OBESITY AND SLEEP APNEA

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Obstructive sleep apnea (OSA) is a sleep-related breathing disorder that is characterized by repetitive episodes of complete or partial upper airway obstruction during sleep (1). Obesity is a major health burden that contributes to increased morbidity and mortality. World Health Organisation suggesting that over 600 million people have a body mass index (BMI) $\geq$ 30 kg/m^2. The association between obesity and OSA seems to be bidirectional; obesity itself increases the risk for OSA, but, on the other hand, OSA may also predispose the individual to weight gain. Weight reduction should always be encouraged for people living with obesity, OSAS, and/or sleep disruptions and resources identified to assist patients in choosing a weight loss approach that will benefit them the most. Untreated, OSA is a potentially lethal disease that increases the risk of numerous health complications, including hypertension, congestive heart failure, atrial fibrillation, coronary artery disease, stroke and type 2 diabetes (2,3). Untreated OSA is associated with an increased risk of all-cause and cardiovascular mortality, and this risk can be reduced with effective treatment (4,5).

Obesity is a major health burden that contributes to increased morbidity and mortality. World Health Organisation suggesting that over 600 million people have a body mass index (BMI) $\geq$ 30 kg/m^2 (6). Obesity, specifically central obesity, is very common in patients with OSA who may gain weight more easily than the equally obese without OSA (7). Overweight is considered as the most important risk factor for OSA (8-10), BMI >29 kg/m^2 increases the risk for OSA by 10-fold. It has been estimated that at least two out of every three patients with OSA are obese. The association between obesity and OSA seems to be bidirectional; obesity itself increases the risk for OSA, but, on the other hand, OSA may also predispose the individual to weight gain (11). In OSAS patients, sleep fregmentation associated with decreased leptin levels and increased ghrelin levels, and therefore, with an increase of hunger and appetite (12). It has been reported that it is more difficult to improve OSA by weight reduction than to develop or further deteriorate OSA by more weight gain (13).

Contuinious positive airway pressure (CPAP) significantly improves insulin resistance in non-diabetic patients with moderate to severe OSA, without significant changes in BMI. Compared with fasting blood glucose at baseline, there was no change in glycemic control with CPAP (14). The cornerstone of treatment of overweight patients must be weight reduction by lifestyle changes (healthy eating habits, food behavior therapy if needed and physical activity) and this should be the first-line treatment for all OSA patients. If necessary, bariatric surgery may represent an option in carefully selected patients who are morbid obese. This finding clearly highlights the importance of maintaining normal body weight by providing general information to the public via prevention programs or in the case of individuals who are overweight, committing them to early control of their condition and more active treatment of their obesity (15).

In Sleep AHEAD (Action for Health in Diabetes) study assessing the effect of weight loss through an intensive life style intervention (ILI), it was found that greatest benefit was observed in men, with more severe OSA at baseline, and in participants who lost the most weight (16). In this study, ILI group had significantly greater reductions in weight and AHI than did the diabetes support and education (DSE) group after 1 year. (16). Four years after that study, , the significant improvement in OSA severity among obese patients with type 2 diabetes and OSA achieved following 1 year of an ILI was maintained at 4 year despite a 50% weight regain over that period (17).

The global epidemic of obesity is no doubt associated with consequent increased prevalence of OSA, which may often be present even in nonsleepy individuals (18). Also abnormalities in neck soft tissue mass is a risk factor for OSA. OSA is associated with both growth hormone (GH) excess and severe GH deficiency in adults. Peker et al, showed that GH therapy does not induce or aggravate OSA in GH-deficient adults (19). In a more recent study of same group, GH treatment increased the severity of OSA in men with abdominal obesity without any effect on subjective daytime sleepiness possibly by GH-induced increase of neck volume (20).

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European Sleep Apnea Database (ESADA) registry suggested that PAP therapy was not associated with systematic weight change in a general clinical sleep laboratory cohort. However, weight gain was seen in a pre-dominantly non-obese subgroup, while there was a modest weight reduction in obese patients under PAP therapy (21).

The major findings of Wong et al meta-anaysis were that in OSA patients: a) bariatric surgery (regardless of type) can lead to substantial weight loss, significant reductions in OSA severity, as well as considerable improvement in daytime sleepiness (assessed using the ESS), b) surgical weight loss is more effective in reducing both AHI and BMI when compared to non-surgical weight loss strategies, c) higher baseline AHI and BMI, as well as a longer duration of follow-up, are associated with greater reductions in weight and AHI, d) there is no relationship between the amount of weight lost and the improvement in AHI, e) a significant proportion of patients still had residual OSA post-surgery despite improvements in clinical symptoms (22).

In a network metaanalysis synthesizing evidence from available studies comparing the efficacies of supervised aerobic exercise training, dietary weight loss, mandibular advancement devices (MADs), and CPAP in the treatment of sleep apnea, authors found that CPAP is the most efficacious in complete resolution of sleep apnea and in improving the indices of saturation during sleep. While MADs offer a reasonable alternative to CPAP, exercise training which significantly improved daytime sleepiness (ESS) could be used as adjunctive to the former two (23).

Weight reduction should always be encouraged for people living with obesity, OSAS, and/or sleep disruptions and resources identified to assist patients in choosing a weight loss approach that will benefit them the most (24). The literature has shown that bariatric surgery has a significant effect on sleep apnoea, inducing resolution or improvement in the majority of cases (25-28).

Bariatric surgery is an effective treatment for OSA, but it is impossible to predict which patients will have persisting symptoms. Bariatric surgery should be at least kept in mind while treating severely or morbidly obese OSA patients. As generally in obesity treatment, multidisciplinary collaboration is needed. Also more long-term follow-up studies are needed to investigate the recurrence rate of OSA after bariatric operations. The number of bariatric operations is constantly increasing, and in 2013 nearly 469,000 bariatric operations were
performed worldwide (29).

REFERENCES

1. American Academy of Sleep Medicine. *International Classification of Sleep Disorders*. 3rd ed. Darien, IL: American Academy of Sleep Medicine; 2014.
2. Punjabi NM. The epidemiology of adult obstructive sleep apnea. *Proc Am Thorac Soc*. 2008;5(2):136–143.
3. Peker Y, Franklin K, Hedner J. Coronary artery disease and sleep apnea. In: Kryger MH, Roth TT, Dement WT, eds. Principals and Practice of Sleep Medicine. 6th Edn. Philadelphia, Elsevier, 2017; pp. 1264–1270. 2
4. Peker Y, Thunström E, Glantz H, Wegscheider K, Eulenburg C. Outcomes in coronary artery disease patients with sleepy obstructive sleep apnoea on CPAP. Eur Respir J. 2017 Dec 7;50(6)
5. Young T, Finn L, Peppard PE, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *Sleep*. 2008;31(8):1071–1078.
6. Obesity and overweight. World Health Organisation (WHO); 2016
7.Phillips BG, Hisel TM, Kato M, Pesek CA, Dyken ME, Narkiewicz K, Somers VK (1999) Recent weight gain in patients with newly diagnosed obstructive sleep apnea. J Hypertens 17:1297–1300
8.Wolk R, Shamsuzzaman AS, Somers V. Obesity, sleep apnea, and hypertension. Hypertension 2003;42:1067-74.
9. Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. JAMA 2004;291:2013-6.
9. Young T, Peppard P, Shahrad T. Excess weight and sleep-disordered breathing. J Appl Physiol 2005;99:1592-9
11. Pillar G, Shehadeh N. Abdominal fat and sleep apnea: the chicken or the egg? Diabetes Care 2008;31:303-9
12 Spiegel K, Tasali E, Penev P, Van Cauter E. Sleep curtailment in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. Ann Intern Med 2004;141:846-50.
13.Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disorders breathing with changes in weight. Arch Intern Med 2005;165:2408-13
14. Yang D, Liu Z, Yang H, Luo Q. Effects of continuous positive airway pressure on glycemic control and insulin resistance in patients with obstructive sleep apnea: a meta-analysis. Sleep Breath. 2013 Mar;17(1):33-8
15. Uusitupa M, Tuomilehto J, Puska P. Are we really active in the prevention of obesity and type 2 diabetes at the community level? Nutr Metab Cardiovasc Dis 2011;21:380-9
16. Foster GD, Borradaile KE, Sanders MH, et al. A randomized study on the effect of weight loss on obstructive sleep apnea among obese patients with type 2 diabetes: the Sleep AHEAD study. Arch Intern Med 2009;169:1619-26.
17. Kuna ST, Reboussin DM, Borradaile KE, Sanders MH, et al. Sleep AHEAD Research Group of the Look AHEAD Research Group. Long-term effect of weight loss on obstructive sleep apnea severity in obese patients with type 2 diabetes. Sleep. 2013 May 1;36(5):641-649A.
18. Peker Y. Platelet activity and cardiovascular risk in obesity and obstructive sleep apnea: compelling need for interdisciplinary research? J Clin Sleep Med. 2011 Apr 15;7(2):179-8
19. Peker Y, Svensson J, Hedner J, Grote L, Johannsson G. Sleep apnoea and quality of life in growth hormone (GH)-deficient adults before and after 6 months of GH replacement therapy. Clin Endocrinol (Oxf) 2006;65:98-105. 1
20. Karimi M, Koranyi J, Franco C, Peker Y, Eder DN, Angelhed JE, Lönn L, Grote L, Bengtsson BA, Svensson J, Hedner J, Johannsson G. Increased neck soft tissue mass and worsening of obstructive

sleep apnea after growth hormone treatment in men with abdominal obesity. J Clin Sleep Med. 2010 Jun 15;6(3):256-63
21. Basoglu OK, Zou D, Tasbakan MS, et al. Change in weight and central obesity by positive airway pressure treatment in obstructive sleep apnea patients: longitudinal data from the ESADA cohort. J Sleep Res 2018:e12705
22. Wong AM, Barnes HN, Joosten SA, Landry SA, Dabscheck E, Mansfield DR, Dharmage SC, Senaratna CV, Edwards BA, Hamilton GS. The effect of surgical weight loss on obstructive sleep apnoea: A systematic review and meta-analysis. Sleep Med Rev. 2018 Jun 19. pii: S1087-0792(18)30020-0
23.ImranH. Iftikhar, Lia Bittencourt, ShawnD. Youngstedt, Najib Ayas, Peter Cistulli, Richard Schwab, Martin,W.Durkin, Ulysses J. Magalang. Comparative efficacy of CPAP, MADs, exercise-training, and dietary weight loss for sleep apnea: a network meta-analysis Sleep Medicine, Volume 30, 2017; 7-14

24. Xanthopoulos MS, Berkowitz RI, Tapia IE. Effects of obesity therapies on sleep disorders. Metabolism. 2018 Jul;84:109-117.

25. Valencia-Flores M, Orea A, Herrera M et al. Effect of bariatric surgery on obstructive sleep apnea and hypopnea syndrome, electro-cardiogram, and pulmonary artrial pressure. Obes Surg 2004;14:755-62.

26. Haines KL, Nelson LG, Gonzalez R et al. Objective evidence that batiatric surgery improves obesity-related obstructive sleep apnea. Surgery 2007;141:354-8.

27. Guardiano SA, Scott JA, Ware JC et al. The long-term results of gastric bypass on indexes of sleep apnea. Chest 2003;124:1615-9. 10.

28. Rao A, Tey BH, Ramalingam G et al. Obstructive sleep apnea patterns in bariatric surgical practice and response of OSA to weight loss after laparoscopic adjustable gastric banding. Ann Acad Med Singapore 2009;38:587-93.

29. Angrisani L, Santonicola A, Iovino P, et al. Bariatric surgery worldwide 2013. Obes Surg 2015;25(10):1822-32.