and Its Correlation With Cervical Posture in Skeletal Class II Malocclusion – A Clinical Study

Priyanka Venkatasubramanian[1], Ratna Parameswaran[2], Devaki Vijayalakshmi[3]

[1]Postgraduate, [2]Professor, [3]Professor and Head, Department of Orthodontics and Dentofacial Orthopaedics, Meenakshi Ammal Dental College and Hospital, Meenakshi Academy of Higher Education & Research, Maduravoyal, Chennai.

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ABSTRACT

AIM: To quantitatively evaluate and compare the body posture and its correlation with cervical posture and plantar pressure in subjects with skeletal class II malocclusion, before and after camouflage orthodontic treatment.

MATERIALS AND METHODS: 18 subjects were considered for the study and subjected to lateral cephalograms and body posture analysis before and after camouflage orthodontic treatment. Cranio-cervical angles were compared before and after treatment using paired T test. A force platform was designed to accommodate the feet with pressure sensors placed at hallux, first metatarsal and medial calcaneus regions to record the loading pressure. The plantar pressure distribution values were correlated with the cranio-cervical angles.

RESULTS: There is statistically significant difference (p value <0.05) in the ANB angle, GoGn/OPT angle between pre and post camouflage orthodontic therapy indicating over extension of the head over the spinal column. Post treatment Pearson correlation coefficient indicates that the cervical curvature (OPT/CVT angle) has a negative correlation with the plantar pressure at medial calcaneus region. However, high statistical significance was found in the plantar pressure distribution before and after orthodontic treatment at all three regions.

CONCLUSION: Cervical curvature increased after camouflage orthodontic therapy, indicating over extension of the cervical spine. Plantar pressure reduced in the hallux, first metatarsal and medial calcaneus regions. The recorded value at the hallux region elicited considerable reduction indicating a shift in the plantar pressure from the most anterior region to the central region.

KEYWORDS: Posture; Orthodontic Treatment; Plantar pressure; Occlusion.

Address for Correspondence

Priyanka Venkatasubramanian
Postgraduate Student,
Department of Orthodontics and Dentofacial Orthopaedics,
Meenakshi Ammal Dental College and Hospital, MAHER
Meenakshi Academy of Higher Education & Research.

INTRODUCTION

The stomatognathic system consists of a complex cybernetic regulatory circuit that interconnects with the other systems.[1] Anatomical variations in the interconnection can alter the development of distinct structures resulting in postural changes and thereby the malocclusions.[2]

Posture is referred to as the position of the human body and its orientation in space. Activation of the muscles controlled by the central nervous system causes postural adjustments.[3] Evidences suggest that the dental occlusion and trigeminal nerve afferents are the key components in influencing the body posture and spinal curvature.[4] when the body maintains the alignment of its segments with minimum effort then it is in good posture.[5] Visual plane, dental occlusal plane and auricular-nasal plane determine the head position. These planes maintain a parallel horizontal pattern to ensure the cranial posture through the mechanoreceptors of the cervical spine.[6]

There are variations in flexion of head in relation to cervical column between skeletal Class II and Class III individuals.[7] This was proved by Solow and Tallgren in 1976. Studies claim that mandibular position influences the hyoid bone, thereby resulting in postural changes in the antero-posterior direction.[3,8] Deficiency of mandible results in inferior positioning of the C1, lack of upright head posture with inward curvature of the lower spine (lordosis). Whereas, angle`s class III individuals with increased mandible length have a superior position of C1 with kyphosis.[9] According to the soft tissue hypothesis given by Solow and Kreinborg [10] in 1977, the muscle pull is the causative agent for the restricted growth of the mandible in case of skeletal class II.

During an individual`s development, at the mixed dentition stage, occlusal development can impact the postural changes. [11] Possibilities that occlusal corrections can correct the postural dysfunctions have been gaining popularity as it outspreads an orthodontist's spectrum of intervention. Along with the overall physiological, functional, and psychological considerations, the cranio-cervical, cranio-facial and postural parameters should be incorporated into the orthodontic diagnosis.

In edentulous patients the transient change of cerival posture often reverts back after denture palcament. [12] Therefore, establishing the accurate vertical dimension in edentulous patients and occlusal height in the dentate patients through the process of orthodontic treatment can alter the cervical and body posture.[13] Occlusion and dentoalveolar height are two important parameters that correlate with cranio-vertical angulation due to the change in vertical jaw dimensions.[14]

Plantar pressure is the distribution of force over the sole of foot. Dental occlusion is the prime and utmost factor influencing the plantar pressure. Maximum mouth opening, maximum intercuspation, the jaw relationship alters the plantar pressure value due to the inter-relation and connection between the neuromuscular components.

Hence, this study is designed to highlight the cervical and body posture changes following conventional fixed orthodontic appliance using plantar pressure. The aim of the study was to quantitatively evaluate and compare the body posture analysis done using plantar pressure and its correlation with cervical spine posture in subjects with skeletal class II malocclusions before and after camouflage orthodontic treatment. The null hypothesis states that there exists no correlation between the cervical posture and body posture before, as well as after camouflage orthodontic therapy.

MATERIALS AND METHODS

The study was approved by the institutional review board (MADC/IRB-XXIII/2018/374). The sample size was evaluated using Sampling software G power version 3.1.9.2. Effect size (Cohen d) was calculated from the parent article and subsequently, sample size was evaluated as 20 with an alpha error of 10% and power of 90%.[15]

Cross sectional study was conducted for individuals above 18 years of age at the department of orthodontics, Meenakshi ammal dental college and hospital, Chennai for a duration of 18 months. Individuals requiring camouflage orthodontic treatment for skeletal class II correction were considered for the study after their consent. History of orthodontic, orthopedic, or orthognathic surgical treatment, TMJ disorder, bruxism, nasal obstruction, spinal problem, craniofacial disorders, syndromes affecting gait and posture candidates were excluded from the study. Extensively filled tooth or missing tooth, mutilated occlusion if present, were not included. Pregnant women were also excluded from the study.

METHOD OF STUDY:

Patients with skeletal class II (because of prognathic maxilla/ retrognathic mandible/ combination of both) who underwent orthodontic treatment were subjected for body posture analysis using plantar pressure. Lateral cephalograms of the participants were taken for the spinal posture evaluation. Pre- and post-treatment frontal and profile full-length photographs were captured to assess the change in the posture, shoulder tilt and pelvic tilt.

CERVICAL SPINE POSTURE EVALUATION:

Individuals were exposed to lateral cephalograms prior to (T0) and after (T1) orthodontic treatment. The x-rays were taken by the same technician with patients subjected to the natural head position, Frankfort horizontal plane parallel to the floor, jaws positioned in centric occlusion, hands freely hanging on the sides and eyes open. (Fig 1)

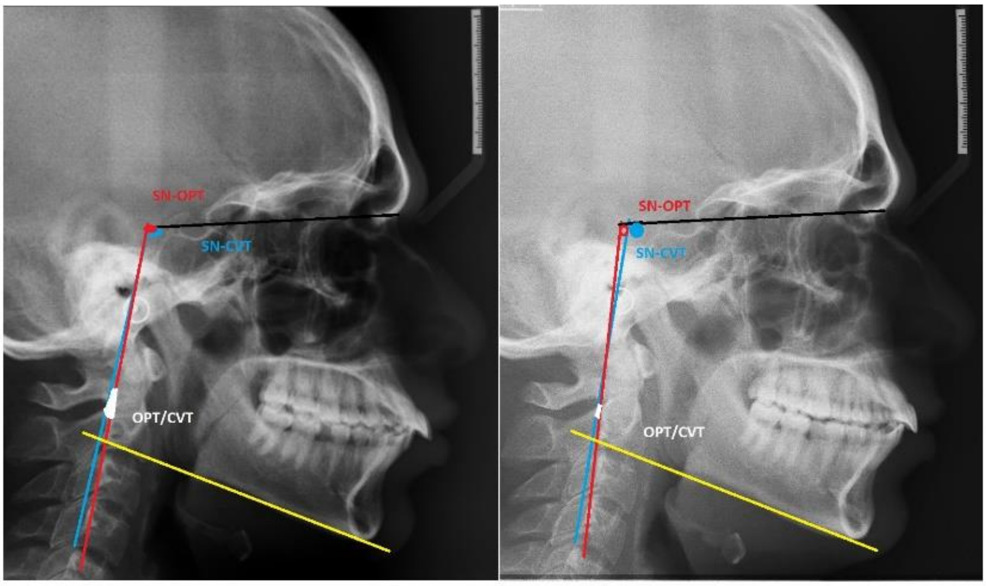

Fig 1: Pre and Post-Treatment Cephalometric Analysis

The parameters that were taken into consideration:

S.NO	PARAMETER	LANDMARK
1	SNA	Angle between anterior cranial base and maxilla
2	SNB	Angle between anterior cranial base and mandible
3	ANB	Angle between maxilla-mandibular complex
4	SN/GoGn	Angle between anterior cranial base and mandibular plane
5	SN/OPT	Angle between anterior cranial base and odontoid process tangent (posterior tangent to odontoid process through cv2ip)
6	ANS-PNS/OPT	Angle between palatal plane and odontoid process tangent
7	Go-Gn/OPT	Angle between mandibular plane and odontoid process tangent
8	SN/CVT	Angle between anterior cranial base and cervical vertebrae tangent (posterior tangent to odontoid process passing through cv4ip)
9	ANS-PNS/CVT	Angle between palatal plane and cervical vertebrae tangent
10	Go-Gn/CVT	Angle between mandibular plane and cervical vertebrae tangent
11	OPT/CVT	Angle between odontoid process tangent and cervical vertebrae tangent.
12	CVT/Hor	Angle between CVT and true horizontal
13	OPT/Hor	Angle between OPT and true horizontal

Five lateral cephalograms were chosen at random from pre-treatment and post treatment groups respectively and were retraced to validate the intra-observer reliability.

BODY POSTURE ANALYSIS

The individuals were subjected to body posture analysis before (T0) and after (T1) orthodontic treatment. The orthodontic treatment comprised of camouflage technique using MBT bracket system involving asymmetrical premolar extraction, all 1st premolar extraction, all 2nd premolar extraction, single incisor extraction to mask the skeletal class II relationship.

Prior to orthodontic bracket bonding, the individual`s body posture analysis was evaluated, and the values were recorded. The orthodontic treatment duration lasted for an average of 15±2 months including levelling and aligning, space closure (if required) and orthodontic settling phase. Ideal overbite, overjet, class I canine relation and acceptable cusp-to-fossa molar relation were achieved at the end of treatment, followed by debonding of the orthodontic appliance. Retainers were provided to the individuals immediately after debonding for retention and stability of the treatment results. Post-treatment postural evaluation was recorded 3 – 4 days after debonding, during which initial post orthodontic settling of occlusion was expected to occur

A force platform, known as the Quanpressurometer (Patency no: A61B 5/00) was devised to quantify static posture (Fig 2a). It had an outline of the right and left feet corresponding to shoe size between 5 – 9 (UK standards), at an angulation of 30 degrees to the midline with pressure sensors at 3 regions – Medial calcaneus (P1; RP1 – right medial calcaneus; LP1 – Left medial calcaneus), first metatarsal (P2; RP2 – Right first metatarsal; LP2 – left first metatarsal) and hallux (P3; RP3 – Right hallux ; LP3 – Left hallux) (Fig 2b). The strain gauge was configured to connect the sensors and adapted to record strain at each of the pressure sensors.

Fig 2a

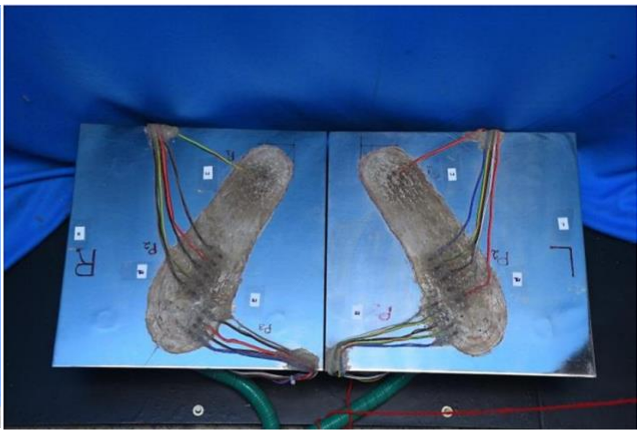

Fig 2b

Fig 2 a: Quanpressurometer; Fig 2b – Force platform with sensors

Two vertical rods comprised of plurality of multiple level holes were fixed to the force platform's both ends and the horizontal rod comprised of plurality of multiple level holes was fixed to top end of the vertical rods to which threads were inserted through the holes of the rods thereby forming a grid with the rods and said platforms for evaluation of inclination of vertebrae with respect to midline of body, pelvic and shoulder tilts. Individuals were instructed to stand on the platform with feet position corresponding to their shoe size. For standardisation, individual`s placement on the force platform was restricted to natural head position, mandibular rest position with eyes open, hands on the sides (Fig 3). Recordings were noted, photographs were taken both in frontal and profile view to compare the shoulder tilt, pelvic tilt, and cervical spine posture.

Fig 3 – Body posture analysis – Patient position

The patients were requested to stand on the force platform twice within a duration of 2 minutes to record the average between the 2 sets of strain values for all 3 regions. The average value was considered as the final data.

INTRA-ORAL EXAMINATION:

Pre-treatment and post treatment intra-oral molar relationships, interdigitations - settling patterns were noted and captured (Fig 4)

Fig 4: Pre-treatment and Post-treatment Intra Oral Photographs

PHOTOGRAPHIC ASSESSMENT

Patients were asked to stand in natural head posture with Frankfort horizontal plane parallel to the floor, hands freely hanging on the sides. Both frontal and lateral full-length photographs were captured (Fig 5) using canon EOS 50D with a 100mm f2.8macro USM lens and canon MR14 EX macro ring flash assembly.

Fig 5: Full length profile and frontal photographs to assess the change in posture, pelvic tilt and shoulder tilt

STATISTICAL ANALYSIS

Statistical analysis was carried out using SPSS Version 20 software (IBM) to analyse the data. Sample size was calculated in accordance with the parent article and estimated to be 20 to attain 90% power of the study. Five pre-treatment and post-treatment lateral cephalograms were randomly chosen to retrace and the interclass correlation coefficient was calculated. To elucidate the difference between the pre-treatment and post treatment cephalometric values, body posture analysis, paired "t" test was used. Further to identify the correlation between the cephalometric and the body posture analysis, Pearson correlation coefficient was performed. P values <0.05 was considered statistically significant.

RESULTS

The study included 20 patients, out of which 2 discontinued orthodontic treatment. Hence, results were calculated for 18 participants. A high interclass correlation coefficient (ICC) score was calculated indicating excellent agreement (0.91) between the initial and retraced cephalometric readings. On the cephalometric comparison between the pre and post orthodontic camouflage treatment (intra group analysis), paired "t" test revealed that ANB angle ($p = 0.003$) and GoGn/OPT angle ($p = 0.043$) were statistically significant (Table 1). An average of 5.7° increase in the GoGn/OPT angle was observed in the post treatment group. Also, SN/GoGn, cranio-cervical angles - SN/OPT, SN/CVT, PP/CVT, GoGn/CVT, OPT/CVT increased after orthodontic treatment, but were not statistically significant. The orthodontic treatment resulted in a decrease in ANB angle by 1°, SNA angle by 1.2°, SNB angle by 0.2°. PP/OPT angle had a non-statistically significant increase by 1.05°, CVT/HOR and OPT/HOR by 1.9° and 1.2° respectively.

TABLE 1: PAIRED SAMPLES TEST (T0-T1) FOR CRANIO-CERVIAL ANGLES AND BODY POSTURE (PAIRED "T" TEST)

	Mean	Std. Deviation	Sig. (2-tailed)
Pre - SNA – Post - SNA	1.27778	2.67462	.059
Pre -SNB – Post -SNB	.27778	2.10896	.584
Pre - ANB – Post -ANB	1.11111	1.36722	.003*
Pre - SN/GoGn – Post - SN/GoGn	-.27778	3.86242	.764
Pre - SN/OPT – Post - SN/OPT	-1.11111	5.38941	.394
Pre - PP/OPT – Post - PP/OPT	1.05556	11.81959	.709
Pre - GoGn/OPT – Post - GoGn/OPT	-5.77778	11.22788	.043*
Pre - SN/CVT – Post - SN/CVT	-.38889	11.34040	.886
Pre - PP/CVT – Post - PP/CVT	-.22222	5.07074	.855
Pre - GoGn/CVT-Post - GoGn/CVT	-2.05556	9.16818	.355
Pre - OPT/CVT – Post - OPT/CVT	-.55556	1.68810	.181
Pre - CVT/Hor – Post - CVT/Hor	1.88889	7.25898	.285
Pre - OPT/Hor – Post - OPT/Hor	1.11111	7.72992	.550

The data collected concluded that plantar pressure is higher at P2 than compared to P3 and P1 for both right and left feet. Similar result was observed in the T1 group (Table 2).

TABLE 2: MEAN VALUE OF BODY POSTURE BEFORE AND AFTER ORTHODONTIC TREATMENT

		Mean	Std. Deviation
Pair 1	PreRP1	.1067	.03850
	PostRP1	.0389	.02763
Pair 2	PreRP2	.3067	.11098
	PostRP2	.1583	.03944
Pair 3	PreRP3	.2533	.07934
	PostRP3	.1028	.03250
Pair 4	PreLP1	.1206	.05428
	PostLP1	.0233	.02086
Pair 5	PreLP2	.3011	.06842
	PostLP2	.1561	.05326
Pair 6	PreLP3	.2322	.05117
	PostLP3	.1089	.03479

However, the mean difference indicates that the camouflage orthodontic treatment resulted in significant change at the hallux region of the right foot and first metatarsal region of the left foot (Table 3). There was high statistical significance between T0 and T1 recorded at the 3 pressure loading areas of both feet (p=0.00).

TABLE 3: PAIRED "t" TEST FOR BODY POSTURE – BEFORE AND AFTER ORTHODONTIC TREATMENT (T0-T1)

		Mean Difference	Std. Deviation	Sig
Pair 1	Pre RP1 – Post RP1	.06778	.04479	.000
Pair 2	Pre RP2 – Post RP2	.14833	.13479	.000
Pair 3	Pre RP3 – Post RP3	.15056	.09932	.000
Pair 4	Pre LP1 – Post LP1	.09722	.05644	.000
Pair 5	Pre LP2 – Post LP2	.14500	.08939	.000
Pair 6	Pre LP3 – Post LP3	.12333	.06231	.000

Figure 6 explains the Pearson correlation between the cranio-cervical angles and body posture analysis at T0. A negative correlation between ANB angle and P3 value, SN/CVT angle and P1 value was evident, but not statistically significant.

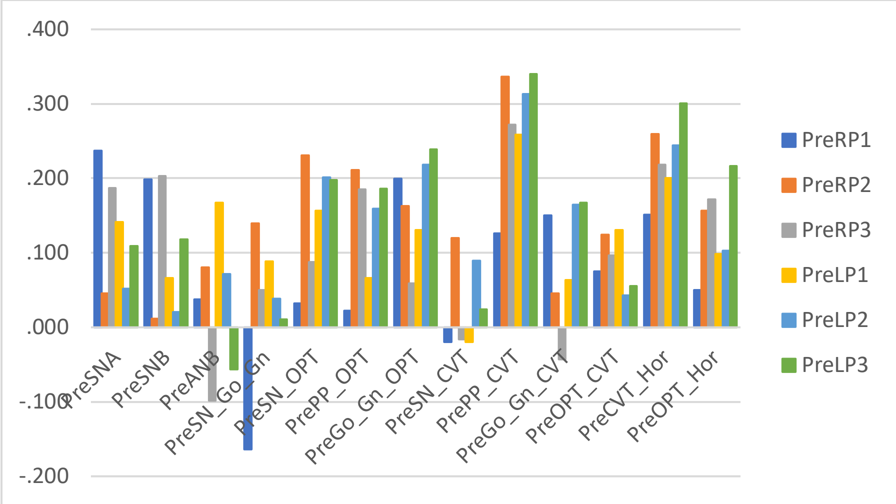

Fig 6: Pearson correlation between pre-treatment cephalometric values and pre-treatment force platform values.

For the T1 group, cranio-cervical angles and body posture values were correlated and tabulated (Figure 7). It suggested that a highly statistically significant negative correlation exists between OPT/CVT and RP3 values and statistically significant negative correlation ANB angle and LP3 values.

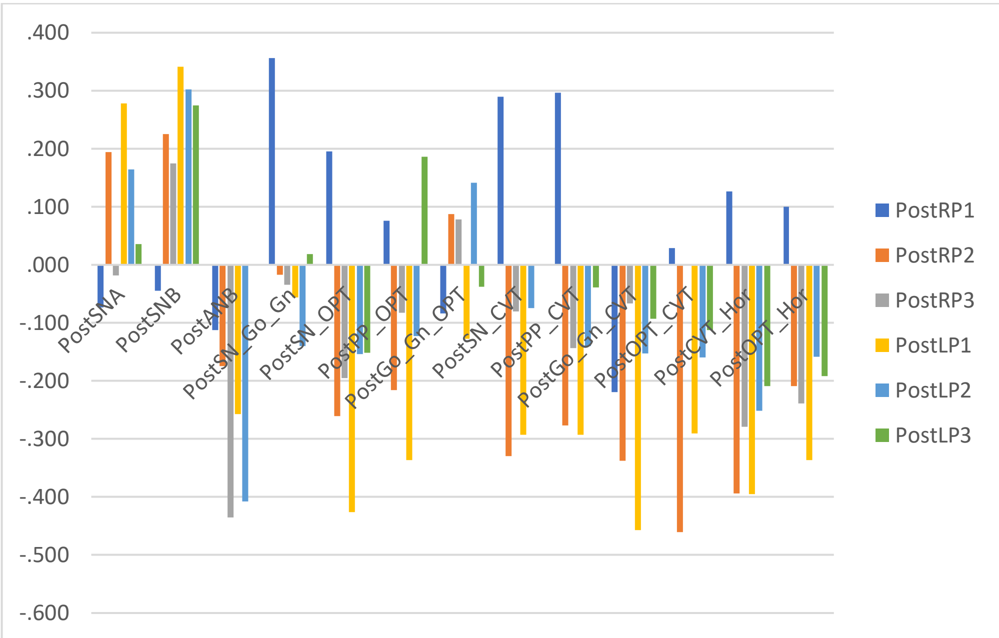

Fig 7: Pearson correlation between post-treatment cephalometric values and post-treatment force platform values.

On photographic assessment, the threads that were used to indicate the right and left pelvic, right and left shoulder became more straighter after treatment than compared to pre-treatment indicating change and betterment in the shoulder and pelvic tilt. The tilt decreased after treatment.

DISCUSSION

It is quite interesting to comprehend that there exists a relationship between the dental occlusion and cervical posture. According to Angle, causes for malocclusion is multifactorial ranging from hereditary, prenatal disturbances, environmental, systemic, habitual and uncoordinated muscular activity.[16] Similarly, malalignment can affect the spinal curvature, cervical and head posture. Therefore, a link is established between the posture and malocclusion.[17]

In this study, the results revealed that the reduction in ANB angle (1°) due to the camouflage correction of skeletal class II was majorly contributed by decrease in the SNA angle (1.2°) than SNB angle (0.28°). As part of extraction treatment mechanics, the retraction of the anterior segment of teeth in the maxilla had caused the change in the position of Pt A, which led to the decrease in SNA angulation. Extraction treatment protocol caused significant change in the pharyngeal airway space and tongue position.[18,19] A significant reduction in the retropalatal and retroglossal oropharyngeal airway is expected following retraction of the extraction space.[20] Due to the increase in the tongue height intra-orally, the tongue bulges and occupies the pharyngeal airway that initiates for the cranio-cervical alterations.[21] Hyoid bone thereby moved inferiorly and posteriorly due to the stretch of the hyoglossal muscle, thereby further restricting the pharyngeal airway. To adapt, the head had to further over-extend, hence the SN-OPT and SN-CVT angle increased, though it was non-statistically significant. Fathih Celebi et al[22], Niall J and McGuiness[23] suggested an average of 1° increase in the SN/OPT angle on maxillary expansion by treating patients with RME for constricted maxilla, which was due to the transient bite opening effect. SN/GoGn increased but not statistically significant (0.3°), stating that there was no evident backward rotation of the mandible. But however, GoGn/OPT angle increased by 5° and was statistically significant denoting that the odontoid process (OPT) moved backward or inclined further backward when compared to T0. Also, GoGn/CVT angle increased by 2°, though not statistically significant, indicating that the cervical vertebrae moved further posteriorly. Hence, an increase of 0.5° of OPT/CVT angle designate that there is worsening of the spinal curvature. This was similar to the result obtained by Fathih et al.[22]

Vertical dimension is another important parameter that influences the posture. The ratio of upper and lower facial height at maximum intercuspation can alter the spinal position with respect to the head and the spinal curvature. According to Urbanowicz [23], an increase of 8mm from the existing vertical dimension, the head was extended from 0.3° to 9°. The increase in vertical dimension results in more extended head position. In the current study, the vertical dimension increase was not considerable to depict a major change in the cervical posture. The posterior dentoalveolar height showed mild increase during the orthodontic phase, but the change in mandibular plane angle (SN/GoGn) was not statistically significant (0.28°). This was in concordance with Root et al [24] and Huggare [25], who also found no significant change in the head posture with increase of vertical dimension.

With regards to the body posture analysis, high statistical significance was found between T0 and T1. An increased loading in the P2 (first metatarsal region) and P3 (hallux) region for both right and left feet for skeletal class II individuals prior to orthodontic treatment indicating a forward leaning posture, in concordance with Nobili et al. [26] As there is extension of the cervical column in skeletal class II, a FEM study by Motoyoshi et al [27] concludes that the stress is majorly experienced by the cervical fifth vertebrae that leads to alteration of the entire spine and thereby, affecting the body posture. Bracco [28] concluded that the posture varies in accordance with the mandibular placement and myocentric jaw position provides equally loading on the feet and thereby helps in achieving a postural balance. When there is morphological change of the jaw base associated with the obstruction of airway, the neuromuscular feedback causes postural change leading to soft tissue stretch that imparts a differential force on the skeletal structure, resulting in the forward lean. Following the orthodontic treatment which provided a better cusp to fossa relationship, balanced occlusion, devoid of premature contacts, the loading pattern remained the same, but the loading values significantly reduced. However, in skeletal class I, the loading is equally distributed among the 3 pressure areas – Hallux, medial calcaneus, first metatarsal.[29] This is because the dental component plays a pivot role in maintaining the body balance. If the dental occlusion is improper, the cervical vertebrae gets mal-aligned causing domino effect reaction. When there is asymmetrical vertical dimension or occlusal loading, there is correspondingly asymmetrical muscle load. So, there will be a stretch of the muscles on the increased loading side, to prevent the collapse on the reduced loading side. This in turn causes tilt in the pelvic inclination. The jaw inclination varies resulting in asymmetrical burden on hyoid musculatures. Due to the constant stretch, muscle undergoes spasm, and the spine is being pulled leading to change in cervical spine posture.[30] Orthodontic treatment has influenced the body posture by distributing the foot loading to all the 3 pressure areas. On the contrary, to the work of Scharnweber[31], who concluded that posture and occlusion are two independent parameters and the change in plantar pressure distribution was due to attain a postural balance only when the occlusion was blocked. According to Marchena – Rodriguez et al[32], there exist a link between the plantar loading and malocclusion. For Class I, the Clark angle that is formed between the tangent of medial aspect of feet and the tangent of the front foot is least whereas, the clinical assessment tool FPI index that records the foot pressure is maximum.

The mean value for the loading was more on the first metatarsal region both before and after orthodontic treatment, followed by hallux and medial calcaneus region. This indicates that the skeletal jaw relationship dictates the loading on the feet. Since the orthodontic treatment only masked the skeletal class II, the forward leaning pattern of body posture remained the same, however, an equal distribution of the loading could be seen post treatment.

In centric occlusion, when the occlusal contacts bilaterally cause change in the peripheral inputs from the stomatognathic system, stability of both head and neck could be acquired. Thus, centric occlusion is more stable position to calculate the body posture. When there is a change in the occlusal contact, the peripheral inputs hamper the harmony of neuroanatomic system thereby resulting in instability of the neck position leading to head position and subsequently the entire body posture.[33] Also, the muscular connection that exists between the sternocleidomastoid (neck muscle) and the cervical muscles dictate the posture. The cervical muscles are responsible for the anterior and posterior balance, whereas sternocleidomastoid is responsible for the lateral balance along with the masticatory muscles.[29,34] In case of imbalance in the tonicity of the involves muscles, the natural postural balance is lost.[35] In skeletal class II, the temporalis muscle activity is more than the masseter muscle activity, due to the alteration in the deglutition and masticatory functions.[36] Improper occlusal contacts worsen the cervical posture. When there is occlusal alteration, there always exists a muscular imbalance, that causes asymmetrical stress distribution.[37] When splints were given to stabilise the occlusion, the posture improved, over a period. Immediate result could not be effective as the muscles had to adapt to the new occlusion, only after which, the postural change was evident. This concludes that the morphology, function, and adaptation of musculature is essential in attaining the desired posture.[38]

Body posture is attained by achieving an equilibrium between the vestibulo-cochlear, visual, and somatic sensation. Neuromuscular compensation with respect to the change in the centre of gravity is essential to maintain the balanced posture. When alterations in leg length occurs as a compensatory mechanism of the domino effect, the posture changes to the side where the leg length is more. This happens because, the head shifts towards the side when the load is more. And hence, class II skeletal malocclusion which has extended neck in the forward direction, corresponds to increased loading in the anterior region (hallux and medial calcaneus).[39]

In the present study, though the pattern of forward leaning in skeletal class II malocclusion after camouflage orthodontic treatment is maintained, there is a shift in the plantar pressure from the most anterior region (hallux) to the central region (first metatarsal) causing redistribution of pressure owing to the change in occlusal loading.

The clinical reference obtained from the study are:

Orthodontic camouflage treatment with extraction biomechanics increases the cranio-cervical angulation resulting in further over extension of the neck to compensate for the pharyngeal obstruction. Hence, retraction should be planned judiciously, taking tongue posture into consideration.

Body posture analysis revealed that the proper establishment of vertical dimension and the occlusal contacts significantly redistribute the plantar pressure. Hence, bite opening mechanics offer a favourable solution in regard to redistribution of plantar pressure which subsequently influences body posture.

The limitations of the study include: The attributing factor for skeletal class II was not taken into consideration. As the force platform was designed to accommodate foot size only between 5-9, the participants were restricted to this criterion. Long term evaluation might provide significant evidence.

CONCLUSION

A statistically significant increase in the GoGn/OPT angle and increase in the OPT/CVT angle indicate the overextension of head over the cervical column and increased spinal curvature respectively.

A highly statistically significant difference between the pre and post orthodontic camouflage treatment designate decrease in the plantar pressure loading at all the three regions- Hallux, medial calcaneus, first metatarsal. But however the plantar pressure still remained more in the anterior region even after orthodontic treatment.

There exists a positive correlation between the cervical posture and body posture in the skeletal class II malocclusion prior to orthodontic camouflage treatment.

The post camouflage orthodontic treatment reveals a negative correlation between spinal curvature (OPT/CVT angle) and loading pressure at the medial calcaneus region.

CONFLICT OF INTEREST

The authors have no conflict of interests to declare.

SOURCE OF FUNDING

Nil

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