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The correlation between obstructive sleep apnea and diabetic neuropathy: A meta-analysis

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ABSTRACT

Background: The aim of this study was to explore the correlation between obstructive sleep apnea (OSA) and diabetic neuropathy.

Materials and methods: After working out searching strategy, literatures were screened from the electronic databases: PubMed, Embase, and the Cochrane library. R 3.12 was utilized to perform meta-analysis, and odds ratio (OR) and its 95% confidence interval (CI) were used to present effect size. Heterogeneity was assessed by χ^2-based Q test and I^2 statistics. Publication bias was estimated by Egger's test and sensitivity was evaluated by leave one out methods.

Results: According to the criteria, a total of 11 studies with 1842 patients were enrolled in this study. With a significant heterogeneity (Q = 31.83, I^2 = 68.60%), the random effects model was utilized to assess the effect size of pooled data. A remarkable correlation was identified OSA and diabetic neuropathy (OR = 1.84, 95% CI: 1.18–2.87) without publication bias (t = 1.68, P = 0.13). Meanwhile, the result of leave one out performed a well sensitivity. Moreover, the subgroup analyses presented that OSA was significantly correlated with type 1 diabetic neuropathy (OR = 1.97, 95% CI: 1.19–3.25), but no remarkable correlation was identified between OSA and type 1 (OR = 1.84, 95% CI: 0.86–3.93) or 1 + 2 (OR = 1.30, 95% CI: 0.43–3.92) diabetic neuropathy.

Conclusion: OSA was significantly correlated with neuropathy in type 1 diabetes, but not in type 2 and type 1 + 2 diabetes.

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1. Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder disease, which is characterized by recurrent partial (hypopnea) or complete (apnea) obstruction of the upper airway [1]. These obstructions will lead to an increased sleep fragmentation, a decline oxygen saturation, and a reduction in airflow companied with loud snoring [2]. Sydrome of OSA is considered as the independent risk factor for a series of cardiovascular disease, including coronary artery disease, systemic arterial hypertension, cerebral vascular events and so on [3]. Moreover, it is also reported that OSA also can lead to on the cognitive disorder [4], metabolism dysfunction [5], and even early mortality [6]. Previous studies had reported that 5–15% adults were suffered with OSA worldwide [7]. However, the management of OSA is still unsatisfied in clinic. Continuous positive airway pressure is an effective therapy to OSA, but it is often abandoned due to its obstructive nature [8]. Oral appliance therapy is another effective method for the OSA treatment, but it is only available for the mild and moderate syndrome [9]. Therefore, it is essential for us to further reveal OSA in both basic and clinical researches.

Mechanism dysfunction is identified strongly associated with OSA, including diabetes [10]. A number of cross-sectional and observation studies have demonstrated that OSA is independently associated with diabetes, insulin resistance, and glucose intolerance in adults [11–13]. Diabetic neuropathy (DN) is a common commodity of diabetes. More and more researches have demonstrated that DN contributes to the genesis of OSA [14]. Tahrani et al. have documented that OSA is closely related to foot insensitivity and diabetic peripheral neuropathy [15]. Further investigation in small fiber neuropathy also revealed that PARP can link OSA to diabetic peripheral neuropathy and endothelial dysfunction in patients with type 2 diabetes [16]. A meta-analysis is also performed to assess the correlation between OSA and neuropathy, but only 5 studies were included [15]. Although a significant correlation is obtained, the result is not stable and no marked results are revealed in the subgroup analyses of type 1 and 2 diabetes.

In the current study, a new meta-analysis with 11 studies was conducted. Meanwhile, the subgroup analyses between OSA and type 1 and 2 diabetes were also estimated. According to this analysis, we hope to further evaluate the correlation between OSA and diabetic peripheral neuropathy, so that can provide a solid evidence for the basic research and clinical treatment.

2. Materials and methods

2.1. Searching strategy

Literatures, which were published in English, were screened from electronic databases of PubMed (http://www.ncbi.nlm.nih.gov/pubmed), Embase (http://www.embase.com) and the Cochrane Library (http://www.cochranelibrary.com) from the first record to March 2017. The search strategy was set as the following terms: obstructive sleep apnea (OR "OSA" OR "obstructive sleep apnea hypoventilation syndrome" OR "Obstructive sleep apnoea") AND diabetes AND neuropathy.

2.2. Inclusive and exclusive criteria

Researches were included if they were meeting the following terms: (1) studies were open access and focused on the research of relationship between OSA and diabetes; (2) patients can be divided into the OSA (OSA+) and non-OSA (OSA−) groups; (3) the number of pathological neurons can be counted and compared between the OSA+ and OSA− groups . Literatures were excluded if the following terms existed: (1) data is insufficient and cannot be used for statistical analysis; (2) studies are reviews, letters or comments; (3) the same dataset is utilized for more than one researcher or duplicated publications; or (4) studies have obvious logical problems.

2.3. Data extraction

Study information and demographic data of patients were extracted including the first author, published year, country, study performed years, type of diabetes, age, gender ratio, body mass index (BMI), duration of diabetes (years), number of neuropathy patients, and the patient numbers of patients in the OSA+ and OSA− groups.

2.4. Statistical analysis

R 3.12 (R Foundation for Statistical Computing, Beijing, China, meta package) was utilized to perform statistical analyses in this study. Odds ratio (OR) and its 95% confidence interval (CI) were used to present the effect size. Heterogeneity among studies were assessed by χ^2-based Q test [17] and I^2 statistics. Significant heterogeneity was considered if $P < 0.05$ or $I^2 > 50\%$ and the effect size of pooled data was determined by the random effects model; otherwise, the effect size was estimated by the fixed effect model [18]. Egger's test was used for the examination of publication bias [19]. Trim and fill method was carried out if the publication bias was existed, and the comparison between the adjusted and the previous effect size was conducted [20]. Finally, the sensitivity was assessed by leave one out method [21].

3. Results

3.1. Primary characteristics of included studies

The procedure of study enrollment is presented as Fig. 1. According to the searching strategy, a total of 295 papers were chosen form the databases of the PubMed, Embase and the Cochrane Library. After removing the duplicated ones, 209 studies were remained. After scanning the title and abstract, total 174 had been deleted which were not consistent with enrolled criteria. Then, the full text was reading and 24 out of 35 were removed out. Finally, 11 studies were enrolled in this study [15,22–31].

Based on the included study, 1842 patients were enrolled, including 840 in the OSA− and 1002 in the OSA+ groups. The primary characteristics of patients were tabulated in Table 1.

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