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DENTAL DEVICE TREATMENT FOR OBSTRUCTIVE SLEEP APNEA SYNDROME

by

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Submitted in partial fulfillment of the requirements
for the Degree of Master of Science in Dentistry

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DENTAL DEVICE TREATMENT FOR

OBSTRUCTIVE SLEEP APNEA SYNDROME

Abstract

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The purpose of this study was to determine if dental appliances used to treat snoring and obstructive sleep apnea produced changes in the craniofacial structure and sleep quality. Specifically, this study compared mean differences in five appliance groups. Group 1 was treated with the SnoreGuard appliance; Group 2 with a mouthguard; Group 3 with device A designed to advance the mandible and increase vertical dimension; Group 4 with device B designed only to increase vertical dimension and Group 5 with device C designed only to advance the mandible. Data was collected on forty-two adult volunteers at three time points: (T0) before using any dental device, (T1) immediately following delivery of a dental device, and (T2) at the end of a two week period of intervention. To evaluate anatomic changes, cephalometric x-rays taken at T0 and again at T1 were

compared in terms of a change in the Craniofacial Risk Index (CRI) and individual cephalometric variables. To evaluate the changes in sleep quality, sleep assessments at T0 and again at T2 were compared in terms of Respiratory Disturbance Index (RDI) and Epworth Sleepiness Scale (ESS). The craniofacial variables which demonstrated significant change following insertion of an appliance were the hyoid to mandibular plane distance,the intermaxillary length, the ratio of the tongue to the intermaxillary area, the tongue length and the ratio of the cranial index to the facial index. The CRI (forced-entry) was significantly reduced in all treatment groups. The CRI (step-wise) was significantly reduced in all groups except Group 2. The RDI was significantly reduced only in the Groups 1 and 3. The ESS was not significantly reduced in any of the treatment groups. In conclusion, the findings from the present study demonstrated that there are some craniofacial changes affected by the placement of an oral appliance. Oral appliances which increased vertical dimension as well as repositioned the mandible anteriorly appeared to be most effective in reducing apneic events.

DEDICATION

To my mother, a biochemist by training and an angel by heart, you have always been a science enthusiast and delivered your Master's thesis defence nine months pregnant with me. Thank you for your lifelong unconditional love and support, for encouraging me to always try my best and for lending me the strength to continue when I was often ready to give up.

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GLOSSARY

Definitions of Anatomic Landmarks

Point/Line	Definition
A	A-point, subspinale: the deepest point in the concavity of the anterior maxilla between the anterior nasal spine and the alveolar crest
A′	A perpendicular projection of A-point onto a reference line drawn perpendicular to the vertical PM plane
ANS	Anterior nasal spine: sharp median process formed by the forward prolongation of the two maxillae at the lower margin of the anterior aperture of the nose
Ar	Articulare (Bjork): a point located at the intersection of the lateral radiographic image of the posterior border of the ramus with the base of the occipital bone
B	B-point, supramentale: the deepest point in the concavity of the anterior mandible between the alveolar crest and pogonion
Ba	Basion: the most postero-inferior point on the clivus
C2	The most posterior-inferior point on the corpus of the second cervical vertebrae
C2tg	The tangent point of which a line from C2 passes through the odontoid process
C3	The most posterior-inferior point on the corpus of the third cervical vertebrae

C3′	The most anterior-inferior point on the corpus of the third cervical vertebrae
C4	The most inferior-superior point on the corpus of the fourth cervical vertebrae
Eb	Base of epiglottis: the deepest point of the epiglottis
FOP	Functional occlusal plane: a line through PreM and Mo bisecting incisal overbite
FOP1	Functional occlusal plane 1: a point formed by the perpendicular projection of ANS onto the functional occlusal plane
FOP2	Functional occlusal plane 2: a point formed by the perpendicular projection of menton onto the functional occlusal plane
Gn	Gnathion: constructed point determined by bisecting the angle between the tangent of pogonion and the tangent of menton
Go	Gonion: constructed point determined by bisecting the angle between line from Me-MIB and line tangent to the posterior border of the ramus passing through articulare
H	Hyoidale: the most superior-anterior point on the body of the hyoid bone
LL1	Lower lingual 1: junction of the lingual surface of the lower central incisor and the functional occlusal plane
MCF	Middle cranial fossa: point represented 40.3 degrees anterior to the line joining Bjork's articulare(Ar) and SE
Me	Menton: the most inferior point on the bony chin
MIB	Most inferior border: most inferior border of the mandible
Mo	Molar: the mesial-buccal cusp tip of the upper first molar

Na	Nasion: junction of the frontal and nasal bones at the naso-frontal suture
Or	Orbitale: the most inferior point on the infra-orbital margin (mid-placed)
P	Palate: the most inferior tip of the soft palate
Phw	Pharyngeal wall: point on the pharyngeal wall at the level of the posterior superior airway space determined by drawing a line from Psp to the pharygeal wall parallel to the from B-point to gonion
Phw1	Pharygeal wall 1: junction of the pharyngeal wall and the functional occlusal plane
PM	Vertical PM a line from SE through the averaged inferior-most points of the left and right pterygomaxillary fissure
PNS	Posterior nasal spine: process formed by united projecting medial ends of the posterior borders of the two palatine bones
Po	Porion: the most superior point of the bony external auditory meatus
Pog	Pogonion: the most anterior point on the bony chin
PreM	Premolar: the buccal cusp tip of the upper first premolar
Psp	Posterior-superior palate: the most posterior-superior point of the soft palate
Ptm	Pterygomaxillary fissure: the averaged inferior-most point of the left and right pterygomaxillary fissure
Pwid1	Palatal width 1: superior point on the soft palate where a line bisecting and perpendicular to PNS-P is drawn

Pwid2	Palatal width 2: inferior point on the soft palate where a line bisecting and perpendicular to PNS-P is drawn
R1	Ramus 1: junction of the anterior border of the ramus and the functional occlusal plane
R2	Ramus 2: junction of the posterior border of the ramus and the functional occlusal plane
REF	Reference line: a horizontal reference line parallel to the FOP drawn from articulare anteriorly
Rgn	Retrognathion: the most inferior-posterior point of the symphysis
S	Sella turcica: the center of the hypophyseal fossa, lodging the pituitary body
SE	Sphenoethmoidal junction: the junction between the averaged right and left greater wings of the sphenoid bone and the floor of the anterior cranial fossa
TH1	True horizontal 1: anterior-most point on the fluid leveler
TH2	True horizontal 2: the posterior-most point on the fluid leveler
Tt	Tongue tip: the most anterior point of the tongue which touches the lingual surface of the mandibular incisor

Lateral and Frontal Cephalometric Measurements

Variables	Interpretation
<BaSn	Cranial base angulation in mid-sagittal plane.
MCF	Middle cranial fossa and antero-posterior maxillary alignment relative to neutral PM. A neutral MCF/PM is an internal angle of 40.3 degrees. When a subject's PM is in front of the neutral PM, a (+) clockwise value results. This forward alignment of the MCF has a tendency to result in a mandibular retrusive effect. When a subject's PM is behind the neutral PM, a (-) counterclockwise value results. This backward alignment of the MCF has a tendency to result in a mandibular protrusive effect. If the neutral MCF coincides with the individual's own MCF, a neutral (0) effect results.
< SNA	Anteroposterior position of the maxilla relative to the anterior cranial base.
<ArN-PM	Posterior wall of the maxilla (vertical PM) relative to the constructed cranial base.
A-PNS	Effective antero-posterior dimension of the maxilla when projected to a line which is perpendicular to PM and passes through the point SE
PNS-Ba	Horizontal position of PNS to basion
<SNB	Anteroposterior position of the mandible relative to the anterior base.

RAM/MCF	The ramus width relative to neutral PM (RAM) is made at the level of REF and is the distance between R1 and neutral PM. If R1 is found behind neutral PM, the value is (-). If R1 is found in front of neutral PM the value is (+). The patient's ramus width relative to posterior maxillary alignment (RAM/MCF) is calculated as follows; RAM minus MCF. If RAM/MCF is (+) this indicates that the anterior border of the patient's ramus is positioned forward of the posterior maxillary alignment. If RAM/MCF is (-) this indicated that the anterior border of the patient's ramus is positioned behind their posterior maxillary alignment.
ArA-ArB	Relative comparison of cumulative maxillary length from Ar to A point with cumulative mandibular point from Ar to B point. The measurements are made along the REF line.
PNS-Ba	Horizontal position of PNS to basion.
Phw-Psp	Posterior-superior airway space (distance measured along a line parallel to B-Go)
T1	Tongue length, measured from Tt-Eb
H-MP	Vertical position of the hyoid bone relative to the mandibular plane.
H-VER	Vertical position of the hyoid bone relative to a line which is perpendicular to PM and passes through SE.
FH- Hor	Head position interpreted by an angle formed by the Frankfort horizontal plane and the True Horizontal (recorded from a fluid level device).
<C2-SN	A craniocervical angle formed by a line from C2 to C2tg and the S-N plane
<C2-C4-SN	A craniocervical angle formed by a line from C2 to C4 and the S-N plane.

Ant. Mx. Ht.	Anterior intermaxillary height, the length of a perpendicular from the palatal plane to menton.
Post. Mx. Ht.	Posterior intermaxillary height, the length of a perpendicular from the palatal plane to the mandibular plane which passes through the point where FOP intersects at Phw.
Int. Mx. Lth.	Length of the intermaxillary space. The linear distance measured along the FOP from the point where it intersects LL1 anteriorly to where it intersects the Phw posteriorly.
Fac. Ht.	Facial height measured on a line from nasion to menton parallel to the vertical PM.
Ar-Go	Effective length of the ramus measured from articulare to gonion.
Go-Gn	Effective length of the body of the mandible measured from gonion to gnathion.
<Go	Angle between the ramus and body of the mandible (gonial angle), measured by the internal angle between the line Me-MIB and a line through Ar tangent to the posterior ramus.
FH-Go	Effective perpendicular length between the Frankfort horizontal plane (Po-Or) and gonion.
<FH-A	Angle between the Frankfort horizontal plane (Po-Or) and A point.
<FH-B	Angle between the Frankfort horizontal plane (Po-Or) and B point.
< Pal-PM	Angle between the palatal plane (ANS-PNS) and the vertical PM plane.
Rgn-H	Effective length between retrognathion and the hyoid bone.

P width	Soft palate width measured from Pwid1 to Pwid2
< C3′-Rgn-H	A craniocervical angle formed by a line from C3′ to retrognathion and a line from the hyoid bone to retrognathion.
Low/Mid	Ratio of the lower face (perpendicular distance from Me to FOP) to the middle face (perpendicular distance from ANS to FOP).
T area	Area of the tongue (outline from Tt along the dorsum of the tongue to the Eb to the hyoid bone to menton along the retrognathion surface back to the Tt).
Int. Mx. Area	Intermaxillary area calculated as follows: (Anterior maxillary height+ Posterior maxillary height)/2 x the Intermaxillary length
T/Int. Mx.	Ratio of the intermaxillary area occupied by the tongue, calculated by T area/Int. Mx. Area.
Facial Index	Facial Height (DFP measurement)/ Facial width (bi-zygomatic width determined from the patient's frontal cephalogram).
Cranial Index	Cranial width/cranial length (clinical measurements taken with the cephalostat)
Biramal width	Biramal width measured from the patient's frontal cephalogram from gonial angle to gonial angle.

INTRODUCTION

An anonymous scholar once said: "Laugh and the world laughs with you, snore and you sleep alone", (Wagner and Price 1987). Snoring and its progression toward a more serious form of the disease, obstructive sleep apnea syndome (OSAS) can have multiple clinical sequelae. Obstructive sleep apnea syndrome is characterized by a constellation of signs and symptoms related to arterial oxygen desaturation and sleep fragmentation caused by pharyngeal obstruction during sleep (Strohl et al. 1986). Clinical symptoms of OSAS in order of prevalence include: snoring, excessive daytime sleepiness, intellectual deterioration, personality changes and morning headaches.

A recent study (Young et al. 1993), in the United States examining the prevalence of OSAS looked at a sample of 602 employed men and women between the ages of thirty and sixty. Nine percent of women and 24% of men had apnea indices greater than five. Two percent of women and four percent of men were estimated to have OSAS based on having an apnea index greater than 5 in addition to excessive daytime sleepiness. Upon closer examination of the

patients between fifty and sixty, 4% of women and 9% of men were found to have apnea indices in excess of 15. While obstructive sleep apnea syndrome has been observed in people of all ages and both sexes, it presents predominantly as a disease of obese, middle-aged hypertensive men.

The etiology and pathogenesis of OSAS is not clearly understood and appears to be multifactorial. There is, however, some evidence to support the hypothesis that craniofacial structures are associated with the development of OSAS as well as neurogenic controls to preserve patency of the upper airway during sleep. Both genetic and environmental factors are risk factors of the disease and include craniofacial features, obesity, alcohol use and ventilatory control.

Management of OSAS can range from conservative medical measures to invasive surgical procedures. Currently available treatment modalities include: weight reduction, positional therapy, pharmacologic agents, oral appliances, nasal continuous positive airway pressure (CPAP), tracheostomy, uvulopalatopharyngoplasty (UPPP), and maxillomandibular osteotomies.

Recently oral appliances have received increased attention because of their efficacy, reversibility and

negligible side effects. This study attempted to examine five dental devices and their ability to effect changes in craniofacial structure and sleep quality. It is hoped that this may reveal important information in regard to appliance design.

REVIEW OF THE LITERATURE

Historical Review and the Clinical Syndrome

Sleep apnea was first discovered in the search for the pathological process behind the Pickwickian syndrome (Gastaut et al. 1965). Pickwickian syndrome was characterized by symptoms associated with obesity, excessive sleepiness, cyanosis, pulmonary hypertension and right sided heart failure (Westbrook 1990). The first polysomnographic study was reported in 1965 by Gastaut and coworkers who began to describe the disorder based on sleep behaviors. The definition of "apnea" was derived from a number of studies: In part from the work of Tassinari in Marseille on the pickwickian patient, partially from the work of Guilleminault in Paris performed on aging poliomyelitic patients with breathing problems during sleep and partially by further work by Guilleminault at Stanford University on normal subjects and non-obese subjects with sleep apnea (Guilleminault 1994). An apnea index (AI) was later established by Guilleminault as the total number of apneas/ total nocturnal sleep time x sixty. The upper limit of "normality" was defined as an AI of 5.

Apnea is defined as complete cessation of nasal or oral airflow for more than ten seconds. Apneas may be classified as central, obstructive, or mixed. Central apnea is the cessation of both airflow and breathing effort. Ventilation ceases because the central nervous system fails to activate the diaphragm and other respiratory muscles (Wiegand and Zwillich 1994). Obstructive apnea is the cessation of airflow caused by a collapsed upper airway in the presence of breathing effort. Mixed apnea is defined as no respiratory effort for at least ten seconds, followed by at least three unsuccessful attempts to inspire before breaking the obstruction (Bonham et al. 1988). Hypopneas occur when there is a 50% decrease in airflow associated with a 4% or greater decrease in oxygen saturation. Hypopneas may also be classified as central, obstructive or mixed. The apnea or hypopnea index indicates the number of such events per hour of sleep. Obstructive sleep apnea is considered mild if the apnea-plus-hypopnea index (AHI) or respiratory disturbance index (RDI) is 6-20; moderate if AHI is 21-50; and severe if AHI is more than 50 (Aboussouan et al. 1994).

In the medical field it is common practice to screen hypertensive patients by measuring blood pressure. The cost-benefit ratio of recording breathing during sleep to

identify apneic patients would be very high. The basis, therefore, of diagnosis is proper history taking and clinical examination. According to the International Classification of Sleep Disorders the diagnostic criteria for obstructive sleep apnea are (ASDA 1990):

A. The patient has a complaint of excessive sleepiness or insomnia. Occasionally the patient may be aware of clinical features that are observed by others

B. The patient has frequent episodes of obstructed breathing during sleep

C. Associated features include:

    1. Loud snoring;

    2. Morning headaches;

    3. A dry mouth upon wakening;

    4. Chest retraction during sleep in young children

D. Polysomnographic monitoring demonstrates:

    1. More than five obstructive apneas, greater than ten seconds in duration, per hour of sleep and one more of the following:

    2. Frequent arousals from sleep associated with apneas;

    3. Bradycardia;

    4. Arterial oxygen desaturation in association with apneic episodes; with or without,

    5. An MSLT that demonstrates a mean sleep latency of less than ten minutes

E. Sleep apnea can be associated with other medical disorders, e.g., tonsillar enlargement

F. Other sleep disorders can be present, e.g., periodic limb movement disorder or narcolepsy

Severity Criteria:

Mild: Associated with moderate sleepiness or mild insomnia as defined above. The majority of habitual sleep period is free of respiratory disturbance. The apneic episodes are associated with mild oxygen desaturation or benign cardiac arrhythmias.

Moderate: Associated with moderate sleepiness or mild insomnia as defined above. Can be associated with moderate oxygen desaturation or mild cardiac arrhythmias.

Severe: Associated with severe sleepiness as defined above. The majority of the habitual sleep period is associated with respiratory disturbance, with severe oxygen desaturation or moderate to severe cardiac arrhythmias. There can be evidence of associated cardiac or pulmonary failure.

Duration Criteria:

Acute: Duration of two weeks or less

Subacute: Duration of more than two weeks but less than six months

Chronic: Duration of six months or more

Obstructive sleep apnea is the most common organic disorder of excessive daytime somnolence seen in sleep disorder clinics today. In almost every report describing large numbers of patients with OSA, the subjects were

predominantly middle-aged, obese men (Chua and Chediak 1994). According to cross-sectional studies minimal prevalence of OSA among adult men is about 1%. There is an age relationship so prevalence of OSAS among men aged forty to fifty nine may be more than 5%. Obstructive sleep apnea is less common in younger and older age groups (Partinen 1994). In the Wisconsin Sleep Cohort Study, (Young et al. 1993), the most comprehensive well designed epidemiologic study to date, a random sample of 602 working men and women between thirty and sixty years of age underwent overnight polysomnography to determine the frequency of apneas and hypopneas during sleep. When the results were extrapolated to the general working population in this age range, the study group determined that 9% of men and 4% of women had fifteen or more episodes of apnea and hypopnea per hour of sleep. Applying more conservative diagnostic criteria, the authors estimated that 4% of men and 2% of women in the middle-aged work force have sleep apnea syndrome.

The clinical hallmark of OSAS is loud irregular snoring and is the most common cause of referral for treatment. Noisy pharyngeal snoring often associated with snorting and interrupted by silences with a very explosive loud expiratory reprise is the most common clinical feature. Patients with sleep apnea also suffer very

commonly from excessive daytime sleepiness. This is chiefly related to fragmented sleep and decreased time spent in the deeper stages of non-REM sleep. There is an increased tendency to doze off easily while watching television and difficulty staying alert while driving long distances. Sleepiness is often more obvious to others in the environment than to the patient (Guilleminault 1994). Excessive daytime hypersomnolence can be related to an inability to concentrate, a deterioration of memory and judgement as well as temporal disorientation. These problems may impair family relations, job performance, and public safety. Patients with OSAS have been reported to have a much higher rate of motor vehicle accidents than other drivers (Findley et al. 1988;1992). Cardiovascular morbidity in OSAS patients may include systemic hypertension, left ventricular dysfunction, myocardial infarction, cardiac arrhythmias, pulmonary hypertension, cor pulmonale and sudden death (Shepard 1992).

Pathophysiology of Obstructive Sleep Apnea

The fundamental problem in OSAS is a collapse of the upper airway during sleep. This a process that often requires arousal for termination. An obstructive apnea involves a sequence of cyclic events (Wiegand and Zwillich 1994). With the initial onset of an obstructive sleep

apnea, the upper airway collapses in the region of the pharynx, and airflow is impeded despite increasing ventilatory effort. Hypoventilation results in progressive asphyxia, which increasingly stimulates breathing efforts against the occluded airway, typically until arousal occurs. With arousal, the upper airway opens, and airflow is restored. A surge in upper airway muscle activity accompanies arousal from sleep, resulting in airway deocclusion and hyperventilation in response to the accumulated asphyxic stimuli. Sleep rapidly returns, pharyngeal muscle activity declines, the pharynx collapses, and the cycle begins again. This series of events may be repeated hundreds of times each night. The patient experiences both hypoxia and hypercapnia and which results in highly disrupted sleep.

The pathophysiology of OSAS includes factors related to upper airway anatomy, upper airway resistance and upper airway muscle function during sleep (Hudgel 1992). Anatomic risk factors associated with OSAS include a number of abnormalities in craniofacial structure. Narrowing of the upper airway is commonly observed, especially at the level of the soft palate and base of the tongue. Fiberoptic visualization in twenty five male subjects with OSAS identified the most common site of obstruction as the

oropharynx (76%). Obstructions were also found at the level of the hypopharynx (11%) and larynx (2%)(Wilms et al. 1982). Cephalometric characteristics linked to OSAS include an increased hyoid to mandibular plane distance, increased soft palate length and decreased posterior airway space. A recent study, at Case Western Reserve University, attempted to differentiate OSA subjects from other habitual snorers based on specific craniofacial risk factors (Pracharktam et al. 1996). This study used cephalometric radiographs to record craniofacial measurements from sixty apneic snorers and sixty non-apneic snorers. A craniofacial risk index (CRI) was constructed using age, body mass index, (BMI) and fourteen cephalometric and anthropometric measurements previously reported to be associated with OSAS. A separating boundary (CRIS) was established using discriminant analysis to differentiate between the two groups. A second sample of nineteen apneic and forty seven non-apneic snorers was identified for the purpose of testing the sensitivity and specificity of the index derived from the first sample (Hans et al. 1997). The CRI was able to correctly classify 72.3% (34/47) of the non-apneic snoring subjects and 73.7% (14/19) of the apneic snorers when all variables were used in the discriminant model. Using four variables (age, BMI, hyoid mandibular

plane distance, and tongue length) selected by the stepwise method, 72.3% (34/47) of the non-apneic snoring subjects and 78.7% (15/19) of the apneic snorers were correctly classified. In addition, seven variables (Cervical Vertebrae-SN, BMI, hyoid to mandibular plane distance, tongue area, the ratio of tongue area to intermaxillary area, intermaxillary length, and tongue length) were found to be significantly different between apneic and non-apneic groups. These results suggest that the stepwise CRI could be used as a adjunctive screening procedure to identify individuals predisposed to OSAS.

Upper airway resistance is relatively increased in sleep apnea patients (Suratt et al. 1983). Inspiratory excitation of upper airway muscles maintains patency when awake (Ono et al. 1996). Excessive relaxation or loss of compensatory excitation of upper airway muscles explains the propensity to collapse during sleep (Remmers et al. 1983).

The mechanics of obstructive sleep apnea from a dentist's perspective (George 1987) are described as follows:

1. As the mouth opens, the clockwise rotation of the anterior attachment of the tongue to the genial tubercle of the mandibular symphysis drives the tongue toward the posterior pharyngeal wall, especially in high mandibular plane angle cases. This decreases

the lumen of the airway, resulting in more rapid movement due to the Venturi effect. The increased velocity creates a greater negative pressure in the airway, which tends to suck the tongue and posterior pharyngeal wall together.

2. Active or passive opening of the mouth initiates a reflex in proprioceptive afferents in the muscles of mastication that inhibits the genioglossus. This antitongue biting mechanism reduces the muscular tonicity of the tongue, allowing it to be sucked back with relatively normal negative airway pressure.

Management of Obstructive Sleep Apnea

The natural history of obstructive sleep apnea is still not completely understood, and currently there are no absolute indices that mandate treatment for apnea frequency, severity of oxyhemoglobin desaturation, or sleep fragmentation. Most clinicians would agree however that patients who have symptoms suggestive of OSAS with greater than twenty apneas and hypopneas per hour of sleep or with severe oxyhemoglobin desaturation should be treated. However, symptomatic patients with fewer sleep disordered breathing events may also benefit from treatment. The decision to treat should be based on an overall assessment of the severity of hypersomnolence and of related neuropsychologic symptoms, cardiac sequelae, the presence of systematic hypertension, and the severity of sleep disordered breathing and sleep fragmentation documented on

polysomnography (Wiegand and Zwillich 1994).

Obstructive sleep apnea remains a therapeutic challenge. The determinants of airway patency during sleep are multifactorial and treatment modalities which address single factors such as anatomical anomalies are not uniformly beneficial. Treatments vary from conservative medical measures to invasive surgical procedures. The following is a synopsis of the most current and popular treatment regimens for OSAS with the exception of oral appliances which will be covered in the next section:

General Measures

The course of therapy for an OSAS patient should be individualized because all treatment modalities are not uniformly effective for all patients. An important part of the management of patients with OSAS involves a search for reversible factors that exacerbate sleep disordered breathing. For example, ethanol and sedative hypnotic use should be eliminated because these agents have been shown to worsen snoring and sleep disordered breathing. Ethanol ingestion may precipitate or aggravate obstructive breathing events in non-apneic snorers and in patients with OSAS (Robinson et al. 1985). Benzodiazepines may also have similar effects. Acute upper airway obstruction has reportedly developed in patients with OSAS who are given

benzodiazepines as preanesthetics (Leiter et al. 1985). Acute upper airway obstruction after barbituate use in patients with OSAS has also been reported.

Weight Reduction

Obesity is a recognized risk factor for upper airway obstruction. Approximately two-thirds of patients with sleep apnea have moderate to severe obesity (Kales 1985). Weight loss may improve breathing during sleep by increasing lung volumes and by decreasing pharyngeal collapsibility (Horner et al. 1989; Thomas et al. 1989). Accordingly, weight loss should be encouraged in all patients with OSAS who have obesity and may correct or reduce the quantity of sleep disordered breathing, particularly if the obesity is moderate (Wittels and Thompson 1990). Small reductions in body weight may result in substantial subjective and objective improvement in some patients with sleep apnea (Bray 1991), and in some patients additional therapy may not be required. However, dietary weight reduction is often difficult to achieve and even more difficult to sustain. In addition, some patients do not have adequate clinical improvement with weight loss or benefit only after substantial weight reduction (Kajaste et al. 1991). Surgical procedures, such as gastric stapling have been successful in selected patients with morbid

obesity (Victor et al. 1984).

Positional Therapy

Apneas during sleep may also be made worse by changes in body position. These are subjects who have apneas in supine position, whose symptoms are markedly ameliorated or abolished by sleeping in the lateral decubitus position (Cartwright et al. 1991; Phillips et al. 1986). Such patients are referred to as positional apneics. This diagnosis can be suspected by taking a careful history from the bed partner. They will report loud snoring and/or have witnessed apneas in only the supine position (Pack 1994). During polysomnography, body position should be monitored so that the respiratory index can be calculated separately for the supine and lateral positions. Patients with positional apnea will have high indices in the supine position (e.g., apnea/hypopneas in the range of 50-100 events per hour) but lower indices (e.g., <10 events per hour) in the lateral decubitus position (Cartwright et al. 1990).

Patients with positional apnea can be treated with position therapy. In essence, patients are advised to sleep with a tennis ball sewn to their pyjamas at the level of their shoulder blades so that sleep in the supine position is uncomfortable. Alternatively, subjects can use a

position-activated sound device that trains the patients with an auditory alarm to avoid supine sleep. After training, some patients no longer sleep supine (Cartwright et al. 1990).

Pharmacologic Agents

Pharmacologic therapy for OSAS has generally been disappointing. There are some reports of improvement in sleep apnea with acetazolamide (Tojima et al. 1988) and nicotine (Gothe et al. 1985). Acetazolamide produces a metabolic acidosis and is most useful in central apneas of the periodic type. Nicotine seems to stimulate upper airway dilating muscles more than diaphragm muscle activity (Westbrook 1990). Most attention has been focused on the use of two pharmacological approaches, medroxyprogesterone and protriptyline.

Medroxyprogesterone is a potent ventilatory stimulant and is most beneficial in obesity hyperventilation syndrome patients (Sutton et al. 1975). These patients hypoventilate during wakefulness and demonstrate carbon dioxide retention while they are awake. Medroxyprogesterone does not, however, exert any specific effects on upper airway motor output. Its effects on obstructive sleep apnea have been disappointing (Strohl et al. 1981; Rajagopal et al. 1986; Cook et al. 1989).

Protriptyline is an another drug that has been employed. Protriptyline, a tricyclic antidepressant, reduces the amount of REM sleep and may stimulate upper airway muscle activity. Animal studies have shown that it increases the respiratory activity of nerves carrying motor output to upper airway muscles (Bonora et al. 1985). Protriptyline has been shown to decrease respiratory disturbance index in at least some subjects (Hanzel et al. 1991). Some studies have suggested, however that the major effect of protriptyline is through reduction of the amount of REM sleep in which apneas can be more frequent and associated with larger falls in oxygen saturation (Smith et al. 1983). The use of this drug is very limited because of its associated anticholinergic side effects such as dry mouth, impotence, urinary hesitancy and constipation (Smith et al. 1983).

Nasal Continuous Positive Airway Pressure (CPAP)

Nasal continuous positive airway pressure (CPAP), was introduced by Sullivan and coworkers in 1981 (Sullivan et al. 1981) and has become the gold standard for treatment of OSAS. With this therapy, pressurized air is applied through the nares and acts as a "pneumatic splint" by elevating the pressure in the oropharyngeal airway and thereby maintaining positive airway pressure throughout the entire

respiratory cycle. Nasal CPAP therapy abolishes apneas and hypopneas, oxygen desaturation, and apnea-related sleep fragmentation in most patients. This results in rapid restoration of normal sleep architecture and improvement in daytime sleepiness. Obstructive apneas are eliminated in more than 99% of patients who can tolerate the device (Westbrook 1990). Patients should be observed in the sleep laboratory to determine the optimal CPAP level, which will vary with individual nasal resistance, upper airway size, compliance, and collapsibility. Continuous positive airway pressures in the range of 5-15 cm H_2O are commonly required (Wiegand and Zwillich 1994). After nasal CPAP therapy is effectively initiated, patients immediately experience a marked rebound in the deep stages of non-REM sleep and REM sleep. The sleep pattern gradually returns to normal during the first few weeks of therapy coincident with dramatic symptomatic improvement, particularly in daytime function and in sleep latency (Hoffstein et al. 1992). Preliminary data from several groups suggest that patients with OSAS initially have less sleep disordered breathing when nasal CPAP therapy is discontinued after longterm use. However, without weight loss, the OSAS returns to its previous degree of severity within a matter of days, suggesting that the changes in upper airway morphology and collapsibility

associated with longterm nasal CPAP are transient (Lamphere et al. 1989). Accordingly, although nasal CPAP therapy is highly effective when it is used regularly, poor patient compliance is likely to significantly reduce any beneficial effects.

Some patients are not able to tolerate nasal CPAP for various reasons: claustraphobia, mask discomfort, intolerance to machine noise, panic reactions, nasal drying or rhinitis and conjunctivitis. Short term compliance was reported at approximately 90% (Westbrook 1990), 95% (Strohl et al. 1986), and 100 of 138 patients (Katsantonis et al. 1988). However, longterm compliance is much lower, 66% (Westbrook 1990), 53% (Katsantonis et al. 1988), and 65-70% (Stokes-Dickens et al. 1989). Selected patients may better tolerate a nasal bi-level positive airway pressure device that allows the independent adjustment of inspiratory and expiratory pressure. Inspiratory pressure assists in inspiration, whereas expiratory pressure retards expiratory airflow and leads to hyperinflation. Thus, reduction of expiratory pressure could lead to less hyperinflation and potentially increase utilization of the device.

Tracheostomy

Tracheostomy was once the standard treatment for OSAS because the pharynx is completely bypassed with this

procedure. While effective, this therapy is not without its adverse effects; there are problems of local recurrent infection and granulation tissue at the site; recurrent bronchitis, presumably related to the loss of upper airway protective mechanisms and psychosocial consequences that can be major (Conway et al. 1981). With the advent of better tolerated options, tracheostomy should be reserved for patients with morbid illness.

Nasal Surgery, Tonsillectomy and Adenoidectomy

The first role to be considered for surgical treatment of obstructive sleep apnea is correction of an obvious upper airway anatomical problem such as nasal polyps, a deviated nasal septum or hypertrophied tonsils and adenoids (Pack 1994). Surgical correction of the deviated septum can improve the degree of respiratory disturbance index during sleep, but it is usually not curative (Heimer et al. 1983). Adenotonsillectomy remains the oldest and most common means of treating OSA in children. It is effective in as many as 90% of patients without craniofacial or neurological abnormalities (Brooks 1993). The results of tonsillectomy in adults are, however, not uniformly successful (Moser and Rajagopal 1987). Patients should be counselled that correction of the structural abnormality may not sufficiently alleviate apnea and that follow-up

polysomnography is required to assess the need for additional intervention (Wiegand and Zwillich 1994).

Uvulopalatopharyngoplasty (UPPP)

Of the various surgical treatments used for all patients with obstructive sleep apnea, UPPP seems to have been the most widely employed. This operation was introduced by Fujita and coworkers in 1981 (Fujita et al. 1981). In this surgical procedure, there is removal of the uvula, a portion of the soft palate, and redundant tissue from the posterior pharyngeal wall. Success rates of this surgery in patients with OSA are highly variable. In a recent study approximately 30% of the initial responders to the surgery had relapsed when they were followed up an average of twenty one months (Larsson et al. 1991). In a study examining the longterm success of UPPP after five years reported that more than 80% of all cases had subjective symptomatic improvement but the actual RDI results were significantly worse (Lu et al. 1995). However, in a third study (Riley et al. 1993), UPPP was reported to be successful in 80% of patients. Patients were treated with nasal continuous positive pressure before surgery and this was the primary method of evaluating success. The surgery was considered successful if the post-operative RDI was equivalent to the pre-operative RDI using nasal CPAP or

was less than 20 with normal oxygenation. In order to improve the overall success rate of UPPP it would seem ideal to be able to identify those patients whose obstruction is in the retropalatal area rather than at the base of the tongue. Using a Muller maneuver with direct visualization of the airway through a nasopharyngoscope, one group was able to identify the level of obstruction and found that retropalatal obstruction was a good predictor of successful UPPP outcome (Sher et al. 1985).

Maxillomandibular Osteotomies and Hyoid Myotomies

The combined Lefort I osteotomy and sagittal split osteotomy is the standard surgical procedure for advancing the maxilla and mandible. Hyoid myotomies allow for isolated advancement of the genial tubercles and genioglossus muscle. Most of the work in this type of surgery has been performed by the Stanford group who currently follow a staged surgical approach for treatment of OSAS (Riley et al. 1993). The first stage of treatment is based on the perceived level of obstruction in wakefulness. Each patient is classified into one of the three types according to the site of obstruction and are treated accordingly: type I, oropharynx (UPPP); type II, oropharynx/hypopharynx (UPPP + genioglossus advancement with hyoid myotomy (GAHM)), type III, hypopharynx (GAHM).

Treatment is considered successful if the RDI is equivalent to that using CPAP, or if the post-operative RDI is less than 20. Overall success rate for stage I of the surgery was 61%. The success rate of the stage II surgery with maxillomandibular advancement was higher,97%. Only twenty four of ninety four patients who failed stage I elected to go on to have stage II surgery. Most of the patients who had stage II surgery were UPPP failures from other institutions. These results are encouraging. Patients who enter and complete the surgical protocol have a greater than 95% success rate which is superior to any other treatment modality. This approach, however, involves major and perhaps multiple surgeries and all the risks that accompany it, not to mention considerable cost, potential relapse and altered dental occlusion.

Oral Appliances

The term "oral appliances" is used as a generic term for devices inserted into the mouth in order to modify the position of the mandible, the tongue and other structures in the upper airway. Over the last several years oral appliances have gained increased popularity for the treatment of snoring and/or obstructive sleep apnea (OSAS). In 1994 there were seventeen commercially available appliances while today there are more than forty. A

conservative estimate based on information from dental laboratories, suggests that there are more than twenty thousand Americans currently wearing a dental appliance for the treatment of snoring and/or OSAS (Lowe 1997).

Each oral appliance can have a primary effect on one or more structures. Many of the appliances position the mandible anteriorly- the Equalizer, Herbst®, Jasper jumper, Mandibular Repositioner, Nocturnal Airway Patency Appliance (NAPA), Sleep and Nocturnal Obstructive Apnea Reducer (SNOAR), SnoreGuard®, Snoring Treatment Appliance, and Klearway™. Other appliances alter the position of the soft palate- the Adjustable Soft Palate Lifter (ASPL) and the Equalizer. The tongue is affected by all the appliances except the ASPL either by direct forward movement of the muscle itself (eg., Tepper Oral Proprioceptive Stimulator (TOPS), Tongue Locking Device (TLD), Tongue Positioner and Exerciser (TPE), and Tongue Retaining Device (TRD)) or by changes secondary to an altered mandibular rest position. A description of the most popular and well documented oral appliances are described in further detail in the following pages.

Adjustable Soft Palate Lifter

This appliance is designed to gently lift the soft palate and uvula preventing them from vibrating against the

pharyngeal wall. This appliance's inventor, Dr. Paskov has claimed a 60% success rate for snoring (Lowe 1994). Prior to presentation of the appliance palatal desensitization exercises are usually recommended (Paskov 1991). The palatal lifter is adjusted backward one eighth of an inch each night by the patient until maximum effectiveness is attained. One case study reported elimination of snoring in a sixty eight year old man who had been snoring for more than ten years. A customized vitallium framework was fabricated with occlusal rests, retentive clasps and extended posteriorly to support the soft palate. This appliance is contraindicated in individuals with a strong gag reflex.

Equalizer

This appliance is designed to advance the mandible, equalize intraoral and extraoral air pressure and elevate the soft palate. One report based on fourteen patients documented a mean RDI of 36.5 before treatment and 18.9 after treatment (Lowe 1994).

Herbst®

This appliance was first utilized as a functional orthodontic appliance in Europe by Herbst in 1905 (Clark et al. 1993). The Herbst is a registered trademark of Dentarum, Inc., Newton, PA and is available from most

orthodontic laboratories. The removable Herbst® is made up of two separate upper and lower full-coverage clear acrylic appliances that snap onto the teeth which are connected with two rod and tube devices that allow opening, protrusive, some side to side movement and no retrusive movement. Dr. Clark recommends the use of bilateral interarch elastics to keep the jaw closed, interproximal ball clasps to increase retention to the teeth and a mandibular advancement of at least 75% of the patient's maximum protrusive position from maximum intercuspation. If the initial response is insufficient, a shim can be added to advance the mandible further (Clark et al. 1993).

For fifteen subjects who had a post-appliance sleep study, the mean pre-appliance respiratory disturbance index of 48.4 $\pm$ 33.4 was decreased to 12.3 $\pm$ 20.6 after appliance treatment. Oxygen saturation levels improved markedly, however there was only a partial return to normal sleep architecture (Clark et al. 1993). In another study of sixteen patients fitted with the removable Herbst®, fifteen claimed improvements of 70-100% improvement in their sleep while one patient was not able to tolerate the device (Rider 1988). In a third study involving nineteen patients who were unable to tolerate CPAP and were fitted with a removable Herbst appliance, RDI decreased from 34.7

± 5.3 to 12.9 ± 2.4 after device therapy. However, there was no change in posterior airway space after mandibular advancement for any subjects contrary to reports of previous studies (Meier-Ewert and Brosing 1987; Schmidt-Nowara et al. 1991). It was observed nonetheless that the distance between the hyoid bone and the mandibular plane decreased significantly for the group as a whole. Because the magnitude of change in RDI varied considerably among the nineteen subjects after appliance therapy, the subjects were divided into subgroups of "responders" and "nonresponders". Responders were defined as having a post-treatment RDI < 10 events/hour (n=10) and nonresponders as having a post-treatment RDI > 10 events/hour (n=10). The results indicated that baseline and post-treatment MP-H distances as well as the post-treatment soft palate lengths (PNS-P) were smaller in the responder group.

There are both advantages and disadvantages of the Herbst appliance. On the positive side, it maintains a continuous, forward tongue position throughout the night and is designed so that oral breathing is still possible if nasal airways are blocked. Disadvantages of this appliance are the possible deleterious side effects, such as TMJ remodelling and subsequent dysfunction as well as occlusal changes (Clark and Nakano 1989).

Patient compliance may also pose as a potential disadvantage. In Clark's study of twenty three subjects only twelve or 52% were still using the appliance successfully at thirty six months. In Eveloff's study, thirteen of fourteen subjects continued wearing their appliance after a mean follow-up time of two years, with a range of 1-3.5 years.

Nocturnal Airway Patency Appliance (NAPA)

NAPA is a modified activator (Soll and George 1985), a variant of the orthodontic appliance developed in 1902 by Pierre Robin as a treatment for upper airway obstruction in infants with mandibular hypoplasia (Robin 1934). NAPA was designed to keep the airway open during sleep by 1) posturing the tongue more anteriorly, 2) inhibiting wide jaw opening, and 3) assuring adequate air intake through the mouth whenever nasal obstruction exists (George 1987). This appliance has eight adams clasps and is designed to protrude the mandible about three-quarters the distance between centric occlusion and maximum protrusion. The mandible is opened vertically just enough to permit an airway between the incisors.

In a preliminary case report (Soll and George 1985), a forty five year old man with a history of sleep difficulty and daytime somnolence was treated with the NAPA. The

patient's snoring disappeared immediately as did his daytime sleepiness. His performance at work improved and his family considered him a new man. Results of his overnight sleep studies demonstrated a decrease in the number of apneic episodes per hour from 79 to 5.3 and his number of arousals from 9 to 2 following appliance therapy. In a second report on an additional five patients treated with NAPA, polysomnography also showed substantial reduction in the number of apneas per hour in all five patients (George 1987). All patients subjectively reported improvement in their sleep, snoring decreased or completely disappeared and daytime somnolence was eliminated or markedly diminished.

A separate study (Bonham et al. 1988) investigated the effect of treatment with NAPA on twelve patients between the ages of thirty and sixty five years. The mean vertical and horizontal changes in mandibular position while wearing the appliance were 8.49 mm and 2.28 mm respectively. The findings indicated that ten out of twelve patients had a mean reduction in apnea index from 53.81 to 35.99 events per hour. The two remaining patients had an increase in respiratory disturbance index after treatment with the NAPA. In this study treatment was considered successful if upper airway obstruction rate decreased by 50% and fell

below 10 events per hour. On the basis of these criteria, treatment with this modified functional appliance was successful in only seven of the twelve patients.

The success achieved with NAPA can be attributed to an increased airway space, a stable anterior position of the mandible and tongue and forward movement of the soft palate. Repositioning the mandible forward and hence the tongue results in an increase in the oropharyngeal airway space. Creation of the bite-block effect with the increased vertical dimension of the appliance results in increased tonicity of the genioglossus muscles inhibiting the posterior displacement of the tongue (Lowe 1988; George 1989). In addition the increased vertical dimension causes the tongue to be carried inferiorly thereby allowing for the soft palate to move anteriorly (Bonham et al. 1988).

Failure to substantially improve OSAS in five of the patients can be explained by two possible reasons. The first reason for lack of success can be attributed to a high mandibular plane angle. The mean SN-MP angle for the seven successfully treated patients was 28.85° and that for the five unsuccessfully treated patients was almost 10° greater; 38.75°. The glenoid fossa in patients with a high mandibular plane would tend to be steep, resulting in more vertical than horizontal translation on mandibular opening.

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Insertion of the NAPA in a patient with a steep mandibular plane would aggravate this, tending to rotate the genioglossus and hyoid musculature closer to the oropharyngeal airway. A second reason for failure can be explained by excessive soft palate length. The mean soft palate length was 44 mm for the seven successfully treated patients and 50 mm for the five unsuccessfully treated patients. Any benefit derived from increased airway space by the appliance was very likely overcome by deep encroachment of the soft palate into the oropharynx.

The advantages of the NAPA are its ease of use and its patient acceptance. After six years of nightly use there does not appear to be any irreversible effects (George 1989). In addition it can be removed and modified or eliminated if the patient's airway anatomy changes after weight loss.

Some disadvantages of the appliance relate to controversy surrounding the effects of prolonged traction on the TMJ. Prolonged nighttime mandibular protrusion with a bionator has been observed to result in a forward posturing of the jaw during the day. This can be attributed to myostatic contracture (foreshortening) of the inferior lateral pterygoid muscle (Graber 1984). In order to prevent this contracture and possible occlusal problems, Dr. George

recommends to his NAPA patients that they clench their teeth three times for five seconds every morning after removing the appliance. This isometric exercise invokes an inverse stretch reflex that relaxes the inferior lateral pterygoids and returns them to their normal resting length (George 1987).

The Tongue Retaining Device (TRD)

The TRD is custom made appliance designed to hold the tongue forward during sleep (Samuelson 1988). An anterior bulb is used to create negative pressure which holds the tongue forward during sleep. A patent nasal airway must be present for TRD to be effective (Cartwright 1985). A modified TRD with lateral airway tubes is also available for those patients with blocked nasal passages (Lowe 1994). The objective is to increase the volume of the air space as the superior surface of the tongue is brought forward and away from the posterior pharyngeal walls (Cartwright and Samuelson 1982).

The TRD is the only appliance that has been studied in various body positions and in conjunction with other forms of therapy. In a preliminary study (Cartwright and Samuelson 1982) that evaluated fourteen subjects reported a mean apnea index (AI) reduction from 55.6 to 27.2 after insertion of the TRD. In addition, improved sleep and

significantly fewer and shorter apneic events were seen on the nights when the device was worn. The sleep architecture also showed a change toward a more normal pattern with less light sleep and more delta-wave and more REM sleep immediately after treatment began. The mean apnea plus hypopnea index while wearing the TRD was shown to be comparable with the rate reported for patients who had been treated surgically by either tracheostomy (Weitzman et al. 1980) or by uvulupalatopharyngoplasty (Fujita et al. 1981), although the tracheostomy group contained more severe cases.

It has long been recognized that obesity is correlated with the severity of sleep apnea (Block et al. 1979). More recently though, sleep position has been identified as another risk factor (Cartwright 1984). In a study of twenty four male OSAS patients, selected for variable sleep posture during the night, the AI was found to be significantly higher during the time spent sleeping in the supine position (mean = 63.6) than in the side sleep posture (mean = 37.8). This difference was found to be marked for those who were no more than 25% above their ideal body weight. For this group, the AI per hour of sleep while on their back (45.5) was significantly higher than their index while sleeping in the lateral decubitus

position (10.8). In a group of sixteen male patients, the TRD was more effective for those who demonstrated an initial position difference in apnea severity. For these patients, the TRD reduced the AI in both sleep positions. For those patients who did not demonstrate an initial postural difference, the TRD was effective in improving respiration only during the portion of the night which they slept in the lateral decubitus position. The criteria for successful treatment in this study was set at achieving an AI within normal limits (0 to 6) or a reduction of the index by at least 50%. On this basis, eleven of the sixteen patients (69%) would be classified as having met that criterion. If only those patients who showed an initial difference in their back and side apnea index had been treated with the TRD, the success rate would have been eight out of nine, or 89%. When obesity, age, and position ratio were entered into a discriminant function analysis, these three variables succeeded in correctly classifying 81.25% of the patients, nine out of eleven successes, and four of five failures.

In another study (Cartwright et al. 1991), a sample of sixty adult men with respiratory disturbance index (RDI) values greater than 12.5 who had two or more times the apnea rate during supine sleep in comparison with their

lateral sleep rate, were assigned to four treatment groups: TRD only, posture alarm, TRD plus posture alarm and health habit instruction. The results reported where that between 53-60 % of the patients in the three single treatment groups (TRD, PA and HH) were at less than 5.5 events/hour. The combined treatment group had the highest success rate at 73% reaching this level of control. The fifteen subjects treated with TRD alone had a reduction in the mean RDI form 27.4 to 11.4. Patency of the nasal airway and an initially low side index were two factors significantly related to successful control of OSAS with the TRD. For the fifteen subjects in the TRD plus posture alarm group, lower initial obesity and higher weight loss during treatment were factors associated with best success. A mean RDI reduction from 30.7 to 7.9 was seen for the latter group.

Previous evidence has shown that a smaller airway size is associated with a hypotonic genioglossus muscle in subjects with OSAS (Guilleminault et al. 1978). To evaluate the effect of the TRD on awake genioglossus activity, ten OSAS subjects were compared to six age and body mass index (BMI) matched symptom-free controls (Ono et al. 1996). In this study, two customized TRDS were used for each subject. The TRD-A did not have an anterior bulb but incorporated lingual surface electrodes to record the GG

electromyographic (EMG) activity. The TRD-B contained an anterior bulb and two similar electrodes. The GG EMG was also recorded while patients used the TRD-B but were instructed to keep their tongue at rest outside the bulb; this condition was referred to TRD-X. The following results were obtained and were consistent in the upright or supine position. The GG EMG activity was greater with the TRD-B than with the TRD-A in control subjects but the GG EMG activity was less with the TRD-B than with the TRD-A in OSAS subjects. Furthermore, there was no significant differences between the GG EMG activity of the TRD-A and the TRD-X in control subjects whereas there was less activity with TRD-X than with TRD-A in subjects with OSAS. It was therefore concluded that the TRD has different effects on awake genioglossus activity in control subjects and patients with OSAS. Nevertheless because TRD has been shown to be an effective treatment modality for reducing apnea, the resultant mechanical enlargement of the upper airway volume seems more important than a facilitation of the hypotonic tongue protruding muscle activity.

SnoreGuard®

The SnoreGuard® (Hays and Meade Inc; Albuquerque,NM) is a prefabricated appliance that is easily fit and adjusted directly in the patient's mouth. The orthosis is

designed to attach securely to the upper teeth and to advance the mandible by means of a projection which engages the lower incisors when the teeth are approximated. An orifice in this projection permits oral airflow. The size of the device is minimized in order to limit discomfort and salivation.

Schmidt-Nowara et al.(1991) used the SnoreGuard® to treat sixty eight patientswho exhibited snoring behavior and varying degrees of obstructive sleep apnea. Seven months after beginning use, 75% of patients were using the orthosis regularly. Snoring, by report was improved in all patients but one and was eliminated in 42%. Sleep quality and sleepiness were also reported improved. Apneas and hypopneas, measured before and after use in twenty patients with obstructive sleep apnea, were reduced from an average of 47 to 20 events per hour. Oxygenation and sleep disturbance were also improved.

In a subsequent study performed at Case Western Reserve University (Hans et al. 1997), two dental appliances were compared in twenty four subjects for their effectiveness in the treatment of snoring and OSAS. Twelve subjects were fitted with device A (SnoreGuard®) designed to increase vertical dimension and protrude the mandible. Another twelve subjects were fitted with device B (a

modification of SnoreGuard®) designed to minimally increase vertical dimension with no mandibular protrusion. Polysomnography was performed at T0, before using any device and again at T1, after using the device for two weeks. The Epworth Sleepiness Scale (ESS)(Johns 1991), a subjective self report was also completed at both time points. With device A the mean RDI was reduced from 35.6 to 21.1 and the ESS scores from 12.0 to 8.2.in ten subjects who completed the study. With Device B the mean RDI increased from 36.5 to 46.8 and ESS scores demonstrated virtually no change from 13.0 to 12.5 in eight subjects who completed the study. Six subjects withdrew for various reasons. Because RDI was decreased in nine of ten subjects with device A and increased in eight of eight with device B, it was concluded that a dental device that advances the mandible and increases vertical dimension to open the upper airway is more effective in reducing the number of apneic and snoring events than one which does not.

Mandibular Repositioners

Of the many oral appliances that have been proposed for the treatment of snoring or sleep apnea, most have designs that use traditional dental techniques to attach the device to one or both dental arches and to modify mandibular posture (Schmidt-Nowara et al. 1995). A recent

report (Menn et al. 1996) evaluated the demographic, polysomnographic and cephalometric radiographic predictive findings of treatment success or failure with the mandibular repositioning device (MRD). The MRD is a device that attaches to the maxillary teeth and advances the mandible by engaging the mandibular incisors. This design is similar to the SnoreGuard appliance (Schmidt-Nowara et al. 1991). Twenty-nine OSAS patients underwent polysomnography and a maintenance of wakefulness test (MWT) before and again after a three month trial with the MRD. During the MWT, the patient was asked to stay awake for a period of forty minutes as opposed to twenty minutes for the multiple sleep latency test (MSLT). The MWT has been shown to be more sensitive to treatment-related improvement in sleepiness (Poceta et al. 1992). Respiratory disturbance index decreased with MRD use (37 ± 23 versus 18 ± 20), and 16 out of 23 patients were considered responders (decrease in RDI $\geq 50\%$ and post-treatment RDI ≤ 20). Mean sleep latency increased from 23 ± 9 to 32 ± 10. The correlation between an increase in MWT mean sleep latency and a decrease in RDI was 0.77. Neither age, body mass index, nor cephalometric measurements were found to be predictive of treatment response. By subjective report, sixteen of twenty three patients (70%) continue to use the MRD nightly after

3.4 ± 0.7 years which is at least comparable to longterm compliance rates with CPAP.

In a report of an appliance called the elastomeric sleep appliance (Lyon et al.,1990), that examined fifteen patients, fourteen reported a marked improvement in snoring. In six additional participants diagnosed with OSAS the apnea/hypopnea index was reduced 47% and all subjects reported a decrease in their subjective symptoms. Based on these results, in the opinion of the authors, patients are more likely to respond favorably to an oral device if they are not over 125% of ideal body weight. In addition they will probably not respond favorably if they are 150% or more of ideal body weight because their obesity limits any increases in pharyngeal airway space.

Three reports discuss treatment results with similar appliances which cover both the upper and lower teeth and hold the mandible forward 3-7 mm in a fixed position. The first is a case report (Arai and Furuta 1997), of a fifty three year old woman with OSAS and nocturnal enuresis that was effectively treated with a dental appliance (DA) and had good compliance and effects during two years of follow-up. The patient's apnea/hypopnea index was 52.6 at pre-treatment, 3.5 after one month with DA therapy and 4.4 at the two year follow-up. A second study by Nakazara et al.

(1992), used an appliance referred to as Prosthetic Mandibular Advancement (PMA). This study evaluated fourteen patients treated with PMA and found it to be therapeutically effective not only on obstructive apnea but also on central apnea. In the third study in which fourteen patients were treated with a "Sleep Splint" (Ichioka et al. 1991), a 50% reduction of the apnea/hypopnea index was demonstrated in thirteen of the patients. It is my opinion, however, that eight of these thirteen were still not within a range of normality.

Customized dental appliances which advance the mandible for the improvement snoring and OSAS can be fabricated not only for the dentate patient (Knudson et al. 1992) but also for the edentulous patient (Meyer and Knudson 1990; Knudson and Meyer 1993).

Klearway™ Appliance

The Klearway™ appliance is the newest and most popular appliance on the market. It has an adjustable hinge that allows progressive advancement of the mandible after initial construction. The mandible can be advanced until an optimal mandibular position is achieved. This appliance requires a minimum of ten teeth in both the maxillary and mandibular arches.

In a prospective randomized crossover study, efficacy,

side effects, patient compliance and preference of both a non-adjustable (SnoreGuard®),(Ferguson et al. 1996) and adjustable (Klearway™),(Fleetham et al. 1996) mandibular advancement appliance and nasal CPAP were compared in fifty one patients with mild to moderate OSAS. Efficacy, side effects, patient compliance, and preference were evaluated by questionnaire and home-sleep monitoring. Forty-eight percent of patients treated with the non-adjustable appliance were treatment successes (resolution of symptoms and reduction in apnea/hypopnea index (AHI) < 10/hour) compared to 61% for the adjustable appliance and 66% for CPAP. Both the appliances and CPAP were effective in reducing symptoms but the appliances were less effective in improving sleep oxygenation. Side effects were more common and the patients less satisfied with CPAP. The long-term preference was overwhelmingly in favor of dental appliance therapy.

A report published by the American Sleep Disorders Association reviewed twenty one publications to describe patients treated with oral appliances for snoring and obstructive sleep apnea (Schmidt-Nowara et al.,1995). The following conclusions were drawn:

1. Despite considerable variations in the designs of the appliances, the clinical effects were remarkably consistent.

2. Snoring was improved in almost all patients and was often eliminated.

3. Mean results of studies showed that OSAS improved in the majority of patients. Approximately half of those who improved achieved an AHI of < 20, but as many as 40% were left with notably elevated AHIs.

4. Sleep was generally improved, although significant sleep disturbance persisted in the patients with residual apnea.

5. Temporomandibular joint complications and occlusal changes appeared to be uncommon.

6. Longterm compliance varied from 50-100% of patients

For OSAS, no currently available treatment provides the ideal combination of a high rate of longterm success and patient acceptance without complications. Nasal CPAP has become the consensus first choice because of its efficacy, but patient acceptance and compliance can be significant problems. Tracheostomy is the only other treatment with efficacy comparable to CPAP, but given today's alternatives, the idea of selecting a treatment requiring a permanent prosthesis in the neck is not appealing. Oral appliances and all other alternatives to nasal CPAP and tracheostomy, either medical or surgical, are effective in a lower proportion of patients. Compared with uvulopalatopharyngoplasty or more complex facial reconstruction, oral appliance therapy costs less and has

the advantage of being terminated without sequelae. Compared with methoxyprogesterone and protriptyline, medications used in the treatment of OSAS, the efficacy of oral appliance therapy is better and side effects appear to be more tolerable. Compared to weight loss, the effects of oral appliance therapy are realized more quickly and the rate of success is higher. Comparison of the risks and benefits of oral appliance therapy with those of other available treatment strategies suggests that oral appliances present a useful alternative.

Snoring and OSAS disorders are the domain of the medical profession and dentists are not medically qualified or legally permitted to diagnose sleep disorders. The dentist's role in treatment should be adjunctive in nature. Dental appliance therapy should only be provided after written request or prescription from a sleep disorders specialist or attending physician. The Standards of Practice Committee of the American Sleep Disorders Association (ASDA) appointed a task force to review the current role of oral appliances in the treatment of snoring and OSAS. The subsequent recommendations were developed by the Standards of Practice Committee and approved by the Board of Directors of the ASDA (ASDA,1995);

Diagnosis

The presence or absence of OSAS must be determined before initiating treatment with oral appliances to identify those patients at risk due to complications of sleep apnea and to provide a baseline to establish the effectiveness of subsequent treatment.

Treatment Objectives

A. For patients with primary snoring without features of OSAS or upper-airway resistance syndrome, the treatment objective is to reduce the snoring to a subjectively acceptable level.

B. For patients with OSAS, the desired treatment outcome treatment includes the resolution of the clinical signs and symptoms of OSAS and the normalization of the apnea-hypopnea index and oxyhemoglobin saturation.

Indications

A. Oral appliances are indicated for use in patients with primary snoring or mild OSAS who do not respond to or are not appropriate candidates for treatment with behavioral measures such as weight loss or sleep-position change.

B. Patient with moderate to severe OSAS should have an initial trial of nasal CPAP because greater effectiveness has been shown with this intervention than with use of oral appliances.

C. Oral appliances are indicated for patients with moderate to severe OSAS who are intolerant of or refuse treatment with nasal CPAP. Oral appliances are also indicated for patients who refuse or are not candidates for tonsillectomy and

adenoidectomy, craniofacial operations or tracheostomy.

Follow-up

A. Follow-up polysomnography is not indicated for patients with either primary snoring or mild OSAS unless symptoms worsen or do not resolve.

B. To ensure satisfactory therapeutic benefit, patients with moderate to severe OSAS should undergo polysomnography, or another objective measure of respiration during sleep, with the oral appliance in place after final adjustments of fit have been performed.

C. Patients with moderate to severe OSAS who are treated with oral appliances should return for follow-up office visits with both the referring clinician and the dentist. These visits should occur at regular intervals to monitor patient compliance, evaluate device deterioration or maladjustments, evaluate the health of the oral structures and integrity of the occlusion, and assess the patient for signs and symptoms of worsening of OSAS. Oral appliances may cause a worsening of OSAS in some patients and appropriate follow-up care is therefore essential.

D. Oral appliances may aggravate temporomandibular joint disease and may cause dental misalignment and discomforts that are unique to each device. Follow-up care by a dentist is necessary to assess the development of any of these complications.

Appliance fitting

A. Oral appliances should be fitted by qualified personnel who are trained and experienced in the overall care of oral

health, the temporomandibular joint, dental occlusion and associated structures. The fitting of tongue-retaining devices may not require any special dental training, although education by and consultation with dentists is desirable.

B. Although cephalometric evaluation is not always required for patients who will use an oral appliance, appropriately trained professionals should perform these examinations when they are deemed necessary.

In addition, a professional society of dentists interested in sleep disorders: The Sleep Disorders Dental Society has issued recommendations to dentists for the implementation of oral appliance therapy as part of overall therapy (Lowe,1994). The following sequence is suggested by the Sleep Disorders Dental Society for the management of dental appliances in patients who are being treated for snoring or OSAS:

1. Medical assessment by the attending physician or sleep specialist
2. Overnight polysomnogram as required by physician or sleep specialist
3. Written referral or prescription and diagnostic report sent to dentist or dental specialist
4. Dental examination
    a. Medical-dental histories
    b. Soft tissue-intraoral examination
    c. Periodontal examination

d. Temporomandibular joint-occlusal examination

e. Intraoral habit assessment

f. Examination of teeth and restorations

g. Initial dental radiographs if films have not been taken in preceding 6 months

i. Panoramic or full mouth survey

ii. Cephalometric radiograph

h. Diagnostic models as appropriate for the specific dental appliance

5. Trial appliances

a.Design, fabrication, fitting, instructions and training

b.Three to seven night trial and evaluation

i. Subjective symptom assessment

ii. Cephalometric radiograph (optional)

6. Final appliance design, fabrication, fitting and placement

7. Final appliance evaluation over 2 to 3 months of regular use

8. Refer patient to attending physician for repeated overnight sleep study

9. Possible modification, redesign, or remake of appliance as required

10. Repeated adjustment and evaluation process

11. Refer to physician for ongoing evaluation

12. Recall appointments and maintenance as requested by patient or physician

The majority of studies evaluating the effectiveness of dental appliances have been case series. None have compared different oral appliances other than the one study published from CWRU (Hans et al. 1997). Very few studies have attempted to explain the mechanotherapy of dental appliances, how and why they work? This study evaluated anatomic changes and sleep quality changes effected by five different appliances. Comparisons were made among the treatment groups in attempt to determine an ideal appliance design.

STATEMENT OF THE THESIS

The purpose of the present study was to determine if 1) dental appliances used to treat patients with a history of loud snoring, with or without apnea, would produce any significant change in the craniofacial structure and sleep quality and if so, 2) were there any signifcant differences among appliance groups? To achieve these objectives, forty two adult volunteers treated with a dental appliance were recruited to address the following specific aims:

1. To evaluate anatomic changes produced by the dental devices, cephalometric x-rays taken at T0 (before any treatment) and again at T1 (time of delivery of the appliance) will be compared in terms of:
    a. A change in the Craniofacial Risk Index (CRI)
    b. A change in the individual cephalometric variables
2. To evaluate the changes in sleep quality produced by the dental devices sleep assessments at T0 (before any treatment) and again at T2 (after wearing the device for 2 weeks) will be compared in terms of:
    a. A change in the Respiratory Disturbance Index (RDI)
    b. A change in the Epworth Sleepiness Scale (ESS)

Identification of variables associated with treatment outcome may aid in designing a dental appliance which could most effectively reduce snoring and obstructive sleep apnea.

MATERIALS AND METHODS

Study Population

The study population consisted of forty two habitual snorers (mean age 52.09 years, SD:10.40, range 29-69 years), recruited for one of two randomized trials examining the effectiveness of dental devices in treating patients with a history of loud snoring with or without apnea. These, otherwise healthy adult volunteers with a self-reported history of loud snoring were recruited by:

1) Poster advertisement in prominent locations throughout the University
2) Advertisement in the "Campus News"
3) Referral from local dentists and physicians
4) Referral from the Veteran's Administration and University Hospitals Sleep Disorders Center

Prior to enrolling a participant in the study, a baseline RDI was determined using home-monitoring polysomnography (Edentrace II, Edentec Corp, Eden Prairie, MN). Individuals with an RDI above 10, who were not referred by a managing physician, were referred to a sleep physician with specialty training in pulmonology for

medical evaluation of pathophysiologic symptoms. Individuals with an RDI greater than 30 were excluded from the study unless they had written approval from their managing physician.The managing physician had to indicate that participation in the randomized trial would not place the participant at increased medical risk of complications related to OSAS.

Individuals who were previously enrolled in a randomized trial examining the effectiveness of dental devices in treating patients with a history of loud snoring with or without apnea were included in the present study if they met the following inclusion criteria:

1) They were delivered a dental device (Clinical Trial I or II)

2) They had a cephalogram with and without the device in place

3) They had a polysomnograph taken at baseline and after two weeks of intervention

4) They were Caucasian

Fifty subjects participated in one of two randomized trials. Clincial trial I compared the effectiveness of two dental devices. Device A (SnoreGuard®) was designed to increase vertical dimension and protrude the mandible. Device B, a mouthguard, (a modification of SnoreGuard®) was designed to minimally increase vertical opening without protruding the mandible. The SnoreGuard® appliance was a

commercially available thermoplastic device. Clinical trial II compared the effectiveness of three dental devices, A,B, and C. Device A was designed to open the vertical and advance the mandible. Device B was designed only to open the vertical and Device C only to advance the mandible. In both trials assignment of subjects to device groups utilized a table of random numbers in order to eliminate selection bias.

Data Collection

Various data were gathered at three time points: T0- before beginning the study; T1- immediately following insertion of the appliance; and T2- at the end of two weeks of intervention.

Questionnaire Data

The Epworth Sleepiness Scale (Johns 1991) was administered by the study coordinator at T0 and T2 to assess sleep patterns, sleep time and subject sleepiness. The questionnaire was subsequently scored and treated as a continuous variable for statistical analyses.

Polysomnographic Data

An unattended in-home 6-channel sleep study was performed for all subjects to ascertain RDI at T0 and T2. The portable monitor allowed for accurate measurement of oxygenation, airflow, snoring, body position, chest wall

movement and heart rate during sleep. Home sleep monitoring has been demonstrated to have a high correlation (r= 0.96) with standard laboratory polysomnographic procedures at the hospital (Redline et al. 1991). The home monitoring device was designed and manufactured for in home use and is non-invasive. Use of this device did not involve any increased risk beyond those encountered in daily living. All of the sleep studies were scored by a single technician blinded to the subjects clinical symptoms.

Anthropometric Data

Anthropometric data included age, sex, Body Mass Index (BMI), as well as head and facial form. Body Mass Index (BMI) was calculated as the weight in kilograms divided by height in meters squared . The mean BMI for the entire sample was 29.71 $\pm$ 5.06 with a range of 19.20 to 41.84 (kg/m^2).

The subject's head was measured using spreading calipers according to standard anthropometric methods. Classification of head form (brachycephaly, mesocephaly, or dolichocephaly) was done by using the cranial index (ratio between cranial width and length). Classification of facial type (euryprosopic, mesoprosopic, or leptoprosopic) was obtained by calculating the ratio of bizygomatic width measured from the lateral radiograph according to Montagu

(1960). The ratio of cranial index to facial index was obtained by dividing the cranial index by the facial index (CI/FI).

Cephalometric Data

Cephalometric radiographs were obtained before treatment (T0) and immediately after insertion of the dental device (T1) to document changes in oropharyngeal dimensions. As in standard cephalometry, the patient was positioned upright with the head held in a modified craniostat. The object source distance was fixed at 60" and the film cassette placed in contact with the patient's left cheek. Prior to radiography, the subject was asked to swallow a teaspoon of barium sulfate esophageal cream (Esophotrast, Roer Pharmaceutical Corp., Collegeville, PA) to clarify the outline of the oropharyngeal soft tissues. The lateral cephalogram was taken using natural head posture, at the end of the expiration phase, with the posterior teeth in contact and without swallowing. Natural head posture was determined by placing a fluid level device on the side of the patient's face parallel to soft tissue Frankfort. The patient was instructed to close their eyes and tilt their head back and forth gently and then to bring their head to a relaxed position. The measure from the fluid level device was recorded. This procedure was

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repeated three to five times and the mode was chosen as the value for natural head position in which the T0 and T1 cephalogram was taken. After the T0 cephalogram was taken the ML distance (the distance from the film to the midsaggital plane) was recorded. This permitted keeping the enlargement of the T1 film on the same subject constant.

All cephalometric radiographs were traced by an investigator blinded to the subject's apneic status. Tracings were done on 0.003 inch matte acetate paper (Masel, Bristol,PA) with 0.3 mm H lead pencil. All cephalometric landmarks were located and digitized using customized software developed for two-dimensional morphologic analysis of anatomy (Dentofacial Planner®, Dentofacial Software, Toronto and GeoCalc®, courtesy of Drs. John Blank, Robert Mensforth, Cleveland State University).

A total of fourteen conventional linear and angular measurements were selected based on the literature and on previous work done at CWRU (Figure 1-4, Glossary). These measurements were Basion to Sella Nasion (BaSN), Cervical Vertebrae to SN (C2C4SN), A-point to Posterior Nasal Spine (A-PNS), Hyoid to Mandibular Plane (H-MP), Intermaxillary Length (Int.Mx.Lth), Soft palate Length (P-PNS), Posterior

Nasal Spine to Basion (PNS-Ba), Superior Posterior Airway Space (Phw-Psp), angle between Frankfort and True Horizontal (Frankfort and True Horizontal (FH-Hor), and Tongue Length (TL). Two measurements from the Counterpart Analysis of Enlow et al., (1971) were used to analyze cranial base alignment (MCF) and ramus width relative to cranial base (RAM-MCF) (Figures 3 and 4). The counterpart analysis is based on an individual's own anatomic features and compares different anatomic parts with each other to identify areas of compensation or imbalance. The relative space occupied by the tongue within the skeletal framework was calculated by taking the ratio of the tongue area (T area) to the intermaxillary space (Int.Mx.area) in the sagittal plane (Vig and Cohen 1974) (Figure 4).

The Craniofacial Risk Index (CRI) was calculated using two discriminant models. The first used the forced entry method and included age, BMI (kg/m2) and fourteen cephalometric and anthropometric variables. The second model used the stepwise method for reducing variables. This model used four variables; age, BMI, hyoid to mandibular plane distance and tongue length to compute the index score.

Statistical Analysis

A Novell based computer network was used for data

management. Data was entered with form oriented tools programmed to identify out-of-range and illogical entries. Statistical analyses were performed using the SPSS for Windows statistical package.

For the purposes of clarity the variables used in the statistical analyses are outlined below:

Predictor Variables:

Dental devices (SnoreGuard®, mouthguard,A,B,C)

Outcome Variables:

a.) Craniofacial Risk Index (CRI)

b.) Cephalometric variables

c.) Respiratory Disturbance Index (RDI)

d.) Epworth Sleepiness Scale (ESS)

Means and standard deviations were calculated for all continuous variables. A two-tailed paired t-test was used to examine differences between the means. A p-value of 0.05 was used to assign statistical significance. An analysis of variance was calculated to compare mean outcomes among the various appliance groups.

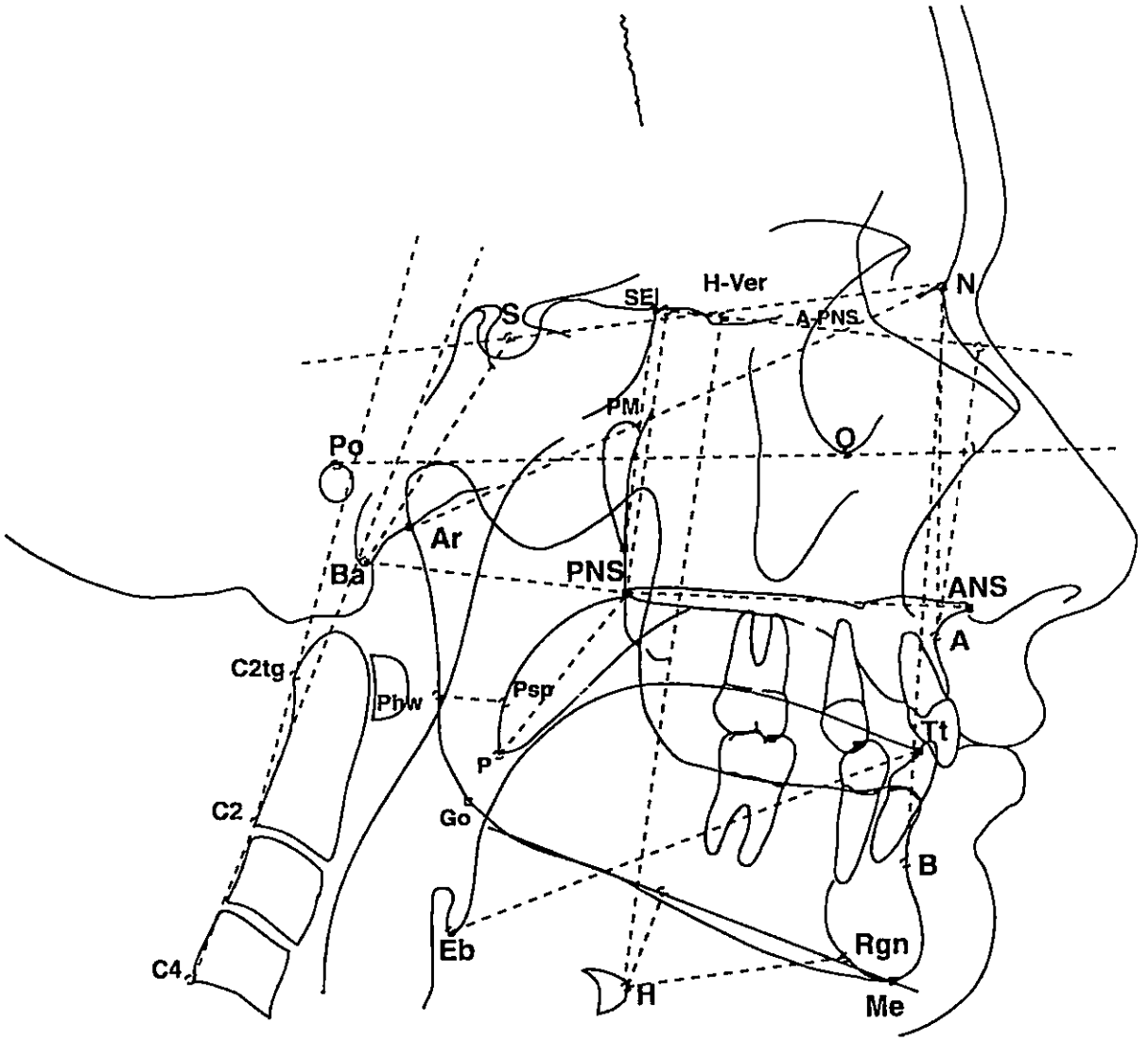


Figure 1. Conventional linear and angular measurements and additional soft tissue measurements.(Refer to the Glossary for an explanation of the abbreviation shown).

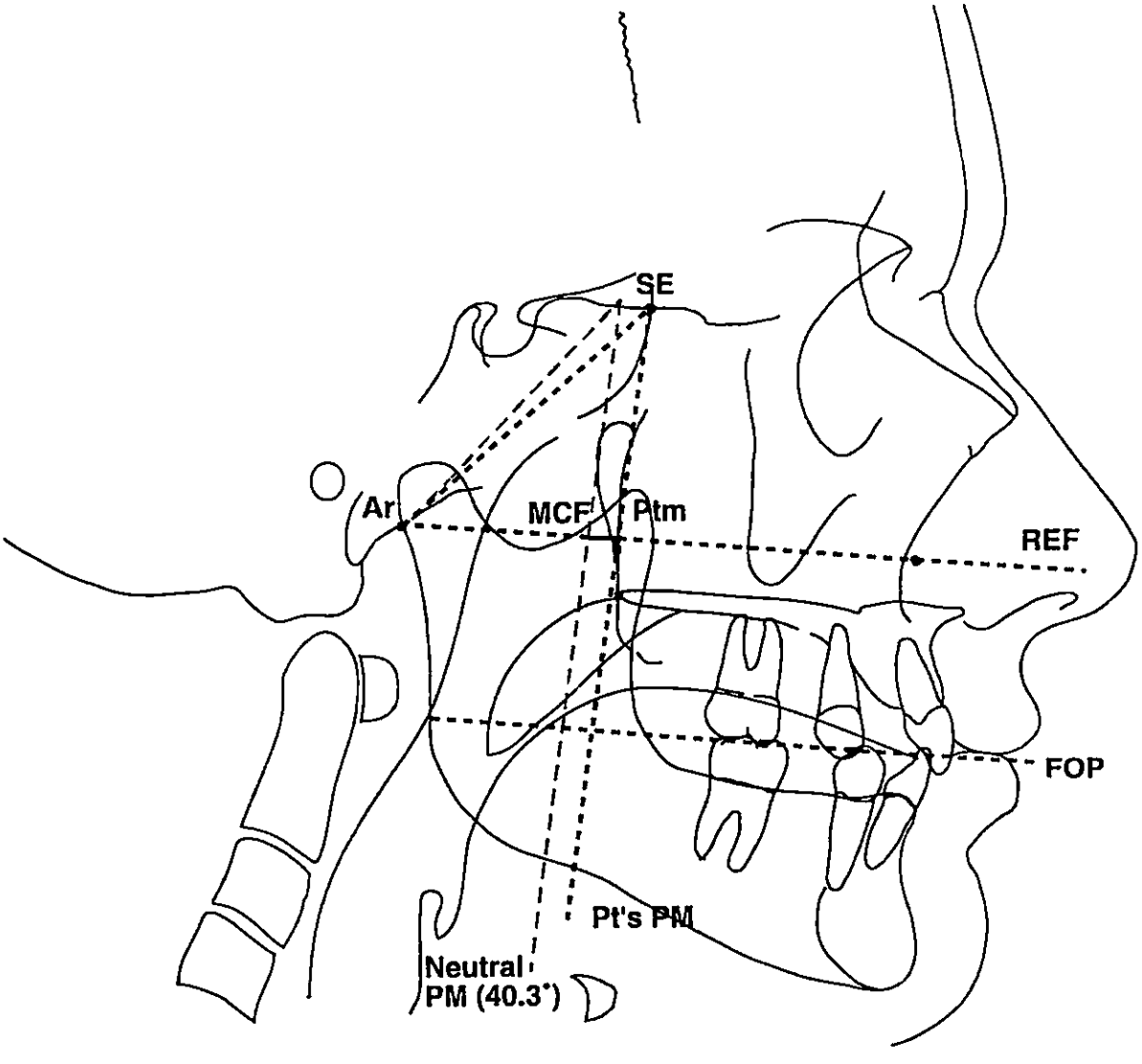


Figure 2. The Counterpart Analysis. This diagram demonstrates the effects of a rotational alignment of the individual's own MCF compared to the neutral MCF on the corresponding maxillary and mandibular placement. A clockwise (+) alignment is shown.(Refer to the Glossary for an explanation of the abbreviation shown).

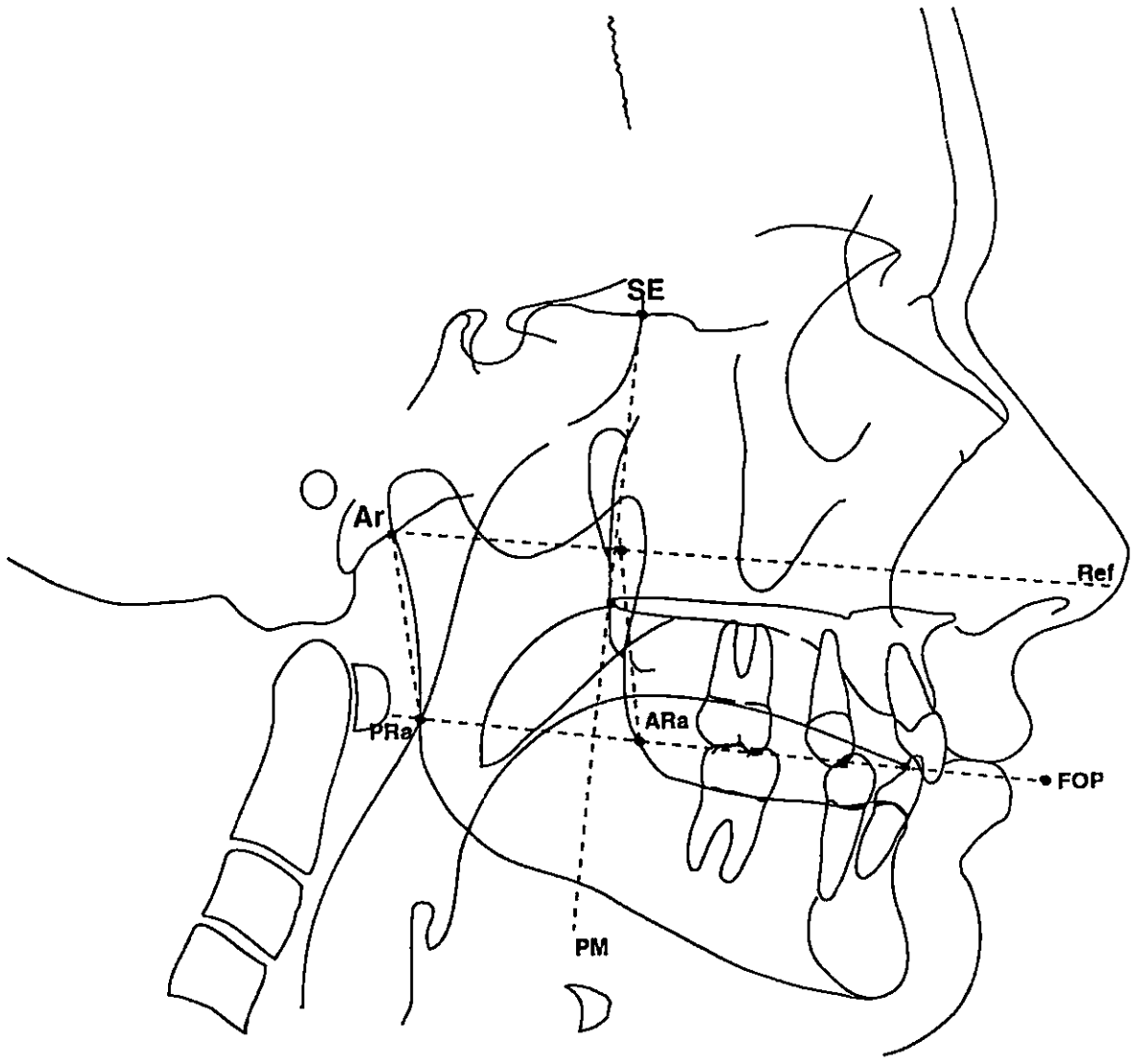


Figure 3. The Counterpart Analysis. This diagram demonstrates a comparison of the horizontal dimension of the MCF with the width of the ramus. This diagram shows a protrusive (-) mandibular effect.(Refer to the Glossary for an explanation of the abbreviation shown).

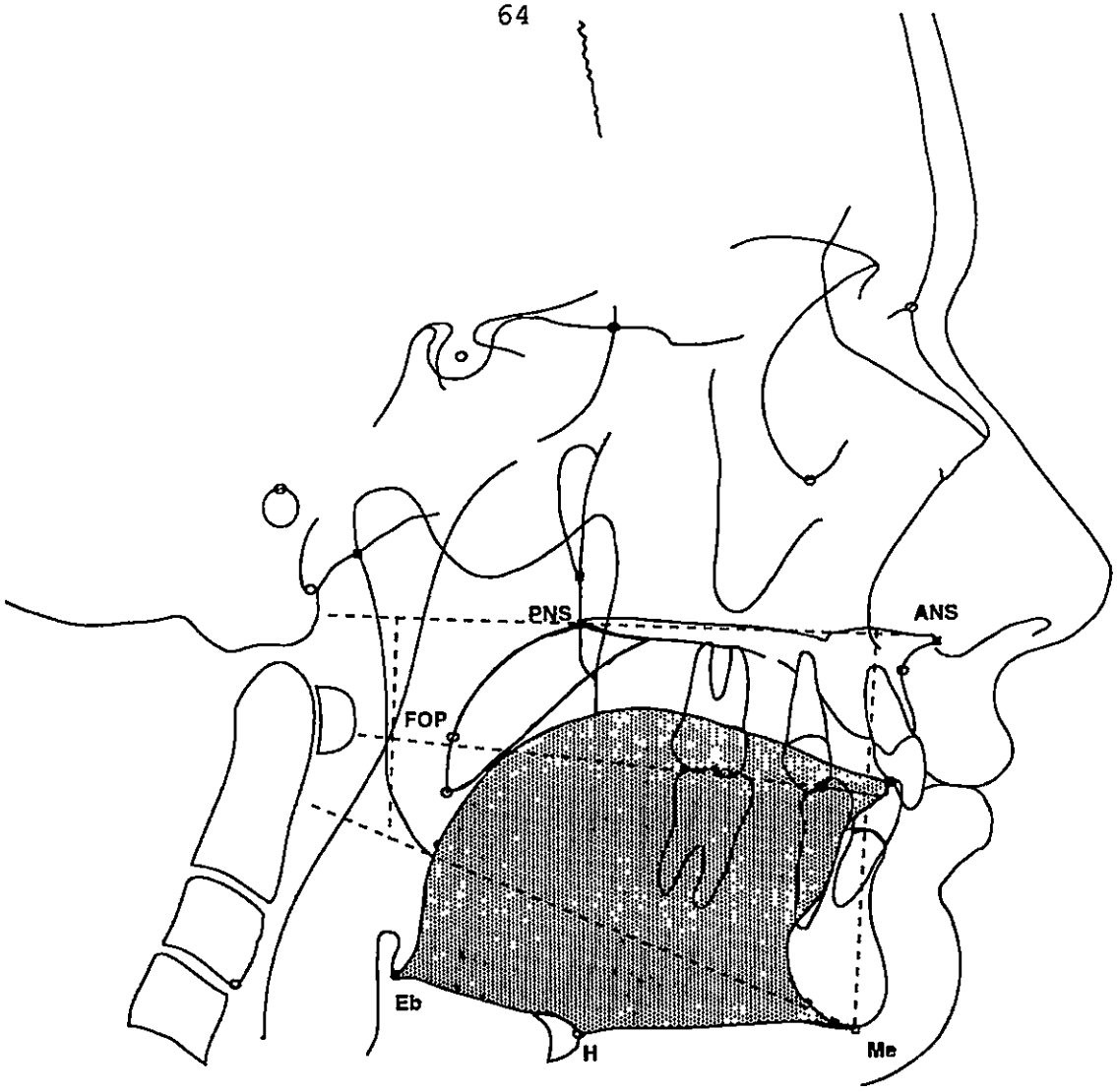


Figure 4. The ratio of the tongue to the intermaxillary area. Anterior intermaxillary space height is the length of a perpendicular from the maxillary plane to the menton; Posterior intermaxillary space height is the length of a perpendicular from the maxillary plane to the mandibular plane which passes through the point where the FOP intersects the pharyngeal wall; Length of the intermaxillary space is a linear distance measured along the FOP from the point where it intersects the tongue tip to where it intersects the pharyngeal wall; Intermaxillary area is calculated by the average of anterior and posterior intermaxillary heights multiplied by intermaxillary length. (Refer to the Glossary for an explanation of the abbreviation shown).

RESULTS

The demographic and anthropometric data for the subjects involved in this study are presented in Table 1. An analysis of variance on baseline measures indicated that there were no statistically significant differences in the variables among the five groups.

The composition of each group was primarily male. The Respiratory Disturbance Indices (RDIs) of subjects in Clinical Trial I (Groups 1 and 2) appeared more severe than those studied in Clinical Trial II (Groups 3,4, and 5) but that difference was not statistically significant.

TABLE 1.--Demographic and Anthropometric Data of the Study Population

Variable	Group 1	Group 2	Group 3	Group 4	Group 5	P
Sex,M:F	8:1	7:0	9:0	7:3	7:0	-
Age	55.1 ± 11.3	48.6 ± 14.1	52.4 ± 10.6	54.1 ± 9.6	47.4 ± 5.7	0.5279
BMI	29.2 ± 4.6	29.8 ± 7.3	29.5 ± 2.4	28.7 ± 6.5	31.5 ± 4.2	0.8569
CI/FI	0.8 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.9 ± 0.1	0.8958
RDI	45.2 ± 29.1	42.7 ± 49.2	23.1 ± 23.3	26.9 ± 28.1	20.3 ± 23.5	0.3700
ESS	11.3 ± 3.9	13.3 ± 4.8	11.0 ± 6.3	12.7 ± 6.0	10.0 ± 5.6	0.7672
CRI^F	0.93 ± 0.95	0.11 ± 1.52	0.14 ± 1.12	0.20 ± 0.96	0.93 ± 0.78	0.2948
CRI^S	0.63 ± 0.87	0.22 ± 1.48	0.51 ± 0.82	0.41 ± 0.95	0.83 ± 0.85	0.8144

*** $p \leq 0.05$

Comparisons of means of fourteen cephalometric variables before and after treatment for each group are presented in Tables 2-6:

TABLE 2.--Comparison of Means of Cephalometric Variables before and after treatment with the SnoreGuard® appliance (Group 1)

Variables	T0	T1	P value
<BaSN	127.4 ± 5.6	127.0 ± 5.2	0.598
MCF	-0.7 ± 0.9	0.8 ± 4.1	0.044
A-PNS	55.2 ± 5.2	53.7 ± 5.1	0.013
PNS-Ba	49.7 ± 3.2	50.4 ± 3.1	0.437
RAM/MCF	4.1 ± 2.4	2.8 ± 4.0	0.008
P-PNS	50.2 ± 7.8	51.3 ± 6.7	0.180
Phw-Psp	4.5 ± 3.6	5.7 ± 2.8	0.393
T1	90.4 ± 8.6	82.9 ± 7.9	0.006
H-MP	24.7 ± 6.0	14.7 ± 5.0	***0.000
<FH-Hor	2.5 ± 6.7	0.5 ± 2.8	0.356
<C2C4SN	109.7 ± 9.9	111.5 ± 10.4	0.152
Int.Mx.Lth.	84.4 ± 7.8	92.4 ± 7.6	***0.000
T/Int.Mx.Area	0.92 ± 0.10	0.73 ± 0.05	***0.000
CI/FI	0.84 ± 0.12	0.78 ± 0.10	0.007

*** Using Bonferroni's correction assessed at p≤0.004

TABLE 3.--Comparison of Means of Cephalometric Variables before and after treatment with the mouthguard appliance (Group 2)

Variables	T0	T1	P value
<BaSN	127.1 ± 3.8	126.9 ± 3.6	0.682
MCF	-0.8 ± 3.7	0.8 ± 3.1	0.066
A-PNS	51.9 ± 3.8	52.5 ± 3.0	0.576
PNS-Ba	47.4 ± 6.6	46.9 ± 6.8	0.946
RAM/MCF	2.3 ± 4.3	1.6 ± 5.1	0.008
P-PNS	47.8 ± 6.1	45.5 ± 7.5	0.472
Phw-Psp	4.5 ± 3.6	5.5 ± 2.5	0.528
T1	89.2 ± 8.6	80.1 ± 8.7	0.008
H-MP	22.4 ± 7.2	16.5 ± 11.2	0.100
<FH-Hor	6.0 ± 6.0	2.1 ± 6.1	0.133
<C2C4SN	115.0 ± 7.0	117.5 ± 6.6	0.094
Int.Mx.Lth.	82.2 ± 4.6	86.1 ± 6.0	0.016
T/Int.Mx.Area	0.94 ± 0.11	0.79 ± 0.09	***0.000
CI/FI	0.81 ± 0.07	0.75 ± 0.06	***0.000

*** Using Bonferroni's correction assessed at $p \leq 0.004$

TABLE 4.--Comparison of Means of Cephalometric Variables before and after treatment with Device A (Group 3)

Variables	T0	T1	P value
<BaSN	132.5 ± 5.2	132.7 ± 5.5	0.690
MCF	-1.3 ± 1.8	-0.3 ± 2.7	0.269
A-PNS	53.8 ± 3.7	52.5 ± 2.3	0.260
PNS-Ba	49.1 ± 2.3	50.4 ± 3.8	0.181
RAM/MCF	2.0 ± 1.8	-1.0 ± 2.7	0.005
P-PNS	52.4 ± 4.6	51.5 ± 5.4	0.076
Phw-Psp	4.1 ± 2.4	5.6 ± 2.8	0.137
T1	93.0 ± 5.2	81.4 ± 9.9	0.008
H-MP	22.5 ± 6.7	18.1 ± 7.3	0.005
<FH-Hor	7.8 ± 5.7	9.7 ± 8.3	0.375
<C2C4SN	117.7 ± 9.0	119.3 ± 8.4	0.119
Int.Mx.Lth.	85.8 ± 5.6	93.9 ± 4.2	***0.000
T/Int.Mx.Area	0.93 ± 0.11	0.74 ± 0.06	***0.000
CI/FI	0.84 ± 0.06	0.78 ± 0.06	0.046

*** Using Bonferroni's correction assessed at $p \leq 0.004$

TABLE 5.--Comparison of Means of Cephalometric Variables before and after treatment with Device B (Group 4)

Variables	T0	T1	P value
<BaSN	129.1 ± 3.1	130.2 ± 3.0	0.185
MCF	0.4 ± 2.5	1.4 ± 2.5	0.033
A-PNS	49.8 ± 3.1	49.3 ± 2.7	0.441
PNS-Ba	46.5 ± 2.7	47.7 ± 2.9	0.021
RAM/MCF	2.2 ± 2.3	2.3 ± 3.2	0.963
P-PNS	45.1 ± 9.0	44.8 ± 6.6	0.836
Phw-Psp	4.9 ± 2.4	4.2 ± 2.0	0.381
T1	85.5 ± 3.3	79.1 ± 6.1	***0.002
H-MP	25.7 ± 6.6	25.9 ± 8.8	0.925
<FH-Hor	4.8 ± 9.1	8.7 ± 7.2	0.110
<C2C4SN	114.9 ± 7.9	120.3 ± 6.4	0.052
Int.Mx.Lth.	81.7 ± 5.5	80.4 ± 5.8	0.115
T/Int.Mx.Area	0.97 ± 0.10	0.90 ± 0.10	***0.000
CI/FI	0.84 ± 0.07	0.78 ± 0.07	***0.000

*** Using Bonferroni's correction assessed at $p \leq 0.004$

TABLE 6.--Comparison of Means of Cephalometric Variables before and after treatment with Device C (Group 5)

Variables	T0	T1	P value
<BaSN	127.0 ± 5.2	127.0 ± 5.5	1.000
MCF	0.4 ± 3.4	1.0 ± 3.5	0.140
A-PNS	55.0 ± 2.3	54.5 ± 2.3	0.570
PNS-Ba	48.3 ± 2.6	49.0 ± 3.9	0.244
RAM/MCF	3.1 ± 2.6	2.4 ± 1.9	0.507
P-PNS	55.3 ± 6.6	54.5 ± 6.6	0.221
Phw-Psp	4.1 ± 1.0	4.2 ± 1.3	0.853
T1	93.8 ± 5.9	85.3 ± 9.4	***0.002
H-MP	26.1 ± 7.3	20.8 ± 5.3	0.038
<FH-Hor	7.0 ± 5.0	5.9 ± 7.5	0.657
<C2C4SN	115.4 ± 5.8	114.6 ± 3.5	0.642
Int.Mx.Lth.	86.3 ± 5.7	90.1 ± 6.1	0.014
T/Int.Mx.Area	0.97 ± 0.04	0.85 ± 0.04	***0.000
CI/FI	0.86 ± 0.08	0.82 ± 0.08	***0.000

*** Using Bonferroni's correction assessed at p≤0.004

In Group 1, after insertion of the SnoreGuard® appliance, significant mean cephalometric changes occurred in the hyoid to mandibular plane distance (H-MP), the intermaxillary length (Int.Mx.Lth.), and the tongue to intermaxillary area ratio (T/Int.Mx.Area).

In Group 2, after insertion of the mouthguard appliance, significant mean cephalometric changes occurred in the tongue to intermaxillary area ratio (T/Int.Mx.Area) and in the cranial index to facial index (CI/FI).

In Group 3, after insertion of Device A, significant

mean cephalometric changes occurred in the intermaxillary length (Int.Mx.Lth.), and the tongue to intermaxillary area ratio (T/Int.Mx.Area).

In Group 4 and 5, after insertion of Device B and C respectively, significant mean cephalometric changes occurred in the tongue length (TL), the tongue to intermaxillary area ratio (T/Int.Mx.Area) and the cranial index to facial index ratio (CI/FI).

Comparisons of means before and after treatment of the other outcome variables are presented in Table 7, Craniofacial Risk Index--forced entry method (CRI^F); Table 8, Craniofacial Risk Index--stepwise method (CRI^S); Table 9, Respiratory Disturbance Index (RDI); and Table 10, Epworth Sleepiness Scale (ESS).

TABLE 7.--Comparison of Means of the Craniofacial Risk Index (forced-entry) before and after Treatment

Group	CRI^F-T0	CRI^F-TI	P value
1	0.93 ± 0.95	-0.93 ± 0.92	***0.0077
2	0.11 ± 1.52	-0.91 ± 1.88	***0.0280
3	0.14 ± 1.12	-1.58 ± 0.91	***0.0117
4	0.20 ± 0.96	-0.47 ± 1.45	***0.0284
5	0.93 ± 0.78	-0.05 ± 0.86	***0.0180

*** $p \leq 0.05$

TABLE 8.--Comparison of Means of the Craniofacial Risk Index (stepwise) before and after Treatment

Group	CRI^S-T0	CRI^S-TI	P value
1	0.63 ± 0.87	-0.59 ± 0.56	***0.0077
2	0.22 ± 1.48	-0.91 ± 1.88	***0.0180
3	0.51 ± 0.82	-1.58 ± 0.90	***0.0077
4	0.41 ± 0.95	-0.47 ± 1.45	0.1141
5	0.83 ± 0.85	-0.05 ± 0.85	***0.0180

*** p≤0.05

TABLE 9.--Comparison of Means of the Respiratory Disturbance Index before and after Treatment

Group	RDI-T0	RDI-T2	P value
1	45.3 ± 29.0	23.0 ± 21.9	***0.0284
2	42.7 ± 49.2	44.9 ± 50.4	0.2367
3	23.1 ± 23.3	12.3 ± 14.7	***0.0077
4	26.2 ± 28.1	22.5 ± 21.8	0.2411
5	20.3 ± 23.5	13.9 ± 12.6	0.4990

*** p≤0.05

TABLE 10.--Comparison of Means of the Epworth Sleepiness Scale before and after Treatment

Group	ESS-T0	ESS-T2	P value
1	11.3 ± 3.9	9.1 ± 4.7	0.1235
2	13.3 ± 4.8	11.7 ± 7.0	0.2049
3	11.2 ± 6.3	9.1 ± 5.2	0.3139
4	12.7 ± 6.0	9.3 ± 3.6	0.0663
5	9.9 ± 5.6	8.1 ± 3.7	0.3454

*** p≤0.05

Mean differences in the craniofacial risk index were significant for all groups when it was calculated using the forced-entry method. However, mean differences in the craniofacial risk index (CRI) were significant for all groups except Group 4 when the CRI was calculated using the stepwise method.

In comparing the means of the respiratory disturbance index before and after treatment, significant changes were only observed in Groups 1 and 3. Examination of the mean differences in the Epworth sleepiness scale demonstrated no significant changes for any of the groups.

An analysis of variance was performed to extrapolate any significant differences for the mean changes of the variables among the five treatment groups. Further, Scheffe's test was performed to identify groups where the difference was signficant. This data are presented in Table 11.

TABLE 11.-- Analysis of Variance of Mean Variable differences

Variable	F-ratio	P value	Scheffe's Test
BaSN	0.8349	0.5118	
MCF	0.3754	0.8247	
A-PNS	2.2406	0.0833	
PNS-Ba	0.5451	0.7037	
RAM/MCF	2.2861	0.0784	
P-PNS	1.8734	0.1357	
Phw-Psp	0.8136	0.5246	
T1	0.8412	0.5080	
H-MP	4.5339	***0.0044	†
FH-Hor	2.1811	0.0902	
<C2C4SN	1.8381	0.1422	
Int.Mx.Lth.	17.6928	***0.0000	†††
T/Int.Mx.Area	11.9443	***0.0000	††††
CI/FI	0.5274	0.7163	
CRI-F	5.5017	***0.0015	††
CRI-S	5.6071	***0.0012	†
RDI	2.2117	0.0866	
ESS	0.2028	0.9352	

*** p≤0.05

† Between groups 1&4 only

†† Between groups 1&4, 3&4

††† Between groups 1&4, 2&4, 3&4, 5&4

†††† Between groups 1&4, 1&5, 3&4, 3&5, 2&4

DISCUSSION

Generally, there is a consensus that dental appliances can be effective in at least some patients in reducing snoring and apneic events (Schmidt-Nowara et al. 1995). Many studies documenting oral appliance efficacy appear regularly in dental and medical journals. However, how and why dental appliances work remains very unclear. Many have postulated that lifting the soft palate, or displacing the tongue and/or mandible in an anterior position prevents obstruction from collapse and thereby improves airway patency (Chua and Chediak 1994).

Previous studies (Meier-Ewert and Brosing 1987; Schmidt et al. 1991) have documented changes in the posterior airway space after mandibular advancement and associate this finding with the reduction in the apnea/hypopnea index. Others, however, have reported no change in this dimension. Instead, Clark and co-workers reported decreases in the distance between the hyoid and mandibular plane in treated subjects (Clark et al. 1993).

The present study documented changes in fourteen cephalometric variables, reported to be important based on

the literature and previous studies at CWRU. Forty-two patients were studied after insertion of one of five appliances. In Group 1, the Snoreguard® appliance produced a decrease in the H-MP distance likely as a result of the mandibular advancement. But, how does decreasing this distance affect airway patency? Perhaps a decrease in H-MP distance is an effect of mandibular advancement rather than a direct cause of RDI reduction.

Increases in intermaxillary length were shown to be significant in both Groups 1 and 3. This increase can be attributed to the anterior repositioning of the lower arch. Increases in the intermaxillary length as well as in the facial height, individually or collectively result in increased intermaxillary area. An increase in intermaxillary area correspondingly resulted in a decrease in its ratio to the tongue area and was shown to be significant in all groups.

A decrease in the tongue length was found to be significant in Groups 4 and 5 and approaches significance in the other groups. Increasing vertical dimension results in the tongue being carried inferiorly, thereby decreasing the distance from its tip to the epiglottis.

Decreases in the CI/FI ratio are simply explained by the increases in facial height as a result of the increased

vertical dimensions relative to the appliances.

The craniofacial risk index was originally developed as a diagnostic test to differentiate snorers from apneics. The separating boundary was defined as zero, above zero as apneic and below it as non-apneic. Using the forced-entry method CRI was significantly reduced from apneic to non-apneic status in all treatment groups. Using the stepwise method CRI was reduced in all treatment groups except Group 4. This group received only an increase in vertical dimension of 15 mm with posterior bite pads. Although Group 2 also received a device designed to only minimally increase vertical dimension, it had a flat plane. This may have inadvertently permitted some protrusion of the mandible, confirmed by the increase in intermaxillary length observed in this group.

Reduction of the RDI was shown to be significant in only Groups 1 and 3. The appliances used in these two groups had both vertical and horizontal components. This suggests that changes in both these dimensions may be important in reducing RDI. Advancing the mandible may increase the airway space at the base of tongue and increased vertical dimension seems important to prevent subjects from opening beyond the ramp during sleep which would allow the mandible to fall backwards. It is crucial

to note that in no treatment group was the RDI reduced to what would be considered a "normal range". This suggests that perhaps dental appliances would be most effective in subjects with only mild to moderate pre-treatment RDI scores.

Subjective symptoms were not significantly reduced in any of the treatment groups. Therefore a reduction in RDI may not be directly related to an improvement in daytime hypersomnolence and other symptoms.

An analysis of variance revealed that H-MP distance and the craniofacial risk index (stepwise method), are reduced significantly more by an appliance which advances the mandible and increases vertical dimension than one which only increases vertical. The craniofacial risk indices (forced-entry method) are significantly reduced with appliances with anterior and vertical repositioning when compared to an appliance which only changes the vertical dimension. Changes in intermaxillary length are more significant in appliances with anterior repositioning than those without. Increases in the intermaxillary area are directly proportional to increases in horizontal and vertical dimension. Appliances which show the biggest increases in those dimensions show the largest decreases in the tongue to intermaxillary area ratios.

Limitations of the Study

The most important limitation of the study was the small sample size. Although there were forty two subjects studied in all, the number of subjects in each treatment group was only between seven and ten patients. This made for large standard deviations in the variables and may have precluded finding significance in the mean differences. The small size of the clinical trial did not convey as much information and may not be as widely applicable or generalizable as a larger trial would have been. In a larger sample, it would have been possible to examine correlations between the changes in the variables and changes in the respiratory disturbance index for each group.

In addition, cephalometric radiography was taken in the awake state, upright position and provided a static two-dimensional image which could not entirely measure a dynamic, three-dimensional upper airway.

SUMMARY AND CONCLUSIONS

The present study attempted to identify anatomical changes in craniofacial structure after placement of one of five oral appliances used to treat patients with a history of loud snoring with or without apnea. The study also examined changes in a craniofacial risk index, respiratory disturbance index, and a subjective report of symptoms before and after treatment. Differences among the treatment groups were evaluated. The study population consisted of forty habitual snorers (mean age 52.09 years, SD:10.40, range 29-69 years). These, otherwise healthy adult volunteers had a self-reported history of loud snoring were included in the present study if they meet the following inclusion criteria:

1) They were delivered a dental device (Clinical Trial I or II)
2) They had a cephalogram with and without the device in place
3) They had a polysomnograph taken at baseline and after two weeks of intervention
4) They were caucasian

The subjects had participated in one of two randomized trials. Clincial trial I compared the effectiveness of two

dental devices. Device A (SnoreGuard®) was designed to increase vertical dimension and protrude the mandible. The SnoreGuard® appliance was a commercially available thermoplastic device. Device B, a mouthguard, (a modification of SnoreGuard®) was designed to minimally increase vertical opening without protruding the mandible. Clinical trial II compared the effectiveness of three dental devices, A,B, and C. Device A was designed to open the vertical and advance the mandible. Device B was designed only to open the vertical and Device C only to advance the mandible. In both trials assignment of subjects to device groups utilized a table of random numbers in order to eliminate selection bias.

Significant craniofacial changes produced by oral appliances were as follows:

1) A decrease in the hyoid to mandibular plane distance
2) An increase in the intermaxillary length
3) A decrease in the ratio of the tongue to intermaxillary area
4) A decrease in tongue length
5) A decrease in the ratio of the cranial index to the facial index

The craniofacial risk index (forced-entry) was significantly reduced in all treatment groups. The craniofacial risk index (step-wise) was significantly

reduced in all groups except in Group 2 in which there was an increase in vertical dimension of 15 mm.

The RDI was significantly reduced only in the groups with dental appliances in which there was an increase in vertical dimension and anterior repositioning of the mandible.

The Epworth sleepiness scale was not significantly reduced in any any of the treatment groups.

In conclusion, the findings from the present study demonstrated that there are some craniofacial changes affected by the placement of an oral appliance. Oral appliances which increased vertical dimension as well as repositioned the mandible anteriorly appeared to be most effective in reducing apneic events. The craniofacial changes responsible for reducing respiratory disturbance index may be a reduction in the hyoid to mandibular plane, a decrease in tongue length, an increase in vertical dimension, an increase in the intermaxillary length or some combination thereof. It is hoped that the suggestions of this study may be further validated by further investigation with larger sample sizes.

APPENDIX A

Human Investigation Consent Form

Human Investigation Consent Form

Consent to Participate in Research Study

I have been asked to participate in a research study entitled: **Dental Device Treatment for Snoring and OSAS**

by:	Mark G. Hans, D.D.S.,M.S.D.	Co-Investigator
	Suchitra Nelson, M.S., Ph.D.	Co-Investigator
	Virginia G. Luks, B.A., D.D.S.	Co-Investigator

I understand that this study involves:

A) Head X-rays (front and side views) before and after treatment while sitting.
B) Polysomnographic testing (sleep monitoring) for diagnosis of Obstructive Sleep Apnea Syndrome.
C) The use of a tooth borne orthopedic appliance to reduce airway obstruction and/or snoring.

I further understand that:

1. The Head X-rays will be taken using the effective minimum X-ray dosage, and a lead apron will be used to further reduce radiation exposure. A spoon of radiographic contrast media (Esophotrast, Rorer Pharmaceutical Corp.) will be required to be swallowed prior to the side view of the head X-ray being taken.

2. Polysomnographic testing (sleep monitoring) will be used to accurately diagnose Obstructive Sleep Apnea Syndrome (OSAS).

3. The tooth borne orthopedic appliance has to be worn as instructed by the investigator. The appliance will temporarily move my lower jaw and possibly relieve apneic and/or snoring conditions. After I am fitted with the device adjustments will be provided for the first month or until the appliance is comfortably and effectively fitted.

4. The outcomes of the study could be beneficial to me because it will be an alternative and conservative treatment for OSAS and/or snoring.

5. I will need to visit a medical doctor if my sleep tests show that I stop breathing more than a person without obstructive sleep apnea. I will need to pay for any doctor's visits and any treatment that I need to treat my sleep disturbance. I will not have to pay for the dental device or for any of the

home monitoring tests that I receive during the time I am participating in the study. All dental device treatment and x-rays will be performed in the Bolton-Brush Growth Study Center, School of Dentistry, Case Western Reserve University, Cleveland, Ohio.

6. I might have pain in my ears, headaches or other jaw pain when I wear the dental device. If I have pain I am to stop wearing the device immediately and call Dr. Luks 368-3249 (Clinic).

7. I may not sleep as restfully with the device in place. If I feel that the device is not helping me rest better or is making me feel worse, I should stop wearing the device immediately and call Dr. Luks.

8. The information from the study is confidential and will be contained in a database for future study.

9. Dr. Virginia Luks will be coordinating this study and will be available to answer any questions. The telephone number for Dr. Luks is (216) 368-3249.

10. I have the right to refuse to participate in this study. In this case, my refusal will not affect the medical or dental care I can receive in the School of Dentistry at Case Western Reserve University.

I have read the above information and understand the risks and benefits involved in participation in this study.

_____ _____

Date Subject/Patient

APPENDIX B

Approval of University Review Committee on Human Studies

CASE WESTERN RESERVE UNIVERSITY
REVIEW COMMITTEE FOR HUMAN STUDIES
NOTICE OF APPROVAL

TO: **Hans, Mark G.**

Dept/School: **Dentistry**

Subject: Notice of (X) Review and approval
( ) Exemption

The committee has reviewed and approved your proposal entitled: **Randomized Clinical Trial of Dental Device for Treatment of Snoring/Obstructive Sleep Apnea Syndrome**

Please be advised that with respect to: (1) the rights and welfare of the individual(s) involved, (2) the appropriateness of the methods to be used to secure informed consent, and (3) the risks and potential benefits of the investigation, the Committee considers your project:

( ) Exempt
(**X**) Fully acceptable
( ) Acceptable with reservations noted
( ) Not acceptable for reasons noted

Follow-up: The Committee wishes to have a status report on this project on **6/17/1997**

SIGNED FOR THE COMMITTEE BY:

Approval Date:
7/01/1996

Ellen Durand
Assistant Director
Office of Research Administration

ED

ORA USE ONLY**********

Type Project: ( ) NEW (**X**) RENEWAL
Human Risk: ( ) Yes (**X**) No
Source of Support: (**X**) Outside Funding ( ) Department/other
Agency (Potential): **AAOF** Agency No.

Are any of the following involved: ( ) Yes (**X**) No
If yes, which category(ies):

() Minors () Fetuses () Abortuses () Pregnant Women
() Prisoners () Mentally Retarded () Mentally Disabled

cc: Dean
Department Chairman
Follow-up (Book)
File

APPENDIX C

Epworth Sleepiness Scale Questionnaire

THE EPWORTH SLEEPINESS SCALE

ID # _____
Today's Date _____

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to work out how they would have affected you. Use the following scale to choose the *most appropriate number* for each situation:

0 = would *never* doze
1 = *slight* chance of dozing
2 = *moderate* chance of dozing
3 = *high* chance of dozing

SITUATION	CHANCE OF DOZING
Sitting and reading	_____
Watching TV	_____
Sitting, inactive in a public place (e.g., a theater or a meeting)	_____
As a passenger in a car for an hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after lunch without alcohol	_____
In a car, while stopped for a few minutes in the traffic	_____

THANK YOU FOR YOUR COOPERATION.

Material in this section from: John MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep, 14(6):540-545

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