INPLASY PROTOCOL

To cite: Wang et al. Response Time of Circulating Biomarkers of Inflammation and Metabolism to CPAP in OSA patients. Inplasy protocol 202160086. doi: 10.37766/inplasy2021.6.0086

Received: 23 June 2021

Published: 23 June 2021

Corresponding author:
Qing Yun Li

liqingyun68@hotmail.com

Author Affiliation:
Department of Respiratory and Critical Care Medicine, Ruijin Hospital, Shanghai Jiao Tong University school of Medicine, Shanghai.

Support: **National Natural Science Found.**

Review Stage at time of this submission: **Formal screening of search results against eligibility criteria.**

Conflicts of interest:
None declared.

Response Time of Circulating Biomarkers of Inflammation and Metabolism to CPAP in OSA patients

Wang, Y[1]; Lin, YN[2]; Zhang, LY[3]; Li, CX[4]; Li, SQ[5]; Li, HP[6]; Zhang, L[7]; Li, N[8]; Yan, YR[9]; Ding, YJ[10]; Sun, XW[11]; Zhou, JP[12]; Li, QY[13].

Review question / Objective: **PICOS format was followed; P: inflammatory markers and metabolic biomarkers (LDL, HDL, TC, and TG), I: CPAP treatment, C; levels of biomarkers before and after treatment, O: improvement in marker levels.**
Eligibility criteria: **1) studies written in English; 2) studies published since January 2000 ; 3) studies performed on adults (>18 years old); 4) full-text manuscripts and quantitative data from before and after CPAP treatment available; 5) studies evaluating the effects of CPAP withdrawal on sleep and physiology were excluded; 6) OSA was strictly defined as an apnea-hypopnea index (AHI) ≥ 5 events/hour measured by polysomnography (PSG); 7) all of the biomarker samples were derived from fasting blood in the morning; 8) studies using bilevel positive airway pressure (BPAP) and other positive airway pressure treatment were also included; 9) studies with identical data sets or the same study subjects were excluded; and 10) data from patients with low adherence (less than 4 h/night on less than 70% nights of use of CPAP) were excluded. In addition, case reports, conference abstracts, and letters to the editor were not reviewed.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 June 2021 and was last updated on 23 June 2021 (registration number INPLASY202160086).

INTRODUCTION

Review question / Objective: **PICOS format was followed; P: inflammatory markers and metabolic biomarkers (LDL, HDL, TC, and TG), I: CPAP treatment, C; levels of biomarkers before and after treatment, O: improvement in marker levels**

Rationale: **Obstructive sleep apnea (OSA) has become a global health burden. The current gold standard treatment for**

moderate-to-severe OSA is continuous positive airway pressure (CPAP). During the past two decades, circulating biomarkers of inflammation, glucose control, and lipid metabolism related to OSA have been investigated to evaluate to the effectiveness to CPAP treatment. However, the duration of CPAP treatment needed to produce a change in these biomarkers is an important unanswered question, and there is no conclusive evidence about timing of CPAP benefits. Thus, we conducted a meta-analysis to explore the response time of several circulating biomarkers to CPAP treatment.

Condition being studied: Obstructive sleep apnea (OSA) has become a global health burden. It is estimated that 936 million adults worldwide aged 30–69 years suffer from OSA, among whom 425 million suffer from moderate-to-severe OSA(1). Observational studies have linked OSA with an increased risk of insulin resistance, dyslipidemia, and cardiovascular diseases. Continuous positive airway pressure (CPAP) is the first-line therapy for moderate-to-severe OSA. Ideally, by relieving nocturnal OXYGEN desaturation and subsequent sleep fragmentation which characterize OSA, CPAP can partially rectify oxidative stress to improve systemic inflammation and abnormal metabolism. During the past two decades, circulating inflammatory and metabolic biomarkers related to OSA, including C-reactive protein, tumor necrosis factor-α, fasting blood glucose, fasting insulin, and lipid profiles, have been explored for the evaluation of the response to CPAP treatment. Several studies have demonstrated time-related benefits of CPAP on biomarkers. For example, Schiza et al reported a gradual decrease in CRP after 3 months of CPAP treatment, and a sharp drop after 6 months of treatment, reaching a plateau after this time point. Simon et al demonstrated that 2 months of CPAP therapy resulted in a significant decrease in both total cholesterol and low-density lipoprotein levels compared to baseline values, and the effect was maintained after 6 months and 5 years of treatment. Moreover, they reported no significant change in serum triglycerides or high-density lipoprotein after 2 months, 6 months and 5 years of CPAP treatment. To date, current evidence is not conclusive about the time-dependent profiles of aforementioned circulatory biomarkers in response to CPAP treatment.

METHODS

Search strategy: PubMed and Embase databases: [(obstructive sleep apnea or sleep disorder breathing or obstructive sleep apnea hypopnea syndromes) and (continuous positive airway pressure or continuous positive pressure ventilation) and (markers or C-reactive protein or tumor necrosis factor-α or fasting blood glucose or insulin or low-density lipoprotein or high-density lipoprotein or cholesterol or triglyceride)].

Participant or population: Adults with OSA.

Intervention: Continuous positive airway presure.

Comparator: Before and after CPAP; experimental and control.

Study designs to be included: RCT, case–control study.

Eligibility criteria: 1) studies written in English; 2) studies published since January 2000 ; 3) studies performed on adults (>18 years old); 4) full-text manuscripts and quantitative data from before and after CPAP treatment available; 5) studies evaluating the effects of CPAP withdrawal on sleep and physiology were excluded; 6) OSA was strictly defined as an apnea-hypopnea index (AHI) ≥ 5 events/hour measured by polysomnography (PSG); 7) all of the biomarker samples were derived from fasting blood in the morning; 8) studies using bilevel positive airway pressure (BPAP) and other positive airway pressure treatment were also included; 9) studies with identical data sets or the same study subjects were excluded; and 10) data from patients with low adherence (less than 4 h/night on less than 70% nights of use of CPAP) were excluded. In addition, case

reports, conference abstracts, and letters to the editor were not reviewed.

Information sources: Electronic databases, trial registers, or grey literature.

Main outcome(s): Changes of levels of biomarkers before and after treatment.

Quality assessment / Risk of bias analysis: the Sackett et al's hierarchy of evidence; Minors scale; Jadad Scale.

Strategy of data synthesis: A random-effect (or fixed-effect) model and standardized mean difference (SMD) meta-analysis model.

Subgroup analysis: According to the duration of CPAP treatment, studies were divided into three subgroups: short-term (<3 months), mid-term (≥3 and <6 months), and long-term (≥6 months).

Sensitivity analysis: Deleting one study at one time.

Language: English.

Country(ies) involved: China.

Keywords: continuous positive airway pressure; obstructive sleep apnea; circulating biomarkers; phase-specific effectiveness.

Contributions of each author:
Author 1 - Yi Wang.
Author 2 - Ying Ni Lin.
Author 3 - Li Yue Zhang.
Author 4 - Chuan Xiang Li.
Author 5 - Shi Qi Li.
Author 6 - Hong Peng Li.
Author 7 - Liu Zhang.
Author 8 - Ning Li.
Author 9 - Ya Ru Yan.
Author 10 - Yong Jie Ding.
Author 11 - Xian Wen Sun.
Author 12 - Jian Ping Zhou.
Author 13 - Qing Yun Li.