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Dentoskeletal changes of anterior openbite cases treated by intrusion of maxillary posterior segments via zygomatic miniplates

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ABSTRACT

Introduction: No one can deny that the successful skeletal open bite treatment depends mainly on intrusion of maxillary buccal posterior segment and an anchorage system. So, intrusion of maxillary posterior segment was a magical orthodontic treatment mechanics granting a clock-wise rotation of the mandible, consequently closure of anterior open bite and improvement of facial profile convexity. So, the aim of this study is to evaluate skeletal and dental effects of intrusion of maxillary posterior segment by surgical miniplates. *Materials and Methods*: The selected sample size was ten patients (4 males and 6 females), ranging from 18 to 29 years of age (22.4 years, SD + 3.20 years), with skeletal anterior open bite were treated by intrusion of maxillary buccal posterior segment with surgical miniplates assisted intrusive device system which composed of zygomatic miniplates (Anchor unit), bonded acrylic maxillary hyrax expander with bite blocks (Reactive unit) and Nickel Titanium closed coil spring. Pre-treatment and Post-treatment lateral cephalograms were compared. *Results*: Maxillary first molars were intruded significantly by -3.85 mm + 0.82 mm($P<0.004$). The lower anterior facial height was reduced statistically by -4.20 mm + 1.13 mm ($P<0.005$). *Conclusion*: The skeletal and dentoalveolar changes produced by zygomatic miniplate assisted maxillary buccal posterior segment intrusion were apparently impressive and sufficient for adult anterior open bite correction. The amount of intrusion produced by the current study was efficient to induce counter-clockwise rotation of the mandible. That amount of autorotation was enough to improve the retrognathic chin to be a prognathic one without the risk of orthognathic surgery.

Keywords: Anterior open bite, intrusion of posterior teeth and zygomatic miniplates

1. INTRODUCTION

No one can deny that the successful skeletal open bite treatment depends mainly on intrusion of maxillary buccal posterior segment and an anchorage system. One of the most skeletal morphological characteristics of anterior open bite was increased maxillary and mandibular posterior dentoalveolar heights (Nemeth and Isaacson, 1974; Arvystas, 1977; Denison et al., 1989). However, most of cases are characterized by over eruption of the maxillary molars (Chudy, 1965). So, intrusion of maxillary posterior segment was a magical orthodontic treatment mechanics granting a counterclock-wise rotation of the mandible, consequently closure of anterior open bite and improvement of facial profile convexity (Hart et al., 2015; Wang et al., 2017). It was interesting that anchorage is a very important element for victorious orthodontic treatment outcomes. So, choosing a correct anchorage appliance will maximize the desired tooth movement and minimize the undesirable tooth movement reaction (Schatzle et al., 2019). Generally, orthodontic treatment remedy used extra-oral and/or intra-oral appliances for anchorage (Ng et al., 2008). Picking anchorage devices independent of patient's cooperation was an excellent choice for fruitful treatment results (Nanda and Kier, 1992) such as skeletal anchorage devices as follows specially designed dental implant (Keles et al., 2003; Block and Hoffman, 1995), anchorage devices as follows especially designed dental implant (Keles et al., 2003; Block and Hoffman, 1995), miniplates (Sugawara et al., 2004; Ohamae et al., 2001), miniscrews (Costa, et al., 1998; Kanomi, 1997; Park et al., 2001; Paik, et al., 2003; Xun et al., 2004), and onplants (Wehrbein et al., 1999; Wehrbein and Merz, 1998).

Miniscrews and miniplates have been popularized in contemporary orthodontic treatment. In spite of miniscrews concept was introduced in 1945 (Gainsforth and Higley, 1945) and used as skeletal anchorage in 1983 (Creekmore and Eklund, 1983), while surgical bone plate was introduced as stationary anchorage in 1985 (Jenner and Fitzpatrick, 1985). However, the miniscrews were more attractive and suitable for orthodontists because of the following: commercially available, low cost, stable anchorage (Liou et al., 2004), minimum pain and discomfort and convenient for placement. Nonetheless, there were complications with miniscrews such as injury to roots and fracture of miniscrews during placement (Kuroda and Tanaka, 2014). Chen et al. (2008) stated that soft tissue inflammation around miniscrews neck and early loading were the most significant factors for their failure.

On the other hand, miniplates provide stationary anchorage, low possibility of root damage, low risk of fracture and high success rate (Sugawara, 2014). Miniplates are often used when the necessary forces are supposed to be high due to their lower risk for failure when compared to miniscrews. In case of miniscrews and miniplates, the rate of failure depends mainly on the bony quality of placement area. In addition, the basal bone has denser bone than the alveolar bone (Chugh et al., 2013). Risk factors and success rate of skeletal anchorage system play an important role in clinician mind to intrude the maxillary posterior buccal segment. So, the aim of this study is to evaluate skeletal and dental effects of intrusion of maxillary posterior segment by surgical miniplates.

2. MATERIALS AND METHODS

Selected Sample Size

The sample size was 10 patients (4 male and 6 females), ranging from 18 to 29 years of age (22.4 + 3.20).

Inclusion Criteria

The criteria of sample selection were as follows:

- Patient's growth completed or near to be completed
- Increased lower anterior facial height (Incompetent Lips)
- Permanent Dentitions
- Anterior open bite between upper and lower incisors of 2mm or greater and extended beyond canines
- Skeletal Class II relationship
- Patients refused orthognathic surgery
- Patients with active periodontal disease were excluded
- No previous orthodontic treatment
- Irrelevant medical history
- Acceptance of treatment protocol

Informed Consent

All patients and/or their parents or guardians had been informed about the detailed treatment plan, complication, success rate, alternative plans, and signed the informed consent.

Diagnostic Records

All the following records were done for the selected sample:

- Comprehensive medical history
- Fully detailed dental clinical examination, diagnosis, and management
- Pre-operative and post-operative intra-oral and extra-oral photographs (Fig 1A & B & Fig 2)

- Pre-operative and post-operative radiographic examination which includes panoramic and lateral cephalometric x ray (Fig. 3 and 4)

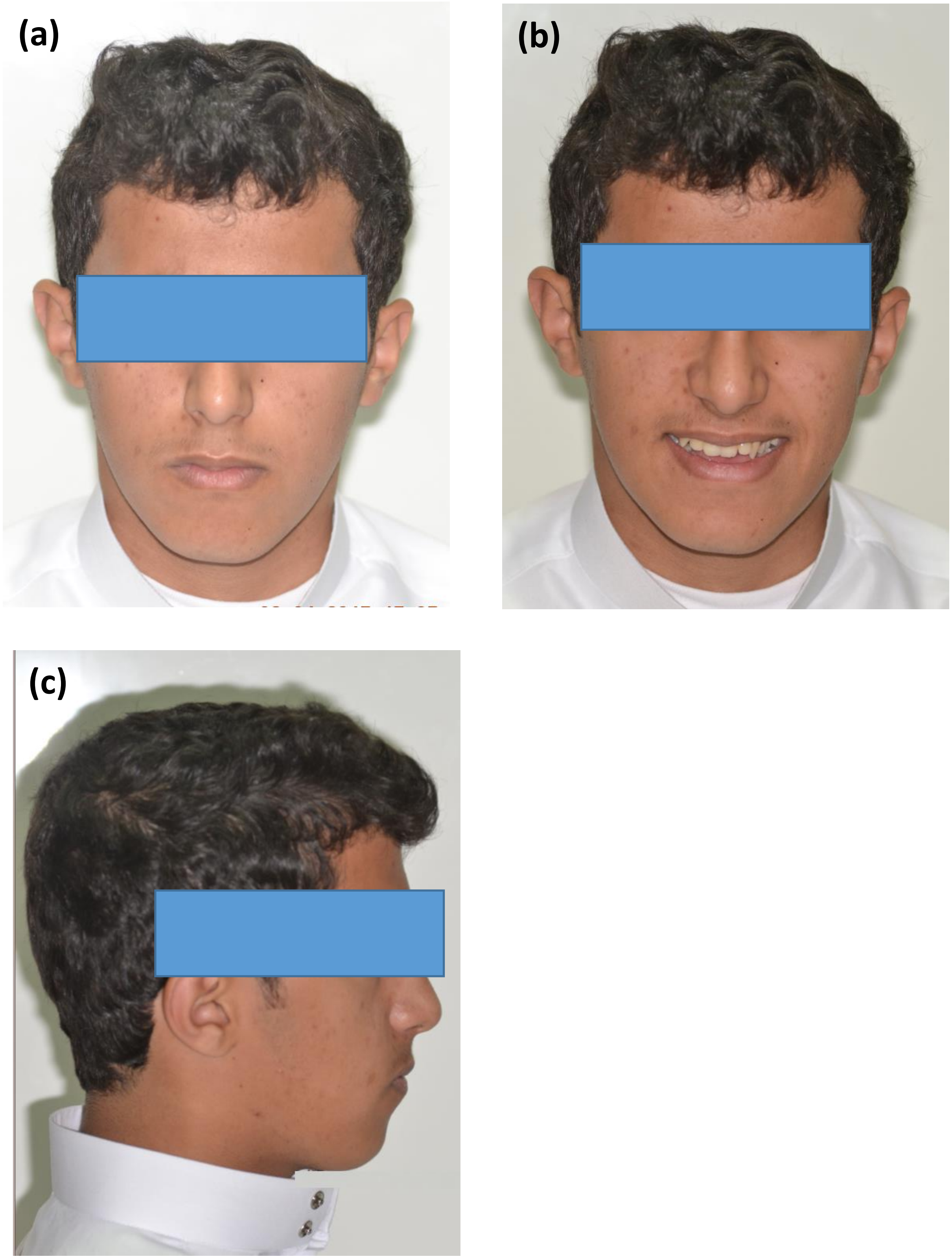


Figure 1A Pre-operative Extra-oral photographs showing: a) Frontal view. b) Frontal view with pose smile. c) Lateral view.

Figure 1B Post-operative Extra-oral photographs showing: a) Frontal view b) Frontal view with pose smile c) Lateral view

Figure 2 Pre-operative Intra-oral photographs showing: a) Frontal view that shows the anterior open bite (6mm). b) Lateral view right side. c) Lateral view left side.

Appliances used in the current study

Acrylic Bonded Hyrax Expander with ball clasps

This appliance was composed of rapid palatal jackscrew with maximum aperture of 9mm (item #19-531-101, international orthodontic service, 12811 capricorn St., Stafford, Tx77477, USA), acrylic cap splint over the upper molars and premolars and ball clasps embedded in the cap splint. The ball clasps was bilaterally between first and second premolars and first and second permanent molars. Some of selected sample had mild narrow maxillary arch. Accordingly, slow maxillary expansion was performed via swivel key (Shilliday, 1992) and the activation was one turn (0.8mm) per two weeks until 4mm of expansion was achieved (Brunetto et al., 2013). However, the expansion stage was done after active intrusion phase.

Zygomatic surgical plate placement procedures

Two T-shaped surgical miniplates (Titanium T-shaped miniplates, In Weiheräcker 778589 Dürbheim – Tuttlingen, Germany) were chosen and modified by opening the holes of the vertical part of the miniplates to facilitate the engagement of closed nickel titanium coil spring (double delta closed coil spring, length 10mm, 250 gm, Ormco, 1717 W collins Ave. orange CA 92867, USA)

(Fig. 5). After sterilization of modified T-shaped surgical miniplates, Oral and maxillofacial surgeon was placed them on the lower contour of each zygomatic process and fixed by three bone screws under local infiltrative anaesthesia (Fig. 6). The vertical arms of the miniplates with opened two holes are exposed into the oral cavity (Fig. 7). After fixation, the incision site is closed and sutured. The patients were advised to take a mild analgesic, an antibacterial mouth wash such as chlorhexidine rinse, and an antibiotic prophylaxis for one week (Kravitz et al., 2007). After suture removal on day 10, the force was applied bilaterally (250gm/side (Fig. 8). Then, the patients were seen in 4-week intervals and progress was observed. The duration of active intrusion was 9.70 ms + 2.07 ms. This research started in february 2017 and ended in may 2019. No surgical plate's failure was observed.

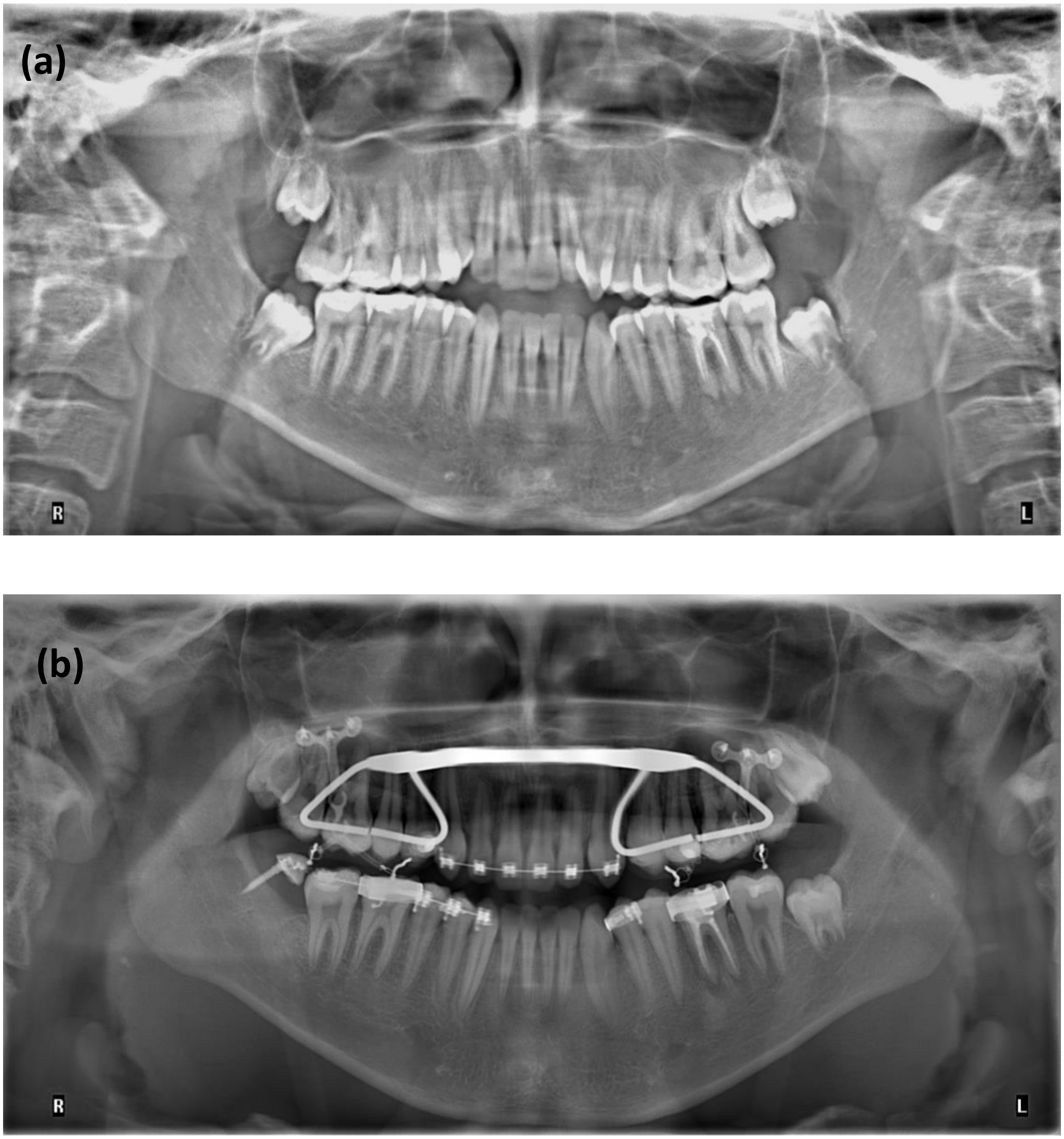


Figure 3 a) Pre-operative Panoramic view before intrusion of maxillary posterior segment. b) Post-operative panoramic view after intrusion of maxillary posterior segment.

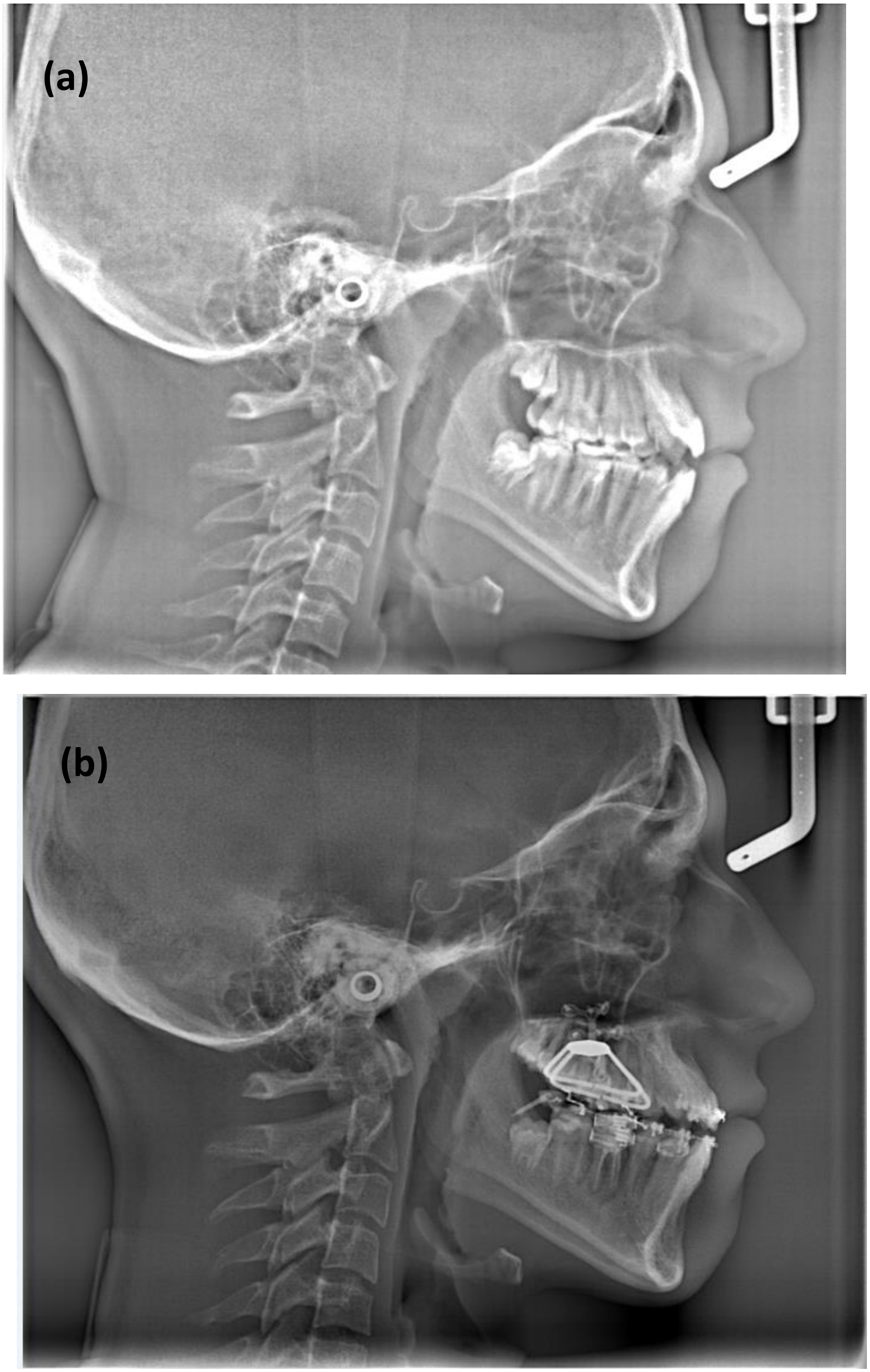


Figure 4 a) Pre-operative Lateral Cephalometric view before intrusion of maxillary segment. b) Post-operative Lateral Cephalometric view after intrusion of maxillary segment.

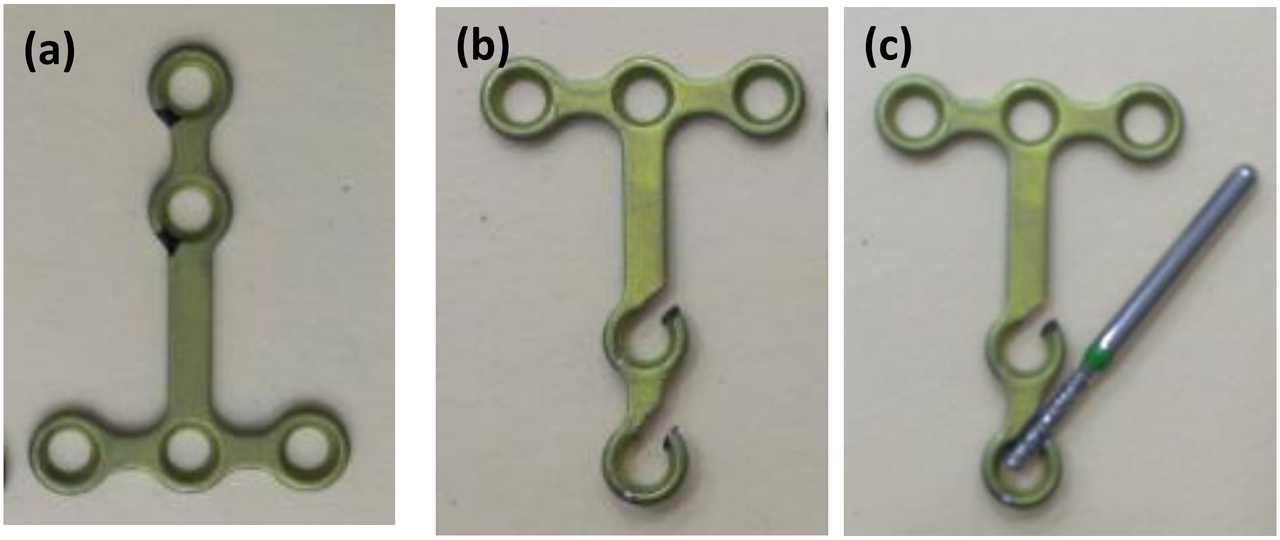


Figure 5 Showing T-shaped surgical miniplates. a) The hole of the miniplates marked by black marker. b) The marked area has been removed. c) The width of the cut similar to the width of the high speed long fissure diamond bur (New technology Instruments – Kahla GmbH, Rotary Dental Instruments Im Camisch 3, D-07768 Kahla-Germany 837, 010C, FG, 83357)

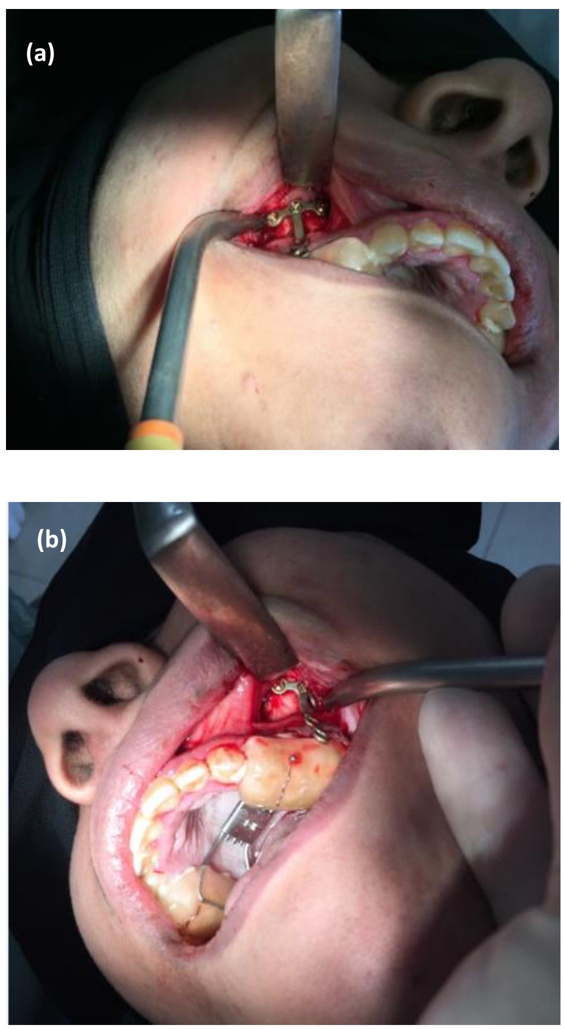


Figure 6 Showing the T-shaped surgical miniplates fixed with 3 bone screws on the lower contour of the zygomatic process while the acrylic bonded hyrax expander with ball clasps: a) Right side. b) Left side.

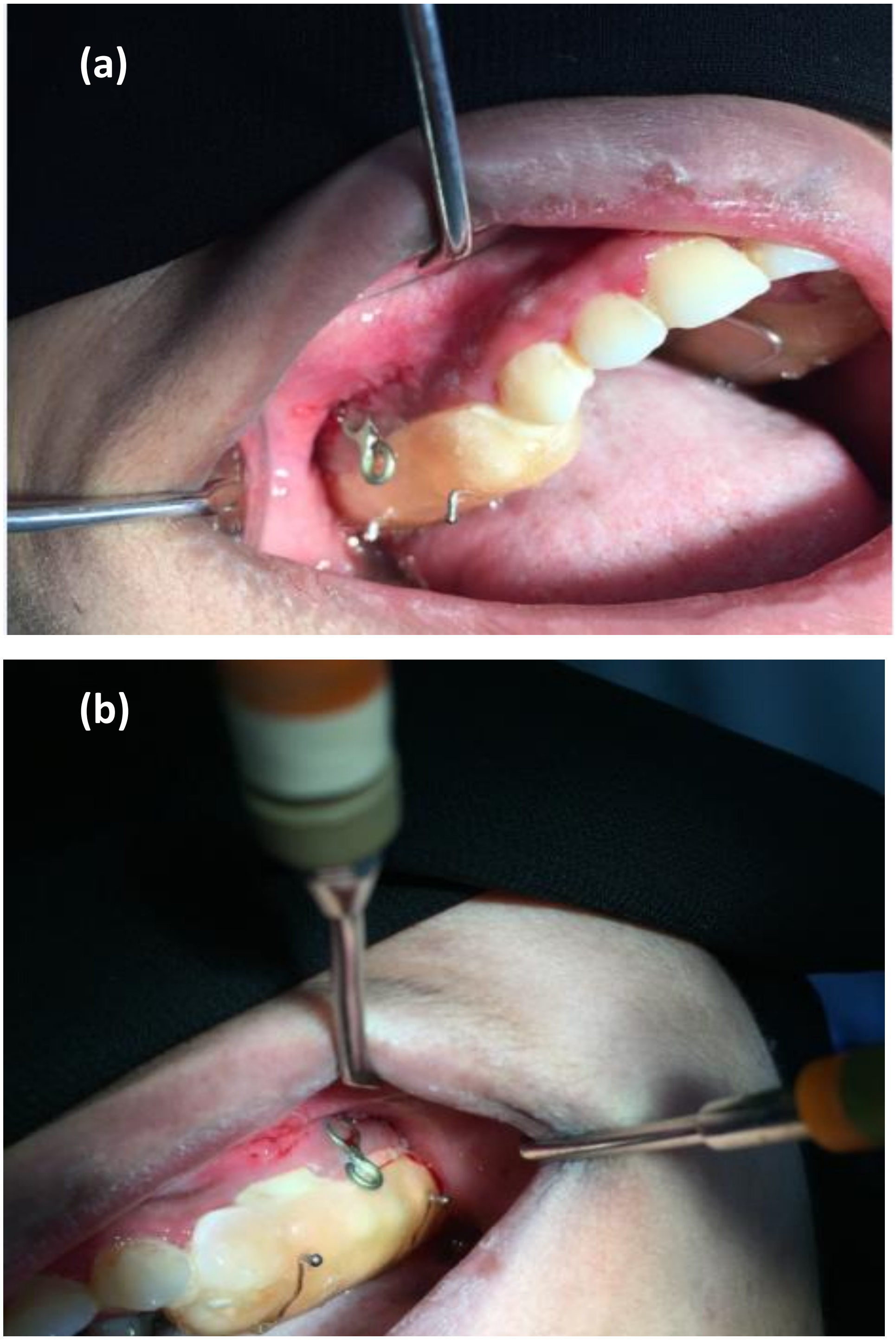


Figure 7 Showing the vertical arm of miniplates exposed into oral cavity at the time of suture removal: a) Right side. b) Left side.

Measurements

For each patient, two lateral cephalometric radiographs were taken at the start and at the end of active intrusion period. Lateral cephalometric landmarks (points and planes) used in the current study were identified as shown in, (Fig. 9) (Chaconas, 1980; Rakosi, 1982; Athanasiou, 1995). The following linear and angular parameters were measured to the nearest 0.5mm and degree from lateral cephalometric radiographs.

1-Lateral cephalometric skeletal angular measurements: Fig. (10)

Horizontal position of the maxilla in relation to cranium (SNA)
Horizontal position of the mandible in relation to cranium (SNB)
Horizontal position of the maxilla in relation to mandible (ANB)
Horizontal position of the most anterior point of the chin in relation to cranium (SN-Pog)
Vertical position of the mandible in relation to palatal plane (Mx-Md)

Facial growth pattern was measured by y-axis which is the inferior facial angle formed by the intersection of the sella-gnathion plane with Frankfort horizontal plane.

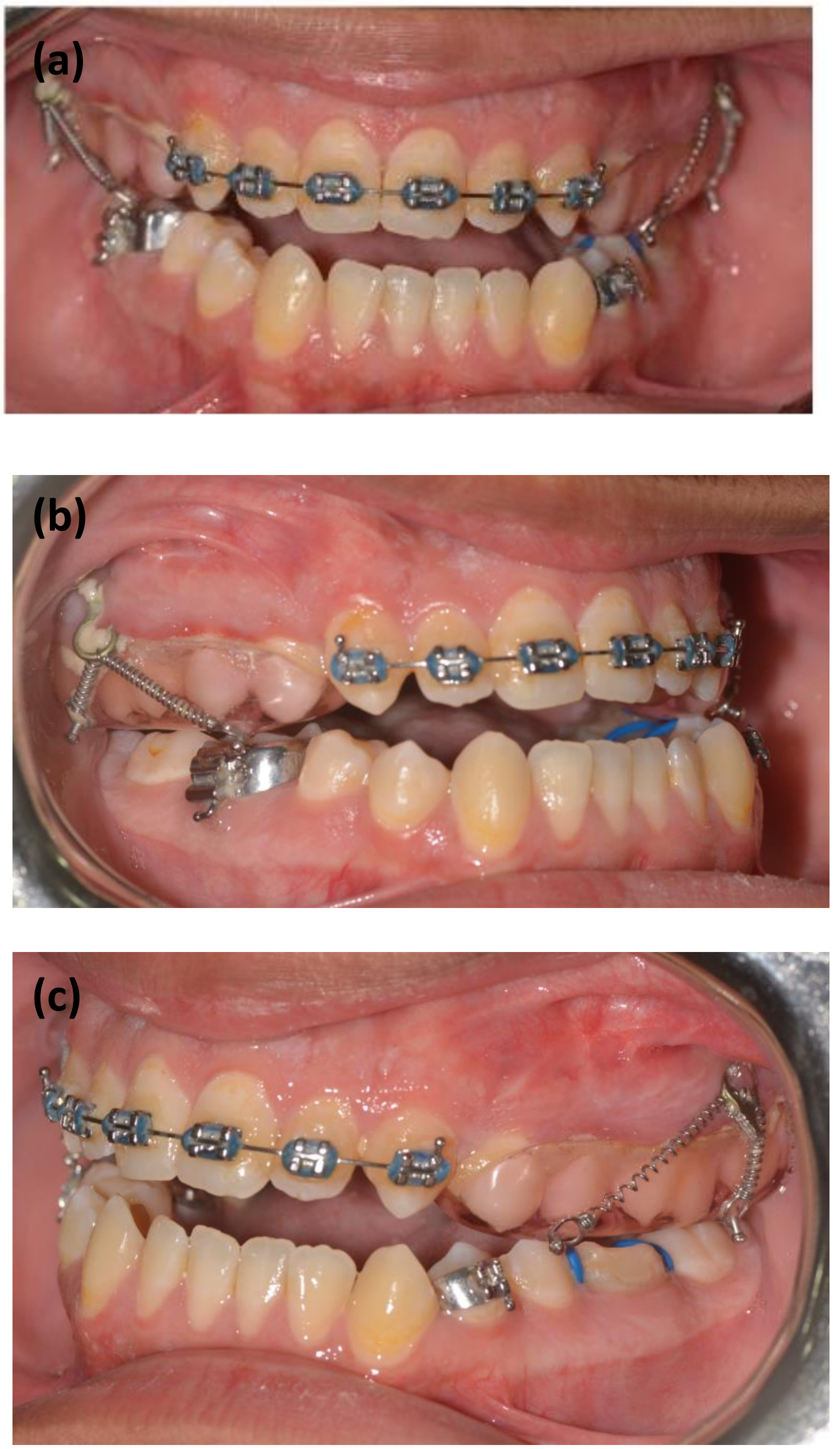


Figure 8 Intra-oral photograph showing Acrylic bonded Hyrax expander with ball clasps loaded with close coil spring; a) Frontal view. b) Lateral view right side. c) Lateral view left side.

2-Lateral Cephalometric linear measurements: (Fig. 11)

A-lateral cephalometric skeletal linear measurements: Measurements of lower anterior facial height was done by measuring the vertical distance between anterior nasal spines (ANS) to Menton (Me).

B-Lateral Cephalometric dental linear measurements: The following measurements were used to indicate the vertical crown movement (Intrusion-Extrusion):

UI to PP: The distance between the incisal edges of maxillary central incisor (U1) to the palatal plane. This line should be perpendicular to palatal plane.

U6 to PP: The distance between the center of the crown of first maxillary permanent molar (CC6) to palatal plane (PP). This line should be perpendicular to palatal plane.

L6 to MP: The distance between the center of the crown of first mandibular permanent molar (CC$\bar{6}$) to palatal plane (MP). This line should be perpendicular to mandibular plane (MP).

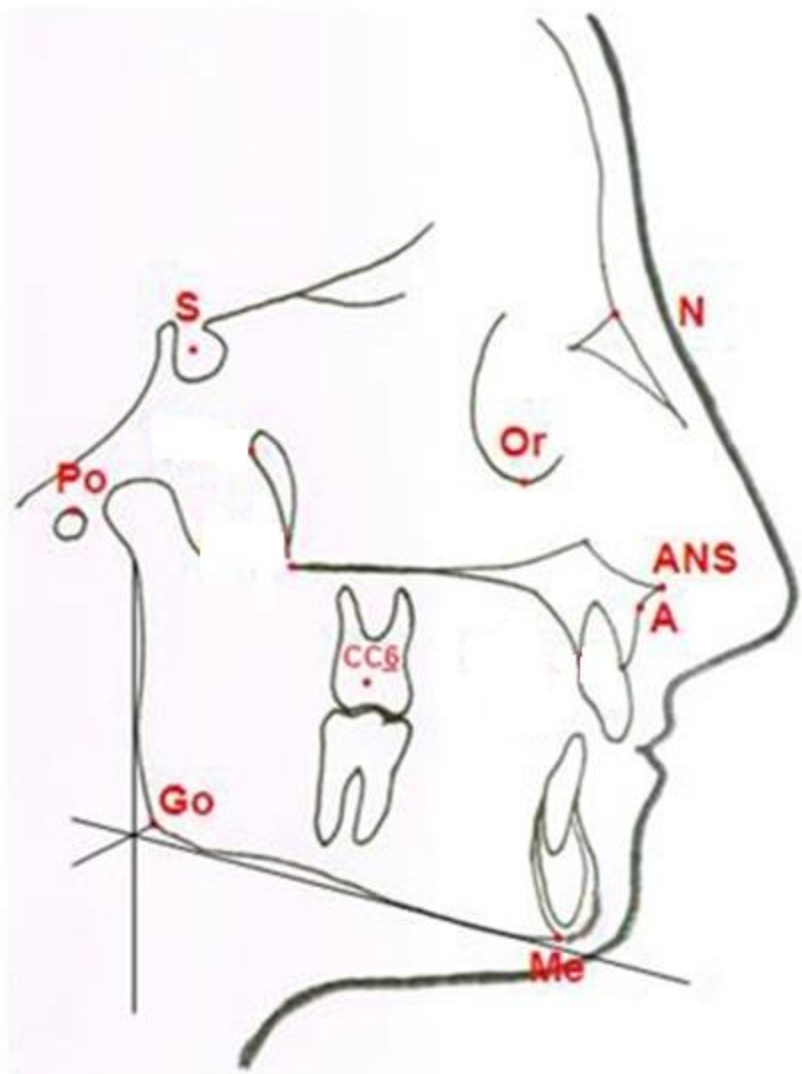


Figure 9 Showing Lateral Cephalometric Landmarks used in the study

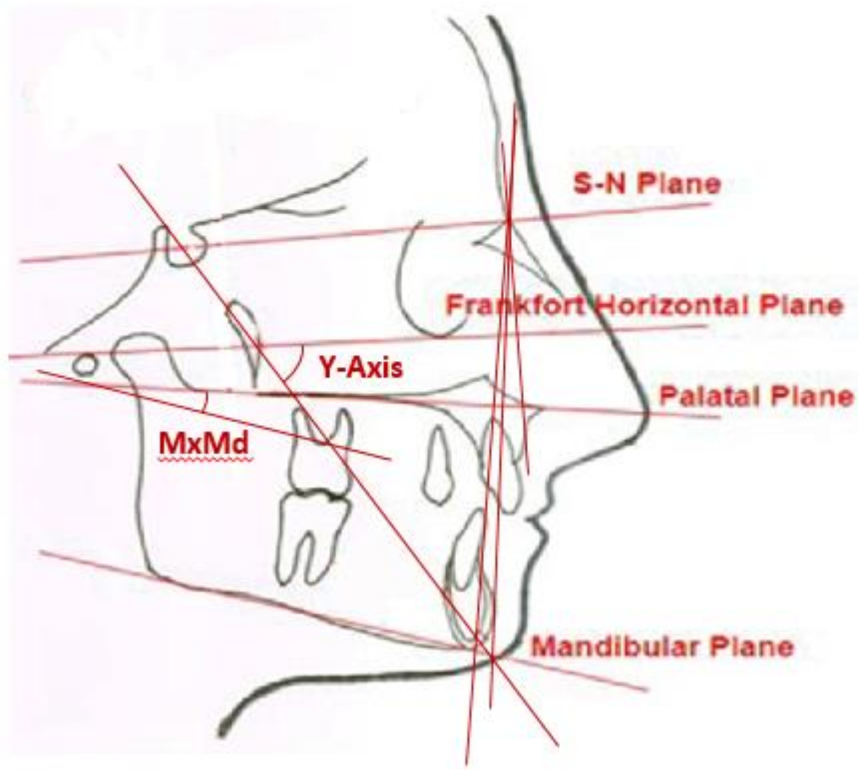


Figure 10 Showing Lateral Cephalometric Skeletal Angular Measurements.

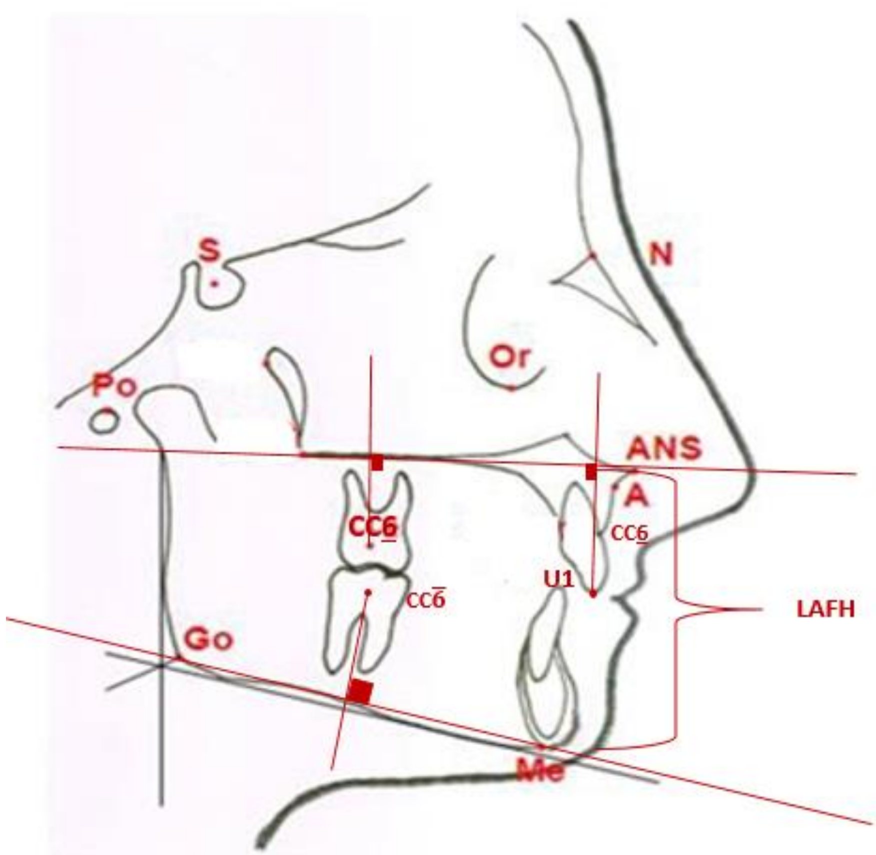


Figure 11 Showing Lateral Cephalometric Skeletal and Dental Linear Measurements.

Statistical Analysis

The collected data was tabulated and statistically analysed via using SPSS version 20.0 statistics software program (SPSS Inl., a subsidiary of IBM, based in Chicago, Illinois) to obtain:

Descriptive statistics:

Mean (x); Standard deviation (SD); Paired "t" test.

This was performed to compare the effect of treatment (pre-operative versus post operative) on different parameters. P value was calculated by Wilcox on Signed Ranks Test.

Intra-observer Error:

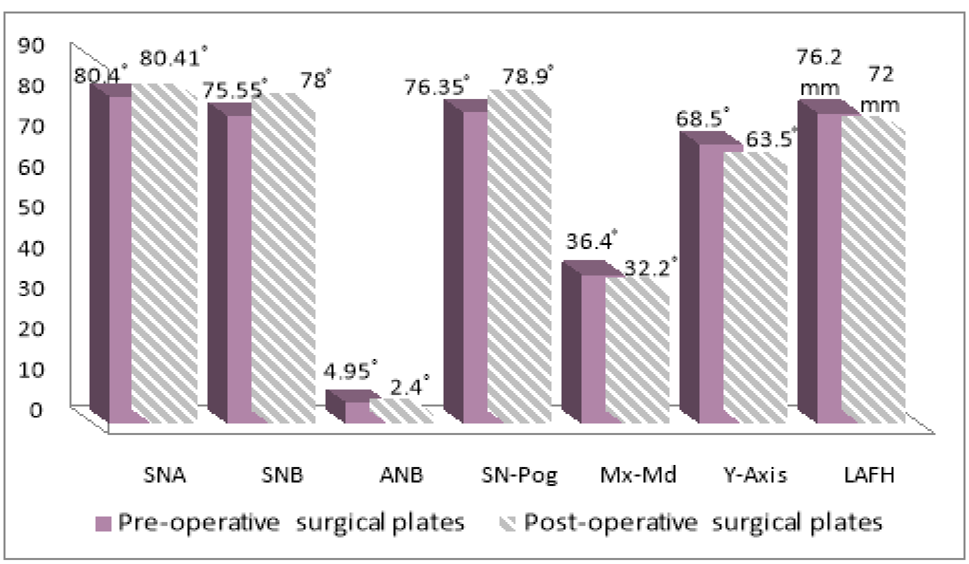
All pre-operative records were measured by one observer at two separate occasions. The error of pre-operative measurements for all parameters was calculated. Paired "t" test was used to evaluate the difference between the two sets of pre-operative measurements.

3. RESULTS

The Cephalometric characteristics of pre-operative and post-operative changes and paired "t" test are shown in Table (2). Statistically significant changes were observed in the most of skeletal and dental cephalometric parameters. Nonetheless, there were no statistically significant changes in the relation of maxilla to the cranium (SNA), the relation of upper incisors (U1) to palatal plane, and the relation of lower first permanent molar (L6) to the mandibular plane. Skeletal Cephalometric analysis results (Table 1 & graph 1).

Table 1 Showing pre-treatment and post-treatment skeletal cephalometric measurements.

	Pre-operative surgical plates (Mean ± SD)	Post-operative surgical plates (Mean ± SD)	Difference (Mean ±SD)	P value
Skeletal analysis				
SNA°	80.40° ± 1.15°	80.41° ± 0.91°	0.01° ± 0.52°	0.86
SNB°	75.55° ± 0.96°	78.00° ± 0.78°	2.45° ± 0.86°	0.005*
ANB°	4.95° ± 1.48°	2.40° ± 1.13°	-2.55° ±1.04°	0.005*
SN-Pog°	76.35° ± 1.06°	78.90° ± 1.10°	2.55° ± 0.83°	0.005*
Mx-Md°	36.40° ± 4.27°	32.20° ± 3.71°	-4.20° ± 0.92°	0.004*
Y-Axis°	68.50° ± 3.34°	63.50° ± 2.83°	-5.00° ± 1.56°	0.005*
LAFH (mm)	76.20 ±2.82 mm	72.00±2.12 mm	-4.20± 1.13 mm	0.005*

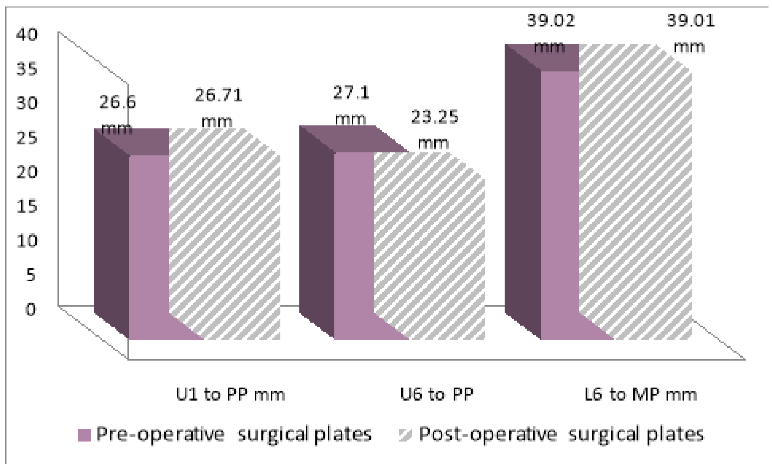


Graph 1 Showing bar graph representing mean of lateral cephalometric skeletal angular and linear changes in pre and post-operative measurements

The relation of mandible relative to cranium was increased by 2.45° + 0.86 (P<0.005). The anteroposterior position of maxilla in relation to the mandible was decreased significantly -2.55° + 1.04° (P<0.005). The anterior point of the chin in relation to the cranium was statistically increased by 2.55° + 0.83° (P<0.005). The maxillary-mandibular plane angle and Y-axis were decreased significantly by -4.2° + 0.92° (P<0.004) and -5° + 1.56° (P<0.005) respectively. Lower anterior facial height was reduced significantly by -4.2 + 1.13 (P<0.005). Dental Cephalometric Analysis result Table (2 & graph 2): The intrusion of maxillary first permanent molar was statistically done by -3.85 + 0.82 (P<0.004).

Table 2 Showing pre-treatment and post-treatment dental cephalometric measurements.

	Pre-operative surgical plates (Mean ± SD)	Post-operative surgical plates (Mean ± SD)	Difference (Mean ±SD)	P value
Dental analysis (mm)				
U1 to PP	26.60±4.25 mm	26.71±4.36 mm	0.11±0.21 mm	0.1
U6 to PP	27.10±1.29 mm	23.25±1.48 mm	-3.85±0.82 mm	0.004*
L6 to MP	39.02±4.07 mm	39.01±4.12 mm	-0.01±0.32 mm	0.92



Graph 2 Showing bar graph representing mean of lateral cephalometric dental linear changes in pre and post-operative measurements.

Intra-observer error results Table (3): The pre-operative measurements for all variables in skeletal and dental cephalometric measurements at different occasions to evaluate the Intra-observer accuracy was varied insignificantly.

Table 3 Comparison of mean and intra observer variation for pre-operative zygomatic miniplates between first and second reading (N= 10)

	First reading (Mean ± SD)	Second reading (Mean ± SD)	P value
SNA°	80.40° ± 1.15°	80.35° ± 1.20°	0.91
SNB°	75.55° ± 0.96°	75.60° ± 1.05°	0.94
ANB°	4.95° ± 1.48°	5.00° ± 1.56°	0.94
SN-Pog°	76.35° ± 1.06°	76.40° ± 1.10°	0.91
Mx-Md°	36.40° ± 4.27°	36.45° ± 4.25°	0.97
Y-Axis°	68.50° ± 3.34°	68.55° ± 3.28°	0.88
LAFH (mm)	76.20 ±2.82 mm	76.10 ± 2.96 mm	0.91
U1 to PP	26.60±4.25 mm	26.50±4.14 mm	0.91
U6 to PP	27.10±1.29 mm	27.20±1.14 mm	0.91
L6 to MP	39.02±4.07 mm	38.96±4.06 mm	0.88

4. DISCUSSION

Orthodontic treatment of skeletal open bite cases with skeletal anchorage system is more suitable for patients and their parents than orthognathic surgery because it is minimally invasive and safe. The most attractive elements of skeletal anchorage system to contemporary orthodontists are miniplates and miniscrews. However, treating skeletal anterior open bite via buccally placed miniscrews needs high placement away from reactive unit to provide acceptable range of action. For the sake of clarity, placement of miniscrews in attached gingiva has more high success rate than in mobile alveolar mucosa because of soft tissue inflammation susceptibility (Kravitz et al., 2007). While, zygomatic miniplates can grant, that without compromising the success rate (stability). Regarding to intrusive force, Park et al. (2003); Yao et al. (2004) used an intrusion force of 200-300gm and 150-200gm respectively to the upper posterior segment which was similar to the current study (250gm). On the other hand, Erverdi et al. (2006); Sugawara and Nishimura (2004) used a 400gm intrusive force which was greater than our study. However, the optimal force levels for maxillary posterior segment intrusion were not confirmed in the literature. Considering the placement area of skeletal anchorage system the zygomatic buttress provide a sufficient cortical bone thickness to afford the primary stability of the screws for miniplate fixation (Prager et al., 2015). Contrarily, there were no many areas of sufficient bone quality in the dentoalveolar buccal bone region to guarantee successful placement of miniscrews (Sugawara et al., 2004).

The Cephalometric evaluation of the amount of molar intrusion depends on the reference planes and points (Ng et al., 2006). The planes that represent the basal osseous bone are reliable such as palatal and mandibular planes (Athanasiou, 1995). It was interesting that the center of molar crowns (crown centroid) were used as a reference point to quantify the amount of molar intrusion. On the other side of the coin, using cusp tips or root tipping might be happened during molar intrusion leading to false evaluation (Burstone, 1977). Fortunately, the palatal planes, mandibular planes and crowns centroid were used in the current study. Through combing the literature, we found that most of zygomatic miniplates assisted intrusive appliances consisted of different design wire frame work (reactive unit) to seize the maxillary posterior dentitions and specific type of zygomatic miniplates (Anchor unit) connecting to each other via certain force system to correct skeletal anterior open bite orthodontically.

Erverdi et al. (2004) reported that ten (10) patients, 17 to 23 yrs old and characterized with an anterior open bite and excessive maxillary dentoalveolar growth. They treated them by I-shaped titanium miniplates were fixed bilaterally with NiTi closed coil spring between the vertical arm extension of miniplates and the transpalatal arch constructed from 0.9mm stainless steel roundwire and adapted 3mm away from the palatal vault. They found that the amount of upper molar intrusion was statistically changed by -2.6mm. Erverdi et al. (2007) evaluated 11 patients with mean age of 19.5yrs and characterized with an anterior open bite and maxillary dentoalveolar growth. They solve them by I-shaped titanium miniplates were fixed bilaterally to zygomatic buttress and a forceof 400g was applied contralaterally with 9mm NiTi closed coil spring between the vertical arm of miniplates and the intrusion appliance was consisted of two shallow acrylic bite blocks. The bite blocks were connected to each other by heavy palatal arch (1.4mm round stainless steel wire) and wire attachments on each buccal side, which were used for force application. They stated that the upper molars were intruded significantly by -3.6mm and lower facial height was decreased statistically by -2.9mm.

Akan et al. (2013) used the same design of Erverdi's appliance of 19 anterior open bite patients with the mean age of 17.7 yrs. They found that the amount of molar intrusion was significantly changed by -3.3mm lower anterior facial height was reduced significantly by -4.1mm. Marzouk et al. (2015) treated 13 anterior open bite patients with mean age 18.8 yrs by miniplate-assisted orthodontic treatment. They used zygomatic miniplates bilaterally, closed NiTi coil sp ring placed contralaterally between the hooks of miniplates just mesial and distal to the first molar buccal tube applying force of 450g per side and double TPA constructed from 1.2mm stainless steel wire connecting the whole posterior buccal segment. They found that the upper molars were intruded significantly by -3.1mm and lower facila height was decreased statistically by -3mm.

In the current study, the amount of molar intrusion was changed significantly by -3.8mm within 9.7 months. It was greater than Erverdi et al. (2004) study which was -2.2mm molar intrusion. This might be attributed to the active intrusion period was short (5.1 months). On the other hand, Erverdi et al. (2007) and Marzouk et al. (2015) studies shouted that the amount of molar intrusion and active intrusion period were -3.6mm/9.6month and -3.1mm/9 months respectively. The aforementioned molar intrusion changes were more or less similar to our study because the active intrusion period was almost the same (9.7 months).

In our study, the amount of lower anterior facial height was reduced significantly by -4.2mm. Akan et al. (2013) was achieved a significant decrease in lower anterior facial height by -4.1mm which was identical to present study. This might be attributed to the use of bite blocks during active molar intrusion phase. The action of bite block is to stretch certain masticatory muscles which place an intrusive force on the posterior teeth which in turn helps control eruption and permits an upward and forward autorotation of the mandible which modify the vertical skeletal pattern effectively (Negan and Fields, 1997; McNamara, 1977). When we compare our study and Akan et al. (2013) study with Marzouk et al. (2015) study, we found that the lower anterior facial height was decreased by -3mm which was less than our study and Akan et al. (2013) study in spite of the amount of molar intrusion were more or less near to each other. This is to clarify that the importance of the presence of posterior bite blocks during treatment of anterior open bite cases. Relating to the changes in the maxillary and mandibular plane angle, In the present study and Erverdi et al. (2004) study showed significant decrease by 4.2° and 2.2° respectively. This big amount of difference may also associate to the use of posterior bite blocks during treatment of skeletal open bite cases.

Regarding to SNB and ANB changes; The results of Akan et al. (2013) and our study showed changes by 2°/-2-4°and 2.4°/-2-5° respectively which were almost similar to each other. However, the other studies such as Erverdi et al. (2004) and Marzouk et al. (2015) showed that minor changes as follows 1.8°/-1.4° and 1.5°/-1.4° respectively. This big gap between these studies might be attributed to the presence of posterior bite blocks. The change in SN-Pog skeletal angle in present study was significant increased by 2-5° which confirmed that there were a true counterclock wise rotation of the mandible due to maxillary posterior buccal segment intrusion which improves chin prominence and facial convexity profile.

Patient's experiences with vertical part of miniplate were satisfactory. However, there was a sort of soft tissue inflammation around the vertical arm or cheek irritations in some patients. These incidences were resolved by proper oral hygiene instruction and prescription of chlorhexidine mouthwashes. Fortunately, there was no miniplate mobility, or removal or replacement. They were remained in their places along the treatment time. The vertical arm of the miniplate was modified by mesial cut to resemble a hook to receive the active component (NiTi closed coil spring) which produced a 250g force per side which was acceptable to produce intrusive action toward the creative unit. This amount of force was similar to the study of Park et al. (2003) and Yao et al. (2004) which were 200-300g force and 150-200g force to each side. On the other hand, the amount of force used in current study was less than the other studies (Sugawara and Nishimura, 2005; Erverdi, 2007; Akan et al., 2013; Marzouk et al., 2015). The intrusive appliance was bonded hyrax expander with acrylic bite block. In some cases, expansion of the maxillary arch was required. Therefore, the maxillary expansion was performed following the active intrusion period.

5. CONCLUSION

The skeletal and dentoalveolar changes produced by zygomatic miniplate assisted maxillary buccal posterior segment intrusion were apparently impressive and sufficient for adult anterior open bite correction. The amount of intrusion produced by the current study was efficient to induce counter-clockwise rotation of the mandible. That amount of autorotation was enough to improve the retrognathic chin to be a prognathic one without the risk of orthognathic surgery.

Acknowledgement

We thank the patients who participated in and contributed samples to the study.

Author Contributions

This research is totally carried out by the author Mohamed G. Elshal.

Funding

This study has not received any external funding.

Conflict of Interest

The authors declare that there are no conflicts of interests.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Ethical approval

This study was approved by the research ethical committee of faculty of Dentistry – Minia University (Minia, Egypt) research No: (23)/2017.

Data and materials availability

All data associated with this study are present in the paper.

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