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RESEARCH ARTICLE

Myofunctional training with negative airway pressure for obstructive sleep apnea: a prospective non-randomized cohort feasibility study [version 1; peer review: 1 approved with reservations, 1 not approved]

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Abstract

Background: Orofacial myofunctional therapy (OMT), for obstructive sleep apnea (OSA) is emerging with recognition of specific phenotypes. Since many OSA sufferers are already familiar with positive airway pressure machines, we designed an OMT protocol involving the modification of such a machine to deliver negative airway pressure. We hypothesized that a three-month trial of using this protocol while awake would reduce the signs and symptoms of OSA.

Methods: Fifteen adults with OSA enrolled for 30-minute sessions/three days a week for a three-month trial of “upper airway muscle physical therapy” while awake. Overnight sleep studies were performed before and after the intervention to determine each subject’s apnea hypopnea index (AHI), the primary outcome measure. Negative airway pressure application was determined by estimation of each subject’s one-repetition maximum (an exercise physiology measure of strength capacity). Exercise sessions consisted of subjects breathing against this pressure for a series of repetitions, and sets.

Results: While the mean post study AHI was slightly improved (-4.3 ± 12.0 [$-10.9, 2.3$], mean $\pm$ standard deviation, 95% confidence interval), it was not statistically significant. The results were similar when the AHI was divided by the sleep state (REM vs. non-REM). The nadir saturation was also essentially unchanged. The eight subjects with mild or moderate OSA (AHI < 30) showed similar results.

Conclusions: Though there was no significant reduction in AHI in this small cohort, the methods elucidate a new daytime use for a machine with which many OSA sufferers are familiar.

Trial registration: ClinicalTrials.gov [NCT02109731](https://clinicaltrials.gov/ct2/show/study/NCT02109731) (registered on April 10th 2015)

Open Peer Review

Approval Status

	1	2
version 1		
27 Oct 2021	view	view

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Any reports and responses or comments on the article can be found at the end of the article.

Keywords

Sleep apnea, therapy, airway pressure

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Abbreviations

AHI: apnea hypopnea index
 BMI: body mass index
 NAP: negative airway pressure
 OMT: orofacial myofunctional therapy
 PAP: positive airway pressure (could be continuous or auto-titrated)
 IRM: one-repetition maximum
 REM: rapid eye movement

Introduction

Obstructive sleep apnea (OSA) is caused by upper airway collapse during sleep resulting in a disruption of regular periodic breathing. The phenotypes of OSA pathology are variable and a particular patient can have the disorder because of anatomical and/or non-anatomical reasons.¹ Continuous or auto-titrated positive airway pressure (PAP) is the current standard treatment; however, other therapies have emerged as alternatives. Mandibular advancement devices (or oral appliances) are currently recommended as a second line therapy²; though the ability to properly track compliance (and thus efficacy) is a challenge. Surgical interventions have targeted anatomical or morphological problems in those unresponsive to standard therapies. However, the evidence supporting its widespread application is lacking.³

We have been studying the collapsibility of the upper airway during sedation-induced sleep by provoking its occurrence through the use of negative airway pressure (NAP).^{4,5} People who are awake can breathe against this NAP (it feels like a vacuum on the back of the throat) down to negative pressures that would readily collapse the airway during sleep or sedation. Awake and healthy OSA patients have been able to tolerate breathing with the application of up to -40 cm of water.⁶ The ability to tolerate these pressures is the result of increased airway muscle tone (both tonic and reflex phasic activation of the airway dilator muscles).⁷

Subjects in our laboratory have commonly described their breathing against this vacuum as a “workout” on their airway. This idea sparked our curiosity to test the ability of NAP application as a therapeutic intervention, exercising the oropharynx, increasing muscle tone and thus decreasing upper airway collapsibility during sleep. Over the last decade, orofacial myofunctional therapy (OMT) has been applied to treat this disorder.⁸ Both as a stand-alone therapy and in conjunction with PAP, OMT has been shown to reduce the apnea hypopnea index (AHI), reduce snoring, and improve quality of sleep and life.⁹ While other OMT protocols involve methods that require specific training,^{8,10,11} we considered that OSA sufferers already familiar with PAP would more easily adapt to our protocol which involves the use of a similar device. The key to our proposed therapy is the use of NAP when awake so that the increased reflex phasic drive to the muscles will result in muscle conditioning. Thus, we developed a regimen similar to OMT, with a primary hypothesis that AHI measured via attended polysomnography after treatment intervention would be %50 reduced compared to baseline AHI.

Methods

Ethical considerations

This study was approved by the University of Rochester Research Subject Review Board (RSRB#24149) and conducted between December 2008 and January 2012. At the time the study was approved, it was not standard practice or mandatory to publicly register trials. This trial’s information was first submitted in 2012, posted in 2014, and results posted in 2015 in [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT02109731) (NCT02109731) after the study was completed, but in line with our understanding of what was evolving as a research standard at that time.

Sample size rationale

All subjects provided written informed consent to participate in this non-randomized, non-blinded feasibility study. The estimated sample size for a one sample comparison of means of AHI utilizing the s.d. of the delta AHI between two measurements was 11 subjects to have a 90% power to detect a 50% difference or a reduction in the AHI of 20 at alpha = 0.05. Taking into account possible dropout of subjects over time, we planned to enroll 15 subjects in the study. For the primary analysis, differences between baseline and follow-up were analyzed using two sample *t*-tests.

Study design and participants

Twenty subjects (>18 years of age) were recruited from local sleep medicine laboratories via flyers or mailing from their treating sleep physicians. Once consented, subjects were additionally screened for inclusion and exclusion criteria and 15 recruited for the study. All subjects had a diagnosis of OSA (apnea hypopnea index, AHI >10) but were not currently using their previously prescribed PAP. Each participant received a targeted history and physical exam to assess for stability of medical conditions, including having a normal electrocardiogram and a negative urine drug test.

Measurements of body mass index (BMI), neck circumference, and an airway exam were collected, and the Epworth sleepiness scale survey was administered.

Exclusion criteria included: major upper airway morphologic abnormality (such as profound micrognathia), history of airway surgery, regular use of central nervous system depressants or alcohol (e.g., > 14 alcoholic drinks per week or >2 per day), morbid obesity (BMI > 40 kg/m²), or unstable medical or psychiatric illness. Participants were also excluded if they were undergoing or planning to undergo an intervention for weight loss, or were pregnant or lactating.

Participants were initially evaluated by the University of Rochester Strong Sleep Disorders Center with an overnight polysomnographic study incorporating 16 electrophysiologic signals: 2-channel electro-oculogram, 8-channel electroencephalogram (Fz, C3, CZ, C4, Pz, Oz, T3, and T4), bipolar mentalis electromyogram, 2 lead electrocardiogram, nasal/oral airflow thermocouple, two respiratory effort sensors, a pulse oximeter, and a channel representing A1/A2. The resulting data were analyzed in 30-second epochs by an independent and certified sleep scorer (LL; see *Acknowledgements*).

Intervention

The NAP myofunctional therapy protocol was designed to minimize the development of muscle hypertrophy and optimize strength and/or endurance.¹² In muscle conditioning therapy, one-repetition maximum (1RM) is the unit designated to describe a maximum weight or resistance that a muscle group can move. For this study, the 1RM was defined as the maximum negative pressure the participant could comfortably tolerate for one breath, not less than -25 cm H₂O. As is conventional in exercise physiology, ideal strength training involves targeting each subject's 1RM repetitiously for 1-5 breaths per set and repeating this set 4-7 times with rests of 1-2 minutes between sets.

Training visits

The initial visit to the University of Rochester outpatient clinical research center was used to familiarize subjects with the apparatus, which appears similar to a typical PAP machine. Subjects were acclimated to both the mask fit (over the mouth and nose) and the feeling of breathing against a negative pressure. Airflow was measured with a pneumotachograph (Hans Rudolph, Shawnee, KS) inserted into the mask, which was calibrated with a rotameter. Mask pressure was measured by connecting a port to a pressure transducer (Validyne, Northridge, CA) calibrated with a water manometer.

Subjects were instructed to breathe through the nose with a closed mouth while sitting in order to minimize any tendency for the upper airway to collapse. At the first visit, the participants were exposed to a variety of negative pressures in an increasing-decreasing manner (from -5 cm H₂O for five breaths and down) and also in random sequence in order to determine each subject's 1RM.

Experiment

Thereafter, the subjects would schedule three observed sessions per week for three months in our clinical research center. As described above, each session entailed the subject breathing NAP at the predefined 1RM for five breaths per set (reps) and repeating this set 4-7 times with rests of 1-2 minutes between sets. Constant observation by study personnel allowed for verification of wakefulness (eyes open) and breathing with the mouth closed during the entire procedure. Each session lasted approximately 30 minutes. After the first and second month, the 1RM was re-evaluated and adjusted, as appropriate. For the following month, the new 1RM of NAP was used for the training exercises. Each subject's BMI and neck circumference were re-measured after the first and second months.

Participants completed a post-intervention overnight sleep study within a week of finishing the prescribed course of airway physical therapy. Data from this study were collected and analyzed in the same manner as the initial overnight sleep study.

Participants were also instructed to maintain nightly sleep diaries. This included recording and rating aspects of sleep quality and sleep-related quality of life on a 1-5 scale (1 = never; 5 = frequently) upon waking, and recording bedtimes, time out of bed, time required to fall asleep, number of awakenings during the night, time awake after falling asleep, time awake before alarm or intended wake time, and time out of bed at night.

Outcome measures

Since this was a pilot study without a control group, the primary outcome was a difference in AHI (as measured by overnight attended polysomnography) between the initial sleep study and the final study in each subject. Specifically, the

study was sized to detect a 50% reduction in AHI or an AHI reduction of more than 10. Other secondary outcomes include nadir saturation, non-REM AHI, and protocol compliance. A pre-planned subgroup analysis of the subjects with a mild to moderate AHI (AHI < 30) was performed.

Table 1. Subject characteristics for all subjects (N = 15 unless noted) and the pre-planned subgroup of subjects with an AHI < 30 (N = 8 unless noted). BMI = body mass index. Data is mean $\pm$ standard deviation.

	Pre-study	Post-study
All subjects (N = 15)		
Age (years)	57.8 $\pm$ 13.3	
BMI (kg/m ²)	32.8 $\pm$ 6.3	32.8 $\pm$ 5.7
Weight (kg)	97.7 $\pm$ 22.9 (N=14)	100.1 $\pm$ 22.5
Neck Circumference (cm)	17.1 $\pm$ 2.3	16.9 $\pm$ 2.0 (N=13)
Mild/Moderate Pre-study AHI (AHI < 30); N= 8		
Age (years)	64.4 $\pm$ 6.22	
BMI (kg/m ²)	30.6 $\pm$ 5.7	31.0 $\pm$ 5.2
Weight (kg)	93.5 $\pm$ 24.2	94.3 $\pm$ 27.6
Neck Circumference (cm)	16.5 $\pm$ 2.0	16.4 $\pm$ 1.6 (N=7)

Figure 1. CONSORT flow diagram.

Statistical analysis

For the primary analysis, the differences between baseline and post-intervention data were analyzed using paired Student's t-tests. Symptoms scores were analyzed nonparametrically.

Data are reported as mean $\pm$ standard deviation and 95% confidence intervals. $p < 0.05$ was considered significant. All statistical analyses were performed using STATA/IC 13.1, (Stata Corp LP, College Station, TX).

Results

Fifteen subjects completed the study and [Table 1](#) provides their demographics, which demonstrates no significant changes in BMI, weight or neck circumference after the training session (see [Figure 1](#) for CONSORT flow chart). The initial airway training pressures ranged from -8 to -18 cm H₂O and all airway training pressures became more negative except for one subject who stayed at -18 cm H₂O ([Figure 2](#)), which was the most extreme pressure utilized for the study.

While the mean post study AHI was slightly improved (-4.3 ± 12.0 [$-10.9, 2.3$]), it was not statistically significant ([Table 2](#)). Six subjects actually increased their AHI, only one subject decreased to below 10 and this was the subject with the lowest pre-study AHI of 10.1 ([Figure 2](#)). The results were similar when the AHI was categorized by the sleep state (REM vs. non-REM). The nadir saturation was also essentially unchanged. The eight subjects with mild or moderate OSA (AHI < 30) showed similar results.

Of the 15 subjects, only 10 completed their sleep diaries. There were no differences noted in sleep quality or feeling refreshed from the intervention.

Discussion

This study demonstrates the novel use of a modified standard PAP machine to provide NAP as a form of quantifiable myofunctional therapy for OSAS. In this small cohort, the intervention did not cause significant changes in AHI. The small size of this pilot study makes it difficult to definitively exclude a clinically helpful effect, but we can exclude a

Figure 2. Changes in AHI and airway pressures used for therapy by subject. The left panel shows the change in the AHI from before and after the training for all subjects. The right panel shows the change in the initial to the final training pressure.

Table 2. Ventilatory outcomes from the overnight polysomnographic studies before (pre-study) and after (post-study) the airway strength training intervention for both the full group and the mild/moderate AHI subgroup. AHI – apnea hypopnea index. The AHI was calculated during rapid eye movement (REM) and non-REM sleep. Data given as mean $\pm$ stand deviation, except for difference which is mean and 95% confidence interval.

	Pre-study	Post-study	Difference (95% CI)
All subjects (N = 15)			
AHI	38.7 $\pm$ 25.7	34.4 $\pm$ 28.5	–4.3 (–10.9, 2.3)
Nadir Sat (%)	76.2 $\pm$ 18.2	77.6 $\pm$ 17.3	1.4 (–2.4, 5.2)
AHI (REM)	41.6 $\pm$ 24.6	38.5 $\pm$ 26.8	–3.1 (–16.7, 10.5)
AHI (non-REM)	36.8 $\pm$ 28.0	33.6 $\pm$ 29.6	–3.3 (–9.5, 3.0)
Mild/Moderate Pre-study AHI (AHI < 30); N = 8			
AHI	19.7 $\pm$ 6.3	14.8 $\pm$ 6.8	–4.9 (–12.8, 2.9)
Nadir Sat (%)	84.1 $\pm$ 7.3	83.6 $\pm$ 4.6	–0.5 (–7.5, 6.5)
AHI (REM)	27.8 $\pm$ 19.5	24.5 $\pm$ 13.3	–3.3 (–25.3, 18.6)
AHI (Non-REM)	15.9 $\pm$ 8.7	12.7 $\pm$ 7.8	–3.2 (–11.3, 4.8)

clinically significant increase in the AHI, thus indicating its safety. However, we believe that sharing the methodology and results may provide clues for further study.

Though PAP therapy remains the gold standard approach for effective treatment of OSA,¹³ compliance remains a challenge.¹⁴ OMT has emerged as a promising alternative or adjunct to standard OSA therapy.⁸ In a recent review of the 11 studies published to date, de Felicio *et al.* provide an analysis of comparative methodology and ideas for further study.¹⁵ In most OMT studies, the intervention exercises target a variety of oral and facial muscles including the tongue, palate, pharynx, mouth, and cheeks. In our study, the NAP therapy was hypothetically the reverse of PAP and may have exercised similar structures. However, we do not know whether NAP targets specific muscles whose tone (or lack thereof) contributes to OSA. With increasing attention being paid to OSA phenotypes, it has been suggested that most would benefit from anatomic intervention.¹ In addition, standardized classification of location, directionality and severity of pharyngeal collapse as determined during drug-induced sedation endoscopy¹⁶ could be explored as a method to target appropriate candidates who might benefit from myofunctional therapy, as it has been used to evaluate success with other OSA interventions such as surgery and electrical stimulation.

We considered that prior familiarity with the PAP machine but failure to adhere to nighttime usage would be a reasonable approach for recruitment of subjects for our study, which included daytime and more limited use of the machine. In hindsight, non-use of PAP may have actually been an inappropriate criterion for inclusion as this may have predicted a phenotype *à priori* which would not benefit from our approach of myofunctional therapy.¹ Most PAP machines can now be interrogated to ensure patient compliance. Future investigations may benefit from recruiting PAP users and assessing devices for sleep-related pressure changes over the course of an exercise intervention during wakefulness.

As was done in our study, OMT is typically utilized during wakefulness as a method to decrease muscle hypotonia during sleep. Theoretically, the frequent repetitions at low levels of resistance may target Type 1 (slow-resistant to fatigue) muscles, such as those found in the tongue.¹⁷ These muscles and Type 2A (fast-intermediate fatigue) muscles have been stimulated electrically.^{18,19} and trained^{11,20} In patients with OSA there are even more type 2A fibers than in normal controls, which could contribute to the increase fatigability.²¹

Our protocol lasted for three months, a time period that is frequently used in muscle training.¹⁵ Unlike other protocols, we chose to have subjects observed in a laboratory and reasoned that visiting three times per week would not be too onerous. Many of the training protocols describe daily exercises, sometimes three^{8,22} to five times²³ per day. It is possible that our training regimen was not sufficient to see an effect.

We asked our subjects to maintain a mouth closed position while performing exercises, mostly as a means to standardize their positions. It has also been shown that mouth breathing exacerbates upper airway obstruction with advocates for mouth closure training to promote airway patency maintenance during sleep.^{24,25}

Despite the limitations of our study, there were no reported adverse events. In contrast, participants shared that they appreciated doing this therapy, and could envision doing it at home were it to become available. We have been contacted by former subjects and a few interested citizens who have located this study on [ClinicalTrials.gov](https://clinicaltrials.gov) to inquire about inclusion in ongoing investigations.

Conclusions

In conclusion, subjects with OSAS were able to tolerate a three-month exercise protocol using the novel application of NAP as orofacial myofunctional therapy. Though was no significant reduction in AHI in this small cohort, the methods elucidate a new daytime use for a machine with which many OSAS sufferers are familiar. Future studies utilizing this protocol may target current PAP users or those whose drug-induced sedation endoscopies indicate this approach as an alternative therapy.

Data availability

Underlying data

Figshare: AirwayPT Data Original 100121.csv, <https://doi.org/10.6084/m9.figshare.16727488.v1>.²⁶

Figshare: pt_sleep_diaries_042412.xls, <https://doi.org/10.6084/m9.figshare.16798138.v1>.²⁷

Reporting guidelines

Figshare: CONSORT checklist for 'Myofunctional training with negative airway pressure for obstructive sleep apnea: a prospective non-randomized cohort feasibility study', <https://doi.org/10.6084/m9.figshare.16818352.v2>.²⁸

Data are available under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/) (CC-BY 4.0).

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In this paper, Karan and coworkers report the results of a small study testing the effects of orofacial myofunctional therapy (OMT) in OSA patients. The rationale was to train upper airway muscles to negative pressure application during wakefulness for 3 months. The protocol was conducted in the laboratory 3 times a week, and the intensity of training was established based on the maximum negative pressure the subject could tolerate for 1 breath (1RM). Negative airway pressure (NAP) was applied for 5 breaths, and each set was repeated 4-7 times with 1-2 min rest between sets. The pressure was adjusted each month. 15 subjects were studied, all of them with OSA and prescription of CPAP but not using it. The study did not show any significant change in the expected outcome, i.e. 50% reduction in AHI or reduction of AHI below 10), although the training pressure decreased during the study in all subjects.

The study is interesting, but the result were negative, raising more questions than answers, especially on the value of this specific training procedure. The study was done between 2008 and 2012, and the possibility to train upper airway muscle has been explored in a more structured way in recent years, and with different devices, some of them using muscle stimulation. I agree with the comments of the previous reviewer and can only add that a more accurate endotyping might show a subgroup of patients especially responsive to this or other treatments aimed at upper airway muscle training. Currently, the treatment discussed in this study cannot be recommended.

Is the work clearly and accurately presented and does it cite the current literature?

Partly

Is the study design appropriate and is the work technically sound?

Partly

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Partly

Are the conclusions drawn adequately supported by the results?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Respiratory sleep medicine

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 09 November 2021

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This is a manuscript based on a therapy called Nap therapy where patients breathe against like a vacuum cleaner with negative pressure. They try to evaluate if this activity can increase the tone of the upper airway muscles and improve OSA patients. Authors considered that breathing against a pipe with negative pressure is an oropharyngeal exercise. This kind of exercise has not developed any improvement in sleep apnea in any worldwide manuscript. Exercises reported by Guimarães KC, *et al.* Those reported by O'Connor Reina *et al.*, have been proven to be effective, but not this kind of activity. We believe there is great issue in the design of this trial as there was no scientific basis to support this. There is no scientific evidence about this therapy to be considered as oropharyngeal exercises.

We believe there is a big misunderstanding by the authors of the concept of orofacial myofunctional therapy. We think the title should be changed to Upper Airway Physical Therapy for the Treatment of Obstructive Sleep Apnea as it was indicated in the clinical trial. On the other hand, authors considered this therapy as a potential use when the results did not reflect this point. On the other hand, authors speak about drug-induced sleep endoscopy as a target for myofunctional therapy but they do not explain what patients are suitable for this therapy.

The study was finished in 2015 and since then, there was no other reports about NAP therapy. Due

this fact, we recommend the authors to rewrite this paper and explain the use of this therapy in the treatment of OSA.

References

1. O'Connor-Reina C, Ignacio Garcia J, Rodriguez Ruiz E, Morillo Dominguez M, et al.: Myofunctional Therapy App for Severe Apnea–Hypopnea Sleep Obstructive Syndrome: Pilot Randomized Controlled Trial. *JMIR mHealth and uHealth*. 2020; **8** (11). [Publisher Full Text](#)
2. Guimarães KC, Drager LF, Genta PR, Marcondes BF, et al.: Effects of oropharyngeal exercises on patients with moderate obstructive sleep apnea syndrome. *Am J Respir Crit Care Med*. 2009; **179** (10): 962-6 [PubMed Abstract](#) | [Publisher Full Text](#)

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

No

Are sufficient details of methods and analysis provided to allow replication by others?

No

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: I am expertise in sleep medicine and myofunctional therapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

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