Influence of combined oral appliance and nose breathing stimulator treatment for obstructive sleep apnea

（閉塞性睡眠時無呼吸症に対する口腔内装置と新規鼻腔拡大装置を併用した場合の治療効果）

Arisa Sawa

Nihon University Graduate School of Dentistry at Matsudo

Oral Function and Rehabilitation

(Director: Prof. Osamu Komiyama)

日本大学大学院松戸歯学研究科 顎口腔機能治療学専攻

澤　ありさ

（指導：小見山　道 教授）

I. Abstract

[Objective]

Oral appliances (OA), a common treatment for obstructive sleep apnea (OSA), are not suitable for patients with nasal obstruction, since high nasal resistance could negatively affect treatment outcomes. Objective assessment of nasal airflow might predict the suitability of OA. We investigated nasal obstruction levels in patients using subjective and objective nasal airflow evaluation, and compared the relationship between them. Furthermore, we aimed to develop a Nose Breathing Stimulator (NBS) for use in combination with an OA to promote nasal breathing.

[Materials and methods]

Research 1: The study included 97 patients with OSA and 105 healthy controls. We examined the correlations between the following variables between the groups: demographics (age and gender), body mass index (BMI), peak nasal inspiratory flow (PNIF), Nasal Obstruction Symptom Evaluation (NOSE) scale scores, apnea-hypopnea index (AHI), lowest SpO_2, Mallampati classification, and Epworth Sleepiness Scale (ESS) scores.

Research 2: Thirteen OSA patients wore a NBS, Max-Air Nose Corns®, Mute with hole®, which expands the nasal cavity from the inside, and Breathe Right®, which expands the nasal cavity from the outside, and compared the resultant changes in respiratory measures with those when a device was not used. The inspiratory flow rate (peak nasal inspiratory flow: PNIF) and visual analogue scale (VAS) scores were measured under five conditions. Furthermore, PNIF was measured under four conditions: OA (-) NBS (-), OA (+) NBS (-), OA (-) NBS (+), and OA (+) NBS (+), and a sleep test was performed.

[Result]

Research 1: Patients with OSA had significantly lower PNIF values and higher NOSE scores than controls. Significant positive correlation was observed between the NOSE scores and Mallampati classification (r=.203, p=.047).

Research 2: PNIF was significantly higher when wearing an NBS compared with the other four devices ($p < 0.001$). In addition, PNIF was significantly higher in OA (+) NBS (+) than that in the other three conditions ($p < 0.001$), and OA (+) NBS (+) improved the respiratory disturbance index ($p < 0.001$), lowest SpO_2 ($p < 0.001$), and Epworth sleepiness scale (ESS) score ($p < 0.001$) on the sleep test.

[Conclusion]

It was suggested that the OSA group had significantly lower nasal inspiratory flow compared to the control group, therefore evaluating the nasal obstruction by screening test is beneficial for sleep dentistry outpatients. Furthermore, wearing the NBS improved breathing in patients who did not benefit from OA treatment alone.

II. Introduction

Obstructive sleep apnea (OSA) is characterized by the repetitive collapse of the pharyngeal airway during sleep, leading to complete or partial airflow obstruction, and thus resulting in perturbations [1]. The first-line treatment of obstructive sleep apnea (OSA) in Europe and the United States is Continuous Positive Airway Pressure (CPAP) [2-3]. In patients with a respiratory disturbance index (RDI) ≧30 [4], CPAP can be used, but for those with an RDI ≧40, CPAP may not be covered by insurance in Japan, so an oral appliance (OA) is also commonly used.

Adherence to CPAP treatment is approximately 50%, and many patients discontinue CPAP treatment due to breathing difficulties caused by nasal obstruction [5]. Further, in severe cases of OSA where CPAP use is rejected, patients can use an OA. These OAs include tongue stabilizing devices (TSD) and mandibular advancement devices (MAD), of which MAD is commonly used for the dental treatment of OSA [6]. In particular, monoblock MAD are commonly used to improve upper airway obstruction in Japan. Such devices function by moving the mandible forward, lifting the hyoid bone, and moving the soft palate forward via the palatoglossal arch, which connects the tongue and soft palate [7]. This mechanism promotes nasal breathing and creates an oral seal by preventing mouth opening and velopharynx occlusion [8]. The treatment efficacy of MAD for OSA patients has been well-established [9-10], though even in cases where the use of an OA improves respiration, its efficacy is reduced if patients are unable to perform adequate nasal breathing. Patients who are diagnosed with OSA in the absence of other sleep disorders must use an OA, even if its efficacy is reduced in cases where nasal breathing is difficult [11] during sleep due to an elongated soft palate [12], as this can result in insufficient improvement in respiratory measures, including lowest SpO_2 and other sleep respiratory measures. We have observed that many of our patients do not experience improvements in the lowest SpO_2, even if their snoring improves, limiting treatment outcomes in those with a MAD. Nasal

obstructions occur in approximately 64% of OSA patients, most of whom exhibit anatomical variations that decrease treatment efficacy [13]. Furthermore, it has been reported that OSA patients have significantly lower nasal airflow compared to healthy participants [14]. Zeng et al. [15] demonstrated that high levels of nasal resistance measured using supine posterior rhinomanometry predicted poor treatment outcome with mandibular advancement. Rhinomanometry is the standard technique for measuring nasal airway resistance through measurement of nasal pressure and airflow. However, it is not readily available in dental sleep clinics. A recent study highlighted the efficacy of a small, lightweight device for easily assessing Peak Nasal Inspiratory Flow (PNIF) in patients with asthma and nasal obstruction [16].

Even if these patients are treated by an otolaryngologist to improve nasal obstructions, some patients have difficulty breaking the habit of mouth breathing. Oral myofunctional therapy (OMFT) can reduce mouth breathing and be effective for sleep improvement in all cases [17]; however, this training takes a long time, and the problem can recur if patients do not continue the training.

Previous studies have attempted to expand the nasal cavity and improve nasal breathing when wearing a special device, either within or exterior to the nasal cavity [18]. However, previous devices have only been able to expand the nasal cavity and improve airflow, but they have never been proven effective in improving sleep apnea [19].

For optimal effectiveness of treatment with an OA, it is important for the patient to make a conscious effort to breathe nasally with a closed mouth to promote airflow; thus, we attempted to develop a novel method to optimize airflow in these patients. This led to the idea of developing not just another nasal clip, but a novel nasal stent—the Nose Breathing Stimulator (NBS). The concepts underlying the NBS development are as follows: I) a polyester elastomer is used as the base material, as it is adequately flexible, resilient, and washable and does not irritate the nasal

mucosa (since it is to be used within the nose); II) the stent is rounded and smoothed to prevent damage to the nasal mucosa; III) a lattice-type structure with an uneven pattern is used for efficient vaporization of nasal secretions or substances entering the nasal mucosa during inspiration; IV) when worn, it affects nasal-valve expansion by pressing the depressor septi at the joint; and V) its design prevents a decrease in airflow at the exits with enhanced diameter differences between the air entry and exit points, along with the dual-plate structure of the exhaust plate at the pharyngeal exit.

The aims of the present study were twofold: first, to investigate awake nasal obstruction by recording PNIF in first-time visitors to our outpatient dental sleep clinic for OSA patients and the healthy participants and second to examine the possibility of using this new device to improve treatment outcomes of patients with OSA.

III. Materials and Methods

Research 1: Assessment of screening for nasal obstruction among sleep dentistry outpatients with obstructive sleep apnea

This study included 97 patients with OSA (65 men, mean age: 47.2 ± 15.2 years; 32 women, mean age: 51.8 ± 15.2 years) who had visited Nihon University School of Dentistry at Matsudo Hospital for OA from July 2019 to January 2020. The control group consisted of 105 adults (68 men, mean age: 34.2 ± 11.2 years; 37 women, mean age: 36.4 ± 11.0 years) with no nasal complaints as assessed by the Nasal Obstruction Symptom Evaluation (NOSE) scale and the Peak Nasal Inspiratory Flow (PNIF) (Table 1). Patients being treated currently for otorhinolaryngologic disorders, athletes such as sumo wrestlers and rugby players, patients with systemic diseases and restrictions to perform vigorous exercise, and patients who could not self-assess were excluded. The study was approved by the Ethics Review Committee of Nihon University School of

Dentistry at Matsudo (approval number EC-18-015: 27/09/2018). The study was performed according to the principles stated in the Declaration of Helsinki. All study participants provided written informed consent prior to inclusion in the study.

The following variables were evaluated using medical records from the first visit in the OSA group: age, gender, Body Mass Index (BMI), apnea-hypopnea index (AHI), lowest SpO_2, PNIF, NOSE scale scores, Mallampati classification, and Epworth Sleepiness Scale (ESS) scores. In the control group, the following variables were evaluated: PNIF, NOSE scores, and Mallampati classification.

A portable PNIF meter (in-check DIAL, Clement Clarke International, Harlow, Essex, UK) was used to assess nasal function (Peak Nasal Inspiratory Flow rate) in the present study. The PNIF assessment is an established, validated clinical tool for evaluating nasal obstruction [20]. Results obtained using this simple, yet reliable procedure correspond strongly with subjective assessment of nasal obstruction. The mean of three approved PNIF measurements for each patient was calculated at the initial visit, with the patient in a seated position with the head held parallel to the floor.

The NOSE scale was developed to assess the impact of nasal obstruction [21]. This scale contains five items (nasal congestion/stiffness, nasal blockage/obstruction, trouble breathing through nose, trouble sleeping, and inability to get enough air through the nose during exercise/exertion) assessed for the last one month and scored along a five-point scale (0 to 4), with 0 representing “not a problem” and 4 representing “a severe problem.” Total NOSE scores are calculated by multiplying the raw score by 5, with final scores ranging from 0 to 100 and classified as: 0, no obstruction; 5–25, mild obstruction; 30–50, moderate obstruction; 55–75, severe obstruction; and 80–100, extreme obstruction. The NOSE scale is a valid and reliable instrument [22-23].

Mallampati scoring is a simple, noninvasive, inexpensive technique that involves visualization of the oropharynx. It is easy to learn and does not need any special equipment or setting. It has been used for more than two decades to assess the ease of intubation in anesthesiology [24]. The patients were asked to sit upright with the head positioned parallel to the floor, to open their mouth as widely as possible, and to protrude the tongue as much as possible. The observer sat opposite the patient at the level of the patient's eye and inspected the pharyngeal structures of the patient with the help of a pen torch. The airway was then classified according to the structures visible, as follows: class I—soft palate, fauces, uvula, pillars; class II—soft palate, fauces, uvula; class III—soft palate, base of uvula; class IV—soft palate not visible at all. The Mallampati score has additional value in diagnosing OSA in adults according to The American Academy of Sleep Medicine [25].

Independent t-tests were used to compare average PNIF measurements between the OSA and control groups. χ^2 test was used to Mallampati classification. Pearson's product–moment correlation coefficients were used to examine the relationship between basic clinical variables and nasal airflow assessments (PNIF and NOSE) in the OSA group. According to Cohen's convention for the size of the effect for the Pearson correlation coefficient, an absolute value of r of 0.1 was classified as small, of 0.3 was classified as medium, and of 0.5 was classified as large [26]. P-values less than 0.05 were considered statistically significant. All statistical analyses were performed using SPSS for Windows version 20.0 software (SPSS, Chicago, IL, USA).

Research 2: A new developed the Nose Breathing Stimulator and oral appliance for treating obstructive sleep apnea

This study included 13 patients with OSA (7 males, average age: 45.0 ± 15.5 years; 6 females, average age: 54.5 ± 4.5 years) who had visited Nihon University School of Dentistry at Matsudo Hospital Snore clinic and were aware of experiencing nasal obstruction daily but had not received

otolaryngologic treatment. This study was approved by the Ethics Review Committee of Nihon University School of Dentistry at Matsudo (approval number: EC-18-029). The study was performed according to the principles stated in the Declaration of Helsinki. All study participants provided written informed consent prior to inclusion in the study.

The participants wore an NBS (Fig. 1), Max-Air Nose Corns®: NC (Sanostec Corp., MA, U.S.A), Mute®: MT (AceJAPAN, Tokyo, Japan), and Breathe Right®: BR (GlaxoSmithKline, Brentford, U.K) (Fig.2) for 15 minutes each; then an otolaryngologist examined each subject for bleeding, redness, swelling, and lacerations of the nasal cavity. In addition, the obstruction was self-assessed by the patient using a 100-mm visual analogue scale (VAS), ranging from 0 (normal nasal ventilation as a control) to 10 (clear nasal ventilation) [27].

Peak nasal inspiratory flow (PNIF) is a measurement of the maximum inspiration volume per minute (L/min) during nasal breathing. PNIF was measured with the NBS, NC, and MT inserted into the nasal cavity and BR applied to the bridge of the nose to objectively evaluate the inspiratory flow in awake participants. In addition, PNIF was measured with "no device" as a control. PNIF was recorded using an inspiratory flow meter (In-check™, Clement Clarke International Limited, Harlow, U.K) (Fig. 3). The participant inhaled maximally through the nasal passage after exhaling fully in a sitting position with the mouth closed. The mean of three measurements correctly performed was recorded. Measurements were taken on three occasions, and the devices were used in random order. To ensure safety, an otolaryngologist examined all participants after each session to evaluate the presence/absence of pain, discomfort, bleeding, or lacerations in the nasal cavity.

Since the safety and effects of NBS were confirmed from the above, the patients were referred to the hospital where an oral examination, an Epworth Sleepiness Scale (ESS) questionnaire assessment [28], and a sleep test were performed in accordance with the usual

methods. Respiratory Disturbance Index (RDI), snoring, and lowest SpO_2 were measured using a level III monitor (WatchPAT: WP—Itamar-Medical, Caesarea, Israel) at home. When OSA was diagnosed, an OA was prepared, mounted, and adjusted for each patient according to the usual method. The OA was a Monobloc-type MAD, with the extent of forward movement being approximately 70%. A re-evaluation was then performed on each patient while wearing the OA. Two weeks later, a sleep test was performed again while wearing the NBS alone to expand the nasal cavity and wearing a combination of OA+NBS and compared among the four conditions, including OA (-) NBS (-), OA (+) NBS (-), OA (-) NBS (+), and OA (+) NBS (+). (+) and (-) are with and without intervention, respectively. PNIF was measured with an intake flow rate measurement tool and compared among four conditions, including OA (-) NBS (-), OA (+) NBS (-), OA (-) NBS (+), and OA (+) NBS (+). The mean of three measurements correctly performed was recorded.

In the subjective and objective evaluation for each nasal dilator, one-way ANOVA was used to compare VAS and PNIF results. The Bonferroni correction was used for multiple comparisons. For PNIF and sleep test results, one-way ANOVA with repeated measures was used to compare to PNIF values, OA (-) NBS (-), OA (+) NBS (-), OA (-) NBS (+), and OA (+) NBS (+). The Bonferroni correction was used for multiple comparisons. P-values less than 0.05 were considered statistically significant. All statistical analyses were performed using SPSS for Windows version 20.0 software (SPSS, Chicago, IL, USA).

IV. Results

Research1: Assessment of screening for nasal obstruction among sleep dentistry outpatients with obstructive sleep apnea

Table 1 shows the demographics, PNIF, NOSE scores, and Mallampati classification level from 105 healthy participants and 97 patients with OSA. In addition, data on AHI, lowest SpO_2 (%), and the ESS scores were collected for the OSA group (Table 1). The group had moderate sleep apnea with a mean AHI of 16.0 ± 9.2.

1. PNIF results between OSA group and control group

The mean PNIF values were significantly lower in the OSA group (101.3 ± 44.4 L/min) than in the control group (134.2 ± 31.5 L/min) ($p < 0.001$). The mean PNIF value remained significantly lower for both males and females in the OSA group than in the control group ($p < 0.001$) (Table 1). Levene's test for homoscedasticity yielded the following results for the patient and control groups: $F = 17.64$, $p < 0.001$. When the analyses were restricted to male or female participants, the F values were 11.73 ($p < 0.001$) and 15.62 ($p < 0.001$), respectively. The standard deviation was significantly larger in the OSA group than in the control group, regardless of gender.

2. NOSE and Mallampati classification between the OSA and the control group

The mean NOSE scores were significantly higher in the OSA group (29.1 ± 22.6 point) than in the control group (8.1 ± 5.5 point) ($p < 0.001$) (Table 1). Moreover, we conducted χ^2 test for Mallampati classification and the results revealed significant differences between OSA group and the control group ($\chi^2(3) = 144.2$, $p < 0.001$). Residual analysis revealed that the mean Mallampati classification was significantly higher in the OSA group than in the control group (Table 2).

3. Correlations between basic clinical variables and nasal obstruction assessment in patients with OSA

We observed a weak yet significant positive correlation between NOSE and Mallampati Classification ($r = 0.203$, $p = 0.047$) and between AHI and BMI ($r = 0.364$, $p < 0.01$). In addition, we observed a significant negative correlation between AHI and lowest SpO_2 ($r = - 0.628$, $p < 0.01$), between age and ESS ($r = - 0.321$, $p < 0.01$), and between BMI and lowest SpO_2 ($r = - 0.20$,

p = 0.048) (Table 3).

Research 2: A new developed the Nose Breathing Stimulator and oral appliance for treating obstructive sleep apnea

Table 4 shows the demographics, age, body mass index, PNIF, RDI, lowest SpO_2, ESS scores, and Mallampati classification. The OSA patients had moderate sleep apnea with a mean RDI of 25.6 ± 15.2 (Table 4).

1. The subjective evaluation of each nasal dilator

The mean VAS scores were significantly higher for the NBS than "no device," NC, MT, and BR (7.5 ± 1.0) ($p < 0.001$) (Table 5).

2. The objective evaluation of each nasal dilator

The mean PNIF values were significantly higher for the NBS than "no device," NC, MT, and BR (135.5 ± 21.7 L/min) ($p < 0.001$) (Table 5).

3. Comparison of OA + NBS with other conditions for sleep outcomes in OSA patients

The mean PNIF values were significantly higher for OA (+) NBS (+) than those for OA (-) NBS (-), OA (+) NBS (-), and OA (-) NBS (+) (168.3 ± 34.8 L/Min) ($p < 0.001$). Moreover, the lowest SpO_2 and RDI were significantly improved for OA (+) NBS (+) compared with OA (-) NBS (-), OA (+) NBS (-), and OA (-) NBS (+) (89.2 ± 4.5%) (6.5 ± 5.2 Event / hr) ($p < 0.001$), and ESS scores were significantly improved for OA (+) NBS (+) compared with OA (-) NBS (-), OA (+) NBS (-), and OA (-) NBS (+) (4.2 ± 2.0 point) ($p < 0.001$) (Table 6).

V. Discussion

Research 1: Assessment of screening for nasal obstruction among sleep dentistry outpatients with obstructive sleep apnea

OA and CPAP treatment can ease obstructive sleep apnea, nasal obstruction may preclude

continuation with these treatments [29]. We therefore performed screening for nasal obstruction in OSA patients and compared that to a group of healthy control participants by means of objective PNIF assessments and the subjective NOSE scale. The patient group with OSA exhibited significantly lower PNIF values than healthy controls, suggestive of impaired nasal airflow. The subjective NOSE scores for the patient group bordered on moderate obstruction (mean 29.1 ± 22.6) and that for the healthy group on normal-mild obstruction (mean 8.1 ± 5.5).

In comparison to a previous multicenter, large-scale study of OA treatment in Japan [30], our study comprised of a large number of female patients, and our overall patient group tended to be younger. In addition, the mean AHI was lower among our outpatients than in previous large-scale studies, indicative of more patients with mild-to-moderate OSA in our study. These results are expected, since our outpatient department specializes in sleep dentistry and patients with mild-to-moderate OSA are referred for OA treatment by nearby sleep clinics. Often, these patients are referred for OA therapy when they have discontinued CPAP treatment. The suburban location of our hospital may also explain the high percentage of female patients in our study.

Our findings for both healthy male and female participants are consistent with those of Ottaviano et al. [31] and Dor-Wojnarowska et al. [32] and confirm the higher PNIF values among men than women. The reason for the higher PNIF in males is the smaller nasal cavity found in females [33]. Differences in lung function may also explain these findings, as previous research has indicated that females have smaller lungs and narrower airways than males of the same age and BMI [34]. Thus, the differences in observed values between the sexes could depend on the difference in the size of the lungs and nasal cavity. Factors other than lung and nasal cavity size, such as an anatomical deviation in the nasal passage, should be considered.

In the OSA group, the PNIF findings obtained are consistent with those of Moxness et al. [35], who also reported lower values in the OSA compared with control group. The Levene's test further revealed that the standard deviation of PNIF values was greater in the OSA group than in

the control group, suggestive of greater individual variation among patients. Moxness et al. [35] reported that the nasal cavity volume was significantly lower in the OSA group than in the healthy controls. In addition, a reduced response to treatment for congestion in the OSA group indicates a high bone-to-mucosa ratio in the inferior turbinate or an inflammatory cause of mucosal edema. Our outpatients may have these causes.

Although rhinomanometry is the gold standard test for assessing nasal airflow [36] and is highly accurate, it is not available in sleep dental clinics, and patients must visit an otolaryngologist for the assessment, making it impractical with regard to time and cost. On the other hand, PNIF measurement is a simple, objective assessment of inspiratory nasal airflow. The ease of obtaining objective data related to nasal airflow in sleep dentistry clinics may provide a means of assessing the degree of nasal obstruction prior to OA/CPAP treatment and thus may help improve adherence to these treatments. However, the daytime PNIF measure does not correlate with any of the sleep apnea variables; it bears no relationship with the AHI or ESS scores, suggesting that PNIF cannot be used to assess treatment outcomes with OA. This measurement was taken with the subjects in an upright posture. A supine PNIF measurement might be strongly associated with AHI, as it is expected to be higher given the reduced pharyngeal diameter while lying down [37]. Thus, supine PNIF would have been a more appropriate measurement for this study.

In the patient group, as expected, the sleep apnea variables were highly correlated, with a high AHI and high BMI predicting a low SpO_2 and increasing age predicting lower sleepiness, SpO_2, and lower subjective nasal obstruction. These findings are in line with previous findings of a positive correlation between AHI and BMI [38] and a negative correlation between BMI and the lowest SpO_2 [39], between AHI and lowest SpO_2 [40], and between age and ESS scores [41].

The NOSE score and Mallampati classification were significantly higher in patients with OSA than in the healthy controls and lower in females than males. Kale et al. [42] had similarly reported a significantly higher Mallampati classification in the OSA group than in the healthy

control group. These subjective evaluations confirm that OSA patients are conscious of their nasal obstruction.

The NOSE scores correlated positively with the Mallampati classification. The NOSE scale, developed and validated by Stewart et al. [21], as a measure of nasal obstruction, is also useful in patients with OSA [43]. Previous studies have reported that high Mallampati grades in patients with nasal obstruction may worsen OSA severity [44], making assessments of Mallampati grade valuable. In addition, Yagi et al. [45] reported that the Mallampati grade predicted severity of OSA linked to anatomical/morphological characteristics in Japanese patients. This may explain the correlation between the NOSE scale scores and Mallampati classification in our patients with mild-to-moderate symptoms. The fact that there was a significant, albeit marginal, negative correlation between PNIF and NOSE ($p = 0.061$, $r = -0.191$) suggests that the perception of nasal obstruction was accurate. The marginal significance may be explained by the small sample size, and we would like to increase the number of participants in future studies.

The present study has some limitations. First, because of the large number of male OSA patients, we saw more male patients than female patients during the 6-month period. In the future, we would like to extend the survey period and derive new data when the numbers of men and women are equal. Second, there was a larger proportion of patients with mild-to-moderate OSA. Third, we measured PNIF in the upright rather than the supine position. Future studies should examine PNIF in the supine position with or without OA for the same patient and systematically evaluate if objective assessments of awake PNIF can help in evaluating the effectiveness for OA/CPAP treatment.

Research 2: A new developed the Nose Breathing Stimulator and oral appliance for treating obstructive sleep apnea

We hypothesized that the treatment for OSA could be improved with the use of NBS in patients with nasal obstruction who cannot use OA, as it is a limitation of OA treatment. Thus, we

developed NBS, and after assessing its potential clinical applicability, the results suggested that the combination of OA+NBS could have the highest treatment efficacy among the other conditions.

Firstly, in the basic clinical data of OSA patients, all Malampati classifications for OSA patients were IV and PNIF was low, suggesting that they are associated with nasal obstruction. In addition, VAS scores were significantly higher for NBS (7.5 ± 1.0) than those for the other nasal dilators. VAS is a commonly used method to evaluate subjectivity [27]. Lekakis et al. [46] reported that nasal obstruction was improved with all nasal dilators, when assessing nasal obstruction subjectively. This is similar to the result of our study. PNIF values were significantly higher for NBS than those for the other dilators (135.5 ± 21.7 L/min). PNIF measurements are commonly used to assess the volume of oxygen entering the nasal passages in one minute (typically in L/min). PNIF is a simple and inexpensive method used to evaluate nasal obstruction objectively [20]. Lekakis et al. [46] reported that the PNIF values were significantly higher for an internal nasal dilator than external nasal dilator. Their results are similar to those of the current study. Therefore, it is suggested that wearing an internal nasal dilator is more beneficial than wearing an external nasal dilator. According to this, the higher PNIF value for the NBS could provide evidence of its favorable effect, not only due to nasal valve expansion, but also due to the effective structural design and further expansion caused by pressing the depressor septi at the joint. Moreover, the difference in the diameters at the air entry and exit points, as well as the dual-plate structure of the exhaust plate at the pharyngeal exit, prevents a decrease in the velocity of air flow at the exits. None of the participants had any issues during the post-session examination of the nasal cavity, which could be attributed to the successful use of the polyester elastomer (which, as described in the Introduction, was adequately flexible, resilient, and washable) as a comfortable base material, while the rounded design prevented damage to the nasal mucosa. Another reason

could be that the NBS was designed to fit the noses of Asian individuals well. It was presumed that wearing an NBS made nasal breathing easier and accelerated the flow velocity, which increased the inspiratory flow rate. The conceptual NBS was expected to accelerate the flow of air that entered the nasal cavity during inspiration so that the air entered the lungs easily. Therefore, the effectiveness of this device was confirmed even during the awake period. As mentioned above, NBS with the highest PNIF was developed, and it was found that the rate of airflow in the nasal passage was subjectively and objectively higher than that with the other nasal dilators. In addition, to examine whether clinical application is possible, the effect with respect to the time of use was examined.

Secondly, the PNIF values were significantly higher for OA (+) NBS (+) (168.3 ± 34.8 L/min) than those for the other conditions, and the RDI, lowest SpO_2, and ESS scores showed improvement on wearing OA (+) NBS (+) compared with OA (-) NBS (-), OA (+) NBS (-), and OA (-) NBS (+). Breathing and snoring, and oxygen saturation measured at the fingertips by the level III monitor were analyzed. Therefore, an improvement in the RDI and lowest SpO_2 indicates a decrease in nasal resistance [47], and it is suggested that air reaches alveoli faster during inspiration. OA (+) NBS (+) showed significant improvement in nasal inspiratory airflow compared with the other three conditions. The effect of combined OA (+) NBS (+) may be more effective than monotherapy. This study is considered a pilot study, as the number of subjects was small; therefore, in future research, a higher number of subjects should be included. The fact that wearing a combination of OA and NBS improved RDI, lowest SpO_2, and ESS scores compared to wearing an OA alone, suggests that the NBS may be effective as a treatment for improving respiration during sleep in patients with OSA and clinical application is possible.

Our findings are consistent with those of a previous study, which reported that a novel OA (O2Vent T, Oventus Medical Limited, Indooroopilly, Australia) could be combined with oral

expiratory positive airway pressure (oral EPAP) and nasal EPAP ventilation during sleep to decrease apnea-hypopnea index scores and improve OSA severity [48].

Nasal obstruction is reportedly one of the key factors contributing to OSA [49]. Based on this concept, our study demonstrated a novel way to avoid nasal obstruction in OSA patients. These findings suggest that combining OA (+) NBS (+) can be efficacious in improving OSA symptoms in patients who cannot wear an OA and in those who do not benefit from OA treatment alone.

VI. Conclusion

It was suggested that the OSA group had significantly lower nasal inspiratory flow compared to the control group, therefore evaluating the nasal obstruction by screening test is beneficial for sleep dentistry outpatients. Furthermore, wearing the NBS improved breathing in patients who did not benefit from OA treatment alone.

VII. References

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VIII. Tables and Figures

Table 1. The characteristics of OSA patients and controls

	Control	OSA	p-value
n	105	97	
Males, n(%)	68 (64.8)	65 (67.0)	
Females, n(%)	37 (35.2)	32 (33.0)	
Age (years)	35.0 ± 11.1	48.7 ± 15.3	
BMI (kg/m^2)	22.6 ± 2.0	24.8 ± 5.1	
AHI (/h)	—	16.0 ± 9.2	
Mild, n(%)	—	49 (50.5)	
Moderate, n(%)	—	42 (43.3)	
Severe, n(%)	—	6 (6.2)	
PNIF (L/min)	134.2 ± 31.5	101.3 ± 44.4	< 0.001
Male (n=68)	143.4 ± 33.6	118.0 ± 45.5	< 0.001
Female (n=37)	117.4 ± 17.7	81.1 ± 34.3	< 0.001
Lowest SpO_2 (%)	—	82.8 ± 7.1	
ESS (point)	—	9.2 ± 5.0	
NOSE questionnaire (point×5)	8.1 ± 5.5	29.1 ± 22.6	< 0.001

N: Number; BMI: Body Mass Index; AHI: Apnea–Hypopnea Index; ESS: Epworth Sleepiness Scale; Lowest SpO_2: Lowest oxygen saturation; PNIF: Peak Nasal Inspiratory Flow; NOSE: Nasal Obstruction Symptom Evaluation.

Sleep apnea severity was classified as mild: 5 ≤AHI<15, moderate: 15≤AHI<30, and severe AHI≤30.

Table 2. χ^2 test for Mallampati classification between controls and OSA patients

	Mallampati classification			
	I	II	III	IV
Controls (N)	5 (4.8%)	45 (42.8%)	55 (52.4%)	0 (0%)
OSA patients (N)	4 (4.1%)	3 (3.1%)	14 (14.4%)	76 (78.4%)

$\chi^2(3) = 144.2$, $p < 0.001$

Table 3. Pearson's product-moment correlation coefficient between NOSE scale, PNIF and patient characteristics

		Age	BMI	AHI	Lowest SpO_2	ESS	NOSE	PNIF	Mallampati classification
Age	r	—	-0.163	-0.069	-0.193	-0.321**	-0.192	0.034	0.116
BMI	r		—	0.364**	-0.201*	-0.077	0.020	0.081	-0.068
AHI	r			—	-0.628**	0.070	0.073	-0.074	-0.129
Lowest SpO_2	r				—	0.045	-0.067	0.030	-0.015
ESS	r					—	0.147	0.034	-0.086
NOSE	r						—	0.061	0.203*
PNIF	r							—	-0.049
Mallampati classification	r								—

NOSE scale; Nasal Obstruction Symptoms Evaluation scale, PNIF; Peak Nasal Inspiratory Flow, Lowest SpO_2: Lowest oxygen saturation, BMI; Body Mass Index, AHI; Apnea Hypopnea Index, ESS; Epworth Sleepiness Scale, *; $p<0.05$, **; $p<0.01$

Table 4. The characteristics of OSA patients

N	13
Male (N)	7
Female (N)	6
Age (yrs)	49.4 ± 12.4
BMI (kg/m^2)	25.6 ± 4.3
PNIF (L/Min)	94.7 ± 30.7
RDI (Event / hr)	25.6 ± 15.2
Lowest SpO_2 (%)	77.7 ± 7.1
ESS (Point)	10.9 ± 2.9
Mallampati Classification (Class)	4 (100%)

BMI: Body Mass Index, PNIF: Peak Nasal Inspiratory Flow, RDI: Respiratory Disturbance Index, Lowest SpO_2: Lowest oxygen saturation, ESS: Epworth Sleepiness Scale

Table 5. The subjective and objective evaluation of each nasal dilator

VAS

Baseline	NBS	Max-Air Nose Corns	Mute with Hole	Breathe Right	F	P
0.0 ± 0.0	7.5 ± 1.0	5.9 ± 1.4	5.2 ± 1.3	4.0 ± 1.2	72.8	< 0.001

PNIF (L/Min)

Baseline	NBS	Max-Air Nose Corns	Mute with Hole	Breathe Right	F	P
94.7 ± 30.7	135.5 ± 21.7	116.3 ± 21.8	110.1 ± 22.6	104.2 ± 24.3	20.8	< 0.001

Table 6. Comparison of OA+NBS with other conditions for sleep outcomes in OSA patients.

	OA(-)NBS(-)	OA(+)NBS(-)	OA(-)NBS(+)	OA(+)NBS(+)	F	P
PNIF (L/Min)	94.7 ± 30.7	138.2 ± 21.0	135.5 ± 21.7	168.3 ± 34.8	11.8	< 0.001
RDI (Event/hr)	25.6 ± 15.2	11.3 ± 7.1	23.9 ± 14.8	6.5 ± 5.2	14.6	< 0.001
Lowest SpO_2 (%)	77.7 ± 7.1	86.2 ± 5.3	79.4 ± 6.4	89.2 ± 4.5	12.4	< 0.001
ESS (Point)	10.9 ± 2.9	6.2 ± 3.0	8.2 ± 2.6	4.2 ± 2.0	72.8	< 0.001

PNIF: Peak Nasal Inspiratory Flow; RDI: Respiratory Disturbance Index; Lowest SpO_2: Lowest oxygen saturation; ESS: Epworth Sleepiness Scale

Figure 1. Photographs of Nose Breathing Stimulator (NBS)

(A): Front view, (B): Back view, (C): Upper view, (D): Wearing NBS

The difference in the diameters at the air entry and exit points, as well as the dual-plate structure of the exhaust plate at the pharyngeal exit, prevents a decrease in the velocity of air flow at the exits. It could be attributed to the use of the polyester elastomer (adequately flexible, resilient) as a comfortable base material, while the rounded design prevented damage to the nasal mucosa.

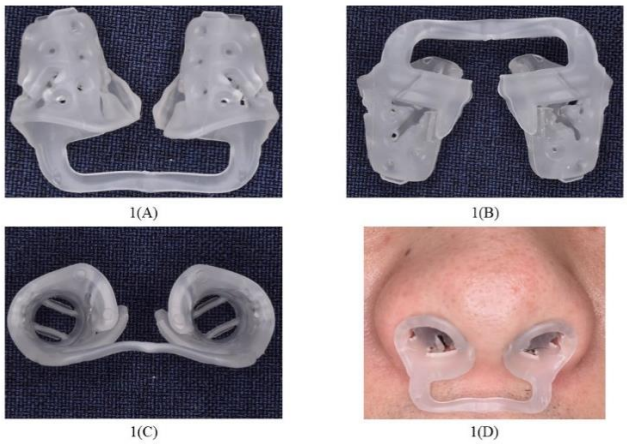

Figure 2. Photographs of wearing the other nasal dilators

They are the other nasal dilators as a control. A is Max-Air Nose Corns® and the participant wearing Max-Air Nose Corns®, B is Mute® with hole and the participant wearing Mute® with hole and C is Breathe Right® and the participant wearing Breathe Right®.

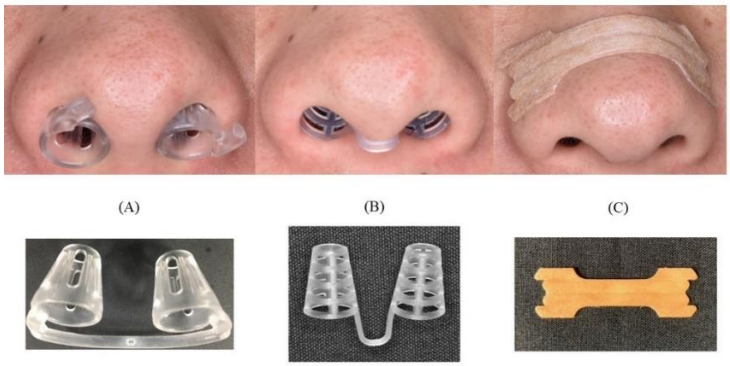

Figure 3. Photographs of the peak nasal inspiratory flow (PNIF) test

(A): PNIF was measured using an inspiratory flow meter, (B): the peak nasal inspiratory flow tool. A portable PNIF meter was used to assess nasal function (peak nasal inspiratory flow rate) in the present study. The PNIF assessment is an established, validated clinical tool for evaluating nasal obstruction. Results obtained using this simple, yet reliable procedure correspond strongly with subjective assessment of nasal obstruction. The mean of three approved PNIF measurements for each patient was calculated with the patient in a seated position with the head held parallel to the floor.

3(A) 3(B)