STUDY20231615

The Impact of Technology in Obstructive Sleep Apnea Myofunctional Therapy

Document Date 5/10/2024

Title: The impact of technology in the myofunctional therapy treatment of Obstructive Sleep Apnea Syndrome

PROJECT PLAN

Background and significance

Obstructive sleep apnea (OSA) affects an important part of the population and is characterized by recurrent partial or total obstruction of the upper airway (UA) during sleep. OSA can negatively affect the individual's quality of life in the short and long term and constitute a significant public health problem for society. The estimated prevalence of OSA in the population is 34% of men and 17% of women, but the values may be even higher since many subjects do not have an adequate diagnosis. Individuals may experience severe lifelong consequences such as cardiorespiratory failure, hypertension, type 2 diabetes mellitus, and neurophysiological deficits associated with increased mortality rate. Currently, any form of SDB should be considered worrisome or even harmful since even the least severe of these conditions can have significant consequences on the quality of life and general health. Orthodontists intervene in the craniofacial complex, and thus, they can assist in the recognition of sleep disorder breathing (SDB) problems, contributing to the identification of dentofacial components involved and, in some cases, to the treatment of OSA, in association with the physician and team.[2]

The upper airway (UA) comprises the nasal cavity, pharynx, and larynx and thus is more relevant for orthodontists because it is close to their area of expertise. The pharynx is a muscular membranous tube that extends from the skull base to the lower edge of the cricoid cartilage. [3] The pharynx is divided into three parts: nasopharynx, oropharynx, and laryngopharynx or hypopharynx.[3,4] The velopharynx is part of the oropharynx and is located between the soft palate and the posterior pharyngeal wall. The UA is responsible for swallowing, speech and breathing. The accomplishment of these tasks depends on the complex interaction of more than 20 muscles that surround the UA: muscles that regulate the soft palate position (elevator and tensor palatini), the tongue (genioglossus, geniohyoid, hypoglossus, and styloglossus), muscles attached to the hyoid bone (hypoglossus, genioglossus, digastric, geniohyoid and sternohyoid) and muscles of the posterolateral pharyngeal walls (palatoglossus and pharyngeal constrictors).[5,6] These muscles act, dilating or constricting the UA lumen. The UA is not a rigid structure (e.g., like the trachea) and is fixed only at its upper (skull base) and lower (cricoid cartilage) ends. The hyoid bone is an important site of attachment for pharyngeal muscles, yet it does not have rigid articulation with other bony structures. Therefore, the pharyngeal cross-sectional area depends on the air pressure in the upper airway lumen, which can collapse due to different factors.[7] Contraction of the upper airway dilator muscles (especially those that control the tongue, soft palate, and lateral pharyngeal walls) maintains respiratory patency during inspiration. A drop in the tone of pharyngeal

dilator muscles results in airway collapse. Upper airway collapse occurs most often in the oropharynx in subjects with obstructive sleep apnea (OSA).

The variety and complexity of vibrations and upper airway collapsibility during sleep depend on sleep stages, muscle tone, body position, head and neck position, and lung volumes. The most common sites of obstruction and vibration are located in the soft palate, on the lateral pharyngeal walls, including the tonsils and tongue base. Obstruction at the epiglottic level occurs less frequently but has clinical significance. Subjects with OSA present with multilevel obstruction, with a collapse in the retropalatal and retrolingual region in a large percentage of cases. Single-level obstruction is more common in subjects with mild OSA, while multilevel obstruction is more characteristic in severe OSA, which is often the reason for the severity of OSA.[8]

The diagnosis and severity of OSA are determined by polysomnography (PSG). It is considered the gold standard exam, in which several sleep and respiratory parameters are monitored simultaneously such as electroencephalogram, electrooculogram, electromyography of the chin region, airflow analysis, oxygen saturation, respiratory effort, electrocardiogram/heart rate, body position, and movements during sleep.[10] One important parameter measured is the apnea-hypopnea index (AHI), which assesses the mean number of apneas and hypopneas per hour of sleep. Apnea is the absence of inspiratory airflow for at least 10 seconds, while hypopnea is a reduction of 30% or more in airflow from baseline associated with a drop in arterial hemoglobin saturation and/or an electroencephalographic awakening.[9] The severity of adult OSA is classified as mild (5≤AHI<15 events/h), moderate (15≤AHI<30 events/h), or severe (AHI≥30 events/h).[9] There is no specific type of physical finding on examination for OSA. Many individuals do not report having sleep disturbances, either because they are asymptomatic or do not realize they have the problem. Specific and validated questionnaires are essential tools to assess an individual's risk of having OSA. Another current trend is to provide the risk assessment for OSA based on the collapsibility of the airway.[16] Ultrasound (US) is emerging as a promising technology that has been evolving to assess the risk for OSA in the last few years. The technique is radiation-free, less expensive, and the equipment is portable, allowing high accessibility for examination and screening.

Preliminary studies

The treatment of OSA should be individualized, considering the disease's pathophysiology, the subject’s individual characteristics, and the treatment goals. Therapeutic possibilities include behavioral changes, oropharyngeal exercises, positive air pressure devices (PAP), intraoral appliances, surgeries, and electrical stimulation.

Oropharyngeal exercises are a non-invasive alternative that should be considered adjunct procedures in treating OSA. The dilator muscles of the upper airway are essential for maintaining respiratory patency during sleep.[11] Some subjects may have flaccidity of the oropharyngeal muscles. This hypotonia is related to the pathophysiology of OSA and deserves therapeutic attention.

Oropharyngeal exercises (myofunctional therapy) are derived from speech therapy and include exercises for the mouth and neck region. They include isometric (continuous) and isotonic (intermittent) exercises aimed at the tongue, soft palate, and pharyngeal lateral walls.[11,12] These oropharyngeal exercises have recently been successfully used in the treatment to reduce the severity of OSA. They are focused on improving the strength, force, and coordination of upper airway muscles.[13] It is believed that strengthening the oropharyngeal muscles, through daily exercises, could prevent upper airway collapse. The main problem with this therapy is the lack of long-term compliance, which is only around 10%. The use of apps associated with smartphones can improve adherence to exercises and training.[13]

Guimarães et al. conducted a randomized clinical study on 31 patients with moderate OSA. The authors concluded that individuals who received oropharyngeal exercise therapy for three months showed significant improvements in disease severity and symptoms compared to the control group.[11] Another randomized clinical trial obtained similar results in patients with primary snoring, indicating oropharyngeal exercises for these individuals.[15] To maintain positive results, the patients should include exercises in their daily routines in the long term, which can cause problems related to treatment adherence.[11,15] New technologies are being developed to aid the treatment adherence and monitoring of sleep disorders patients. The use of apps provides a permanent record of feedback and accuracy of exercises performed.[15]

Çakmakc et al. found that oropharyngeal exercise training may have improved respiratory muscle strength, sleep quality, and health-related quality of life in the exercise group. Forty-one patients with moderate and severe OSA were included in the study (20: exercise group; 21: control group). Each patient was assessed with CPAP usage time, maximal voluntary ventilation (MVV), maximum inspiratory and expiratory pressure (MIP-MEP), neck circumference, body mass index (BMI), waist-hip ratio, Epworth sleepiness score, Pittsburgh sleep quality index (PSQI), and short-form health survey (SF-36) in the first visit. The OPE was prescribed in addition to CPAP for the exercise group and performed by the patients for 3 months. At the end of the third month, groups were re-assessed with the same parameters. Most of the patients were men, and the mean age of the study population was 51.9±7.4; the mean apnea-hypopnea index (AHI) in the last polysomnography report was 53.3±27.4. In the exercise group, MVV ($p=0.003$), MIP ($p=0.002$), MEP ($p=0.024$), and SF-36 energy/fatigue ($p=0.020$) were observed to increase while the total PSQI score ($p=0.036$) decreased. The neck circumference ($p=0.006$) and BMI ($p=0.013$) were found significantly decreased in the exercise group.[16]

Myofunctional exercises are now available as application in smartphones, claiming to help increase adherence, and achieve better results than traditional methods. There are no studies at this point comparing the myofunctional therapy through an app versus traditional methods.

Aim of the study

1) Compare the effects of myofunctional exercises in subjects diagnosed with OSA when using a smartphone app versus a traditional analog method, after 3 months of myofunctional therapy.

2) Compare the compliance maintained when using a smartphone app versus a traditional analog method, after 3 months of myofunctional therapy.

Experimental design, methods, and statistical analyses planned

After IRB approval, subjects 18 to 75 years old with mild, moderate, and severe OSA that were being treated at the Division of Sleep Medicine of University Hospitals of Cleveland and who rejected/failed CPAP or other therapeutic options will be invited to participate in the study. The ones who agree to participate will sign a written consent form agreeing to participate in the study, and will be given a $100 gift card as incentive, built in as 4 increments of $25 earned by presence in each visit (baseline, month 1, month 2, and final visit at month 3). The subjects in the app group will receive the cost of the app included in the gift certificate. Subjects should have a recent (within 5 years) in-lab polysomnography or home sleep apnea testing (HSAT) performed, following the American Academy of Sleep Medicine guidelines. The test results will be used to define the severity of OSA, according to the apnea-hypopnea index (AHI) in mild (5–14 events/h of sleep), moderate (15–29.9 events/h), and severe (30 events/h or over). A total need of 60 subjects was calculated, based on the maximum inspiratory pressure (MIP) from the Çakmakc et al. study. The power sample calculation was performed with a 0.05 α value and 80% power, using the G*Power program for Windows.[16]

Exclusion criteria will include:

a. Age lower than 18 or higher than 75.
b. BMI > 40
c. Alcoholism or drug abuse
d. A-fib, pacemaker, CHF, strokes, narcotics
e. Neuromuscular disease
f. Use of benzodiazepine hypnotics (may affect muscle tone)
g. Restricted tongue movement
h. Permanently blocked nose
i. TMJ disorder.
j. Lost to follow-up
k. Gained or lost ≥5% of body weight during 3 months

The baseline protocol will include the following data:

Variable	Collected
Age	Self-reported
Sex	Self-reported
Neck Size	Measured on-site
Waist	Measured on-site
BMI	Measured on-site (height and weight)
Tongue Strength	IOPI device
Lip Strength	IOPI Device
OSA Risk Assessment	STOP-Bang Questionnaire
Nasal Breathing Efficiency	NOSE questionnaire
Sleep Quality	Pittsburgh Sleep Quality Index
Sleepiness Assessment	Epworth Sleepiness Scale
Insomnia Assessment	Insomnia Severity Index
Airway Collapsibility	AmCAD Ultrasound
Oxygen Saturation	Belun Ring Wearable
Heart Rate Variation during sleep	Belun Ring Wearable
Sleep Stage Assessment	Belun Ring Wearable
Sleep Efficiency	Belun Ring Wearable
Airway muscle tone	Surface Electromyography (EMG)
Snoring Presence, quality and quantity.	SnoreLab Application

Regular biometric measurements will be taken in the orthodontic clinic at Case Western Reserve University, using a calibrated scale which included a height measuring device.

Below is a description of the equipment specific for this project which will be used to capture and measure all monthly collected variables, from baseline to months 1, 2, and the final visit on the third month.

Iowa Oral Performance Instrument (IOPI)

The IOPI is a validated intra oral device that measures tongue elevation strength and endurance, and well as lip strength and endurance in kPa (Figure 1). The IOPI is a pressure transducer connected to a battery-operated amplifier, signal-conditioning circuit, and digital voltmeter. A peak holding circuit displays peak pressure in kPa on a digital readout. The IOPI will be used to measure the variables up to three times and the highest value will be recorded. The IOPI will be used at baseline and at every monthly visit, to evaluate the myofunctional therapy progress.

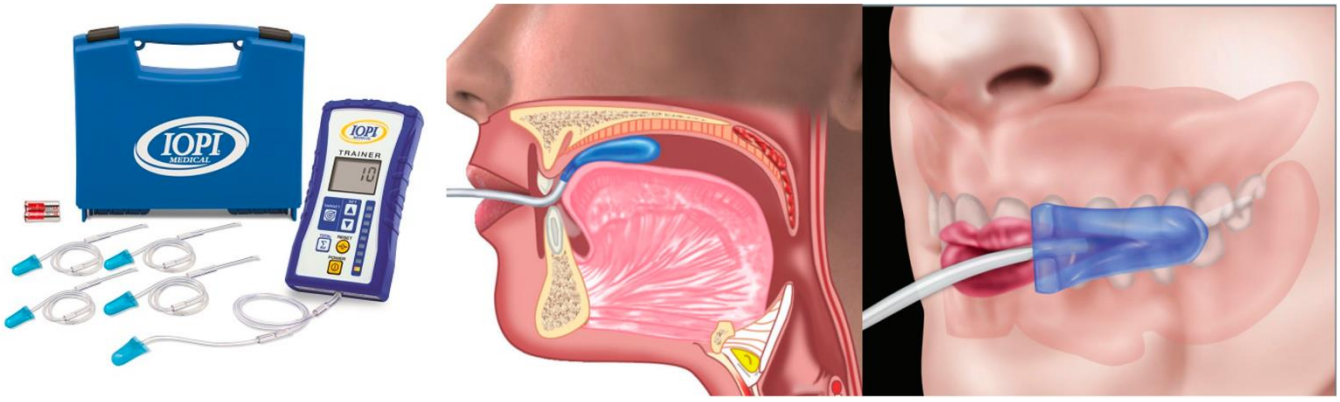

Figure 1. Iowa Oral Performance Instrument (IOPI) kit, and diagrams showing data collection for the tongue elevation strength and lip strength.

Belun Ring

Belun Sleep Platform (BSP, Belun Technology Company, Hong Kong) is a deep learning (DL) neural network-enabled, PPG-and-accelerometry-based wearable developed primarily for detecting OSA (Figure 2). The Belun Ring sensor is an FDA-cleared Class II pulse oximeter that is positioned on the proximal phalanx of index finger (proximal phalangeal radialis indicis artery). It measures oxygen saturation, heart rate, heart rate variability, and accelerometer signals (movement) to derive total sleep time, classify sleep stages (wake, NREM, REM), and number of apnea/hypopnea events per hour of sleep. The Belun ring showed great correlation with PSG (r=0.89), a sensitivity of 0.88 and a specificity of 0.83 when categorizing the apnea/hypopnea index (AHI).[17]

Figure 2. The Belun ring and how it is positioned on the index finger. The data collected is uploaded from the ring directly to a computer by placing the ring on its charging cradle, and connecting the cradle with an USB cable.

AmCAD-UO Ultrasound

The ultrasound is a non-invasive exam using a remote-controlled submental ultrasound device to detect obstructive sleep apnea (AmCAD-UO and AmCAD-US software). The AmCAD-UO system aims to standardize the ultrasound transducer pathway to reduce intra-observer variations and make the assessment more consistent. The software compares the images obtained in the two situations (normal breathing and Müller's maneuver and provides a risk assessment for OSA based on the collapsibility of the airway (Figure 3). The analysis is based on the VOTE Classification, which refers to the primary structures that contribute to upper airway obstruction in sleep-disordered breathing: **V**elum, **O**ropharyngeal lateral walls (including the tonsils), **T**ongue**,** and **E**piglottis. [8]

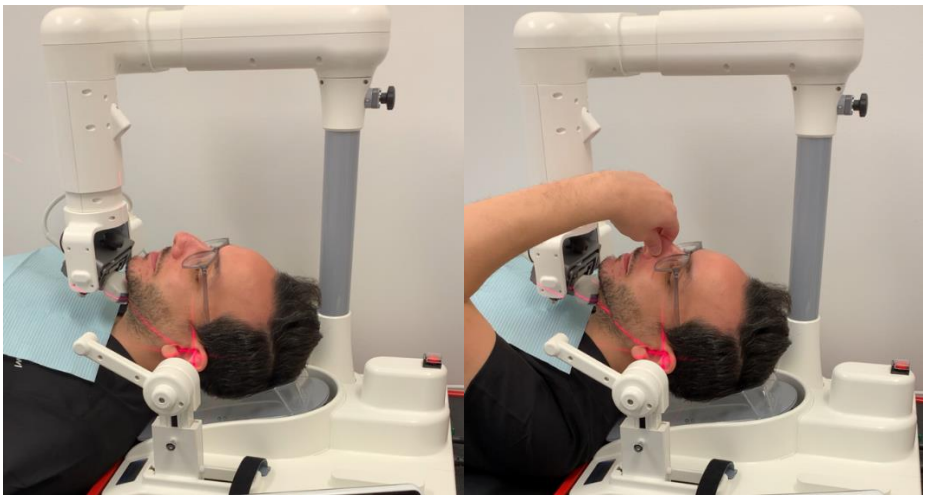

Figure 3. AmCAD-UO taking a normal breathing and a Mueller Maneuver ultrasound volume. Both airway volumes are compared in order to assess the airway collapsibility, and its tone.

The Mueller maneuver will be standardized in this study by using an inspiratory exercise device (spirometer) which when the subject inspires, balls are raised and remain floating while inspiration is taking place (Figure 4). This way we will be certain that the inspirational movement is taking place.

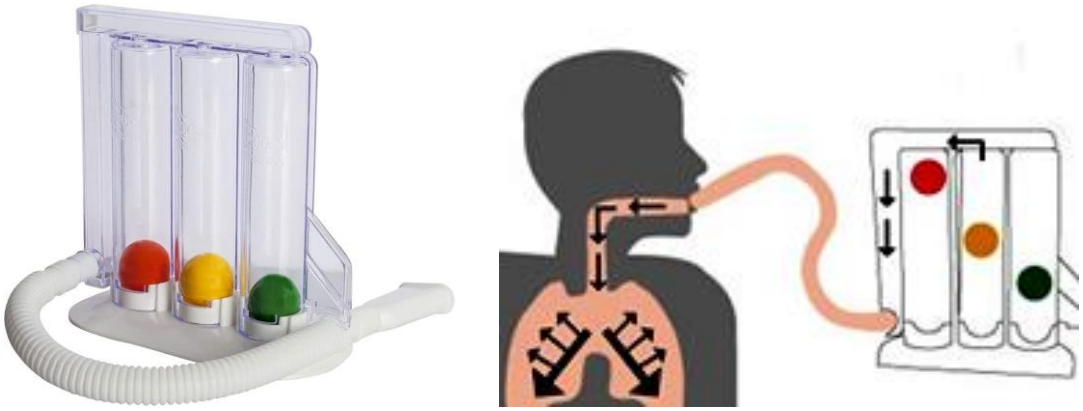

Figure 4. Spirometer used to assure inspiratory activity while performing the Mueller maneuver.

Airway Gym

The Airway Gym is a smartphone app which teaches and aids in the performance of several airway related exercises, using a smartphone pressure sensors to evaluate progress and monitor proper performance (Figure 5). The Airway Gym app includes proprioceptive exercises that are aimed to strengthen the lingual and pharyngeal muscle tone. Those muscles are considered responsible for the upper airway collapse during sleep. The Airway Gym app will be installed in the subject's smartphone belonging to the App Group. After the baseline exams, subjects will be instructed to perform the myofunctional exercises under the guidance of the Airway Gym app. The main objective of these exercises is to increase the tone of the extrinsic muscles of the tongue (genioglossus, hyoglossus, styloglossus, and palatoglossus)[15]. An initial session will be scheduled to train the subject in using the app and the exercises. The average training time proposed is 20 min/day, five days/week. There are nine exercises to enhance the tonicity of the various muscles involved in the pathogenesis of OSA [15]. Before every exercise, there is an animated gif demonstration that shows the subject how to perform the exercise. Subjects can follow the development of their activity daily overtime using the app. After each exercise, the subject receives feedback on their performance with a point score. When the subject finishes the exercises, they are saved for further evaluation.

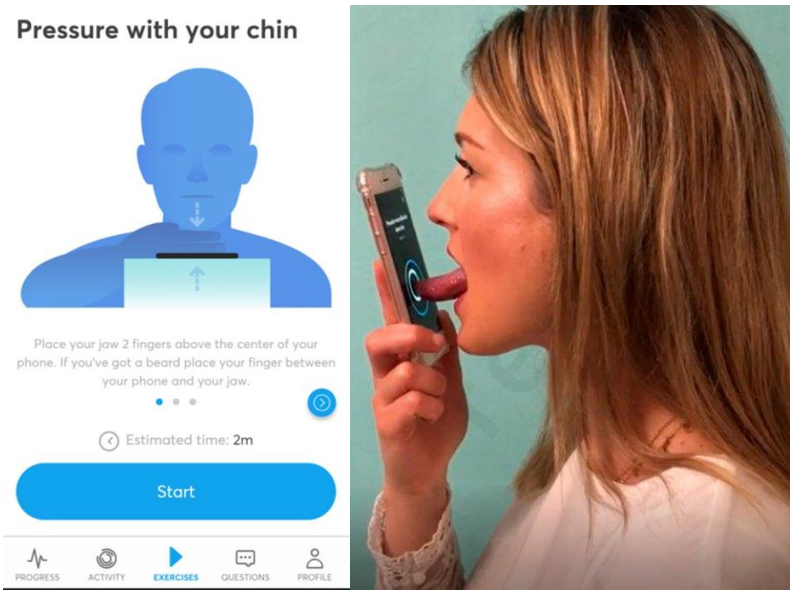

Figure 5. Example of Airway Gym training interface, and picture showing a subject performing a proprioceptive exercise using Airway Gym.

SnoreLab

SnoreLab is a smartphone app that uses the device's microphone to capture snoring, and uses an algorithm to evaluate snoring intensity and length during sleep (Figure 6). The SnoreLab app has been

used in several scientific studies, showing good correlation with PSG, but sometimes showing differences in data depending on the devices condition. For this reason, in this project we plan on installing SnoreLab on iPads, and loan the iPad to the subject whose snoring is being evaluated. All iPads will be tested and calibrated as to provide a standardized result. The iPads will be recalibrated everytime it is received back from a subject. The Snore app will be used to detect the snoring intensity and length during the exercise period, in both app and analog groups.

Figure 6. SnoreLab app reporting snoring intensity and length during sleep.

Surface Electromyography (EMG)

Surface Electromyography (EMG) will be used to assess the tone of the oropharyngeal musculature while performing exercises in both app and analog groups. Surface EMG is a non-invasive reliable and accurate alternative to the needle EMG, commonly used to evaluate muscle tone and activity. Surface EMG will aid in identifying the specific muscles that are being activated, and if one group is having better results than the other after performing their exercises.

Questionnaires

The STOP-Bang questionnaire is a sleep apnea risk assessment tool with 4 self-reported (STOP: snoring, tiredness, observed apnea, and high blood pressure) and 4 demographic (Bang: body mass index [BMI, age, neck circumference, and gender) variables. In its validation study, the STOP-Bang questionnaire demonstrated a sensitivity of 84%, 93%, and 100% to detect all OSA (mild, moderate, and severe, respectively). The STOP-Bang questionnaire will be filled on a monthly basis by all subjects in both groups.

The Pittsburgh Sleep Quality Index (PSQI) is a self-report questionnaire that assesses sleep quality over a 1-month time interval. The index consists of 19 individual items, with 7 components which produce one final score. The questionnaire takes an average of 5–10 minutes to complete. The Pittsburgh Sleep Quality Index will be filled on a monthly basis by all subjects in both groups.

The Epworth Sleepiness Scale (ESS) is a validated, widely used self-administered questionnaire that poses 8 different situations and provides a level of sleepiness ranging from “not a chance of dozing” to high chance of dozing”.

The Insomnia Severity Index is a 7-item self-administered questionnaire that assesses the severity of both daytime and nighttime components of insomnia.

Data Collection

Baseline data will be collected at the first visit, followed by monthly progress data, and final data will be at the 3-month mark.

Statistical Approach

A normality test will be applied to the data to determine if parametric or non-parametric statistics are to be used. A combination of descriptive and comparative analysis will be performed in order to determine if there are statistical significant differences between the groups.

A Bonferroni correction will be applied if too many t-tests are performed.

SPSS 28 will be used for all statistical analysis.

Expected outcomes

The hypothesis is that the app group will show better compliance and better results due to the constant reminders and interactive approach used by the app.

Alternative approaches if outcomes are not as expected

Due to the non-invasive nature of this project we do not expect problems during the project.

If outcomes are not as expected, this means that there is no significant differences between using an app or an analog method, which would be helpful information for future projects.