Original Article

Semi-fixed versus fixed oral appliance therapy for obstructive sleep apnea: A randomized crossover pilot study

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Abstract *Background/purpose:* Although mandibular advancement oral appliances (OAs) are the most widely used and accepted therapeutic modality for obstructive sleep apnea (OSA), whether these maxillary and mandibular appliances should be semi-fixed or fixed remains uncertain. This randomized crossover pilot study compared the efficacy, side effects, and patient preference of semi-fixed and fixed OAs for the treatment of OSA.
Materials and methods: Patients with mild to moderate OSA were recruited and randomly assigned to either the semi-fixed or fixed OA group, whereby they used their assigned OA for the first 4 weeks, followed by assessments for sleep parameters (including the Apnea-Hypopnea Index [AHI]) and temporomandibular joint pain as a side effect. After a two-week washout period, patients were switched to the alternative OA for 4 weeks, followed by repeated assessments. Patient preference was assessed at the end of the completed treatment period.
Results: Fifteen patients were enrolled and completed the full study protocol. Both types of OAs were efficient in reducing the patient's AHI in comparison to baseline (i.e., without OA). However, there was no significant difference in AHI reduction between the semi-fixed and fixed OA devices. Regarding the side effect of temporomandibular joint pain and patient preference, the semi-fixed OA device was superior to the fixed OA device on both measures.
Conclusion: While both semi-fixed and fixed OAs are effective in treating patients with OSA, semi-fixed OAs are superior in regards to both patient preference and reduced side effects. Thus, semi-fixed OAs may be the preferred therapeutic modality for OSA.

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Introduction

Obstructive sleep apnea (OSA) is a common sleep-related respiratory disorder characterized by an apnea—hypopnea cycle with upper airway collapse or sleep fragmentation and intermittent hypoxia.[1] Untreated OSA patients have a poorer quality of life, including an increased risk of both cardiovascular and cerebrovascular events and developing dyslipidemia and diabetes.[2,3] Nasal continuous positive airway pressure (nCPAP) and oral appliance (OA) therapy are the current standard treatments for OSA.[4,5] OA therapy is a non-invasive and highly adherent therapy compared to nCPAP, but its therapeutic effect is inferior. The American Academy of Sleep Medicine (AASM) guidelines recommended OA therapy for patients with mild to moderate OSA, or who are nCPAP intolerant, or who prefer an alternate therapy.[6] Recently, OA therapy for patients with mild to moderate OSA has been reported to both improve apnea and hypopnea, and reduce the risk of complications such as hypertension, arrhythmias, ischemic heart disease, and cerebrovascular disease.[7,8]

Among the various types of OA devices, the mandibular advancement OAs are the most widely used and accepted therapeutic modality for patients with OSA.[5–7] Mandibular advancement OAs expand the upper airway by repositioning the mandible anteriorly, thus preventing obstruction during sleep.[9,10] Generally, it has been reported that OA therapy has better patient adherence than nCPAP,[7,8] but there are cases in which OA therapy is discontinued due to patient preference and comfort. Mandibular advancement OAs can be either fixed (i.e., the degree of mandibular advancement cannot be changed) or semi-fixed (i.e., the degree of mandibular advancement can be adjusted). Since OA treatment for OSA is covered under health insurance in Japan, fixed OAs are more commonly used due to the reduced cost compared to semi-fixed OAs. Fixed OAs have a relatively high risk of TMJ disorder and dental/occlusal changes, although they provide a reliable therapeutic effect.[11,12] On the other hand, semi-fixed OAs are reported as both effective and comfortable devices that permit slight mouth opening and lateral jaw movement.[13–16] Semi-fixed OAs using NK connector®, as used in our institution, have demonstrated satisfactory clinical outcomes.[15,16] Recently, a systematic review using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework reported that mono-block (fixed) OAs were more effective than bi-block (semi-fixed) OAs for the treatment of OSA.[11] However, it remains unclear whether maxillary and mandibular appliances should be semi-fixed or fixed, as semi-fixed and conventional fixed OAs have not been sufficiently compared with regards to side effects and patient preference, in addition to efficacy.

The purpose of this randomized crossover pilot study was to compare the efficacy, side effects, and patient preference between semi-fixed and fixed OAs in the treatment of patients with mild to moderate OSA.

Materials and methods

Study design

This was a randomized, open-label, crossover pilot study comparing efficacy, side effects, and patient preference between semi-fixed and fixed OAs for the treatment of patients with OSA. Each OA was used for 4 weeks with a two-week washout period in-between. This clinical study was conducted in accordance with both the Clinical Research Law enacted in April 2018 in Japan and the tenets of the 2013 Declaration of Helsinki. The study protocol was registered with the Japan Registry of Clinical Trials (jRCT) on September 6, 2019 (JRCT ID: jRCTs072190026). Ethical approval was obtained from the Clinical Research Review Board at Nagasaki University (No. CRB19-009-1).

Participants

This study included OSA patients referred to the Department of Oral and Maxillofacial Surgery, Nagasaki University Hospital for OA treatment between October 2019 and April 2020. The inclusion criteria were as follows: patients aged 20 years or over with mild to moderate OSA (Apnea-Hypopnea Index [AHI] between 5 and 30 events/h) based on diagnostic polysomnography (PSG). The exclusion criteria were as follows: patients with problems in judgment; severe OSA (AHI > 30 events/h); or judged by the investigator to be inappropriate as a participant. Written informed consent was obtained from each patient prior to their inclusion in the study.

Interventions

The OAs were comprised of two lateral connectors and individual customized appliances for the maxilla and the mandible, as previously reported.[15,16] The appliances were made of clear transparent polyethylene terephthalate glycol thermoplastic (DURAN®, Scheu-dental GmbH, Iserlohn, Germany), and the degree of mandibular advancement was set at slightly less than the maximum anterior position so as not to exceed the limit the patients could comfortably tolerate. In fact, the position was determined at 70—80% of the maximum protrusion. The semi-fixed OAs were joined to each other using a connector composed of a polyethylene toothed belt (NK connector®, Morita Co. Ltd, Osaka, Japan), which permits slight mouth opening and lateral movement of the mandible (Fig. 1a). The fixed OAs were joined to each other using resin, thereby restricting mouth opening (Fig. 1b).

Patients were randomly assigned to either the semi-fixed or the fixed OA group, whereby they used their assigned OA for the first 4 weeks of the treatment period, followed by outcome assessments. After a two-week washout period, patients were switched to the alternative OA for the final 4 weeks of the treatment period, followed by the same
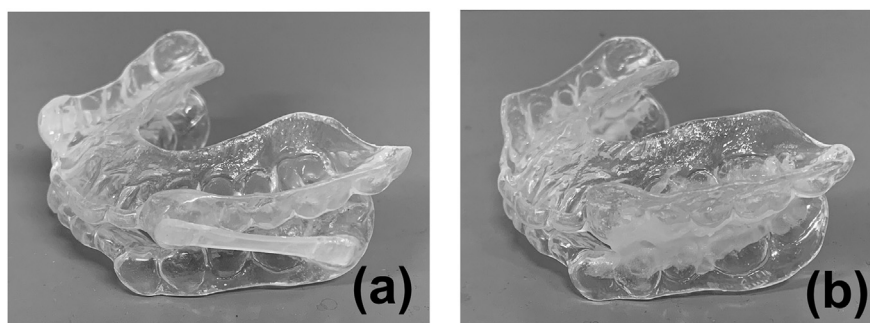
Figure 1 The oral appliance. (a) The semi-fixed oral appliance was comprised of two lateral connectors and individual customized appliances for the maxilla and mandible. (b) The fixed oral appliance consisted of appliances fixed together with resin.

outcome assessments. In addition, patient OA preference was assessed at the end of the treatment period.

Outcomes

The efficacy of both OAs was evaluated at home using WatchPAT (Itamar Medical Ltd., Caesarea, Israel). WatchPAT is an FDA-approved portable sleep test device, which can measure peripheral arterial tone (PAT) signal, pulse rate, oximetry, actigraphy, body position, snoring, and chest motion.[17] WatchPAT is considered a simple and reliable alternative that is well-correlated with PSG.[18] The AHI, 3% oxygen desaturation index (ODI), and lowest oxygen saturation (SaO_2) were evaluated. A successful treatment response was defined as a reduction in the AHI of $\geq 50\%$ compared to baseline, plus a decrease in the AHI to <5 events/hour.

The assessment of temporomandibular joint (TMJ) pain was performed using a Likert scale. This scale used the following response anchors: "not at all", "a little", "fairly much" to "much", and the opportunity to respond "do not know". TMJ pain was classified as a side effect if the patient endorsed a response of "fairly much" or "much".

Patient preference was assessed by asking whether the participant would prefer to use the semi-fixed or fixed OA at the end of the study.

The primary outcome was the difference in the AHI between the baseline and 4 weeks of OA treatment. Secondary outcomes included the difference in 3% ODI, lowest SaO_2, TMJ pain, and patient preference.

Randomization

Since this was a pilot study, a sample size calculation was not conducted. Rather, all eligible patients enrolled during the study period were included. All enrolled patients were randomly assigned to one of two sequences. The randomization was performed using a computer-generated block randomization method overseen by one investigator (MM). The sequence remained concealed after enrollment until assigning the first OA.

Statistical analysis

Data analyses were performed using SPSS version 24.0 (Japan IBM Co., Tokyo, Japan). All variables are reported as medians and interquartile ranges (IQRs). Between treatment (i.e., semi-fixed versus fixed OA) comparisons of categorical variables were assessed using Chi-squared tests or Fisher's exact tests, as appropriate. Between-treatment comparisons of continuous variables were assessed using non-parametric Wilcoxon signed-rank tests. In all analyses, a 2-tailed *p-value* of <0.05 was considered statistically significant.

Results

Patients' characteristics

Fifteen patients were enrolled in the study and randomized to one of the two treatment sequences. One patient withdrew due to intolerance of the OA at an early stage, and two patients withdrew for job-related reasons. Twelve patients completed the full study protocol, as shown in the CONSORT flow diagram (Fig. 2).

The patients' baseline characteristics are shown in Table 1. The median age of the patients was 50.0 (31.5—69.0) years, and seven males and five females were included in this study. The median body mass index (BMI) was 23.2 (21.4—28.2) kg/m^2. The median AHI, 3% ODI, and Lowest SaO_2 were 12.5 (8.9—17.0) events/h, 6.7 (5.6—13.1) events/h, and 87% (81.0—89.5%), respectively.

Outcomes

As reported in Table 2, the average AHI significantly improved from 12.5 (8.9—17.0) at baseline to 5.0 (2.6—12.0, $p < 0.05$) after semi-fixed OA treatment and 5.8 (2.1—8.5, $p < 0.05$) after fixed OA treatment. Similarly, the average 3% ODI and lowest SaO_2 also significantly improved from baseline after semi-fixed and fixed OA treatment. There was no significant treatment difference in AHI, 3% ODI, and lowest SaO_2 between the semi-fixed and fixed OA. A successful treatment response was observed for 7 of the 12 patients (58.3%) in the semi-fixed OA treatment, and for 6 of the 12 participants (50.0%) in the fixed OA treatment. There was no statistical difference in the successful treatment response between the semi-fixed and fixed OA ($p = 0.707$).

A participant who withdrew at an early stage after being assigned to the fixed OA first was intolerant, not because of side effects such as TMJ pain, but simply due to discomfort.
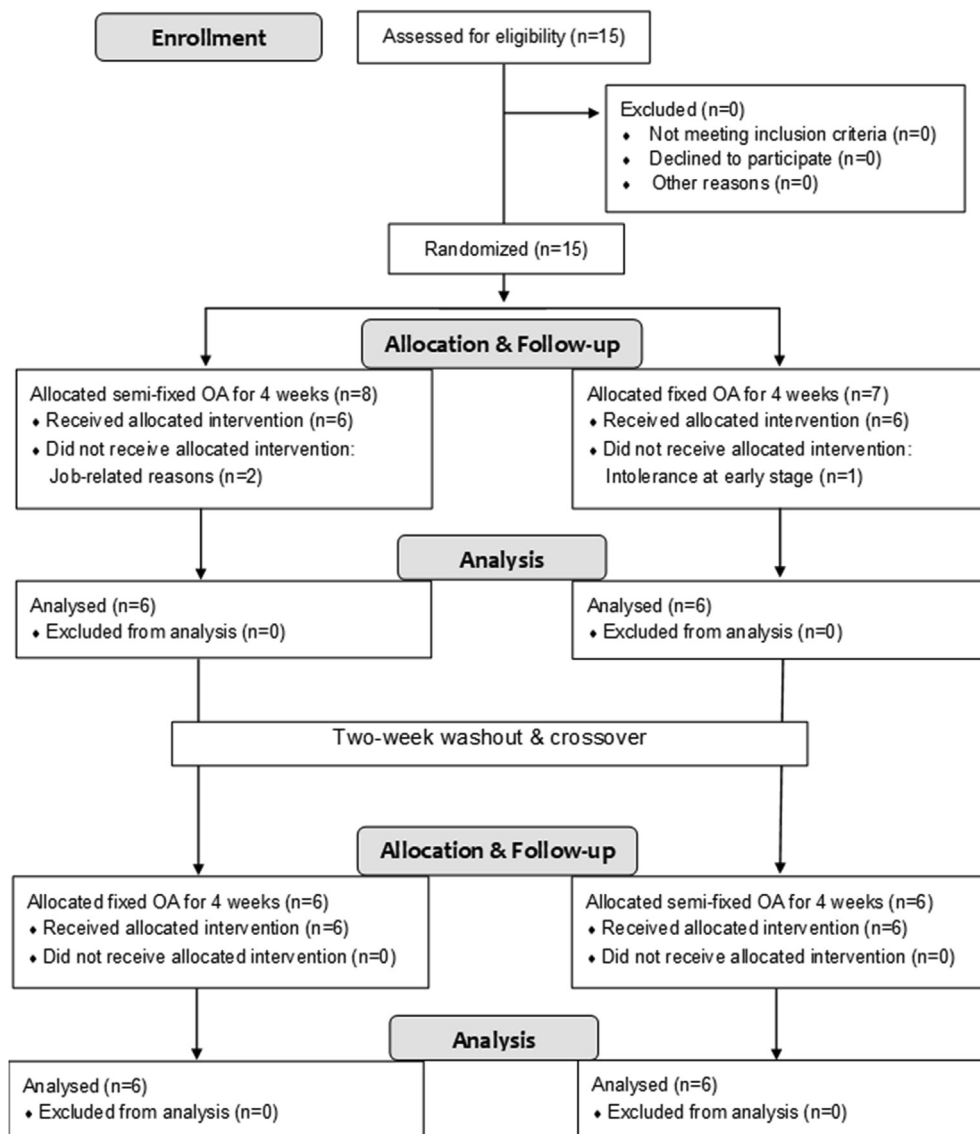
Figure 2 Flow diagram. Twelve participants completed the full study protocol, with six participants allocated to each treatment.

Table 1 Patients' characteristics at baseline.

Characteristic	All patients ($n = 12$)
Age (years), median (IQR)	50.0 (31.5–69.0)
Age (years), range	25–85
Sex (Male/Female)	7/5
BMI (kg/m^2), median (IQR)	23.2 (21.4–28.2)
AHI (events/h), median (IQR)	12.5 (8.9–17.0)
3% ODI (events/h), median (IQR)	6.7 (5.6–13.1)
Lowest SaO$_2$ (%), median (IQR)	87 (81.0–89.5)

IQR: interquartile range; BMI: body mass index; AHI: Apnea Hypopnea Index; ODI: oxygen desaturation index; SaO$_2$: oxygen saturation.

No participant withdrew due to the side effect of TMJ pain; however, the fixed OA resulted in a significantly higher incidence of TMJ pain compared to the semi-fixed OA (fixed OA: 4/12 patients, semi-fixed OA: 0/12 patients, $p = 0.047$).

After the complete treatment, more patients preferred the semi-fixed OA compared to the fixed OA (fixed OA: 3/12 patients, semi-fixed OA: 9/12 patients, $p = 0.021$).

Discussion

OA therapy for patients with OSA has recently received attention, and its application is increasing. Several recent studies have shown that OA treatment, which is simpler and more cost-effective than nCPAP, may be recommended over other treatment modalities in mild to moderate OSA patients.[7,8,19] A standardized form of OA treatment has not yet been established, including whether fixed or semi-fixed OAs are superior, Rather, treatment specifications vary between institutions. This study provides evidence that both OAs were efficient in reducing the patient's AHI after 4 weeks of treatment; however, there was no significant difference in the degree of this reduction between the semi-fixed and fixed OA devices. Regarding the

Table 2   Treatment effects of semi-fixed and fixed oral appliance.

Outcomes	Baseline, $n = 12$	Semi-fixed OA, $n = 12$	Fixed OA, $n = 12$	P value (semi-fixed versus fixed)
AHI (events/h), median (IQR)	12.5 (8.9–17.0)	5.0 (2.6–12.0)*	5.8 (2.1–8.5)*	0.388
3% ODI (events/h), median (IQR)	6.7 (5.6–13.1)	2.3 (0.8–4.8)*	1.9 (0.9–4.6)*	0.398
Lowest SaO_2 (%), median (IQR)	87 (81.0–89.5)	90 (88.5–91.0)*	90 (88.5–92.5)*	0.655
Treatment success	—	7/12	6/12	0.707
TMJ pain	—	0/12	4/12	0.047
Patient preference	—	9/12	3/12	0.021

IQR: interquartile range; AHI: Apnea-Hypopnea Index; ODI: oxygen desaturation index; SaO_2: oxygen saturation; TMJ: temporomandibular joint.
*$P < 0.05$ versus baseline.

improvement in the 3% ODI and lowest SaO_2, similarly, there was no significant difference in the degree of improvement between the two OA devices. Regarding the side effect of TMJ pain and patient preference, the semi-fixed OA was superior to the fixed OA.

Zhou and Liu[14] et al. reported that fixed OAs were more effective in reducing AHI than semi-fixed OAs, and were preferred by the majority of patients. In contrast, Bloch et al.[13] reported no significant difference in the AHI reduction between semi-fixed and fixed OAs, but fixed OAs were superior in regards to patient comfort and sleep. A systematic review incorporating these results concluded that fixed OAs are more effective than semi-fixed OAs.[11] However, this study found no significant differences between the two OA types in OSA-related sleep parameters, and, conversely, semi-fixed OAs caused less TMJ pain and were more preferred by patients than fixed OAs. Therefore, based on this preliminary evidence, we would suggest that semi-fixed OAs are superior to fixed OA.

This study had some limitations. As this was a pilot study were inherently a small number of patients, and the treatment intervention was of a short duration. Ideally, TMJ pain and patient preference should be evaluated after long-term use of each OA type. In addition, while fixed OAs are almost uniform devices, semi-fixed OAs are highly variable. Therefore, it is difficult to directly compare the outcomes of semi-fixed OAs from this study to other, similar, clinical trials using this type of OA.

In conclusion, the results of this study indicated that both of semi-fixed and fixed OAs were effective in reducing the AHI of patients with OSA. While there was no significant difference between OA types in their treatment effect on OSA-related sleep measures, semi-fixed OAs resulted in less TMJ pain and were more preferred by patients compared to fixed OAs. Therefore, we would suggest that semi-fixed OAs are the preferred choice in OA therapy for OSA, based on their superior safety and patient preference. However, further studies with more patients and a longer treatment duration are required to validate this preliminary evidence supporting the efficacy of semi-fixed OAs for patients with mild to moderate OSA.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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