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Review

Effect of continuous positive airway pressure on lipid profile in patients with obstructive sleep apnea syndrome: A meta-analysis of randomized controlled trials

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ABSTRACT

Background: Obstructive sleep apnea syndrome (OSAS) is an independent risk factor for development of dyslipidemia. Continuous positive airway pressure (CPAP) is the first-line treatment for OSAS. However, it is unclear whether CPAP improves lipid metabolism.
Objectives: To review the effect of CPAP on lipid profile of patients with OSAS.
Methods: We searched PubMed, Embase, and the Cochrane Library to identify eligible articles published prior to October 30, 2013. Six randomized controlled trials (RCTs) were subjected to meta-analysis using Comprehensive Meta-Analysis software.
Results: Six RCTs meeting the inclusion criteria were enrolled. The total numbers of measurements of total cholesterol (TC), triglyceride (TG), low-density lipoprotein (LDL) cholesterol, and high-density lipoprotein (HDL) cholesterol, in CPAP intervention patients and sham/control groups, were 370 and 371, 330 and 328, 276 and 274, and 269 and 266 respectively. The pooled estimate of the difference in the mean TC level between the CPAP and sham CPAP/control groups was significantly different (−0.15 [95% confidence interval, −0.27 to −0.03]; $p = 0.01$). Subgroup analysis revealed that OSAS patients of younger age, who were more obese, and who had been treated via CPAP for a longer duration, showed a significant decrease in TC levels (the differences in the means were −0.27, −0.24, and −0.20; and the p values 0.001, 0.01, and 0.04, respectively).
Conclusion: We confirmed that CPAP decreases the TC level, especially in OSAS patients who are younger, more obese, and who use CPAP for a longer period. CPAP did not alter TG, LDL, or HDL levels, suggesting that CPAP may have no clinically important effect on lipid metabolism.

Contents

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1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a common sleep disorder, affecting about 24% of middle-aged males and 9% of middle-aged females [1]. OSAS is characterized by repetitive episodes of partial or complete upper airway obstruction during sleep, causing intermittent hypoxia, in turn triggering oxidative stress or inflammation [2]. An increasing body of research shows that OSAS is an independent risk factor for development of cardiovascular events and morbidity, including dyslipidemia [3–5].

Continuous positive airway pressure (CPAP) therapy is the first-line treatment for OSAS [6]. The benefits of CPAP include elimination of upper airway collapse, micro-arousals, and oxidative stress during sleep; and improvement in clinical symptoms, including snoring and excessive daytime sleepiness [7,8]. Previous studies have shown that CPAP exerts a positive effect on metabolic syndrome [9]. In particular, the influence of CPAP on the levels of total cholesterol (TC), low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and triglyceride (TG), were investigated [10–15].

Several articles exploring the beneficial effects of CPAP treatment on blood lipid levels have been published in the past few years [10–16]. These include randomized controlled trials (RCTs), original studies, and a review. However, few definite conclusions can be drawn. Recently, three new RCTs exploring the effects of CPAP on the blood lipid profile have been conducted [12–14]. These RCTs enrolled more OSAS subjects than did all prior studies combined. It was thus necessary to systematically review and meta-analyze all relevant RCTs to explore the effects of CPAP therapy on lipid profile.

2. Materials and methods

We strictly followed the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analysis) [17]. Our registration number is CRD42013005732.

2.1. Search strategy and selection of trails

We systematically searched PubMed, Embase, and the Cochrane library. All pre-September 2013 literature examining the effects of CPAP on blood lipid profiles was included. No language or other restriction was imposed. The search terms used were: (Continuous positive airway pressure or CPAP) and (obstructive sleep apnea or OSA) combined with (lipids or lipid profile or metabolic profile or dyslipidemia or cholesterol or TC or triglycerides or TG or HDL or LDL). In addition, we manually searched for relevant published studies and review articles.

We selected RCTs that met the following inclusion criteria: (1) only adults (aged $\geq$ 18 years) with newly diagnosed OSAS were studied; (2) CPAP was applied; (3) the duration of CPAP therapy was $\geq$2 weeks; and, (4) the level of at least one of TC, TG, LDL, or HDL was measured both before and after application of CPAP. Reviews, abstracts, case reports, letters, and non-human studies were excluded. Other exclusion criteria were: (1) treatment of adolescents (age $<$ 18 years); (2) diagnosis of OSAS in a manner other than by determination of the AHI (AHI $\geq$ 5) or the oxygen desaturation index (ODI) (ODI $\geq$ 7.5); (3) failure to record lipid levels both before and after CPAP therapy, or the inadequacy of supplied information in terms of allowing such values to be estimated; and/or, (4) a duration of therapy of less than 2 weeks. Two investigators (Drs. Xu and Guan) screened all relevant published material using the abovementioned criteria. If disagreement arose, a third reviewer (Prof. Yin) participated in resolution of the issue by discussion.

2.2. Quality assessment

We evaluated the quality of each study with the Jadad score. The Jadad score represents the quality of randomization, blinding, withdrawal reporting, generation of random numbers, and allocation concealment. One point was allotted to each of these features, and the score thus varied from 0 to 5 (the highest quality level). Quality assessment was subjected to sensitivity analysis, because low-quality trials may influence outcome measures. Quality was independently assessed by two investigators (Drs. Xu and Guan).

2.3. Data extraction

Data were extracted from RCTs meeting the inclusion criteria. These data were the first author; year of publication; the country in which the work was performed; study design; number of subjects; sex, age, body mass index (BMI), and AHI or ODI values of the participants; the duration of CPAP intervention; the extent of adherence to CPAP; post-intervention TC, TG, LDL, HDL, weight, BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting glucose, and/or homeostasis model assessment of insulin resistance (HOMA-IR) data from both the CPAP and the sham CPAP/control groups; and the mean differences in the levels of TC, TG, LDL, HDL, and weight, BMI, SBP, DBP, fasting glucose, HOMA-IR between the test and control groups. Our final analysis featured examination of these differences and the associated confidence interval (CI). The differences were calculated if not directly provided.

2.4. Quantitative data synthesis

Data on differences in TC, TG, LDL, HDL levels, and weight, BMI, SBP, DBP, fasting glucose, and HOMA-IR between the two groups were analyzed using pooled estimates of the differences in means, and the associated CIs were calculated. Funnel plots of standard errors and differences in means were used to assess publication bias. We also used Begg's test and the Mazumdar rank correlation approach to this end [18]. Heterogeneity was assessed with the aid of the I-squared index. If a p value was $<$0.10, the existence of statistical heterogeneity was suggested and the data were analyzed using a random-effects model. Otherwise, the data were considered to be homogeneous and a fixed model was employed. Comprehensive Meta Analysis software, version 2.2.064, was used to analyze all data.