Effect of respiratory therapy on patients with sleep bruxism and associated respiratory events: Study protocol for a randomized controlled clinical trial

Efeito da terapia respiratória em pacientes com bruxismo do sono e eventos respiratórios associados: Protocolo de ensaio clínico randomizado controlado

Efecto de la terapia respiratoria en pacientes con bruxismo del sueño y eventos respiratorios asociados: Protocolo de estudio para un ensayo clínico controlado aleatorizado

Abstract

Aim: The aim of this study will be to perform respiratory physiotherapy on patients with sleep bruxism and associated respiratory events (apnea and hypopnea). Methodology: The study will be a randomized, controlled, double-blind, clinical trial with a sample of individuals with sleep bruxism and associated respiratory events. Respiratory (inspiratory and/or expiratory) physiotherapy will be performed using the THRESHOLD IMT and PEP and the results will be compared to a placebo group. Discussion: Regarding respiratory events, there is a broad variety of possible treatments for sleep apnea depending on the physiopathology, severity and patient preference, with CPAP considered the gold standard. However, data on CPAP are inconsistent, with adherence to therapy reported to be between 45 and 89%. Thus, other forms of treatment are proposed, including respiratory training. Understanding obstructive sleep apnea syndrome as the loss of the dilation strength of the pharynx and the inability to maintain the path open for air, respiratory muscle training could assist in increasing dilation strength, enabling the passage of air during sleep. Taking into consideration that sleep bruxism may be associated with events of apnea and hypopnea, the intervention to treat obstructive respiratory events related to sleep may have a positive impact on events related to sleep bruxism (rhythmic activity of the masticatory muscles). To determine this, we will measure the apnea/hypopnea index (AHI) and number of contractions of the masseter muscle (characteristic of the
activity of bruxism) before and after the intervention using polysomnography. Trial registration: The trial was registered with the REBEC platform: RBR-9F6JKM (ensaiosclinicos.gov.br).

**Keywords:** Sleep bruxism; Respiratory therapy; Sleep apnea.

**Resumen**

Objetivo: El objetivo de este estudio será realizar fisioterapia respiratoria en pacientes con bruxismo del sueño y eventos respiratorios asociados (apnea e hipopnea). Metodología: El estudio será un ensayo clínico aleatorizado, controlado, doble ciego, con una muestra de individuos con bruxismo del sueño y eventos respiratorios asociados. Se realizará fisioterapia respiratoria (inspiratoria y/o espiratoria) utilizando el THRESHOLD IMT y PEP y los resultados se compararán con un grupo de placebo. Discusión: En cuanto a los eventos respiratorios, existe una amplia variedad de posibles tratamientos para la apnea del sueño en función de la fisiopatología, la gravedad y la preferencia del paciente, siendo la CPAP considerada el estándar de oro. Sin embargo, los datos sobre CPAP son inconsistentes, y se informa que la adherencia al tratamiento está entre el 45 y el 89%. Por tanto, se proponen otras formas de tratamiento, incluido el entrenamiento respiratorio. Entendiendo el síndrome de apnea obstructiva del sueño como la pérdida de la fuerza de dilatación de la faringe y la incapacidad de mantener el camino abierto para el aire, el entrenamiento de los músculos respiratorios podría ayudar a aumentar la fuerza de dilatación, permitiendo el paso del aire durante el sueño. Teniendo en cuenta que el bruxismo del sueño puede estar asociado a eventos de apnea e hipopnea, la intervención para tratar los eventos respiratorios obstructivos relacionados con el sueño puede tener un impacto positivo en los eventos relacionados con el bruxismo del sueño (actividad rítmica de los músculos masticatorios). Para determinarlo, mediremos el índice de apnea / hipopnea (IAH) y el número de contracciones del músculo masetero (característica de la actividad del bruxismo) antes y después de la intervención mediante polisomnografía. Registro del ensayo: El ensayo se registró en la plataforma REBEC: RBR-9F6JKM (ensaiosclinicos.gov.br).

**Palabras clave:** Bruxismo del sueño; Terapia respiratoria; Apnea del sueño.

**1. Introduction**

Bruxism is a recurrent issue in the dental clinic and is charged with uncertainties regarding its diagnosis, the need for treatment and the effectiveness of therapeutic modalities. In some situations, bruxism may be associated with oral problems, such as sensitivity/pain upon palpation of the masticatory muscles, headache and symptoms of temporomandibular disorder (Castroflorio et al, 2015). On other occasions, it may be considered a physiological effect of respiratory and swallowing mechanisms during sleep, in which bruxism is the result of the motor activity required for the increase in the patency of the upper airways through jaw movements (Mayer et al, 20017).

For an understanding of the etiological factors of bruxism, it is necessary to understand its definitions. Sleep bruxism (SB) is defined as a movement disorder during sleep characterized by involuntary motor activity of the masticatory muscles in an episodic and repetitive manner. Muscle contractions, also called rhythmic activity of the masticatory muscles (RAMM)
during sleep often produce teeth grinding sounds, which are related to sleep bruxism (Kapur et al, 2016). Episodes of RAMM are found in 60% of the general adult population as physiological activity of the masticatory muscles during sleep (Lavigne et al, 2001). In individuals with sleep bruxism, each maximum contraction during RAMM is threefold more frequent and 40% shorter in comparison to individuals without sleep bruxism (Hasegawa et al, 2013; Jadidi et al, 2011). This activity is also found in numerous sleep disorders, such as somnambulism, night terrors and obstructive sleep apnea/hypopnea syndrome (Lavigne et al, 2003). Many other forms of masticatory and facial muscle activity also occur during sleep, such as swallowing, coughing, smiling, lip smacking and jaw movements (Lavigne, Manzini e Huynh, 2011).

The consensus in the literature is that the diagnosis of SB has three categories: ‘possible’, which is based on a self-report with the use of questionnaires or the patient history part of the clinical examination; ‘probable’, which is based on the self-report and a clinical examination; and ‘definitive’, which is based on the self-report, clinical examination and polysomnography, preferably with both audio and video recordings (Lobbezoo et al 2018).

Sleep bruxism may occur alone (primary SB) or with one or several associated comorbidities (secondary SB). In some complex cases, SB should be differentiated from other types of facio-mandibular activity that occur during sleep, such as facio-mandibular myoclonus, respiratory disorders (respiratory effort-related arousals, apnea and hypopnea), abnormal swallowing, gastroesophageal problems (acid reflux), night terrors, dyskinetic movements of the jaw during sleep (dystonia, tremors, chorea and dyskinesia) and sleep-related epilepsy (rare) (Lavigne, Manzini e Huynh, 2011; Carra, Huynh & Lavigne, 2012). Thus, obstructive sleep apnea/hypopnea syndrome (OSAHS) may be a sleep disorder that is concomitant with SB (Inoko et al, 2004; Kato et al, 2003; Sjoholm et al, 2000; Okeson et al, 1991).

Positive effects have been reported in studies involving inspiratory exercises for individuals with obstructive sleep apnea (Vranish et al 2016; Souza et al 2018; Lin et al, 2020) indicating a direction for effective treatments with greater adherence on the part of patients in comparison to the use of CPAP (Weaver & Grunstein, 2008; Olsen, Smith & Oei, 2008). Likewise, expiratory exercises have been successful at improving sleep quality and markers related to obstructive sleep apnea (Kuo, Song, Bernard & Liao, 2017; Herkenrath et al, 2018).

2. Methodology

Objective:

As sleep bruxism may be related to events of apnea and hypopnea, interventions for the treatment of obstructive respiratory events during sleep could have a positive impact on events related to sleep bruxism (rhythmic activity of the masticatory muscles). Therefore, individuals with sleep bruxism and associated respiratory events (apnea and hypopnea) will be randomized in a double-blind clinical trial to receive therapy with inspiratory exercises (inspiratory group), expiratory exercises (expiratory group) or no intervention (placebo group). The apnea/hypopnea index (AHI) and number of contractions of the masseter muscle (characteristic of bruxism) will be determined before and after the intervention.

The following hypotheses will be tested:
1. The inspiratory exercise promotes a reduction in the AHI.
2. The expiratory exercise promotes a reduction in the AHI.
3. The inspiratory exercise promotes a reduction in the number of contractions of the masseter muscle during sleep.
4. The expiratory exercise promotes a reduction in the number of contractions of the masseter muscle during sleep.
Design

The study will be a randomized, controlled, double-blind, clinical trial with a sample of individuals with sleep bruxism and associated respiratory events. Respiratory (inspiratory and/or expiratory) physiotherapy will be performed using the THRESHOLD IMT and PEP and the results will be compared to a placebo (non-intervention) group.

Participants and eligibility

The population for this phase of the study will be composed of 15 individuals identified with sleep bruxism and associated respiratory events (apnea and hypopnea). Recruitment for the study will begin in December 2019 exclusively in the city of Curitiba, Brazil, until the number of participants is reached.

Inclusion criteria:
1. Age 18 to 65 years;
2. Sleep bruxism and associated respiratory events (mild to moderate apnea and hypopnea) identified through polysomnography.

Exclusion criteria:
1. Age less than 18 years;
2. Use of intraoral splint;
3. Severe apnea/hypopnea;
4. Severe skeletal abnormalities that affect the upper airways;
5. Chronic medical conditions that affect OSAHS, such as stroke.
6. Inability to sign the statement of informed consent.

Recruitment

Participants will be recruited through a public call via social networks and from among the individuals who seek the University with a complaint of sleep bruxism. Those who meet the eligibility criteria after polysomnography will be included in the study.

Interventions: Allocation

Randomization and blinding

A person not otherwise involved in the study will manage this phase of the study, ensuring that the evaluators of the outcome are blinded to the allocation of the participants to the different groups. The website program randomization.com will be used for the generation of the random sequence. The proportion of the three groups (inspiratory, expiratory and placebo) will be 1:1:1.

The evaluator of the main outcome (physician in charge of the polysomnography analysis and therefore evaluator of the pre-intervention and post-intervention AHI, oxygen desaturation index and contractions of the masseter muscle) will be blinded to the allocation. The participants will also be blinded; they will not know to which group they are allocated because they are not familiar with the intervention. Likewise, the person in charge of the data analysis will not be directly involved in the study.
Interventions

The participants will be randomly allocated to the Inspiratory Group, Expiratory Group and Placebo Group. The three groups will have the same clinical conditions. The participants will not know to which group they have been allocated.

Maximum respiratory pressures will be determined with the aid of a pressure gauge. The measurement of maximum inspiratory and expiratory pressures (MIP and MEP) is a noninvasive method that is widely used to evaluate the strength of the inspiratory and expiratory muscles (Almeida, Bertucci & Lima, 2008). MIP and MEP values do not depend only on the strength of the respiratory muscles but also on the lung volume with which the measurements are made and the corresponding elastic recoil pressure of the respiratory system (Silva, 2011).

Pressure readings will be performed prior to initiating respiratory muscle training to determine baseline values and enable the quantification of the increase in muscle strength achieved by the respiratory exercises (Souza et al, 2019). Inspiratory and expiratory muscle strengthening will be based on resistance breathing using nonlinear or linear load devices. The method of choice will be the Threshold® IMT for inspiratory muscle training and Threshold® PEP for expiratory muscle training (Ohayon, Li & Guilleminault, 2001).

The physiotherapist will first verify the resistance to be applied. The load will be adjusted to 70% maximum inspiratory or expiratory capacity in the intervention groups. No load will be applied in the placebo group. The load will be adjusted weekly based on a new measurement of maximum respiratory capacity. The intervention will be performed for 12 weeks at a frequency of five times per week and the exercises will consist of 30 respiratory cycles (inspiration + expiration) per day.

Data collection and management

Plans for data collection and evaluation of results

The data will be entered onto an Excel spreadsheet by a secondary participant in the study. The baseline data will be entered first and the final data will be entered after the 12-week interventions.

Confidentiality

The researchers commit to maintaining the confidentiality of the data until the publication of the results in a scientific journal. None of the participants will have their identities revealed.

Statistical methods

The data collected during the study will be organized and submitted to univariate (descriptive: frequency of variables) and bivariate (association and/or correlation tests and comparisons between groups) statistical analyses. The Student's t-test will be used to determine the effectiveness of respiratory therapy. The significance level will be set at 5%.

Reported adverse events and arms of intervention

The risk of the study regards expiratory and inspiratory muscle fatigue due to the exercises proposed as therapy. To minimize this possibility, the participants will be accompanied by a physiotherapist with experience in respiratory physical therapy who will immediately suspend the therapy upon observing signs of fatigue and will take the necessary measures to reverse the situation.

Criterion for discontinuing or altering the allocation in the intervention group

Participants who exhibit signs of respiratory fatigue will be removed from the intervention group and will be excluded
from the study.

**Strategies for ensuring adherence to the interventions**

The patients will be monitored weekly in person and telephone contact will be maintained to encourage the daily performance of the exercises.

**Concomitant treatment permitted or prohibited during the clinical trial**

During the interventions, the participant cannot undergo any other treatment for obstructive sleep apnea/hypopnea or sleep bruxism. Moreover, the use of sleeping pills will be prohibited.

**Prediction of post-trial care**

At the end of the study, if one therapy proves superior to the other, it will be made available to all participants so that they may perform the intervention with the greater benefit.

**Outcomes**

The primary outcomes will be the apnea/hypopnea index (AHI), oxygen desaturation index (ODI) and number of contractions of the masseter muscle per hour, measured by polysomnography. The secondary outcome will be sleep quality measured using Pittsburg Sleep Quality Index. The evaluator of the primary outcomes will be blinded to the allocation of the individuals to the different groups.

**3. Results and Discussion**

An epidemiological study published in 2001 suggests that patients with sleep-related respiratory disorders have a greater chance of exhibiting SB (Hosoya et al, 2014). Despite a weak but significant association between SB and OSAHS, the cross-sectional design of the study did not enable the determination of causality between the two conditions. Through polysomnographic analyses, studies have demonstrated that masticatory muscle activity tends to occur soon after the end of apnea or hypopnea events (Inoko, Shimizu & Kohno, 2004; Sjoholm et al, 2000; Okeson et al, 1991; Saito et al, 2016). Some studies support the hypothesis described above and conclude that most bruxism events are secondary to apnea and hypopnea events, making apnea a risk factor for SB (Saito et al, 2016). However, these findings are inconclusive, since not all SB events occur in this sequence or have a temporal association with respiratory events (Sullivan, Berthon-Jones & Eves, 1981). If the theory that bruxism is secondary to apnea and hypopnea is confirmed, an improvement in the respiratory condition could lead to a reduction in the occurrence of bruxism.

Regarding respiratory events, there is a broad variety of possible treatments for sleep apnea depending on the physiopathology, severity and patient preference, with CPAP considered the gold standard (Remmers et al, 1978). However, data on CPAP are inconsistent, with adherence to therapy reported to be between 45 and 89% (Weaver & Grunstein, 2008; Olsen, Smith & Oei, 2008). Thus, other forms of treatment are proposed, including respiratory training. Understanding obstructive sleep apnea syndrome as the loss of the dilation strength of the pharynx and the inability to maintain the path open for air (Van de Heyning et al, 2012), respiratory muscle training could assist in increasing dilation strength, enabling the passage of air during sleep (Stollo et al, 2014; Boutron et al, 2017).

**Trial Status**

Recruiting
4. Final Considerations

Among the interventions evaluated in clinical trial have a potential positive impact on OSA and bruxism symptoms. The therapy with inspiratory and expiratory exercises, can be considered on future an alternative for the management of OSA/bruxism patients, improving the quality of sleep an increase in functional capacity.

This study show a possible treatment option in generating a positive impact on events related to sleep bruxism.

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