Introduction:

Obstructive sleep apnea/hypopnea syndrome (OSAHS) has become one of the more serious health problems worldwide.(Mendes et al., 2014) Because of its relationship with obesity, its prevalence and incidence have been increasing and it is associated with morbidities such as cardiovascular and cerebrovascular diseases. The classic treatment of this disease is based on dietary measures, losing weight, and exercise, and the use of a continuous positive airway pressure (CPAP) machine, a device that reduces collapsibility of the upper airway by emitting a flow of air. Other options are upper airway surgery treating the obstacle of the airway or correcting the muscles that do not perform their function properly, and mandibular advancement devices (MAD), which protrudes the tongue forward to avoid it falling backward and collapsing the airway. The success rates and treating the obstacle of the airway or correcting the muscle are variable .Indications for all treatments depend on the adherence to the treatment and severity of the disease (Mendes et al., 2014).

Myofunctional therapy (MT) has become one of the newest treatments for sleep-disordered breathing.(Macario Camacho et al., 2015).MT is based on daily exercises using oropharyngeal muscles in an attempt to strength them and facilitate opening of the airway. OSAHS originates from the lack of an optimal function of the dilator muscles of the airway. Therefore, MT is a therapy designed theoretically to deal with the underlying mechanism of this disease. (Korhan et al., 2015).MT is based on oropharyngeal exercises described by diagrams, videos, and instructions from a myofunctional therapist on a weekly basis. The pa- tient is instructed to perform the exercises regularly, for at least 3 months, between 20 to 40 min daily. In some cases, patients perform exercises by themselves at home without substantial feedback and without giving an exact information to the therapist about their performance of the exercises. (O'Connor Reina et al., 2020).

Most existing mHealth Applications for OSAHS patient focus on diagnosis of snoring or OSAHS((Isetta et al., 2017), while a few are designed to promote adherence to treatment to CPAP(M. Camacho et al., 2015). So far, to our knowledge, there are none focused in the treatment of OSAHS. However mobile technology could be especially valuable in treating OSAHS patient because of its potential to promote patient empowerment and self- management((Iftikhar et al., 2017a).

One of the best treatments for OSAHS is performing exercises and reducing weight.((Iftikhar et al., 2017b)(Guimaraes KCC., 2009) Because time is limited, we consider that there will be a greater probability of patients performing the exercises if they are able to do so while sitting comfort- ably and watching television. Therefore, we

designed and developed a novel mHealth Application software (App) to promote oropharyngeal exercises while interacting with a smartphone. In this prospective randomized multicentre clinical trial we want to regarding adherence to the App and its effectiveness in a group of patients with severe OSAHS compared with a control group.

Hypothesis:

The periodical use of the App Airway Gym designed to perform and increase adherence in Myofunctional therapy (MT), improve obstructive sleep apnea/hypopnea syndrome (OSAHS) in patients with severe disease (AHI>30) increasing the tone of the upper airway muscles.

OBJETIVES.

The main objective will be to study the evolution of the use of the App “Airway Gym” based on MT in patients diagnosed with severe OSAHS.

Secondary Objective:

1) To evaluate the influence of the MT with an App in the change of the Apnea Hipopnea Index in patients diagnosed with severe OSAHS.
2) To evaluate nadir and O2 desaturation index.
3) To evaluate scores obtained with IOPI (Iowa Oral Permoance Instrument) to evaluate genioglossus muscle one and buccinator muscle tone.
4) To evaluate subjective morning somnolence and sleep quality score with Epworth Sleepiness Score and Pitsburg questionnaires.

Methods

Design: Prospective controlled clinical trial quasi-experimental in patients with severe OSAHS (AHI>30)

Place.

Patients diagnosed and/or treated with severe sleep apnea in the Neumology and Otolaryngology Units of Hospitales Quironsalud Marbella and Campo de Gibraltar and will be developed in their installations

Population.

Patient recently diagnosed with severe sleep apnea and accepted to participate in this clinical trial.

Inclusión criteria

1)Age between 18-75 years

2) Recently diagnosed with severe sleep apnea and do not have any previous experience or information with this pathology.

3) Consent report signed.

Exlusion criteria

- ✓ IMC>40.
- ✓ Inhability to fill up questionnaires
- ✓ Severe drug or alcohol abuse.
- ✓ Hipnotic medication.
- ✓ Not controllled coronary disease
- ✓ Descompenated Heart failure
- ✓ Stroke
- ✓ Sistemic Disaease associated with inflammatory diagnosed entity (artritis, sarcoidosis, vasculitis, lupus…)
- ✓ Neuromuscular disease (like Duchenne)
- ✓ Cranefoacial deformities.
- ✓ Active oncologic process.
- ✓ Any antecedents of MT treatment, or other treatment for sleep apnea could affect study results of the study (surgery, DAM or CPAP).

Once patient accepted and signed consent report and meet inclusion criteria is attended by Ent specialist to rule out:

1) Severe upper airway obstruction (Complete nose obstruction, Tonsills grade IV/IV).
2) Presence of tongue tie (Marchesani Protocole) with limitation of tongue movements.
3) Antecedents or presence of temporomandibular joint disorders.

If present these features patients are excluded from study despite acceptance

Sample size calculation and sampling procedure.

Evaluation of the Efectiveness in the use of the App in perfoming MT in patients with severe OSAHS will be held with the values obtained in the longitudinal study, from the percentage of improvement in the AHI observed during the follow-up of the study. This percentage has been calculated upon results reported in previous MT studies published and presented in the bibiliography. With a statistical confidence level of 95%,and the power of 80% and estimating an improvement of the AHI of 60% the sample size will be 30 patients (15 experimental group,15 control group). In order to compensate potential lost in the inclusion process, (including patients with selection biass), early withdrawal or lost in follow up, we will increase the sample size in 100%, thereby sample size will be 60 subjects. Simple size was calculated with software XLSTAT for Excel.

Randomization Will be depending upon the number of the subject for consecutive order, being odd number group 1 or experimental (patients treated with the App) and even numbers group 2 or control (patients without complementary therapy).

Patient wihtout smarthpone Will directly recruited in group 2 or control.

VARIABLES DEFINITION

Age, Sex, Weight, Height, IBM ,waist circumference (belly button height),neck circumference, IOPI lingual and buccinator, IAH, O2 desaturation index and O2 Nadir.

Questionnaires: Friedman stage, Epworth sleepiness scale and Pittsburg-

PROCEDURE

For experimental group we are going to apply the Mhealh App Airway Gym developed by Otolaryngology Department form

This App is a smartphone App created in a collaboration between the Sleep Units of Hospital Quirónsalud Marbella and Campo de Gibraltar and their Engineering Informatics Departments and developed by Apnea Bye company. It was presented last November 2018.

We can think of this App as a portable gym with athletes instead of patients and trainers instead oftherapists. The novelty of this App is that it is the first in the health-care market where the patient can interact directly with the smartphone without any other device, which provides feedback about the efficacy of the exercises performed and focused on sleep apnea disease. There are nine exercises based on MT that attempt to enhance the tonicity of the various muscles involved in the pathogenesis of OSAHS. Before every exercise, there is an animated gif demonstration and a video that shows the patient how to perform the exercise (Figs. 1a–c). App's users can follow the development of their activity daily over time (Figs. 2a–c). At the conclusion of each exercise, the patient receives feedback about the success of their performance with a point score (Fig. 3). When the patient finishes the exercises, they are saved on networked online storage (in the Cloud) and a therapist (Fig. 4) can evaluate the perform- ance of the exercises and achievements. A chat function is available where the patient can contact the therapist directly. There is a reminder every 5 days if the patient "forgets" to perform the exercises. The English-language version of this App is now available on Android and the iOS platform via Google Play and the App Store, respectively. Full information about the App is provided in a Web Page https://airwaygym.App/. Therapists can use it to enroll and follow up their patients.

This App was developed with the most cutting-edge technologies (e.g., Ionic, Angular provided by Google and TypeScript by Microsoft) and the most consolidated software languages (such as HTML5, CSS3, and PHP). The App takes advantage of 3D Touch technology, a capacity available in the latest Apple devices to accurately measure the pressure that is produced on the mobile screen. This App complies with regulation 2002/58/ CE and (UE) 2016/679 about Data protection.

The main objective of these exercises was to increase the tone of the extrinsic muscles of the tongue (genioglossus,hyoglossus,styloglossus and palatoglossus).

The exercises are based on those described by Guimaraes in 2009(KCC 2009), adapted to obtain a feedback with the phone.

Due to hygienical reasons we recommend to cover the screen with cling film or a hypoallergenic plastic wrap in all exercises. See exercises annexed.

In the **control group** we do not use any therapy for OSAHS for 3 months

All patients Will assist to hospital once a month to measures variables (Weight, Height, IMC , Neck and belly diameter, and fill up questionnaires, IOPI scores)

Distribution hospital visits:

SELECTION VISIT

Patient diagnosed with newly diagnosed severe OSAHS with an in lab polysomnography with measures of IAH, saturation o2 and O2nadir All sleep studies were manually interpreted by a sleep technician according to the standard criteria of the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events and were reviewed by certified physicians. Inclusion and exclusion criteria, evaluate type of móbil pone used, previous experience with app, information about the study is provided and after questions and doubts resolved, patient accepted and sign consent report.

INITIAL VISIT: Patient is evaluated by ENT specialist, Oropharyngoscopy, rhinofibrolaryngoscopy , Friedman stage , Marchesani protocole and examination about temporomandibular joint dysfunction were performed. If patient presents Tonsil grade IV, complete nose obstruction, anquiloglosia or problems with temporomandibular joint dysfunction were considered selection failure.

SECOND VISIT: After ENT examination, variables are measured (Weight, Height, IMC , Neck and belly diameter, and fill up questionnaires, IOPI scores) and randomization were performed to control group and experimental group. Patients in the experimental group were instructed about the use of the App and exercises to perform.

- **Follow up visits** :
- **Experimental group**: Patient performed exercises daily about 20 minutes daily. One visit follow up is performed after one month (visit 3), and 2 months later (visit 4), in this visits variables are measured, questionnaires filled and assuring performance of exercises.
- **Control group:** One visit follow up is performed after one month (visit 3), and 2 months later (visit 4), in this visits variables are measured, questionnaires filled and assurance no other therapies are being followed.
- **Final visit:** It will be 3 months in both groups, questionnaires are filled, variables are measured again, in lab polysomnography is performed

Total study duration for each patient are 3 months-

DISCONTINUATION CRITERIA

Patient Will be excluded from the study if:

1) Do not perform exercises at least 85% sessions requested, or lost in follow up due not attend visits in both groups.

2) Loss of weight of 5% during study participation.

STATITISCAL ANALYSIS:

Data will be collected in a database. Nominal variables were described by their frequency distribituion Quantitative variables were assessed by calculating the arithmetic mean and standard deviation Baseline characteristics of patients with OSAS according to the group assigned were compared by two-tailed paired *t* tests for continuous variables and Xi squared or Fisher exact test for nominal variables. For variables with skewed distribution, we performed Mann-Whitney test. Two-way repeated- measures analysis of variance and Tukey test were used to compare differences within and between groups in variables measured at baseline and after 3 months. In addition, we performed Pearson correlations between changes in AHI with changes in possible explanatory variables, including BMI, abdominal circumference, and neck circumference. A value of P , 0.05 was considered significant. IBM SPSS Statistics for Windows software (version 20; IBM Corp, Armonk, NY, USA) was used for statistical analysis.

The main concerns will be poligraphy findings at the beginning and at the end of the study

Iopi Scores at the beginning and at the end of the study

Epworth and Pitsburgh questionnaires in all visits

Weight in kg height in cm BMI in m/k2 and Measurement neck and belly circumference in cm all visists

ETICAL APPROVAL:

After evaluating and revising the protocol the Investigation Ethical Committee from Costa del Sol approved the study with the code AWGAPN-2019-01. Before starting the trial, all participants should have signed and dated all consent reports approved by Ethical Committee.

Accest to Data and Data protection.

In order to warranty data confidentiality from study data, original data will be conserved in the Hospital and only will have Access the investigators and the Investigation Ethical Commitee:

It will be applied etichal principles from the last revisión from Helsinki Declaration and Good Clinical Practice..Confidence will be warranted to all participants (Organic Law Personal Data Protection 15/1999), likewise all information only wil be used to the aim specified in the trial. Personal data that could identify patients will be separated from the rest of information obtained in the trial. Every patient will have an indentification number and it will appear in the database.

UTILITY:

This App could improve the IAH , improve quality of life of patient and reduce clnical symptoms and needs for treatment.

CHRONOGRAM:

Activity (months)	1	2	3	4	5	6	7	8	9	10	11	12
Inicio, diseño base de datos y coordinación. Starting, Database and cordiation												
Recruitment												
Followup												

Collecting and entering data												
Statistical analyis and report results												

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