Title: Respiratory effect associated with use of occlusal orthotics in temporomandibular disorder patients

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Running title: Respiratory effect of occlusal orthotics in TMD patients

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Abstract

Occlusal orthotics are widely used to manage temporomandibular disorder (TMD). However, the respiratory effects of the use of occlusal orthotics in TMD patients are unclear. The primary purpose of this study was to determine the effect of increased the vertical dimension by an orthotic on the apnea hypopnea index (AHI) and oxygen desaturation index (ODI) of TMD patients. The secondary purpose was to determine whether these effects differed between maxillary and mandibular orthotics.

A total of 26 participants (eleven males and 15 females, average age 36.4 ± 15.9 years old) who were diagnosed TMD were recruited for this study. The orthotic group with bruxism performed the Nox-T3 monitor test to obtain the AHI and the ODI, one night without the use of an orthotic (baseline) and the other night two weeks after they began using an orthotic (follow-up). The control group without bruxism performed the Nox-T3 monitor test for two nights without the use of an orthotic. The AHI and ODI were compared between the baseline and follow-up. In the orthotic group, half of the patients were randomly allocated to the maxillary orthotic group; the other half were allocated to the mandibular orthotic group. The AHI and ODI were compared between maxillary and mandibular orthotic groups.

Increasing the occlusal dimension with the orthotic statistically reduced the AHI both in the non-supine (p<0.01) and supine positions (p=0.04). Moreover, the maxillary appliance decreased all AHI and ODI, and mandibular appliance showed the decrease of only AHI.

This study concluded that increase vertical dimension by use of occlusal orthotics in TMD patients reduced respiratory disturbances in non-supine and supine positions.

1. Introduction

Temporomandibular disorder (TMD) affects approximately 33% of the population, such that they exhibit at least one TMD symptom, such as muscle pain, temporomandibular joint (TMJ) noise, restricted jaw mobility, or TMJ dislocation. Approximately 3.6-7% of patients with TMD symptoms seek treatment [1]. To manage TMD symptoms, occlusal orthotics are frequently used as a noninvasive treatment. There are many proclaimed benefits for occlusal orthotics, such as relaxation of muscles, protection of teeth and associated structures from bruxism, reduction of joint loading, or mitigation of periodontal ligament proprioception. Notably, more than 3,000,000 occlusal orthotics are fabricated in

the United States [2]. However, clear evidence for the use of occlusal orthotics is controversial and their mechanism of action remains unclear [3, 4].

Obstructive sleep apnea (OSA) is a disorder that carries risks of hypertension, daytime sleepiness (which increases the risk of transportation or work accidents), altered memory, and periodic limb movement during sleep [5, 6, 7]. Although primary care physicians report that OSA prevalence among their patients is low, at 2.2% [8], some researchers have calculated that the prevalence of objectively measured, moderate to severe obstructive sleep apnea, in men aged 40 years and older, is around 26% [9, 10, 11].

Patients who are diagnosed with OSA are often treated with mandibular advanced devices (MADs), which are oral appliances to move the jaw vertically and protrusively. This repositioning brings the jaw and tongue forward, thus opening the oropharyngeal airway and reducing the likelihood of airway collapse. However, some studies have indicated that increasing the vertical dimension alone, using thick orthotic or MAD without any protrusive modification will rotate and retrude the mandible, thereby reducing tongue space. This change then results in an increased apnea hypopnea index (AHI) and oxygen desaturation index (ODI) in OSA patients. [12, 13, 14].

We assume that wearing a occlusal orthotic modifies the vertical dimension in a similar manner to that of a MAD, without protrusion. However, the respiratory impact on breathing, when TMD patients were modified the vertical dimension using a TMJ "night guard," remains unexplored.

Therefore, an important clinical question is whether the use of a TMJ orthotic could aggravate the AHI or ODI. Additionally, there has been no research comparing the impact of maxillary versus mandibular TMJ orthotics on AHI and ODI.

The primary purpose of this study was to determine the effect of increasing the vertical dimension on AHI and ODI, using a TMJ orthotic. The secondary purpose was to determine whether these effects differ between maxillary and mandibular occlusal orthotics.

2. Materials and methods

2.1. Subject recruitment

Participants who were diagnosed as TMD at the University of California, Los Angeles (UCLA) Orofacial Pain & Dental Sleep Medicine Clinic were recruited for the present study. All subjects were

18 years old or older and had a sufficient number of teeth in good health to support the dental appliance. Patients with severe dental disease, inadequate dental retention, OSA, medication usage that could influence sleep (e.g., selective serotonin reuptake inhibitors or benzodiazepines), and surgical cases that might require invasive interventions (e.g., arthrocentesis) were excluded. Patients with a high score on the Epworth Sleepiness Scale (score>10) and/or STOP-Bang (score>3) were also excluded, because they had a higher chance of diagnosis with OSA [15, 16].

The scientific and ethical aspects of the protocol were reviewed and approved by the institutional review board of University of California Los Angeles (#17-001949).

2.2. Data acquisition

The Nox-T3 sleep monitor and software (Nox Medical, Inc., Reykjavik, Iceland), which records nasal pressure, snoring, rib cage and abdominal movement, pulse activity, superficial masseter activity, and body position, was used to record AHI and ODI [17, 18].

The software program defined apnea as >90% reduction in airflow from baseline, for at least 10 seconds. Hypopneas were defined as >30% reductions in respiratory signals for >10 seconds, associated with a >4% reduction in oxygen saturation. The AHI on Nox-T3 recording was calculated as the average number of apneas and hypopneas per hour of analyzed time. The ODI was calculated as the number of oxygen desaturations >3% per hour.

Supine position was detected with a position monitor; supine AHI (AHI-sup) and supine ODI (ODI-sup) were calculated.

2.3. Study protocol

2.3.1. Orthotic group

The participants who had sleep bruxism and need orthotic for the treatment of TMD were allocated to the orthotic group. The diagnostic criteria of Seep related movement disorders from international classification of sleep disorder were used to determine the participants had sleep bruxism [19]. After written informed consent was obtained, all orthotic group patients underwent the following protocol.

At the first visit, as an initial assessment, full medical and dental history data were collected, including the Epworth Sleepiness Scale, the STOP-Bang, the Berlin Sleep Questionnaire, and the modified Mallampati classification.

Impressions were taken with Jeltrate® alginate impression material (Dentsply Sirona) by a trained dentist. Bite forks which has 2-mm thickness were held at the bilateral maxillary first molar by the dentist. The dentist guided the patient to close the jaw with a habitual closing movement until the mandibular closing teeth came in contact with the bite forks. The space between maxilla and mandible was filled with the Patterson® Rigid bite registration-fast set (Patterson Dental Supply, Inc.). Bite registration was used to make an orthotic with 2-mm thickness at the first molar level.

A trained dentist taught the participants to apply all Nox-T3 sensors. They were instructed to re-apply the sensors at home by themselves, just prior to bedtime, in order to obtain baseline AHI, AHI-sup, ODI, and ODI-sup for one night for the baseline data (i.e. no orthotic was worn during baseline recording).

At the second visit, each subject's TMD orthotic was delivered and adjusted by a trained dentist. Articulating paper was used for occlusal adjustment on the flat surface of the occlusal orthotic in the maximal closing position.

After two weeks of nightly orthotic use, follow-up data for AHI, AHI-sup, ODI, and ODI-sup were collected by Nox-T3 with the orthotic in situ for one night.

2.3.2. Control group

The participants who didn't have bruxism and didn't need orthotic for the treatment of TMD were allocated to the control group. After written informed consent was obtained, all control group patients underwent following instructions.

At the first visit, as an initial assessment, full medical and dental history data were collected, including the Epworth Sleepiness Scale, the STOP-Bang, the Berlin Sleep Questionnaire, and the modified Mallampati classification.

A trained dentist taught the participants to apply all Nox-T3 sensors. The participants were instructed to re-apply the sensors at home, just prior to bedtime, in order to obtain baseline AHI, AHI-sup, ODI, and ODI-sup for one night.

At 2 weeks after the first visit, follow-up data of AHI, AHI-sup, ODI, and ODI-sup were collected by Nox-T3 in situ for one night.

2.3.3. Maxillary and mandibular orthotic group

The orthotic group participants drew a paper which had word “maxillary” or “mandibular” from an envelope. Following the paper, the participants were randomly allocated into maxillary occlusal orthotic therapy group or mandibular occlusal orthotic therapy group.

2.4. Intra-oral device

All orthotic group participants received either maxillary or mandibular occlusal orthotic. The appliance was fabricated with hard acrylic resin with 2-mm thickness at the level of the first molar.

The orthotic covered the entire dental arch and had two ball clasps as stabilizers between molars and premolars on each side. The orthotic did not come into contact with the patient's soft tissues.

After the impression were taken, dental casts were made with NEW PLASTONE II LE (GC). The casts were sent to the Glidewell Laboratories (Los Angeles, CA, USA), and occlusal orthotics, Astron CLEARsplint hard processed acrylic, were fabricated at the laboratory.

2.5. Statistical analysis

Participants’ basic data were summarized by the calculation of mean and standard deviation. Qualitative variables were compared with the chi-squared test; continuous variables were compared with kolmogrov-Smirnov test and Student’s t-teat. A paired t-test was used to compare the AHI, ODI, AHI-sup, and ODI-sup between baseline and post-treatment, as well as to compare the data between maxillary and mandibular orthotic groups. The level of statistical significance was set at 0.05 for all tests. Data were processed using a statistical software package (SPSS Ver. 18.0).

3. Results

3.1 participants recruitment

As Fig. 1 shows, a total of 26 participants were enrolled in the study. Eighteen participants using the TMJ orthotic for management of TMD with sleep bruxism were recruited to the orthotic group (seven males and 11 females, average age 36.4 ± 15.9 years old); eight participants with other TMD without sleep bruxism were allocated to a control group (four males and 4 females, average age 29.4 ± 2.7 years old).

The orthotic group participants were randomly allocated into two groups: maxillary occlusal orthotic therapy group (two males and 7 females, average age 30± 12.4 years old) and mandibular occlusal orthotic therapy group (five males and 4 females, average age 42± 16.4 years old).

Table 1 shows the characteristics of the participants in this study. There were no statistical differences between the orthotic and control groups.

3. 2 Comparison between orthotic and control groups

The outcomes of occlusal orthotics are shown in Table 2. The AHI and AHI-sup significantly decreased in the orthotic group (paired t-test showed $p<0.01$ and $p=0.04$ respectively). There was no significant effect of ODI on the orthotic group. Furthermore, the control group did not show any differences between baseline and follow-up. Fig. 2 shows the distribution of AHI and ODI of the orthotic group. Notably, AHI decreased for 16 (88.9%) participants at the time of follow-up; the same number of participants showed the reduction of ODI. The control group did not exhibit any statistical differences between baseline and follow-up (Table 2, Fig. 2).

3. 3 Comparison between maxillary and mandibular orthotic groups

Participants who received maxillary orthotics showed significant reductions of all AHI, AHI-sup, ODI, and ODI-sup (paired t-test showed $p=0.002$, 0.03, 0.004, and 0.02 respectively). Seven (88.9%) participants showed reductions in AHI, AHI-sup, and ODI; eight (100%) participants showed reductions in ODI-sup.

In contrast, only AHI decreased in the group that received mandibular occlusal orthotics (paired t-test showed $p=0.001$). Notably, seven (88.9%), five (62.5%), six (75.0%), and five (62.5%) participants exhibited reductions of AHI, AHI-sup, ODI, and ODI-sup, respectively (Table 3, Fig. 3).

4. Discussion

The primary clinical question in the present study was whether the modification of vertical dimension by occlusal orthotic for TMJ treatment can vary AHI and ODI. The results showed that increasing the vertical dimension with occlusal orthotics reduced the AHI both in non-supine and supine positions in the orthotic group.

These results may explain by the tongue position. Oral appliances, such as occlusal orthotics or MAD, open the vertical dimension, which makes the tongue space larger, thereby preventing re-positioning of the tongue posteriorly. The airway patency is reduced during sleep, especially in a supine position, because the tongue is re-positioned posteriorly and tends to collapse the airway during sleep [20, 21]. Our study showed that, even in a supine position, AHI was improved among participants.

Nikolopoulou et al. reported that the use of a stabilization splint raised the AHI significantly; this occurred in all 10 patients [14]. Other studies also concluded that increased vertical dimension would risk aggravation of AHI in OSA patients [12, 13, 14]. Some previous studies found no significant change of AHI when the vertical dimension was raised in OSA patients; other researchers reported that AHI was increased only at the individual level [12, 13]. Aarab et al. assumed that single maxillary appliances did not impact the respiratory system, and used this as a placebo appliance to examine AHI variability between baseline and follow-up PSG recordings [22]. In contrast, Anitua et al. reported that 30% of samples showed the best response with no mandibular advancement; 10 of 26 participants with >50% reduction in AHI had zero advancement. They concluded that the zero advancement position was sufficient to maintain the patency of the upper airway and stabilize pharyngeal tissue [23, 24]. A meta-regression analysis showed that the extent of mandibular advancement does not significantly influence the AHI [25]. However, these studies focused solely on patients who were already diagnosed with OSA, which is considered a multifactorial disorder. Obesity, age, nasal airway restriction, such as allergy, adeno-tonsillar hypertrophy, and dental arch abnormalities, such as retrognathia and narrow maxilla, can be a causation factor of OSA [26, 27]. Therefore, it is difficult to evaluate the impact of just for an oral appliance for the OSA patients. Our current is the only study to have targeted undiagnosed OSA patients. Our participants' complaints were TMJ problems. Therefore, we were able to determine the respiratory effect of raising the vertical dimension with less complexity.

The secondary clinical question was whether there was a difference in respiratory effects between the maxillary and mandibular occlusal TMJ orthotics. Our study reported that the maxillary orthotic showed better respiratory effects on each of the following parameters: AHI, AHI-sup, ODI, and ODI-sup; those were in contrast with the mandibular orthotic, which improved AHI alone.

As we mentioned earlier in this paper, other researchers have shown the impact of raising the vertical dimension in OSA patients: their participants exhibited either aggravation of AHI or showed no impact. In

contrast, the targets of our study were patients who were not diagnosed with OSA. In this present study, the maxillary and mandibular orthotics were randomly allocated to participants. However, the baseline AHI for the mandibular orthotic group was 9.8, while the baseline AHI for the maxillary orthotic group was 4. The baseline AHI of the mandibular orthotic group was higher than that of the maxillary group. Moreover, the baseline AHI of the mandibular orthotic group was higher than the score 5, which is the criterion by which patients are diagnosed with OSA using polysomnography [19]. Therefore, baseline AHI may be an important factor in obtaining a better respiratory effect at a non-protrusive position.

In our study, even the mandibular orthotic group, which had a higher average AHI score (AHI>5), showed significant lowered AHI; this did not lead to aggravation of other scores (AHI-sup, ODI, and ODI-sup). Further studies should be performed with OSA patients to determine the impact of increasing the vertical dimension in a larger number of patients, because all prior studies (mentioned above) that reported no respiratory impact upon raising the vertical dimension in OSA patients [14] were performed with a limited number of participants. Therefore, it remains unclear whether increasing vertical dimension without protrusion plays a particular role among OSA patients. If raising the vertical dimension in OSA patients leads to a better respiratory effect, the clinical impact may be considerable because the protrusive position has some side effects, such as bite change by shortening of the lateral pterygoid muscle, muscle, tenderness, or joint tenderness [28].

Our study is the first study to have directly investigated the impact of the difference between maxillary and mandibular appliances; no other studies performed this comparison. A prior study showed that two of eight patients showed modest reduction of RDI with the maxillary device, whereas six showed increases in RDI [29]. Another study reported that mandibular appliances did not increase the AHI, compared with the baseline value. Based on the findings of the present study, it remains unclear which patient characteristics are responsible for the impact of raising the bite upon using of orthotics in TMD patients. We previously suggested the necessity for further studies with larger numbers of OSA patients, in order to determine the respiratory impact of increased vertical dimension. For further research to determine the differences in the respiratory impact of maxillary and mandibular orthotics is also required in patients without OSA. However, for this type of study, more careful participant selection, such as the requirement of a pre-sleep study to eliminate participants with higher AHI, must be considered.

Although we targeted the participants who had never been diagnosed with OSA, many participants had a higher AHI (>5) score; those were possible OSA patients. The significance of this finding is that dentists must always maintain awareness of the possible OSA within a patients dental and medical history, even for patients without any complaints regarding sleep, snoring, or tiredness. The OPPERA prospective cohort study reported that a high likelihood of OSA was associated with higher odds of chronic TMD [30]. Although this study concluded that occlusal orthotics did not aggravate the respiratory disturbance, clinicians should always provide the best treatment option for patients; patients who have OSA should be delivered MAD.

The main effect of the orthotic is to manage the symptom of TMD. We didn't get the evaluation from TMD aspect for orthotic in this study since we combined some other treatments depend on each patient necessity such as stretch therapy, moist heat therapy, medication therapy, trigger point injections. Other reports already showed the effects of orthotic therapy for TMD patients [31]. This time, we showed the side effect of using orthotic from the respiratory aspect.

To increase the accuracy of this present study, multiple sleep recordings are required for each participant, because the studies with multiple PSG recordings showed night-to-night variability in AHI [32]. Further, the first night effect should be considered [33]. Participants did not have to go to sleep lab because the Nox-T3 is designed for at-home use. However, the participants had to sleep with many codes on their faces and bodies, which may have changed their sleep condition. Several nights of this research would eliminate the first night effect.

This study was limited by its small sample size. For future studies, 49 participants would allow an 80% chance of detecting a difference in AHI as large as the one found in the present study, at the usual level of statistical significance (alpha=.05). We will continue collecting data to update this study for greater accuracy. Additionally, the long-term effects of orthotic respiratory effects on TMD patients should be assessed in a future longitudinal study, because most patients use this type of orthotics for long periods of time.

5. Conclusions

This study concluded that the increase of vertical dimension of TMD participants using OO didn't show respiratory disturbances in non-supine and supine position. It showed clinician can provide OO to

TMD patients without any complication to respiratory system. We need to have a further research with larger number of participants to see the difference of the effect between maxillary and mandibular OO.

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Figure Legends

Fig. 1 Flow diagram of participants' sex and age distribution.

Fig. 2 Distribution of orthotic group and control group apnea hypopnea index (AHI) and oxygen desaturation index (ODI) for baseline and follow-up assessments.

Fig. 3 Distribution of maxillary and mandibular orthotic group apnea hypopnea index (AHI) and oxygen desaturation index (ODI) for baseline and follow-up assessments.

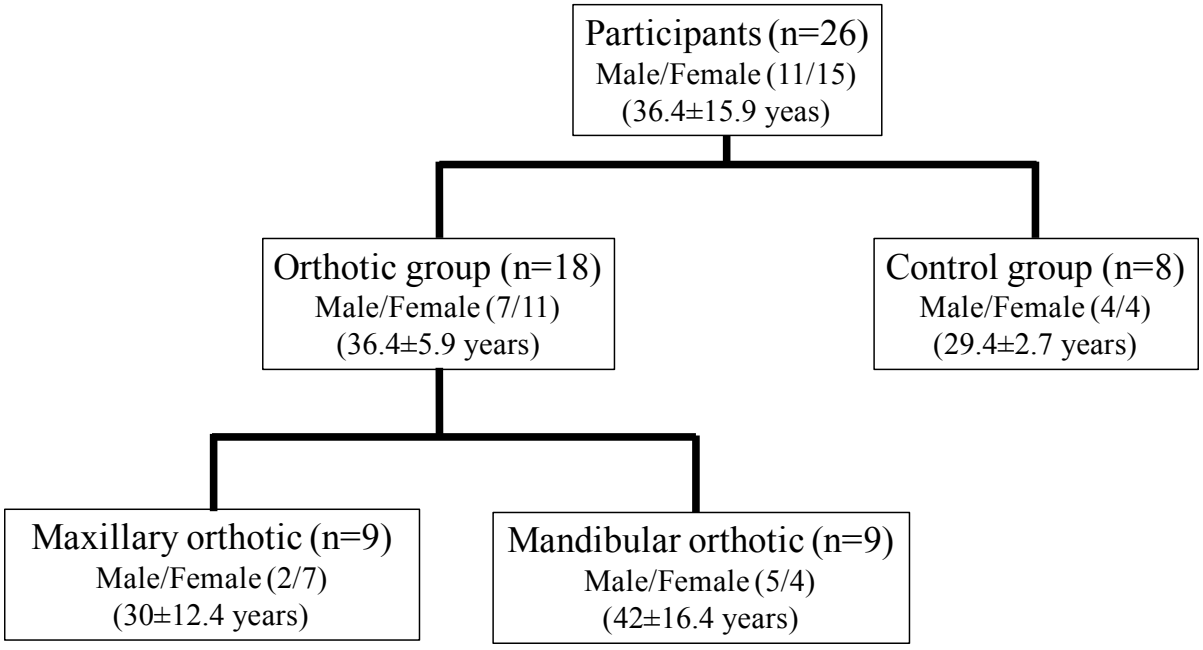

Fig. 1

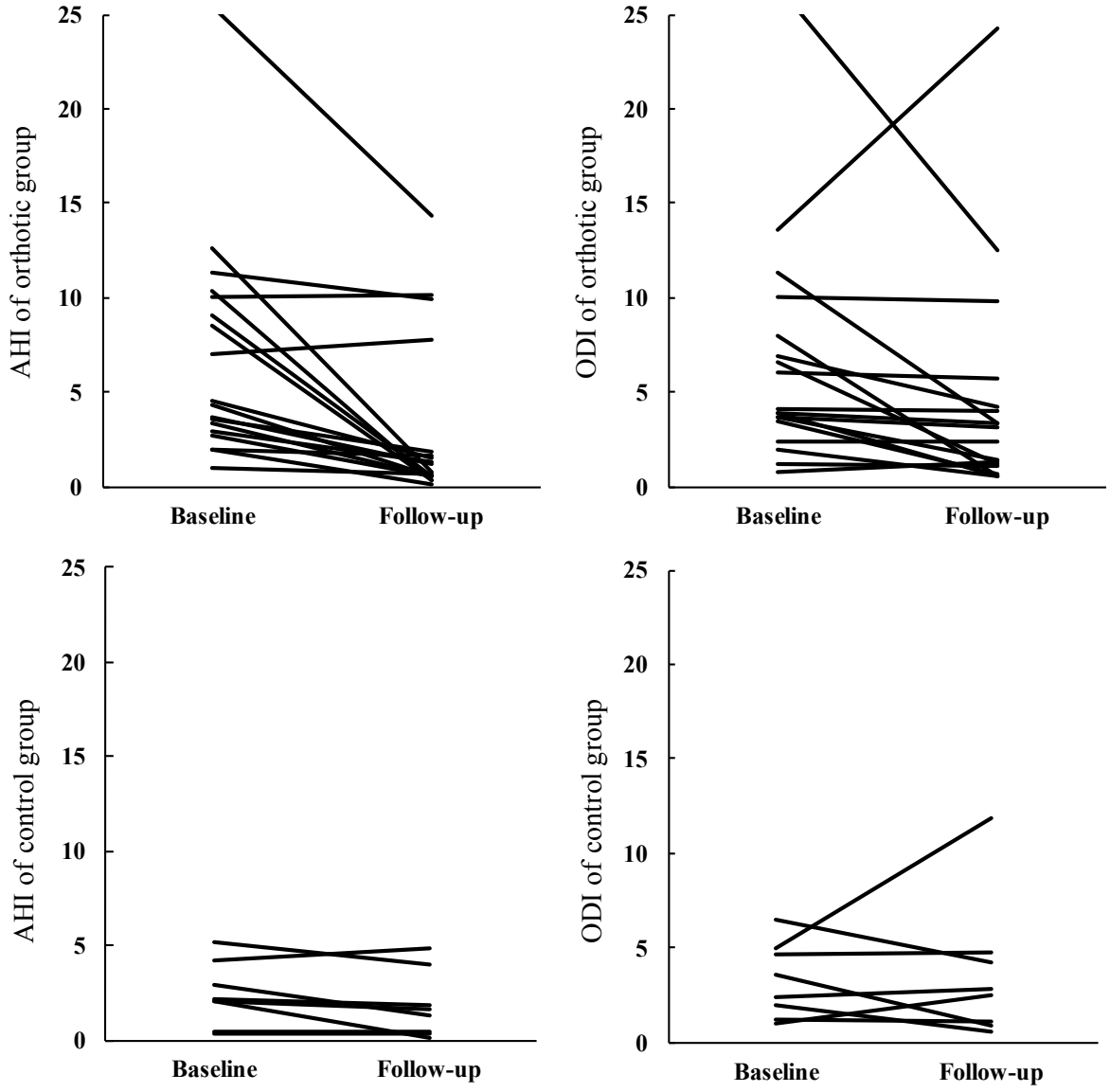
AHI of orthotic group
ODI of orthotic group
AHI of control group
ODI of control group
25
20
15
10
5
0
Baseline
Follow-up

Fig. 2

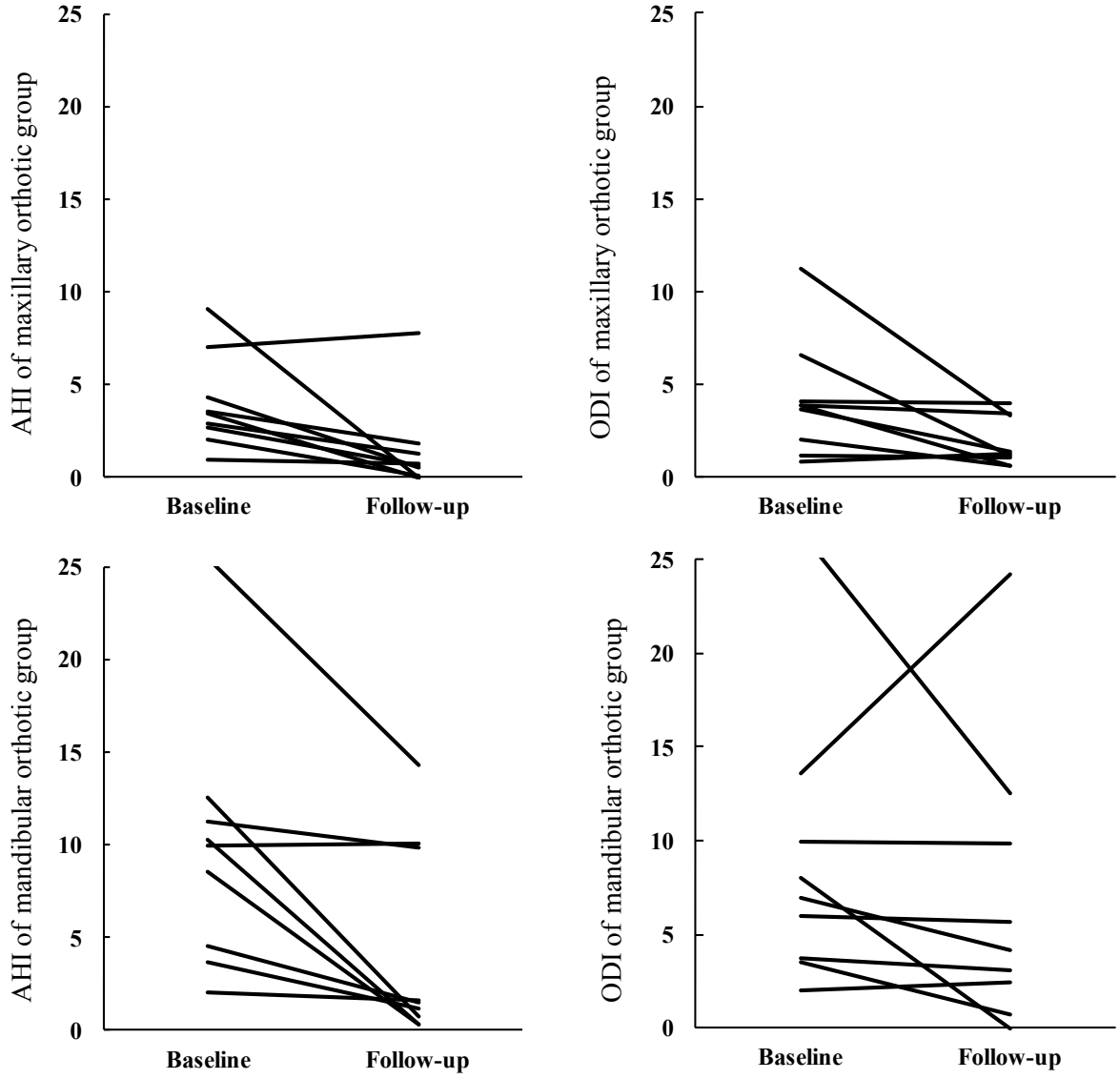
AHI of maxillary orthotic group
ODI of maxillary orthotic group
AHI of mandibular orthotic group
ODI of mandibular orthotic group
25
20
15
10
5
0
Baseline
Follow-up

Fig. 3

Table 1. Characteristics of the participants in the study

	Orthotic group	Control group	*p*
Variable	Value	Value	Value
[a]Male, n (%)	7 (41.2)	4 (50)	0.61
[b]Age (year) (s.d.)	36.4 (15.9)	29.4 (2.7)	0.23
[b]Body mass index (s.d)	26.8 (4.8)	22.3 (3.7)	0.39
[b]Epworth sleepiness score (s.d)	6.1 (2.7)	5.6 (2.7)	0.72
[b]STOP-Bang score (s.d)	1.2 (1.0)	0.6 (0.5)	0.18
[b]Berlin questionnaire (s.d)	0.93 (1.1)	1.0 (0.7)	0.92
[b]Mallampati score (s.d)	2.7 (0.9)	2.4 (0.7)	0.37

s.d: standard deviation

[a] chi-squared test

[b] Student's t-test

Table 2. Apnea hypopnea index (AHI) and oxygen desaturation index (ODI) mean score and s.d for orthotic and control groups

	Orthotic group			Control group		
	Baseline	Follow-up	*p*	Baseline	Follow-up	*P*
AHI (s.d)[§]	6.9 (5.7)	2.3 (4.3)	<0.01*	2.3 (1.6)	1.8 (1.6)	0.09
AHI-sup (s.d)	9.0 (10.1)	3.6 (5.1)	0.04*	2.8 (2.1)	3.7 (2.8)	0.08
ODI (s.d)	6.6 (6.0)	4.4 (5.9)	0.08	3.3 (1.8)	3.6 (3.4)	0.78
ODI-sup (s.d)	8.0 (7.8)	6.0 (7.6)	0.22	3.6 (2.0)	6.8 (4.6)	0.11

s.d: standard deviation

* $p<0.05$

[§] base line comparison between orthotic group and control group showed statistical significance ($p=0.004$)

Table 3. Apnea hypopnea index (AHI) and oxygen desaturation index (ODI) mean score and s.d for maxillary and mandibular appliances

	Maxillary orthotic group			Mandibular orthotic group		
	Baseline	Follow-up	*p*	Baseline	Follow-up	*p*
AHI (s.d)[§]	4 (2.3)	1.4 (2.3)	0.002*	9.8 (6.5)	4.5 (5.0)	0.001*
AHI-sup (s.d)	4.8 (3.2)	1.6 (2.5)	0.03*	12.6 (12.7)	5.4 (6.0)	0.17
ODI (s.d)	4.2 (3.0)	1.9 (1.2)	0.004*	8.9 (7.1)	7.0 (7.1)	0.46
ODI-sup (s.d)	5.0 (4.1)	2.2 (2.4)	0.02*	10.9 (9.2)	9.5 (8.9)	0.6

s.d: standard deviation

* $p<0.05$

[§] base line comparison between maxillary orthotic group and mandibular orthotic group showed statistical significance ($p=0.03$)