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Continuous positive airway pressure to improve insulin resistance and glucose homeostasis in sleep apnea

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Abstract

Obstructive sleep apnea syndrome (OSAS) is a relatively common disorder in the adult population. It is associated with alterations in glucose metabolism and increases the risk for diabetes mellitus. Continuous positive airway pressure (CPAP) is the treatment of choice for OSAS. It may also have a favorable effect on insulin resistance and glucose metabolism, although relevant data is conflicting. Additional research is still needed to fully establish the effect of CPAP on glucose homeostasis. It should ascertain which patients may benefit most and how long treatment takes to induce favorable changes. Finally, patient compliance is being appreciated as a major factor influencing therapeutic outcomes, and this needs to be further examined.

Key words: Continuous positive airway pressure; Diabetes mellitus; Glucose homeostasis; Obstructive sleep apnea syndrome

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INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a common disorder affecting approximately 3%-7% of adult men and 2%-5% of adult women in the general population[1]. OSAS is characterized by repeated episodes of complete or partial obstruction of the upper airway during sleep and is being increasingly recognised as an important cause of morbidity and mortality[1]. The main symptoms of OSAS are nocturnal respiratory pauses interrupted by loud snoring and excessive daytime sleepiness. Rapidly accumulating data from both epidemiological and clinical studies suggest that OSAS is independently associated with alterations in glucose metabolism and that it places patients at an increased risk for the future development of type 2 diabetes[2,3].

CONTINUOUS POSITIVE AIRWAY PRESSURE TO TREAT OSAS

Continuous positive airway pressure (CPAP) is the treatment of choice for OSAS[4]. It has proven to be efficacious in eliminating obstructive respiratory events during sleep and in improving sleep architecture, daytime sleepi-

Table 1 Summary of the 3 randomised controlled trials which examined the role of continuous positive airway pressure on glucose homeostasis

Author	Patients	Duration	Methods	Results
Lam *et al*[10]	61	1 wk 12 wk	Short insulin tolerance test	Increase in insulin sensitivity after 1 wk of CPAP use. Further improvement after 12 wk in subjects with BMI < 25 kg/m^2
West *et al*[11]	42	3 mo	Hyperinsulinemic euglycemic clamp, HOMA index, HbA_{1C}	No difference after 3 mo of APAP use
Coughlin *et al*[12]	24	6 wk	Fasting glucose, insulin, HOMA index	No difference

CPAP: continuous positive airway pressure; APAP: automatic positive airway pressure; BMI: body mass index; HbA_{1c}: haemoglobin A_{1c}.

ness and quality of life[5,6]. CPAP is commonly used to treat OSAS by delivering a constant pressure throughout inspiration and expiration to maintain upper airway patency during sleep. It consists of a flow generator that delivers airflow at a constant pressure to the patient through a mask via a tubing system. CPAP technology has improved considerably over the years. This technological progress notwithstanding, patient adherence to CPAP treatment remains suboptimal and its use during sleep time shows substantial variation between patients[7].

CONTINUOUS POSITIVE AIRWAY PRESSURE: ITS ROLE IN GLUCOSE HOMEOSTASIS

Not only is CPAP the established treatment for OSAS, it may also have a favorable effect on insulin resistance and glucose metabolism in such patients. It has been postulated that CPAP can ameliorate intermittent hypoxia and sympathetic overactivation, both pathophysiological mechanisms responsible for the impaired glucose metabolism in OSAS patients. This additional therapeutic benefit conferred by CPAP is now attracting considerable interest but is still an issue of ongoing debate[8]. Indeed, findings from numerous studies on the effect of CPAP treatment on glucose metabolism, both in diabetic and non-diabetic populations, have been rather conflicting. This can be attributed to differences between the studied populations (i.e. diabetic, non-diabetic, obese or non-obese patients), the primary outcomes, the method of assessment of glucose metabolism (i.e. fasting glucose, glycated hemoglobin, hyperinsulinemic euglycemic clamp *etc*.), the period of CPAP application (ranging between 1 night and 2.9 years)[8] and the patient's adherence to CPAP use[9]. Unfortunately, only three randomised control studies have so far examined the effect of CPAP on different parameters of glucose metabolism[10-12] and only one, the most recent, has shown a favorable effect.

The latter[10] demonstrated an increase in insulin sensitivity among the 31 patients with moderate/severe OS AS who received CPAP treatment, as opposed to no improvement among the 30 controls receiving sham CPAP. An additional improvement was also recorded after 12 wk of CPAP use in subjects with body mass index exceeding 25 kg/m^2[10]. The authors have used the short insulin tolerance test, a rapid and simple test that has been validated against clamp studies[13] and whose short duration inhibits interference from counter regulatory hormones[14]. Additional strengths of the study include good CPAP adherence and exclusion of OSA patients with comorbidities, a fact that allows a clear delineation of the impact of OSA per se on glucose metabolism.

Conversely, two further randomised control studies indicate that CPAP treatment does not improve glucose metabolism. The first one by West *et al*[11] compared 20 OSAS patients receiving automatic positive airway pressure (APAP) therapy with 22 OSAS patients receiving sham therapy for 3 mo (Table 1). All patients were male with established type 2 diabetes mellitus. There was no significant change in haemoglobin A_{1C} (HbA_{1c}), insulin sensitivity assessed by euglycemic clamp and HOMA in either group[11]. Even after excluding 8 patients with poor compliance, changes remained insignificant[11]. The other study by Coughlin *et al*[12] was a randomised placebo-controlled blinded cross-over trial, comparing 6 wk of therapeutic and sham CPAP in 34 obese OSAS patients. No change occurred in fasting glucose and insulin levels or insulin resistance, as assessed by HOMA[12]. Nonetheless, it should be borne in mind that the study period was rather short. Indeed, the authors themselves queried whether a prolonged longer study period would be necessary to reveal significant changes[12].

Clearly, the role of CPAP in the improvement of glucose metabolism and insulin sensitivity has not been defined yet[8]. Results are conflicting which may be explained by the differences in recruited populations (diabetic or non-diabetic), adherence to CPAP use, as well as in study design (duration of follow-up) and endpoints (different parameters of insulin resistance and glucose homeostasis)[8]. In addition, other issues such as the role of diet and exercise should always be addressed.

CONCLUSIONS AND FUTURE DIRECTIONS

In the light of current knowledge, further research therefore needs to revisit the effect of CPAP on glucose homeostasis[8]. It is important to define which patients stand to benefit and how long the treatment takes to produce favorable changes. Moreover, the magnitude of the effect needs to be re-evaluated in terms of quantifying the

changes in insulin sensitivity, fasting and post-prandial glucose levels and HbA_{1c}. These issues should be addressed by large-scale, long-term, randomised controlled trials. In the authors' opinion, the accumulating evidence for a positive effect of CPAP on glycemic control is very promising and warrants careful attention. It has recently been realised that OSAS aggravates glycemic control, even at the earliest stages of glucose intolerance[15], opening rich perspectives for application of CPAP. Patient health care is anticipated to have improved by 2020 and physicians will be able to make better and more individualised use of CPAP to affect favorable changes in glucose homeostasis, targeting both hypoxia and hyperglycemia.

REFERENCES

1 **Punjabi NM**. The epidemiology of adult obstructive sleep apnea. *Proc Am Thorac Soc* 2008; **5**: 136-143
2 **Lévy P**, Bonsignore MR, Eckel J. Sleep, sleep-disordered breathing and metabolic consequences. *Eur Respir J* 2009; **34**: 243-260
3 **Spiegel K**, Tasali E, Leproult R, Van Cauter E. Effects of poor and short sleep on glucose metabolism and obesity risk. *Nat Rev Endocrinol* 2009; **5**: 253-261
4 **Malhotra A**, Ayas NT, Epstein LJ. The art and science of continuous positive airway pressure therapy in obstructive sleep apnea. *Curr Opin Pulm Med* 2000; **6**: 490-495
5 **Giles TL**, Lasserson TJ, Smith BH, White J, Wright J, Cates CJ. Continuous positive airways pressure for obstructive sleep apnoea in adults. *Cochrane Database Syst Rev* 2006; **3**: CD001106
6 **Gordon P**, Sanders MH. Sleep.7: positive airway pressure therapy for obstructive sleep apnoea/hypopnoea syndrome. *Thorax* 2005; **60**: 68-75
7 **Weaver TE**, Kribbs NB, Pack AI, Kline LR, Chugh DK, Maislin G, Smith PL, Schwartz AR, Schubert NM, Gillen KA, Dinges DF. Night-to-night variability in CPAP use over the first three months of treatment. *Sleep* 1997; **20**: 278-283
8 **Steiropoulos P**, Papanas N, Nena E, Maltezos E, Bouros D. Continuous positive airway pressure treatment in patients with sleep apnoea: does it really improve glucose metabolism? *Curr Diabetes Rev* 2010; **6**: 156-166
9 **Steiropoulos P**, Papanas N, Maltezos E, Bouros D. Is there a metabolic effect of continuous positive airway pressure in sleep apnoea? Adherence should not be underestimated. *Eur Respir J* 2009; **34**: 1209-1210; author reply 1210-1211
10 **Lam JC**, Lam B, Yao TJ, Lai AY, Ooi CG, Tam S, Lam KS, Ip MS. A randomised controlled trial of nasal continuous positive airway pressure on insulin sensitivity in obstructive sleep apnoea. *Eur Respir J* 2010; **35**: 138-145
11 **West SD**, Nicoll DJ, Wallace TM, Matthews DR, Stradling JR. Effect of CPAP on insulin resistance and HbA1c in men with obstructive sleep apnoea and type 2 diabetes. *Thorax* 2007; **62**: 969-974
12 **Coughlin SR**, Mawdsley L, Mugarza JA, Wilding JP, Calverley PM. Cardiovascular and metabolic effects of CPAP in obese males with OSA. *Eur Respir J* 2007; **29**: 720-727
13 **Bonora E**, Moghetti P, Zancanaro C, Cigolini M, Querena M, Cacciatori V, Corgnati A, Muggeo M. Estimates of in vivo insulin action in man: comparison of insulin tolerance tests with euglycemic and hyperglycemic glucose clamp studies. *J Clin Endocrinol Metab* 1989; **68**: 374-378
14 **Wallace TM**, Matthews DR. The assessment of insulin resistance in man. *Diabet Med* 2002; **19**: 527-534
15 **Steiropoulos P**, Papanas N, Bouros D, Maltezos E. Obstructive sleep apnea aggravates glycemic control across the continuum of glucose homeostasis. *Am J Respir Crit Care Med* 2010; **182**: 286

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