Sleep apnea and diabetes – a complex relationship

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AIMS

- To provide an overview of the association of sleep apnea (with focus on obstructive sleep apnea, OSA) and diabetes mellitus, DM (with focus on type 2 DM)
- Explore the update evidence for an independent detrimental role of OSA on glucose homeostasis of subjects who do not yet have diabetes
- Explore the update evidence for a detrimental effect of untreated OSA on glycemic control with diabetes mellitus and on clinical outcomes of DM
- Summarise the current state of knowledge and suggest points of note in clinical management

SUMMARY

Introduction

Obstructive sleep apnea (OSA) and glucose intolerance/type 2 diabetes mellitus often co-exist due to the common risk factor of obesity. Glucose regulation is closely linked to tissue response to insulin (insulin sensitivity/resistance) and insulin secretion from pancreatic beta-cells. Insulin resistance is a harbinger of type 2 diabetes mellitus, but frank diabetes only develops when compensatory insulin secretion is insufficient to maintain glucose homeostasis. There is also a phase of prediabetes. OSA is postulated to cause or aggravate impaired glucose-insulin regulation through induction of neurohumeral activation, oxidative stress and inflammation, with variable degree of evidence supporting the role of such mediating mechanisms, while there is much less research on the opposite direction of causality.

In the discussion of diabetes mellitus, it is worthwhile to note the close relationship of diabetes mellitus (or insulin resistance) as one of the core components of metabolic syndrome, alongside central obesity, hypertension and dyslipidemia. The contribution of obesity in the relationship between sleep apnoea and diabetes mellitus is difficult to dissect completely.

Association between OSA and a spectrum of glucose abnormalities:

It is important to understand the tools for assessment of glucose metabolism in critical appraisal of literature.

A number of population-based studies have shown positive and independent association between prevalence or severity of sleep disordered breathing and various indicators of adverse glucose metabolism, including insulin resistance or impaired insulin sensitivity, glucose intolerance and type 2 diabetes on cross-sectional analysis. Most clinical studies have also identified an independent association between OSA and adverse glucose metabolism, despite adjustments for known confounding factors.
Some but not all studies show a dose-dependent effect of severity of OSA on the prevalence and/or severity of insulin-glucose abnormalities. Several, though not all, longitudinal cohorts in the community or clinics show that baseline OSA is associated with incident diabetes. There is also recent evidence to suggest that OSA or experimental intermittent hypoxia in healthy subjects may impair insulin secretion.

**Association between OSA and type 2 DM:**

Studies of subjects with type DM have demonstrated a high prevalence of OSA, ranging from 10% to more than 70%, substantially higher than that in the corresponding general community population. Vice versa, subjects presenting with OSA at the sleep clinic not uncommonly have previously undiagnosed prediabetes or diabetes.

There is less data on the association of OSA and type 1 DM, but one study showed that about 10% of non-obese type 1 DM subjects suffer from moderate OSA, postulated to be due to autonomic neuropathy.

**Impact of Treatment of OSA on glucose metabolism in diabetics and non-diabetics:**

Studies have evaluated the impact of treatment of OSA on glucose metabolism in non-diabetic subjects as well as diabetic subjects. Interventional studies of CPAP treatment of OSA were mostly observational in nature, and have yielded conflicting results on measures of insulin-glucose metabolism in non-diabetic subjects or glycemic control in diabetics. Although there is evidence supporting that glucose metabolism is improved in the short term (1-2 weeks) of OSA treatment in non-diabetics or prediabetes, evidence from randomized controlled trials conducted over 3-6 months in either DM or subjects without DM have not been consistent. The discrepancy in results may be attributed to the multiple endogenous and environmental determinants of diabetes and glycaemic status which may overwhelm or mask any positive impact of OSA control. Consistent adherence to CPAP may not be easily achievable over long term in large groups of subjects, thus hindering proper evaluation of effectiveness. The severity and duration of diabetes may also affect any potential modification of glucose metabolism by treatment of OSA.

Hence, despite suggestive data of a detrimental effect of OSA on glucose metabolism, there are many unknowns and uncertainties which require much more rigorous and definitive research evidence.

In diabetes, presence of OSA may produce adverse effect on microvascular or macrovascular diabetic complications, and there is emerging interest in the study of potential detrimental impact of OSA on diabetic nephropathy, hypertension, retinopathy etc.

In terms of clinical management, it is important to be aware of the high co-existence of both OSA and DM. Looking for OSA is recommended in updated guidelines for the management of diabetes mellitus, while screening for glucose intolerance or diabetes is easily achievable. The identification of metabolic syndrome is useful for holistic healthcare. Both OSA and DM require its own appropriate treatment, while weight reduction in the obese and other lifestyle measures where relevant should benefit both diseases.

**SELECTED READING**


