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Original Article

Continuous positive airway pressure and diabetes risk in sleep apnea patients: A systemic review and meta-analysis

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ABSTRACT

Background: The study assessed the effect of continuous positive airway pressure (CPAP) therapy on the risk of developing type 2 diabetes by evaluating change in the homeostasis model assessment of insulin resistance (HOMA-IR) fasting blood glucose (FBG) and fasting insulin following CPAP treatment in non-diabetic patients and pre-diabetic with obstructive sleep apnea (OSA).

Methods: Medline, PubMed, Cochrane, and EMBASE databases were searched until August 24, 2015. The analysis included randomized controlled trials (RCTs), two arm prospective studies, cohort studies, and retrospective studies. The primary outcome measure was change of HOMA-IR in pre-diabetic patients receiving CPAP treatment.

Results: Twenty-three studies were included with 965 patients who had OSA. Nineteen studies were prospective studies and four were RCTs. CPAP therapy resulted in a significant reduction in the pooled standard difference in means of HOMA-IR (-0.442, $P = 0.001$) from baseline levels compared with the control group. Change in FBG and fasting insulin from baseline levels was similar for the CPAP and control groups. For RCT studies ($n = 4$), there was no difference in change in HOMA-IR or FBG levels from baseline between CPAP and control groups. The combined effect of RCTs showed that CPAP was associated with a significant reduction in change from baseline in fasting insulin than the control group (standardized diff. in means between groups $= -0.479$, P value $=$ 0.003).

Conclusion: These findings support the use of CPAP in non-diabetic and pre-diabetic patients with OSA to reduce change of HOMA-IR and possibly reduce the risk of developing type 2 diabetes in this patient population.

1. Introduction

Obstructive sleep apnea (OSA) is a prevalent disorder characterized by repetitive upper-airway obstruction during sleep resulting in intermittent hypoxia and fragmentation of sleep. Approximately 9% of women and 24% of men are affected by OSA [1]. In the adult population, OSA is an independent risk factor for development of type 2 diabetes [2–7]. Cross-sectional epidemiologic studies and cohort and clinical studies found an association between OSA and deterioration in glycemic control, insulin resistance, and metabolic syndrome [6–15]. OSA is present in patients with type 2 diabetes, ranging from 58% to 77% [10], and there is some evidence of a direct relationship of OSA and the risk of developing the disease [3,7]. Intermittent hypoxia and sleep fragmentation induced by OSA may cause disorders in various systems, such as the sympathetic nervous system, oxidative stress reactions, systemic inflammation, hormone system that regulate appetite, and the hypothalamic–pituitary–adrenal axis, which in turn contribute to the development of insulin resistance, poor blood glucose control, and increase the risk of type 2 diabetes [16].

Continuous positive airway pressure (CPAP) is the primary treatment for OSA, which reduces hypoxia and improve subjective sleep quality [17,18]. However, prior studies investigating whether CPAP can improve insulin resistance of glucose control in OSA patients have resulted in conflicting findings. Some work found CPAP treatment resulted in a significant reduction in HbA1c and improvement in glycemic control [13,14,19–21], while other studies found no effect of CPAP on diabetes-related outcomes [22–26]. Similarly, some but not all studies, found CPAP therapy improved insulin sensitivity [14,19,21–23,26–28]. Three previous meta-analyses have investigated the effect of CPAP on measures of glycemic control and insulin resistance in patients who did not have type 2 diabetes [6,28,29]. Among those studies, two meta-analyses found CPAP was associated with improved homeostasis model assessment of insulin resistance (HOMA-IR) [6,29]. However,

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another article reported no change in insulin resistance following CPAP therapy [28]. Consequently, it is currently unclear if CPAP-therapy can have therapeutic benefit for preventing type 2 diabetes in patients with OSA. In this meta-analysis, we included both prospective and retrospective studies to evaluate whether CPAP treatment improved insulin resistance and sensitivity in non- or pre-diabetic patients with OSA treated with CPAP.

2. Material and methods

2.1. Search strategy

The study was performed in accordance with the PRISMA guidelines. Medline, PubMed, Cochrane, and EMBASE databases were searched until August 24, 2015 using the following terms: sleep apnea AND obstructive AND (continuous Positive Airway Pressure OR CPAP) AND (Diabetes Mellitus OR Insulin Resistance OR insulin sensitivity). Randomized controlled trials (RCTs) and prospective studies were included. Eligible studies had to include patients without diabetes or who were pre-diabetic. Based on the American Diabetes Association criteria, patients who met the impaired fasting glucose (IFG) (fasting plasma glucose of 100–125 mg/dL), impaired glucose tolerance (2-hour plasma glucose of 140–199 mg/dL), and/or HbA1c value ranged from 5.7 to 6.4% were diagnosed as pre-diabetes [30]. In included studies, data for body mass index (BMI), waist circumference, adiposity evaluation were reported. Patients had to have a diagnosis of OSA by polysomnographic analysis and evaluation of apnea-hypopnea index (AHI). Studies also had to use CPAP for treatment intervention, and specify duration and patient compliance with treatment. Treatment efficacy needed to be evaluated by measurement of SpO2, and biomarkers for type 2 diabetes and metabolic syndrome had to be quantitatively reported before and after CPAP intervention. Studies were excluded if they included patients with type 1 or type 2 diabetes, who had central sleep apnea, or who were already receiving CPAP treatment (therapeutic or sub-therapeutic) prior to start of the specific study. Studies were also excluded if they did not report outcomes of interest quantitatively, or were letters, comments, editorials, case report, proceeding, or personal communications. Two independent reviewers identified studies for inclusion, data extraction, and quality assessment. In cases of uncertainty, a third reviewer was consulted.

2.2. Data extraction and quality assessment

The following information/data were extracted from studies that met the inclusion criteria: the name of the first author, year of publication, study design, number of participants in each group, participants' age and gender, and the major outcomes including the HOMA-IR, fasting blood glucose (FBG), insulin sensitivity index (ISI), and fasting insulin.

The quality of the included studies was evaluated using Cochrane Collaboration's tool for prospective two-arm studies [31] and Modified 18-items Delphi checklist [32] for single-arm studies.

2.3. Outcome measures

The primary outcome measures were changes of HOMA-IR from baseline in pre-diabetic and non-diabetic patients receiving CPAP treatment. Secondary outcome included change in FBG and fasting insulin from baseline after CPAP treatment.

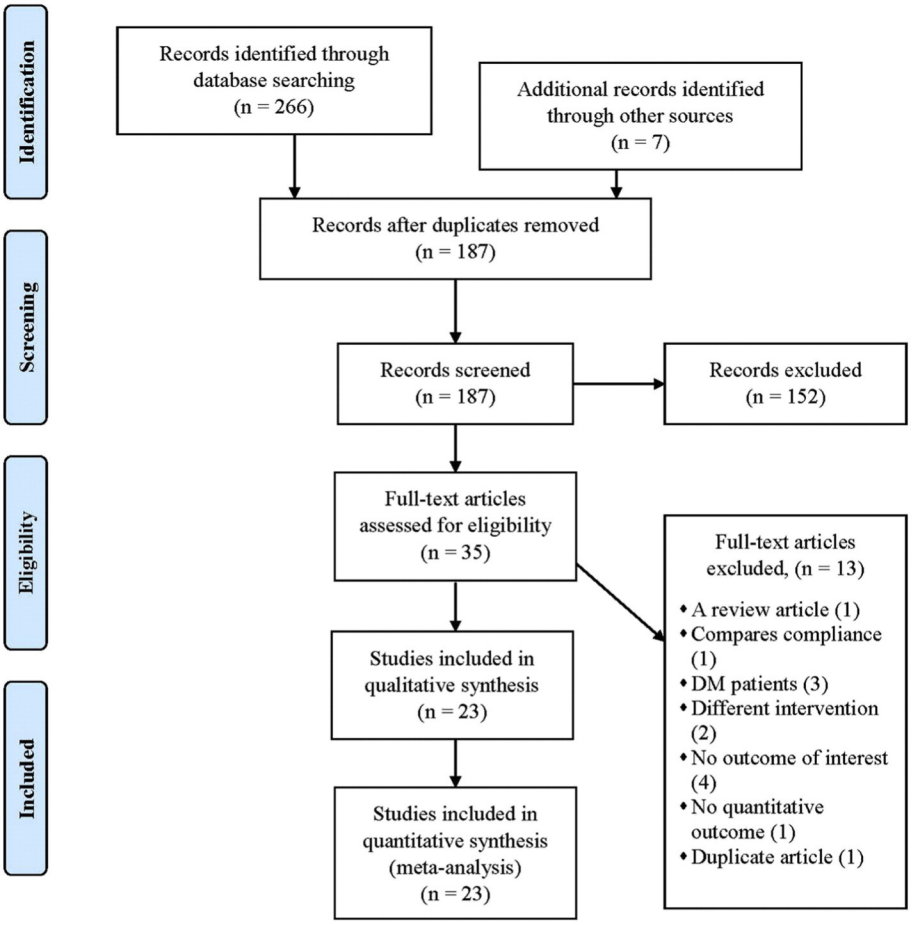

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

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