Health Psychology

Manuscript version of

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Funded by:

- National Institutes of Health

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Support for Dr. Whited provided by NIH grant K23HL109620. Support for Dr. Waring provided by NIH grants KL2TR000160 and U01HL105268, and support for Dr. Busch was provided by K23HL107391. Support for Dr. Pagoto and Dr. Ma provided by 5R01HL094575 and K24HL124366. The parent study was funded by Dr. Ma's grant 5R01HL094575.

Abstract

Objective: The purpose of this study was to examine if adults with obesity and metabolic syndrome who screen as high risk for OSA lose less weight as part of a weight loss intervention than those who screen as low risk.

Methods: We conducted a secondary analysis of a randomized trial comparing two weight loss interventions consisting of dietary counseling for adults with obesity and metabolic syndrome. Participants were screened for sleep apnea using a validated screening questionnaire. Percent weight loss was calculated from weight measured at baseline and intervention end (12 months). Weight loss of 5% or greater was considered clinically significant. Multivariate linear and logistic regression models estimated the association between OSA screening status (high versus low risk) and percent weight loss and clinically significant weight loss, adjusting for gender, age, education, marital status, baseline body mass index, self-reported sleep duration, and intervention condition.

Results: Nearly half of participants (45.8%) screened at high risk for OSA. Participants who screened at high risk for OSA lost less weight (1.2%$\pm$4.2% vs 4.2%$\pm$5.3%) and were less likely to lose 5% or greater (24.4% vs. 75.6%) than participants without OSA.

Conclusions: Among adults with obesity and metabolic syndrome, those at high risk for OSA lost less weight in response to a dietary counseling intervention than adults with low risk of OSA. Routine OSA screening should be considered as part of weight loss treatment programs. Additional research is needed to determine how to tailor weight loss treatment for those with high risk for OSA.

Keywords: Sleep Apnea, Metabolic Syndrome, Weight Loss, Sleep Disordered Breathing, Metabolic Dysfunction, Dietary Intervention

Obstructive Sleep Apnea and Weight Loss Treatment Outcome among Adults with Metabolic Syndrome

Obstructive sleep apnea (OSA) is a condition in which the airway is obstructed or partially obstructed during sleep resulting in interrupted breathing and partial or full awakenings (Epstein et al., 2009) resulting in poor sleep quality, daytime sleepiness, and dysregulated autonomic function (Mansukhani, Kara, Caples, & Somers, 2014; Trombetta et al., 2010). OSA is also associated with metabolic dysregulation, obesity (Strobel & Rosen, 1996), and cardiovascular disease (Drager, Togeiro, Polotsky, & Lorenzi-Filho, 2013). OSA and obesity are intimately related, as obesity is a principal risk factor for sleep apnea, and treatment of obesity has been shown to improve OSA (Epstein et al., 2009). Obesity increases fatty tissue in the upper airway and abdominal area placing additional weight on the chest and requiring greater muscular effort for inspiration thus increasing the likelihood of sleep disordered breathing (Drager et al., 2013). The effect of additional adipose tissue on breathing difficulty is most evidently observed among adinotonsillectomy patients, as those with obesity show much higher levels of sleep disordered breathing post-operation than lean patients (Mitchell & Kelly, 2007). Obesity is also associated with hormones (i.e., leptin) and inflammatory processes which influence respiratory control (Ong, O'Driscoll, Truby, Naughton, & Hamilton, 2013). Conversely, OSA is independently associated with cardiometabolic risk factors similar to those observed in metabolic syndrome (Drager et al., 2013), and dysregulated appetite hormones (leptin sensitivity and increased ghrelin secretion) (Ong et al., 2013). Most importantly, obesity and OSA additively contribute to cardiometabolic risk factors, and risk for cardiovascular disease (Drager et al., 2013; Trombetta et al., 2010).

Clinical guidelines state that a formal diagnosis of OSA must be made via polysomnography (PSG) and that subsequent treatment involves a combination of weight loss and continuous positive airway pressure (CPAP), which involves a device that uses forced air to keep the airway open during sleep (Epstein et al., 2009). Other treatments (e.g. surgery, oral appliances) may also be utilized if indicated, but it is recommended that CPAP and weight loss are offered to all patients with OSA and obesity. Weight loss has beneficial effects on both OSA (Foster, Borradaile, Sanders, & et al., 2009; Strobel & Rosen, 1996) and the metabolic dysfunctions that accompany obesity (Bassi et al., 2014) indicating a high potential for the beneficial effects of weight loss, especially among individuals with metabolic syndrome. Poorly studied, however, is whether OSA itself causes weight gain and/or interferes with weight loss (Ong et al., 2013). Two studies have documented an increase in weight subsequent to an OSA diagnosis (Phillips et al., 1999; Phillips, Kato, Narkiewicz, Choe, & Somers, 2000). However, no studies have examined whether OSA is associated with poorer weight loss in the context of a weight loss intervention. This knowledge would have clinical implications and could support routine OSA screening and treatment as part of weight loss programs.

Using data from a randomized controlled trial (RCT) of two dietary interventions for weight loss among adults with obesity and metabolic syndrome (Ma et al., 2015), we compared weight loss outcomes among adults who screened at high risk versus low risk for OSA on a validated screening questionnaire. We hypothesized that individuals screening as high risk for OSA would lose less weight during a weight loss intervention than individuals who screen as low risk for OSA.

Methods

The RCT compared two 14 sessions dietary counseling interventions which differed only in the content of the dietary recommendations provided (Ma et al., 2015). Results indicated significant weight loss within each condition, and no significant differences in weight loss between conditions (Ma et al., 2015). The STOP (Snoring, Tiredness during the day, Observed apnea, and high blood Pressure) questionnaire (Chung et al., 2008) was added to the baseline assessment partway through enrollment. Of the 240 RCT participants, all 175 participants enrolled after the addition of the STOP questionnaire were screened for OSA. Procedures were approved by the University of Massachusetts Medical School Review Board. Participants provided written informed consent prior to completing the following measures.

Assessment of Obstructive Sleep Apnea

The STOP questionnaire, (Chung et al., 2008) a four-item scale assessing snoring, tiredness, observation of halted breathing by others, and high blood pressure (or treatment for it), was used to screen for OSA. The STOP questionnaire has acceptable validity in identifying participants with OSA compared to the apnea-hypopnea index derived from PSG (Chung et al., 2008). The STOP questionnaire has shown high sensitivity for detecting moderate (74.3%) and severe (79.5%) OSA with poorer and acceptable sensitivity for mild OSA (65.6%) (Chung et al., 2008). Answering "yes" to two or more of the 4 items on the STOP questionnaire indicates high risk for OSA. Participants also reported whether they had been previously diagnosed with OSA. A subset of sequential participants screening as high risk for OSA in the final 20% of the study were also asked whether they had a confirmatory PSG and treatment (type not specified) for their OSA.

Assessment of Anthropometric measurements, Energy Intake, and Physical Activity

All measurements were recorded at baseline and 12 months. Body weight and height were assessed using a calibrated balance scale (Detecto 339 Model scale; Webb City, MO, USA). Percent weight loss at 12 months was calculated. Clinically significant weight loss was defined as losses of 5% or greater of baseline weight. Participants completed 3 telephone 24-hour diet recalls (two weekdays, one weekend day, randomly selected) within a 3-week window surrounding each study visit. Recalls were conducted by unaffiliated dietitians trained in the use of University of Minnesota's Nutrition Coordinating Center's Nutrition Data System for Research software (versions used: NDSR 2008-2012), and also included assessment of physical activity (including occupational, housework, and sport/leisure activities) and sleep/wake times. We calculated average daily energy intake in kilocalories (kcal), minutes of moderate or greater intensity physical activity (all types), and sleep duration (time spent in bed during each 24-hour recall period) to examine as potential covariates.

Statistical Analyses

Chi-square tests or two-sample t-tests were utilized to compare demographic and other characteristics at baseline (age, gender, educational attainment, marital status, baseline body mass index (BMI), caloric intake, physical activity, and sleep duration) in relation to OSA screening status (high vs. low risk). Multiple linear regression analyses examined the relationship between screening status and 12-month percent weight loss. Multivariate logistical regression models estimated the association between OSA screening status and clinically significant weight loss (i.e., 5% or greater at 12 months). We constructed unadjusted regression models and then regression models adjusted for gender, education, marital status, sleep duration, age, baseline BMI, and treatment condition.

Results

Of the 175 participants who were administered the STOP questionnaire, we excluded 2 participants with missing data on the STOP questions, resulting in an analytic sample of 173 adults with obesity and metabolic syndrome. Among this sample, OSA screening status was not associated with the likelihood of completing the 12-month assessment [odds ratio (OR = 1.5, 95% confidence interval (CI): 0.7, 3.3], nor was OSA status associated with number of treatment sessions attended [regression coefficient (β) = 0.3, 95% CI: -0.9, 1.5]. The majority (82.1%) of participants had available weight data at both baseline and 12 months and data for all covariates resulting in an analytic sample of 142 (age M=53.3 years, SD=9.1 years; gender=76% female; BMI M=34.8 kg/m^2, SD=3.0 kg/m^2).

Nearly half of participants (45.8%) screened as high risk for OSA. Of those screened as high risk, thirty participants (21.1%) self-reported a prior OSA diagnosis;. Only baseline BMI differed by OSA status (Table 1). Adults that screened as high risk for OSA had higher baseline BMI than those that screened as low risk (p=0.04).

Participants screening as high risk for OSA lost significantly less weight at 12 months (1.2% SD=4.2%) than participants who screened as low risk (4.2%, SD=5.3%; β = -2.9%, 95% CI: -4.5%, -1.3%). Results were similar in the adjusted model (β = -2.7%, 95% CI: -4.4%, -1.0%). Adults who screened as high risk for OSA were less likely to achieve 5% or greater weight loss (n=10, 24.4% vs. n=31, 75.6%; unadjusted OR = 0.3, 95% CI: 0.1, 0.7; adjusted OR = 0.3, 95% CI: 0.1, 0.6). Five participants self-reported an OSA diagnosis, but screened as low risk, so we repeated the above analyses excluding these participants and significant results remained for both percent weight loss (β = -2.5%, 95% CI: -4.2%, -0.7%) and proportion reaching 5% weight loss goal (OR = 0.3, 95% CI: 0.1, 0.8). Twenty-four participants reported currently undergoing some type of OSA treatment; of these, the 4 screening as low risk lost an average of 6.5% weight

(SD=4.2%), and the 20 participants who screened as high risk for OSA lost an average of 0.6% (SD=3.6%).

Discussion

Among adults with obesity and metabolic syndrome participating in a weight loss intervention consisting of dietary counseling, nearly half screened as high risk for OSA. Participants who screened as high risk for OSA achieved less than one-third the weight loss as those who screened as low risk for OSA, and were 70% less likely to achieve a clinically significant 5% weight loss. Results suggest that an OSA screening indicating high risk identifies individuals who will struggle to lose weight when participating in a weight loss intervention despite equal attendance at treatment sessions and study assessments. Findings of this study suggest that OSA is a significant barrier to weight loss. While we found that participants reporting current OSA treatment had greater weight loss (6.5% vs. 0.6%), the small sample of individuals receiving OSA treatment (n=24) precluded statistical comparison.

Whether routine OSA screening, PSG-derived diagnosis, and subsequent OSA treatment should be routinely implemented to enhance weight loss treatment success must be considered in light of two studies suggesting that concurrent CPAP use does not enhance weight loss treatment (Chirinos et al., 2014; Kajaste, Brander, Telakivi, Partinen, & Mustajoki, 2004). These studies, however, either did not report CPAP adherence rates (Kajaste et al., 2004), or had a low threshold for CPAP adherence: 4 hrs/night on $\geq$ 70% of nights (Chirinos et al., 2014). Results of these studies do not contraindicate OSA treatment for individuals undergoing weight loss treatment. However, these studies do suggest that OSA treatment should be recommended for the primary purpose of improving metabolic and cardiovascular risk factors as opposed to enhancing weight loss. Most importantly, these studies did not target individuals with metabolic syndrome,

and improvement of the metabolic dysfunction associated with OSA via direct OSA treatment including CPAP may have more beneficial effects on weight loss among this population than among those with obesity alone. In the current study, nearly all participants who reported receiving OSA treatment screened as high risk on the STOP questionnaire, suggesting that treatment was not successful in eliminating OSA symptoms. Future research should carefully examine adherence to recommended CPAP regimens, and subsequent improvement in OSA symptoms and associated metabolic dysfunction, in order to thoroughly evaluate the impact of OSA treatment on weight loss treatment efficacy.

The current study has several limitations. The study sample was predominantly female and well-educated, which limits generalizability. The STOP questionnaire was only administered in the final 60% of the participants, and engagement in OSA treatment was only assessed in the final 20%. Some participants who reported undergoing treatment screened as high risk on the STOP questionnaire; had we assessed the method of diagnosis, the nature of the treatment, and treatment adherence, we could explain this discrepancy. Implementation of these efficient assessments went smoothly, but the STOP questionnaire is a screening tool and does not replace PSG for identifying the presence and severity of sleep apnea (Chung et al., 2008; Epstein et al., 2009), future research designed to more definitively test our hypotheses is needed. Daytime sleepiness also would have been a preferable covariate to sleep duration. Finally, studies using lifestyle interventions that include both diet and exercise instruction may yield different results.

Conclusion

Screening as high risk for OSA among adults with obesity and metabolic syndrome identified individuals who lost less weight and were less likely to achieve clinically significant weight loss in response to dietary intervention. OSA screening as a standard component of

weight loss interventions has a high potential for usefulness as identified individuals can be targeted for more intense or comprehensive treatment. The benefits of OSA treatment as a standard part of weight loss interventions among individuals with obesity and metabolic syndrome has yet to be determined, and future research must include examination of adherence to both OSA and weight loss intervention components. A thorough understanding of OSA and its effects on weight loss and metabolic risk factors in the context of a weight loss intervention will allow treatment providers to effectively intervene upon individuals with obesity, metabolic syndrome, and OSA to reduce the risk for cardiovascular disease conferred by these comorbid conditions.

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