Pilot Study of Oral Negative Pressure Therapy for Obstructive Sleep Apnea-Hypopnea Syndrome

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Abstract

Background: Although the continuous positive airway pressure is the gold standard therapy for patients with moderate to severe obstructive sleep apnea-hypopnea syndrome (OSAHS), there are several treatment options such as mandibular advancement devices, tongue-retaining devices, and nasal airway stent devices. Recently, newly developed intraoral pressure gradient therapy system, iNAP® Sleep Therapy System, was introduced as an alternative treatment for OSAHS patients.

Purpose: This feasibility study explored the effectiveness of the iNAP® device for patients with mild to moderate OSAHS.

Materials and Methods: The iNAP® device consisted of an oral interface, a tube set with a saliva container, and a negative pressure console. Negative pressure is introduced directly from the oral interface and the pressure pulls the tongue anteriorly, resulting in improving the obstruction or narrowing of the upper airway. A total of 5 male and 4 female patients with mild to moderate OSAHS, aged between 32 and 62, with 50.6 years+11.7 years were recruited in the study.

Results: The baseline apnea-hypopnea index (AHI) was 17.2 events per hour+4.7 events per hour, while AHI with the iNAP® device was 12.7+5.4 (p<0.01). Regarding the sleep architecture, a significant reduction in wakefulness after sleep onset (WASO) on the initial night of treatment from 97 min+50.0 min to 70.7 min+36.9 min (p<0.05) was observed; however, other sleep parameters was not.

Conclusion: This study demonstrated that negative pressure therapy with the iNAP® device improved the apnea severity in patients with mild to moderate OSAHS, the degree of whose amelioration of AHI was marginal but significant. Although the number of patients recruited was small, this study is the first report on the effectiveness of the intraoral pressure gradient therapy.

Keywords: Obstructive sleep apnea-hypopnea syndrome; Intraoral pressure gradient therapy; iNAP® Sleep Therapy System

Introduction

Obstructive sleep apnea-hypopnea syndrome (OSAHS) is a common condition characterized by repetitive obstruction of the upper airway resulting in daytime sleepiness due to sleep fragmentation caused by an airway obstruction. There are several papers on the prevalence of OSAHS showing that 7% to 26% of men and 2% to 13% of women have an apnea-hypopnea index (AHI) of more than 15 events per hour [1-5].

In Japan, the prevalence of OSAHS in the male working population has increased over the past decade, being estimated at 22.3% in patients with moderate to severe sleep-disordered breathing (SDB) [6]. It is significantly correlated with cardiovascular morbidity and mortality [7-8]. For patients with moderate to severe OSAHS, standard treatment is the continuous positive airway pressure (CPAP) ventilation. Compliance with and tolerance of CPAP are not always favourable, whose adherence rate is low, being 40% to 83% [9-10].

In Japan, CPAP treatment is not covered by health insurance for OSAHS patients with AHI of less than 20 events per hour. Consequently, one of the oral appliances (OA), prosthetic mandibular advancement (PMA), is a solid alternative to manage patients with mild to moderate OSAHS.

PMA causes protrusion of the mandible and tongue and enlarges and stabilizes the upper airway during sleep. Although the PMA has been shown to be effective for patients with mild to moderate OSAHS, adherence is poor [11,12]. Studies on PMA treatment have indicated that about 75% of patients remained adherent after 12 months of treatment, which may decrease to 50% after 5 years. In the PMA treatment, there are several side effects including tooth pain, pain of the temporomandibular joint (TMJ), gum disease, and dry mouth. Therefore, PMA treatments are not indicated for use in all patients who prefer PMA to CPAP, who do not respond to CPAP, or who show failed treatment attempts with CPAP. It is consequently important to develop other treatment options besides PMA for sleep apnea.

A newly developed intraoral pressure gradient therapy system (IPGT), the iNAP® Sleep Therapy System (Somnics Inc., Hsinchu, Taiwan), was introduced as an alternative treatment for OSAHS [13].

The feasibility study explored the abilities and safety of the new device, the iNAP®Sleep Therapy System, for patients with OSAHS in our clinical sleep laboratory using full-night polysomnography.

Materials and Methods

Participants

A total of 5 males and 4 females' patients with mild to moderate OSAHS aged between 32 and 62 years visiting the Fukuoka Urasoe Clinic were recruited. The chief complaint of each patient was daytime sleepiness, witnessed apnea, and/or loud snoring.
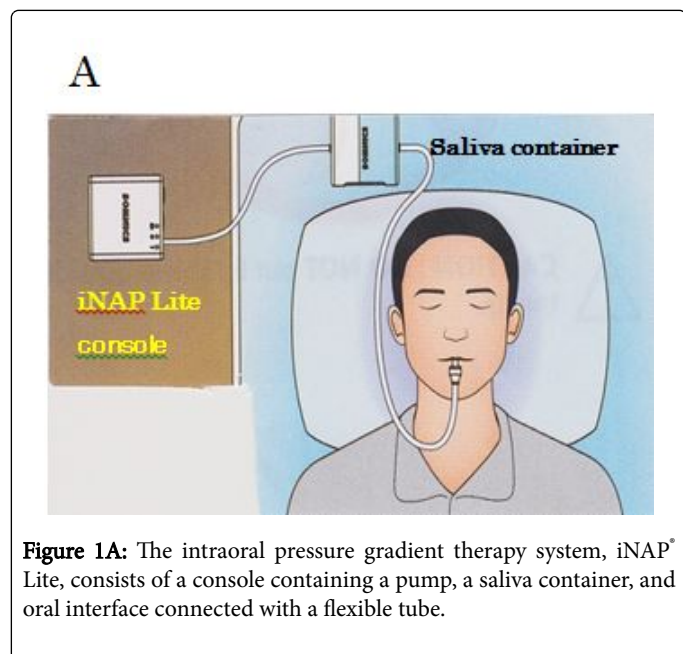
All the patients were required to undergo diagnostic polysomnography (PSG). Patients with no history of cardiovascular diseases, cerebrovascular diseases, or diabetes mellitus (DM) were enrolled in this study.

This study was approved by the Institutional Ethics Committee at the Nakamura Clinic, Urasoe, and Okinawa, Japan. Informed consent was obtained from all patients before enrollment in this study, which was performed in accordance with the Helsinki Declaration.
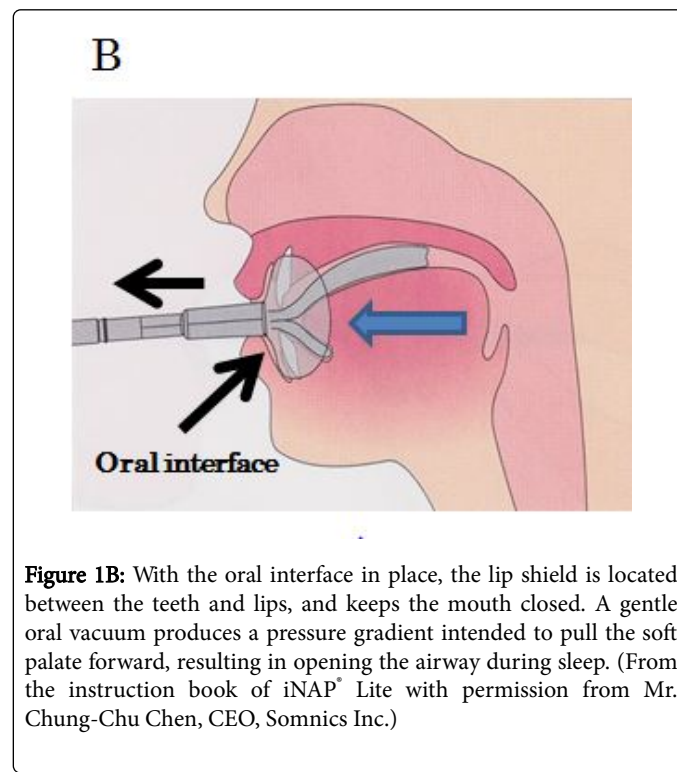
Protocol design and device description

This study was a single-center, non-controlled, non-randomized, proof-of-concept, single-treated night study in which subjects underwent a non-treatment PSG followed by a second PSG with the iNAP® Lite Sleep Therapy System.

The device, the intraoral pressure gradient therapy system, consisted of an oral interface, a tube set with a saliva container and a negative pressure console (Figure 1A).

Figure 1A: The intraoral pressure gradient therapy system, iNAP® Lite, consists of a console containing a pump, a saliva container, and oral interface connected with a flexible tube.

Negative pressure is introduced from the oral interface and the pressure pulls the tongue, soft palate, and uvula formed in order to keep the oropharynx stable during sleep (Figure 1B). The device detects the air pressure within the oral cavity and automatically adjusts the pressure gradient applied to the airway as needed.

The system in a console provides the negative pressure with 2 AA-sized batteries, which have a running life of approximately 7 days.

Figure 1B: With the oral interface in place, the lip shield is located between the teeth and lips, and keeps the mouth closed. A gentle oral vacuum produces a pressure gradient intended to pull the soft palate forward, resulting in opening the airway during sleep. (From the instruction book of iNAP® Lite with permission from Mr. Chung-Chu Chen, CEO, Somnics Inc.)

Polysomnography

As shown in our previous study, standard overnight PSG included continuous monitoring with a central electroencephalogram (EEG), electrooculogram (EOG), submental and anterior tibial electromyogram (EMG), and electrocardiogram (ECG) using conventional leads. Airflow was monitored with oral and nasal thermistors, and respiratory effort by respiratory inductance plethysmography with transducers placed around the chest and abdomen. Oxyhemoglobin saturation was continuously recorded with a pulse oximeter (3900P, Datex-Ohmeda Co., Louisville, CO, USA). All variables were continuously recorded using REMbrandt™ version 8.0 (Embla, Broomfield, CO, USA) and RemLogic™ version 3.2 (Embla, Thornton, CO, USA). All recordings were scored directly on the screen by polysomnographers certified by the Japanese Society of Sleep Research using the 2014 guidelines from the American Academy of Sleep Medicine (AASM) [13]. Apneas were defined as >90% reduction in tidal volume lasting >10 seconds. Hypopneas were defined as >30% reduction of the pre-event baseline using nasal pressure lasting >10 seconds with a >3% oxygen desaturation from the pre-event baseline or an event associated with an arousal.

Statistical analysis

All subjects who had an AHI greater than 5 events per hour during the baseline night were included in the data analysis. A paired t-test was used to test the change from the baseline to treatment within each patient. Statistical analyses were performed using StatMate ver. 5.01 (Atoms, Tokyo).

Results

Patient characteristics

Five men and four women were included in the study, whose ages ranged from 32 years to 62 years with a mean+standard deviation (SD) of 50.6 years+11.7 years. The body mass index (BMI) ranged from 21.3 kg/m^2 to 31.8 kg/m^2 with a mean+SD of 24.6 kg/m^2 ± 3.4 kg/m^2. No patients enrolled in the study were refused, and all subjects tolerated the use of the iNAP® device.

The effectiveness of iNAP® therapy

The baseline AHI was 17.2 events per hour+4.7 events per hour (mean+SD), while AHI with the iNAP® device was 12.7+5.4 (p<0.01) (Figure 2).
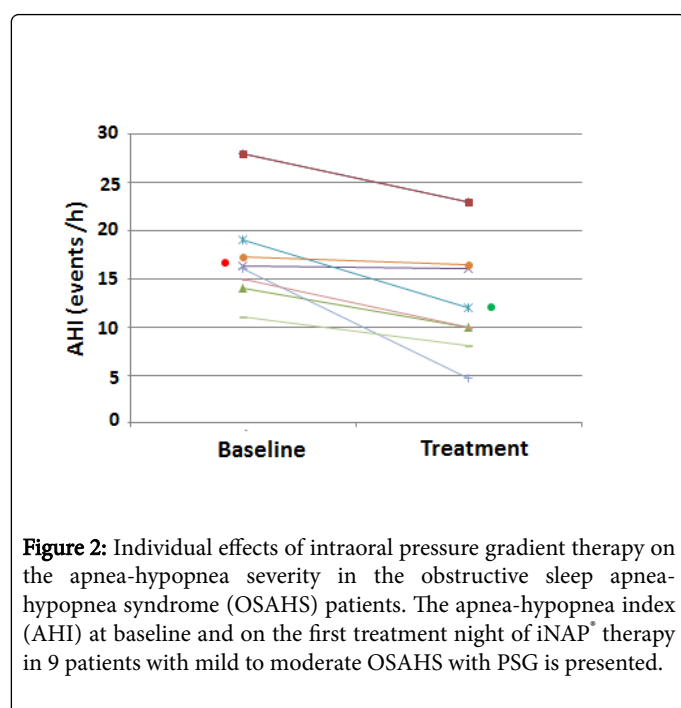

Figure 2: Individual effects of intraoral pressure gradient therapy on the apnea-hypopnea severity in the obstructive sleep apnea-hypopnea syndrome (OSAHS) patients. The apnea-hypopnea index (AHI) at baseline and on the first treatment night of iNAP® therapy in 9 patients with mild to moderate OSAHS with PSG is presented.

Regarding sleep architecture, a significant reduction in wakefulness after sleep onset (WASO) on the initial night of treatment from 97.0 min+50.0 min to 70.7+36.9 min (p<0.05) was observed. However, other sleep parameters including sleep efficiency, stage N1, arousal index, and desaturation was not (data not shown). There were no serious adverse events in the 9 subjects who used the device during PSG.

Discussion

Our study confirmed that intraoral pressure gradient therapy (IPGT) study is well tolerated by OSAHS patients. In addition, the results of the present study show the improvement of apnea severity and WASO in patients with mild to moderate OSAHS. However, the improvement of AHI in patients with AHI of less than 30 events per hour was only 26%, with a decrease from the baseline AHI of 17.2 to treatment AHI of 12.7, which was marginal but significant.

In our data, the improvement rate of AHI in patients between those younger than 50 years and older than 50 years was 40 and 17.6%,

respectively. Although the number of patients analysed in our study was small, the IPGT might appear to be more effective in younger rather than elderly patients.

In this study, the subset of OSAHS patients who were strong responders to the IPGT could not be clarified. However, in those who showed a clinically significant effect, the benefits were observed on the first night of treatment. In the future, more studies should be conducted to further define patients who can be managed successfully. How to select appropriate patients for IPGT has been an on-going clinical challenge.

As the present study was a clinical feasibility research, there are important limitations that should be recognized for evaluating this study and in planning future studies. With data from only a single night of treatment for each patient, the durability of the treatment effect cannot be evaluated and a study of long-term treatment is needed. Whether or not long-treatment with IPGT leads to the reduction of daytime sleepiness should be investigated,

It is difficult to establish a treatment control (sham oral device) because subjects are aware of the sensation of oral negative pressure produced by the iNAP® device. In addition, each patient feels differently with the oral interface. Accordingly, one of the reasons why responses to IPGT in patients are different might be due to the unfavourable positioning of the mouthpiece in the oral cavity relative to the tongue. Optimizing the oral interface shape, size, and applied negative pressure might increase comfort. It is important to further define what subset of OSAHS patients are most indicative for the negative pressure therapy.

In this study, the first PSG was carried out in order to study the AHI severity at the baseline, and the second PSG was performed to evaluate it on treatment. In consequence, concern about a potential "first-night effect" might be raised regarding the effectiveness for apnea severity. Based on the fact that several studies have uniformly reported no first-night effect on respiratory parameters [14-16], it has been considered that the improvement of apnea severity with the iNAP® device is not likely to be due to the first-night effect. However, the amelioration of WASO with the iNAP® device might be due to the first-night effect.

The main limitation factors of this study were the small number of patients recruited. The study was not supported by any corporate sponsors and a large number of patients with OSAHS could not be enrolled because of economic limitations in our clinic. However, the data from this study are the first report showing the role of iNAP® device to treat patients with mild to moderate OSAHS.

Another device that reduces airway obstruction and airflow during sleep by moving the soft palate anteriorly with negative pressure produced by the pump in the console via a mouthpiece, oral pressure therapy (OPT) (ApniCare, Inc., Redwood City, CA, USA) was recently developed [17]. There are several advantages of negative pressure therapy using iNAP® compared with OPT. iNAP® can still be used for edentulous patients or those with poor dentition. In addition, iNAP® is light, small, and compact, and can work with 2 AA batteries for 7 days. Therefore, this device is very travel-friendly, and can be used on a long-distance airplane or coach travel.

In conclusion, this study demonstrated that the negative pressure therapy using the iNAP® Sleep Therapy System improved the apnea severity in patients with mild to moderate OSAHS, whose degree of amelioration of apnea severity was marginal but significant. In the study, although the number of patients recruited was small, this paper

is the first to report on the effectiveness and safety of IPGT. Future studies should be carried out with more patients with mild to severe OSAHS, and the daytime sleepiness or quality of life should be evaluated by long-term treatment with the device.

Acknowledgment

Conflict of Interest

Somnic Inc. was not involved in any part of the study. We declare conflict of interest related to this study.

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