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Physical exercise related improvement in obstructive sleep apnea. Look for the rostral fluid shift

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ABSTRACT

Obstructive sleep apnea (OSA) is a common and underdiagnosed medical disorder. OSA is associated with the symptoms of excessive daytime sleepiness (EDS). These patients typically follow a sedentary lifestyle, and sedentary behavior is related to impaired fluid dynamics in the lower body, particularly the legs. In a supine position this fluid can move towards the neck, with a subsequent increase in upper airway (UA) resistance and UA collapse. Several studies have shown that rostral fluid shift worsens OSA; however, whether physical activity can influence this has not been tested.

Physical activity related improvement in OSA severity cannot be fully explained by a weight loss in the performed studies, which is of particular importance. One of the potential additional pathways is via an improvement in leg fluid dynamics, with a subsequent decrease in the supine fluid shift toward the neck, since physical activity improves leg fluid dynamics.

It is likely that patients with fluid overload states such as heart failure, chronic kidney disease and resistant arterial hypertension, as well as patients with EDS are likely to benefit the most from physical exercise in terms of better leg fluid clearance, and potentially in terms of OSA severity.

However, none of the studies have directly assessed the potential effect of physical activity on the leg fluid volume, and more importantly on the supine fluid shift and OSA severity. These questions should be addressed in future studies of the effects of physical exercise on OSA severity.

Introduction

Obstructive sleep apnea (OSA) is a common medical condition and a form of sleep disordered breathing, which is characterized by repetitive complete and/or partial collapses (apnea and hypopnea, respectively) of the upper airways (UA). The disease is classified into mild, moderate and severe forms based on the number of apneas and/or hypopneas per hour of sleep, which is called the apnea-hypopnea index (AHI). The AHI is measured by instrumental sleep monitoring [1]. The risk factors for OSA are shown in Table 1.

OSA is not only a disease of the UA, but should be rather approached as a medical condition with systemic features. Indeed, OSA is associated with cardiovascular metabolic diseases such as arterial hypertension, coronary artery disease, heart failure, arrhythmias, stroke, type 2 diabetes mellitus, renal disease and liver disease [2–7], as well car accidents and neuropsychiatric disease, which are more common in patients with OSA than in the general population [8,9].

Subjects having OSA often complain of excessive daytime sleepiness (EDS). Several clinically helpful questionnaires are available for the detection of patients with symptoms of EDS, with the Epworth Sleepiness Scale (ESS), being the most commonly used [10]. Patients with EDS are at much greater risk for car and work related accidents; therefore, abolishing EDS is of major clinical and social importance.

A shift of fluid from the lower body, particularly from the legs toward the neck can increase the collapsibility of UA and, thus worsen OSA. On the other hand, patients with EDS are likely to follow a sedentary lifestyle, which is associated, with fluid accumulation in the lower extremities due to decreased muscle work. First, we will briefly discuss the data on the physical activity and fluid accumulation in the legs. Second, we will review the effects of fluid shift on the OSA severity. Third, we will discuss the data on the physical activity and OSA course.

Hypothesis

Research data suggest that a sedentary lifestyle and decreased ambulation are related to a greater leg fluid volume. This association may be explained by the fact that the leg muscles are of a major importance in the local venous fluid dynamics. This mechanism

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Table 1
Risk factors for OSA.

Age
Male gender
Obesity
Smoking
Alcohol
Sedatives
Craniofacial parameters
Neck circumference $\geqslant$40.6 cm in women
Neck circumference $\geqslant$43.2 cm in men
Resistant arterial hypertension
Congestive heart failure
Chronic kidney disease/end stage renal disease

may contribute to the OSA severity, given the fact that many patients with OSA experience EDS and are likely to be sedentary. Furthermore, strong scientific data exist on the role of the fluid shift from the legs toward the neck, leading to the worsening of OSA. The impact of the rostral fluid shift is even more important for patients with OSA and concomitant hypervolemic states such as chronic kidney disease, resistant hypertension and heart failure. These hypervolemic conditions are independently associated with reduced physical endurance; therefore, the concomitant presence of these pathologic states may have additive effects on the impact of OSA severity. It is noteworthy to mention that physical activity is of no cost to the healthcare system and it is well known that the active lifestyle is associated with cardiac and metabolic well-being. Therefore, physical activity is a very attractive in terms of research and health care policy in the field of OSA.

Below we will review the existing data on the impact of lower extremity fluid dynamics and OSA severity. Potential implications of the hypothesis will be subsequently discussed.

Physical activity and fluid accumulation in the lower extremities

Patients with OSA and symptoms of EDS have decreased physical endurance during exercise and increased daytime fatigue [11]. Indeed, patients with OSA and EDS may fall asleep at different times, even while sitting. It is well known that a sitting position is associated with an increased leg fluid volume, due to gravity forces [12–15].

Others have shown that sedentary behavior is associated with leg swelling [16,17]. It is also important to note that physical activity may, in fact, greatly diminish the fluid accumulation in the lower extremities [18].

However, it is essential to mention that these studies were not performed in OSA patients, but, it seems possible that sedentary and sleepy patients with OSA have a similar clinical profile.

Rostral fluid shift and OSA severity

Chiu et al. recruited 11 healthy non-obese participants and measured their neck circumference, leg fluid volume and pharyngeal airflow resistance [19]. Afterwards, participants were randomized to lower body positive pressure (LBPP) application and control period, and the variables were measured at 1 and 5 min intervals. They found that volume redistribution from the legs towards the upper body via the application of LBPP increases the neck circumference and pharyngeal airflow resistance.

In a later study, the same group in a later study recruited 27 healthy participants and applied LBPP [20]. They found that LBPP application increased neck circumference and reduced UA cross-sectional area. Based on their results, men were found to have a higher sensitivity of UA to rostral fluid shift than women, which may in part explain the different OSA prevalence between genders [21].

Redolfi et al. recruited 23 non-obese male referred to a Sleep Center because of suspected OSA [22]. Prior to a sleep, study, the recruited participants spent most of their time in a sitting position. The research group found that an overnight increase in the leg volume correlated with change in the neck circumference, time spent sitting and worsened OSA severity.

In a later work, Redolfi et al. applied venous compression stockings and assessed changes in leg fluid volume, neck circumference and OSA severity [23]. A decrease in leg fluid volume was associated with an improved OSA severity and a reduction in overnight neck circumference. In a similar study with venous compression stockings in OSA patients with chronic lower extremity venous insufficiency the investigators found an improvement in OSA severity as well as a reduction of neck circumference and a decreased leg fluid volume [24].

However, Jafari and Mohsenin failed to find any association between rostral fluid shift and OSA severity [25]. The difference in the studied population may underlie the negative findings. For a more detailed review and discussion the reader is referred to a review article on this topic [26].

Physical activity and OSA improvement

It is well known that physical activity decreases weight and can help prevent obesity. Obesity, on the other hand, is a significant risk factor for OSA. Thus, it is necessary to keep in mind the potential for a weight change as a potential confounder, when studying the potential impact of exercise on the OSA severity.

Indeed, several studies have bolstered the notion that physical exercise has beneficial effects on the OSA severity [27–30]. However, the weight decreased substantially in these studies, and thus, the improvement in OSA severity was likely mediated via this mechanism. On the other hand, a decrease in weight can be to a lesser extent explained, by physical exercise related improvement in leg fluid dynamics and its clearance.

It is pertinent to mention that Giebelhaus et al. found that exercise mitigates OSA without any significant weight loss [31]. In a later study, a group from Brazil showed that physical activity is associated with an OSA improvement in patients with heart failure [32]. Of particular relevance is the fact that patients with heart failure are volume overloaded and that the impact of rostral fluid shift on the OSA severity is likely greater than in the general OSA population.

Other groups have confirmed that physical activity is associated with a better OSA control, and this association could not be entirely explained by weight loss [33–35].

In a recent study performed by Kline et al. it was shown that physical exercise and activity led tom improvement in daytime performance in patients with OSA [36].

However, none of these studies directly assessed the potential effect of physical activity on the leg fluid volume, and more importantly on the supine fluid shift and OSA severity. These questions should be addressed in future studies on the effects of physical exercise on OSA severity.

Implications of the hypothesis

Prospective studies should assess the impact of regular physical exercise on the lower extremity fluid dynamics and its impact on the rostral fluid shift and subsequently OSA severity. Given the fact that this intervention is of no financial cost and is associated with