NCBI

Effects of Exercise Training on Sleep Apnea: A Meta-analysis

Imran H. Iftikhar, Christopher E. Kline, and Shawn D. Youngstedt

Abstract

Background

Several studies have shown a favorable effect of supervised exercise training on obstructive sleep apnea (OSA). This meta-analysis was conducted to analyze the data from these studies on the severity of OSA (primary outcome) in adults. Secondary outcomes of interest included body mass index (BMI), sleep efficiency, daytime sleepiness and cardiorespiratory fitness.

Methods

Two independent reviewers searched PubMed and Embase (from inception to March 6, 2013) to identify studies on the effects of supervised exercise training in adults with OSA. Pre- and postexercise training data on our primary and secondary outcomes were extracted.

Results

A total of 5 studies with 6 cohorts that enrolled a total of 129 study participants met the inclusion criteria. The pooled estimate of mean pre- to postintervention (exercise) reduction in AHI was −6.27 events/h (95 % confidence interval [CI] −8.54 to −3.99; $p < 0.001$). The pooled estimates of mean changes in BMI, sleep efficiency, Epworth sleepiness scale and VO_2 peak were −1.37 (95 % CI −2.81 to 0.07; $p = 0.06$), 5.75 % (95 % CI 2.47–9.03; $p = 0.001$), −3.3 (95 % CI −5.57 to −1.02; $p = 0.004$), and 3.93 mL/kg/min (95 % CI 2.44–5.42; $p < 0.001$), respectively.

Conclusions

This meta-analysis shows a statistically significant effect of exercise in reducing the severity of sleep apnea in patients with OSA with minimal changes in body weight. Additionally, the significant effects of exercise on cardiorespiratory fitness, daytime sleepiness, and sleep efficiency indicate the potential value of exercise in the management of OSA.

Go to:

Introduction

Obstructive sleep apnea (OSA) is a common medical condition characterized by repetitive upper airway obstruction during sleep [1, 2]. OSA is linked to a wide range of adverse health consequences, including daytime sleepiness, cognitive impairment, and several cardiovascular and metabolic disorders [3, 4].

The American Academy of Sleep Medicine recommends the use of continuous positive airway pressure (CPAP) [5] or oral appliances for treating mild to moderate OSA, whereas CPAP is recommended as the first-line and oral appliances as second-line treatments for severe OSA patients [6]. Although highly efficacious when used, the utility of CPAP is limited by poor patient adherence to CPAP. Other treatment options for OSA include weight loss [7–9] and upper airway surgery [10, 11]. However, the effects of weight loss on the severity of OSA could be delayed [12]. Surgical modifications of the upper airway for the treatment of OSA continue to evolve, and the data are not as robust due to the relative paucity of randomized, controlled trials (RCTs) [13].

Exercise training in patients with sleep apnea has received accelerated attention. Not only has exercise been shown to be effective in improving OSA, but it also has been found to decrease the severity of central sleep apnea in chronic heart failure patients [14, 15]. Moreover, exercise could be uniquely helpful to ameliorate numerous sequalae of OSA, including cardiovascular disease, impaired glucose tolerance, and fatigue. Additionally, analyses from a large community-based cohort showed that vigorous physical activity was associated with a decrease in the prevalence of OSA [16]. The mechanisms by which exercise training leads to improvement in OSA are not well-understood. Of course, exercise could reduce OSA indirectly by facilitating decreases in body weight and fat. However, epidemiologic [17, 18] and experimental studies [19–21] have shown that the effect of exercise on sleep apnea is independent of body weight reduction. Besides the beneficial effects on OSA severity, regular physical activity also has been found to be associated with subjective well being in patients with OSA irrespective of the severity [22].

The primary purpose of this study was to evaluate the efficacy of exercise training on OSA severity reduction in adults with OSA. Secondary objectives were to evaluate the effects of exercise training on body mass index (BMI), sleep efficiency, daytime sleepiness, and cardiorespiratory fitness. In much of the literature on the effects of exercise on OSA, the degree to which participants indeed exercised or were encouraged to do so has often been unclear. Therefore, the present meta-analysis was restricted to studies that documented exercise training via improvements in cardiorespiratory fitness.

Methods

This meta-analysis was performed according to the guidelines reported in meta-analysis of observational studies in epidemiology [23] and preferred reporting items for systematic reviews and meta-analyses statements [24].

Search Strategy and Selection Criteria

We searched PubMed and Embase databases from their inception to March 6, 2013. We used combinations of the following keywords: “exercise,” “obstructive sleep apnea,” and “sleep-disordered breathing.” The search from PubMed yielded all the studies included in this meta-analysis. To ensure a thorough search of the literature, we hand-searched the reference lists of the included studies and previously published meta-analyses [25, 26] on lifestyle interventions and OSA severity. For inclusion in our meta-analysis, we considered only those studies that reported exercise as a primary component of an intervention and also reported changes in cardiorespiratory fitness. Inclusion criteria for RCTs included a diagnosis of OSA and randomization to exercise training or to control condition. The control condition could include individuals who received either stretching exercises or were left untrained. We excluded studies that reported additional intervention with CPAP. We also excluded studies that reported data in median and interquartile range. If the required data from articles were ambiguous or missing, we contacted the study authors; after two unanswered attempts, we excluded these studies from the analysis.

Two investigators (IHI and CEK) independently searched the studies and performed the final screening. In those instances when there was a disagreement between the investigators, a third investigator (SDY) reviewed the article and disagreements were resolved through discussion. Figure 1 summarizes the results of the selection and exclusion process.

Study Outcomes

Our primary study outcome was OSA severity, as measured by the apnea hypopnea index (AHI; i.e., number of apnea or hypopnea events per hours of sleep). Secondary outcomes included changes in BMI, sleep efficiency, daytime sleepiness, and cardiorespiratory fitness. As a measure of body mass, BMI was calculated as weight in kilograms divided by height in meters squared. As an indicator of overall sleep quality, sleep efficiency was measured by overnight polysomnography and expressed as a percentage of time in bed that was spent asleep. Subjective daytime sleepiness was measured by the Epworth Sleepiness Scale [27]. Cardiorespiratory fitness was indicated by peak oxygen consumption (VO_2 peak, measured in mL/kg/min) obtained during a graded cardiopulmonary exercise test.

Data Abstraction

Data were extracted on a prespecified worksheet. This included first author's name, year of publication, number of participants, mean of pre- and postexercise training AHI, BMI, sleep efficiency, Epworth Sleepiness Scale, and VO_2 peak with standard deviations. One study reported separate data for the two exercise intervention arms (aerobic exercise and combined aerobic/resistance exercise) [28]; as a result, these two groups were separately analyzed in our analyses. Some data were specifically requested from the corresponding authors of two studies included in our meta-analysis [20, 28]. Kline et al. [20] confirmed that Epworth Sleepiness Scale and cardiorespiratory fitness data were published separately from the included study [29, 30]. The authors of two studies provided additional BMI data for their study populations [19, 26]. One of the studies reported cardiorespiratory fitness data as metabolic equivalents (METs) [31]. Therefore, we transformed the data to peak relative oxygen consumption using the following equation: 1 MET = 3.5 mL O_2/kg/min. Five of the study participants in one study [31] used CPAP during the intervention. Because individual pre- and postexercise training AHI data were provided, for our meta-analysis on the effects of exercise training on AHI, we excluded the data of those who concurrently used CPAP.

Quantitative Data Synthesis

The mean changes in the outcomes from exercise training along with their 95 % confidence intervals (CIs) were estimated by pooling available data using comprehensive meta analysis software version 2.2.064. Results are displayed in the form of forest plots (Figs. 2, ,3,3, ,4,4, ,5,5, ,6).6). Similarly, we also conducted separate analyses of the difference in each outcome between control and exercise groups in RCTs. We conducted both random-effects methods and fixed-effects meta-analyses to account for variance between and within the studies, respectively [32]. However, we chose to include the results from the random-effects method to account for any heterogeneity within and between the studies. Statistical heterogeneity was assessed with the I^2 statistic [33]. An $I^2 > 60$ % indicated significant heterogeneity. We also performed sensitivity analyses to assess the influence of each study on estimates of the overall effect. This was done separately for the pooled estimates of change in AHI, BMI, sleep efficiency, and VO_2 peak. To check for publication bias, we constructed funnel plots of effect size and standard error [32, 34] and also analyzed results by using the Begg and Mazumdar rank correlation test [35].

Results

We reviewed 498 citations and identified 5 studies [19, 20, 26, 29, 31] for inclusion in our meta-analysis (Fig. 1). Our search strategy yielded three studies that used exercise as the sole intervention [20, 21, 28]. In two other studies, exercise was the primary intervention but study participants also underwent some dietary intervention [31, 36]. Altogether, these studies enrolled a total of 129 participants. Table 1 outlines the baseline characteristics of the population in each study. Table 2 summarizes the exercise interventions used in each study. On average, study participants were ≥42 years old and had a mean BMI ≥ 26. The duration of exercise intervention lasted between 12 and 24 weeks. There were three RCTs [20, 21, 28] and two single group intervention studies [31, 36]. Two [20, 31] of the studies were conducted in the United States, one [21] in Turkey, one [28] in Brazil, and one [36] in Australia.

Effect on Primary Outcome

The effect of exercise training on our primary outcome, AHI, was assessed by using two approaches. First, the pre-to postintervention analysis of five studies (six cohorts) showed a pooled estimate of mean change in AHI of −6.27 events/h (95 % CI −8.54 to −3.99; $p < 0.001$) with an I^2=0% (Fig. 2), which reflected a 32 % reduction in AHI from baseline in the intervention groups. Second, a separate analysis of the data from three RCTs showed an AHI reduction of 7.17 (95 % CI −1.86 to −12.48; $p = 0.008$) in favor of the exercise groups, with an $I^2 = 0$ %. This effect corresponded to an improvement in AHI by 42 % following exercise compared with the control treatments (Table 3). The I^2 statistic for these analyses showed no significant heterogeneity.

Effect on Secondary Outcomes

Data for the secondary outcomes of BMI, sleep efficiency, and VO_2 peak were available for five studies (6 cohorts), whereas Epworth Sleepiness Scale data were available for four studies. The analyses showed significant improvements following exercise training for sleep efficiency (5.75 %; 95 % CI 2.47–9.03; $p = 0.001$, $I^2 = 53.29$ %), VO_2 peak (3.93 mL/kg/min; 95 % CI 2.44–5.42; $p < 0.001$, $I^2 = 65.89$ %) and for Epworth Sleepiness Scale scores (−3.3; 95 % CI −5.57 to −1.02; $p = 0.004$,$I^2 = 82.52$ %) but no significant change in BMI (−1.37; 95 % CI −2.81 to 0.07; $p = 0.06$,$I^2 = 76.92$ %). These results are shown in the form of forest plots (Figs. 3, ,4,4, ,5,5, ,6).6). The I^2 statistic for these analyses showed moderate to high heterogeneity. The results corresponded to an improvement of 8 % in sleep efficiency, 24.6 % in VO_2 peak, and 28 % in Epworth Sleepiness Scale scores compared with baseline following intervention. Similar results were obtained from separate analyses of the data from RCTs (Table 3). These results showed that, compared with the controls, there was a significant increase in VO_2 peak and sleep efficiency in the exercise groups, but BMI did not decrease significantly. These effects corresponded to an improvement in VO_2 peak and sleep efficiency by 17.65 and 5.8 % respectively, following exercise compared with the control treatments.

Sensitivity Analysis

Sensitivity analyses, done by systematically removing one study at a time, demonstrated that no single study changed the statistical significance of the overall results.

Publication Bias

The Begg and Mazumdar rank correlation tests of funnel plots for the analyses on AHI, BMI, sleep efficiency, VO_2 peak, and Epworth Sleepiness Scale did not show any publication bias (see Supplementary Material, only funnel plot for data on pre- and post-AHI is provided).

Discussion

Our findings indicate that exercise training has a statistically significant effect on AHI that seems to be independent of changes in BMI. An important finding of our meta-analysis is that the reduction in OSA severity was achieved without a significant reduction in body weight. This suggests a possible role of exercise in the treatment of sleep apnea. Using a pre- to postintervention model and pooling the mean differences in AHI across the studies, we found that exercise training resulted in a mean AHI reduction of 6.27 events/h. Limiting the results to studies that used exercise as the sole intervention and using change scores to calculate the difference in AHI between the cohorts that received exercise as an intervention and the controls, we found a similar reduction in AHI. Our meta-analysis shows that BMI did not change with exercise, but there was a significant improvement in sleep efficiency and daytime sleepiness.

The AHI reduction seen in our meta-analysis seems modest compared with similar meta-analyses that evaluated the effects of dietary weight loss, surgery, oral appliances, and CPAP on OSA severity. Anandam et al. [25], in a meta-analysis of studies on dietary weight loss intervention showed a reduction in AHI by 23.1 events/h (95 % CI 8.9–37.3, $p = 0.001$) corresponding to a 44 % reduction compared with baseline. In another meta-analysis, oral appliances were found to reduce AHI by 12.07 events/h (95 % CI −9.7 to −14.3, $p < 0.01$), suggesting an improvement of 60.25 % postintervention [37]. Finally, Greenburg et al. [38] showed that bariatric surgery reduced AHI by 38.2 events/h (95 % CI 31.9–44.4), possibly suggesting a 71.11 % improvement compared to baseline.

An important finding of our meta-analysis is that the reduction in OSA severity was achieved without a significant reduction in body weight. This is an important distinction, as epidemiologic research estimates that a reduction in body weight of approximately 10 % would be necessary to achieve the 25–30 % reduction in OSA severity that we documented with exercise [7]. Furthermore, complete amelioration of OSA is not necessary to obtain significant health benefits; even modest differences in OSA severity have been associated with significantly reduced risk of adverse health outcomes (e.g., hypertension) [37]. Finally, whereas CPAP and oral appliances are dependent upon nightly use to obtain the effects, evidence indicates that exercise training elicits chronic reduction in the severity of OSA [19].

Besides changes in OSA severity, the improvements in secondary outcomes following exercise training are noteworthy. The improvement in cardiorespiratory fitness has unique health and longevity benefits [39]. Moreover, the improvement in sleep efficiency with exercise is similar to what is typically achieved with CPAP [40, 41]. Likewise, the effects on daytime sleepiness (as measured by the Epworth Sleepiness Scale) with exercise training is similar to that seen with CPAP [42, 43]. Therefore, although based upon a small number of studies, these preliminary findings suggest that the effects of exercise in adults with OSA extend past AHI reduction.

Although converging evidence suggests beneficial effects of exercise training on the severity of sleep apnea, the current body of evidence remains inconclusive on the exact mechanisms of these effects. Different theories have been proposed. An earlier study in canines found increased tone in the genioglossus muscle when the gastrocnemius muscle and sciatic nerve were stimulated [44]. Later, two studies in humans raised some interest in the possible role of strength of respiratory muscles in relation to exercise [31, 45]. However, contrary to this hypothesis, Sengul et al. [21] found no change in the strength of respiratory muscles in OSA patients who received breathing and aerobic exercise training.

Some authors have also suggested that exercise can lead to decreased leg fluid accumulation and, hence, prevent the nocturnal rostral fluid shift that may be implicated in upper airway collapse [46–50]. This mechanism would more likely be associated with a potential acute effect of exercise rather than a training effect, which could nevertheless be important if repeated frequently. However, a recent study by Jafari and Mohsenin [51] casts some doubt on this study, as they found no progressive worsening in OSA despite a demonstrable fluid shift overnight.

Slow wave sleep (SWS) has been found to be associated with decreased severity of sleep apnea [52, 53]. In the study by McSharry et al. [53] this effect was thought to be related to the increased genioglossus single motor unit activity during SWS, making the airway more stable and resistant to collapse. It also is known that exercise training is associated with increased SWS [15]. Is it possible that the effects of exercise on reducing sleep apnea severity could be related to the protective effects of SWS that it induces?. Proving such a relationship in a well designed study would indeed be more insightful. However, it is possible that no single mechanism is responsible and perhaps there is a complex interplay of factors associated with exercise training that leads to improvement in the severity of sleep apnea.

Our meta-analysis has numerous strengths. First, our analysis had enough power to detect an effect of exercise intervention in the included studies. Given a total of 87 participants that received exercise intervention, we estimate that our meta-analysis had a power of 100 % to detect a change in AHI of 12.8 assuming a standard deviation of nine. Second, there was no evidence of publication bias by funnel plots. Third, our sensitivity analyses showed no significant change in the overall statistical significance of the results. Fourth, the analysis for the change in AHI based on the pre- and postintervention effects of exercise showed no significant heterogeneity. Finally, our study showed that significant effects from exercise training occurred despite the fact that studies differed in the mode, frequency, intensity, compliance, and levels of supervision of the exercise interventions.

However, there also are limitations to our study. Most of the studies had a small sample size and the length of intervention in most studies ranged from 12 to 24 weeks. Therefore, this meta-analysis does not address the long-term efficacy of exercise training on OSA severity. With so few studies thus far, it was not possible to evaluate which exercise characteristics were associated with more favorable OSA outcomes. It also is a limitation of our study that the data on secondary outcomes had moderate to high heterogeneity.

In conclusion, our meta-analysis demonstrates that exercise training leads to a significant reduction in AHI, improvement in sleep efficiency, and daytime sleepiness, independent of the effects on BMI. Although the effect size in AHI reduction seems smaller compared with CPAP and oral appliances, exercise training may be an ideal adjunct therapy, especially considering its effects on sleep efficiency and daytime sleepiness. Given the preliminary nature of our findings, RCTs involving a larger number of participants and longer duration of intervention are needed to determine whether the beneficial effects of exercise training in patients with sleep apnea can be sustained over a longer period of time.