INTRODUCTION

RESPIRATORY-RELATED ACTIVATION OF THE UPPER-AIRWAY-DILATING AND TONGUE-PROTRUDING MUSCLES IS WIDELY KNOWN to be effective in reducing the tendency of the upper airway and tongue to collapse during sleep. The electromyographic (EMG) activity of the genioglossus (GG) muscle increases in the head-up and/or supine position and thereby acts to maintain upper airway patency. However, sleep-related reduction of the upper airway-dilating EMG activity may cause respiratory disturbances which include snoring and/or obstructive sleep apnea (OSA). Anterior displacement of the mandible accompanied by a forward migration of the tongue enlarges the upper airway and counteracts partial or complete obstruction. Mandibular advancement oral appliances have been established as one treatment modality for primary snoring and/or mild OSA and the usefulness of oral appliances for the treatment of such sleep-related disorders is no longer in question. In addition, oral appliances have been recommended for moderate to severe OSA patients who cannot tolerate or refuse nasal continuous positive airway pressure (nCPAP) or for subjects who are not suitable surgical candidates. However, the precise relationship between the degree of mandibular advancement and the morphological changes in the upper airway has not been well evaluated except for the maximum mandibular protrusion. It was reported that the upper airway in OSA patients was significantly enlarged at the most protrusive mandibular position while awake and under general anesthesia. If we could determine a less protruded mandibular position that provided the same effect as the maximum protrusion in terms of enlargement of the upper airway, therapy using oral appliances would be simplified. Furthermore, it could provide less discomfort or strain to the jaw muscles and/or the temporomandibular joint, leading to increased patient compliance.

The purpose of this study was to define the precise relationship between the degree of mandibular advancement and changes in upper airway structures using a titratable oral appliance. Morphological changes in the upper airway and its ambient structures were evaluated in healthy males using awake supine lateral cephalograms.

MATERIALS AND METHODS

This study was carried out on 10 non-apneic adult males [age: 27.8±3.2 (mean±S.D.) years, body mass index: 22.1±3.2 kg/m²]. Informed consent was obtained from each subject before the study. Subjects were accepted into the study if they revealed no limitation of jaw movement and had an adequate dentition (>10 teeth in each of the maxillary and mandibular arches) with a skeletal Class I relationship. Subjects who were unable to give informed consent, had evidence or a past history of temporomandibular disorders or respiratory disease were excluded.

Ten Klearway™ oral appliances (Great Lakes Orthodontics, NY, USA) were fabricated on plaster casts of maxillary and mandibular dental arches and a wax-bite registered at the

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most retruded mandibular position (Figure 1). The maxillary and mandibular components of the titratable oral appliance are made from thermoactive acrylic resin which firmly fits not only on the dentition but also has flanges extended to undercut areas of the alveolar bone. The two arch components are connected with an adjustable screw mechanism positioned close to the palatal arch. The screw mechanism enables an 11.0 mm range of anteroposterior mandibular movement in a total of 44 increments of 0.25 mm. The titratable oral appliance allows significant retention and reliable titration and decreases teeth soreness and soft tissue discomfort. An atypical experimental vertical separation of 5 mm instead of the standard clinical separation of 2 mm was obtained between the maxillary and mandibular incisors so as not to interfere with smooth forward displacement of the mandible from the most retruded (RP) to maximum protrusion (MAX) positions when the titratable oral appliance was in place.

Each subject was instructed to lie on a flat table with the head supported by a pillow constructed of a soft sponge material and designed to facilitate the subject’s simulation of a natural and habitual sleep posture. The ear rods of a cephalostat attached to the table were inserted into external auditory meatus to fix the subject’s head in a given position. The exposure factors included a tube voltage of 95 kVp, while the tube current and the exposure time were set at 3 mAs, which were half as much as that of a conventional cephalogram. A set of supine lateral cephalograms were obtained with the titratable oral appliance in place for each subject at end expiration in four mandibular positions; RP, MAX, 33% of MAX (MAX33), and 67% of MAX (MAX67). All cephalometric radiographs were taken 10 minutes after insertion of the appliance.

Analyses of each lateral cephalogram were performed by an experienced orthodontist. The cephalometric landmarks and analysis have been described in detail elsewhere. In addition to landmarks that were frequently used, unique landmarks and variables were defined (Figure 2 and Table 1). Changes in the anteroposterior width of the upper airway, position of the hyoid bone, the third cervical vertebra and the mandible were compared between the four mandibular positions in the 10 subjects. The superior level of the velopharynx was defined as the backward extended palatal plane, whereas the inferior margin of the velopharynx and superior margin of the oropharynx were lines drawn through the tip of the soft palate parallel to the palatal plane. The inferior part of the oropharynx was defined as a line going through the tip of the epiglottis parallel to the palatal plane. One-way repeated-measure analysis of variance (ANOVA) followed by contrast for multiple comparison was used to establish statistical significance.

RESULTS

When the mandible was advanced using the titratable oral appliance, significant morphological and positional changes were induced in the upper airway and its related structures. With regard to upper airway variables, the anteroposterior width of the velopharynx significantly increased but that of the oropharynx did not (Figure 3). Although there were no differences in the SPPS and MPS between RP and MAX33, there were significant increases in the SPPS (p<0.05) and MPS (p<0.01) between RP and MAX67. In addition, there were significant increases in the
The hyoid bone moved forward significantly when the mandibular position was changed from RP to MAX (p<0.01), MAX33 (p<0.01) and MAX67 (p<0.01) (Figure 4). In addition, a significant difference in the anteroposterior position of the hyoid bone between MAX and MAX33 (p<0.01). The hyoid bone also showed a superior movement when the mandible was advanced by the titratable oral appliance. There were significant movements in the PNS-H between RP and MAX33 (p<0.01), MAX67 (p<0.01) and MAX (p<0.01). In addition, there was a significant difference in the superoinferior position of the hyoid bone between MAX and MAX33 (p<0.01).

As in the case of the hyoid bone, similar forward movement was also demonstrated in the position of the third cervical vertebra (Figure 5). The third cervical vertebra moved forward significantly when the mandibular position was changed from RP to MAX33 (p<0.05), MAX67 (p<0.01) and MAX (p<0.01) (Figure 4). In addition, there was a significant difference in the anteroposterior position of the third cervical vertebra between MAX and MAX33 (p<0.01). The third cervical vertebra also showed a superior movement when the mandible was advanced by the titratable oral appliance. There were significant movements in the PNS-H between RP and MAX33 (p<0.05), MAX67 (p<0.01) and MAX (p<0.01). In addition, there was a significant difference in the superoinferior position of the third cervical vertebra between MAX and MAX33 (p<0.01).

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Both H-RGN and C3-RGN increased significantly with anterior movement of the mandible (Figure 6); there was significant (p<0.01) lengthening in both the H-RGN and C3-RGN in MAX67 and MAX when compared to those in RP. In addition, there were significant differences in both the H-RGN and C3-RGN between MAX and both MAX33 and MAX67. This indicated that the forward movement of the mandible outreached that of the hyoid bone and third cervical vertebra. However, the distance between the hyoid bone and the third cervical vertebra (C3-H) remained constant.

**DISCUSSION**

This study has shown that a titratable oral appliance increases the anteroposterior dimensions of the supine velopharynx in normal subjects during wakefulness. However, mandibular advancement with the titratable oral appliance did not effect the oropharynx. The maximum mandibular protrusion yielded the largest changes in the SPPS and MPS of all 10 subjects, and there were significant differences between MAX67 and MAX. This suggests that more than 67% of maximal protrusion is required to obtain the same effect as maximal protrusion in terms of anteroposterior dimensions of the velopharynx in awake control subjects.

Our findings on the upper airway enlargement site using the titratable oral appliance are consistent with recent studies which employed videofluoroscopy.15,17 Ryan and co-workers17 demonstrated that the same titratable oral appliance used in this study significantly enlarged the velopharynx and a notable reduction in the Apnea Hypopnea Index (AHI) was observed in OSA patients. Additionally, they found that the cross-sectional area of the oropharynx was not increased but there was a tendency for that of the hypopharynx to increase.17 Lowe and co-investigators15 also reported that the cross-sectional area of the velopharynx increased and the Respiratory Disturbance Index decreased in a group of OSA patients after insertion of the Klearway™ appliance. However, they found that there were no significant differences in hypopharynx or oropharynx cross-sectional areas.15 On the other hand, it was reported that the anteroposterior dimension of the velopharynx showed a significant reduction in both skeletal Class I male patients with OSA and controls when the body position was changed from upright to supine.22 Thus, it appears that the titratable oral appliance has a direct effect on the velopharynx by increasing the anteroposterior dimension and may improve airway patency at the same site in the supine posi-

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**Table 1—Definition of variables used in cephalometric analysis**

<table>
<thead>
<tr>
<th>No.</th>
<th>Description</th>
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<tbody>
<tr>
<td>1</td>
<td>SPPS Superior posterior palatal space. Width of the pharynx measured between the posterior pharyngeal wall and the dorsum of the soft palate on a line parallel to the Frankfort Horizontal (FH) plane that runs through the middle of the line from PNS to the tip of the soft palate (P).</td>
</tr>
<tr>
<td>2</td>
<td>MPS Middle posterior palatal space. Space between the posterior pharyngeal wall and the dorsum of the tongue on a line parallel to the FH plane that runs through P.</td>
</tr>
<tr>
<td>3</td>
<td>IPS Inferior posterior palatal space. The width of the pharynx measured between the posterior pharyngeal wall and the dorsum of the tongue on a line parallel to the FH plane that runs through C2 (the most anteroinferior point on the second cervical vertebra).</td>
</tr>
<tr>
<td>4</td>
<td>N(\perp)H Linear distance between N(\perp)line (the line perpendicular to the FH plane through Nasion) and H (the most superoanterior point on the body of the hyoid bone).</td>
</tr>
<tr>
<td>5</td>
<td>PNS-H Linear distance between PNS (posterior nasal supine) and H.</td>
</tr>
<tr>
<td>6</td>
<td>N(\perp)H-C3 Linear distance between N(\perp)line and C3 (the most anteroinferior point on the third cervical vertebra).</td>
</tr>
<tr>
<td>7</td>
<td>C3-PNS Linear distance between C3 and PNS.</td>
</tr>
<tr>
<td>8</td>
<td>H-RGN Linear distance between H and RGN (the most posterior point on the mandibular symphysis).</td>
</tr>
<tr>
<td>9</td>
<td>C3-H Linear distance between C3 and H.</td>
</tr>
<tr>
<td>10</td>
<td>C3-RGN Linear distance between C3 and RGN.</td>
</tr>
</tbody>
</table>

SPPS (p<0.01) and MPS (p<0.01) between RP and MAX. Moreover, both the SPPS (p<0.01) and MPS (p<0.05) in MAX were significantly longer than those in MAX67. When compared to values in MAX, there were several significant differences between the different mandibular positions; significant differences were found in the SPPS (p<0.01) and MPS (p<0.05) between MAX and MAX67. Likewise, significant differences were found in the SPPS (p<0.01) and MPS (p<0.01) between MAX and MAX33. In contrast, such differences were not found in the IPS between the four mandibular positions.
tion. Since the most constricted and collapsible site is located in the retropalatal region in both patients with OSA and normal subjects, forward displacement of the mandible with a titratable oral appliance may be an effective therapy for the treatment of upper airway obstruction.

Interestingly, the third cervical vertebra moved anterosuperiorly together with the hyoid bone (Figs. 5 and 6). This movement of the third cervical vertebra virtually caused no change in the sagittal dimension of the oropharynx. Lowe et al. demonstrated in skeletal Class I male OSA patients that the C3-H was signifi-
significantly lengthened when the body position was changed from upright to supine. This suggests that there is a compensatory mechanism for impaired control of airway patency in these patients. However, coordinated reflex mechanisms to maintain the distance between the hyoid bone and the third cervical vertebra may exist when the oropharyngeal airway is not collapsible. In other words, the C3-H does not appear to correlate with the effectiveness of the oral appliance in the treatment of OSA. Instead, the relative positions of the hyoid bone and the third cervical vertebra to the mandible and/or the cranium may be better correlated. Indeed, Liu and co-workers demonstrated in 16 OSA patients that the distance from the hyoid bone to the mandibular plane or the C3-RGN line significantly decreased after insertion of the titratable oral appliance. Likewise, our study showed that the PNS-H was significantly decreased in MAX33 or a more protruded mandibular position. The degree of forward movement of the hyoid bone was less than that of the mandible in the present study (Figure 6). We speculate that some extrinsic tongue muscles which connect to the hyoid bone and/or the soft palate, the posterior belly of the digastric muscle and the infrapharyngeal muscles could restrict the anterior movement of the hyoid bone.

Although the significant difference between 67% of MAX and MAX in the velopharyngeal configuration in controls may help to simplify oral appliance therapy (Figure 3), it would not be appropriate to apply the results to OSA patients. Ryan et al. reported that mandibular advancement increased the lateral dimension of the velopharynx more than the antero-posterior dimension in OSA patients. However, the site of enlargement following mandibular protrusion may not be the same between controls and OSA patients on account of the different shape of the upper airway. In addition, the different reflex activity of the GG muscle between controls and OSA patients may provide more complicated configurational changes in response to mandibular advancement. Further investigation is needed to determine the effects of mandibular protrusion on the relationship between the anatomy and muscle activity of the upper airway.

There are also some significant limitations to this study. The effects of sleep on upper airway enlargement are unknown. It may be possible that the amount of mandibular protrusion during sleep could be more than that when awake in order to obtain the same upper airway enlargement, since supine upper airway dimension decreased during sleep compared to during wakefulness. The influence of gender on airway size after the insertion of an oral appliance should be discussed. Since men had a more compromised airway in the supine position than women, and female awake GG muscle activity was augmented compared to males, it appears that the female upper airway is less collapsible and that male subjects may need more mandibular advancement to obtain the same effect. The subjects in this study were younger than most of the OSA patients. Liu et al. reported that the younger patients significantly reduced the AHI more than the older patients using the same titratable oral appliance we used in this study. Since the dimension and collapsibility of the upper airway decrease with age in both men and women, the same amount of protrusion may not give the same enlargement in individuals with advancing age. Finally, there is a certain limitation in a two-dimensional evaluation when compared to a three-dimensional structural analysis. However, cephalometry has been widely used as a convenient and easy tool for both upright and supine body positions. Supine cephalometric analyses as used in this report where the vertical dimension is kept constant and the mandible is not allowed to open passively may offer unique advantages over previous supine studies.

Currently, it seems that the demand is growing for alternatives to nCPAP and/or surgery for the treatment of OSA. Although there are a number of oral appliances commercially available, the ideal combination of adjustability, retention, titration, and compliance for the patient has not been determined. Gradual forward and/or backward titration of the mandible with-

![Figure 5](image-url)
out fabricating a new appliance is especially necessary when the initial jaw position proves inadequate. The titratable oral appliance possesses better adjustability than other oral appliances and reduces the need for multiple appliance changes for a single subject. It is also well worn by patients throughout the night. With regard to the efficacy of the appliance, Liu and colleagues investigated the relationship between the initial cephalometric variables and reduction of the AHI after insertion of the titratable oral appliance. They concluded that a good response was seen in subjects where the cross-sectional area of the hypopharynx increased after insertion of the appliance.

In conclusion, in normal males during wakefulness, the titratable oral appliance significantly enlarged the supine upper airway caliber of the velopharynx together with a forward displacement of the hyoid bone and the third cervical vertebra. However, the titratable oral appliance did not affect the anteroposterior dimension of the oropharynx.

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