The interaction of obstructive sleep apnea and obesity on the inflammatory markers C-reactive protein and interleukin-6

Ema S. Arnardottir,1,2,3, Greg Maislin3, Richard J. Schwab3, Bryndis Benediktsdottir,2,isleifur Olafsson4, Thorarin Gislason1,2,*, Allan I. Pack PhD2,3,*. Co-senior authors.

1 Department of Respiratory Medicine and Sleep, Landspitali - The National University Hospital of Iceland. 2 Faculty of Medicine, University of Iceland. 3 Center for Sleep and Circadian Neurobiology and Division of Sleep Medicine/Department of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania. 4 Department of Clinical Biochemistry, Landspitali – The National University Hospital of Iceland.

Introduction

Obesity and obstructive sleep apnea (OSA, Figure 1) commonly coexist and have many shared pathways such as inflammation (Figure 2). The aim of the study was to investigate the relevant effect of OSA and obesity on interleukin-6 (IL-6) and C-reactive protein (CRP) levels. Also to assess if the effect of OSA on IL-6 and leptin differs by the degree of obesity.

Demographics

The untreated OSA patients (n=454) included in this study had a mean±SD age of 54.4±10.6 yrs, mean BMI 32.6±5.3 kg/m², mean apnea hypopnea index (AHI) 40.1±16.1 events/hour and mean oxygen desaturation index (ODI) 31.5±14.0 events/hour. 84% of the cohort was male. Subjects were divided into 3 BMI tertiles, BMI<30 (n=158), BMI 30-35 (n=163) and BMI≥35 (n=133). See Figure 4.

Materials and Methods

454 untreated OSA patients had a sleep study, magnetic resonance imaging (MRI) for total abdominal and visceral fat volume (Figure 3), and had fasting morning IL-6 and CRP levels in serum measured. A multiple linear regression model with higher order and interaction terms was performed to estimate the interaction between OSA severity and obesity on IL-6 and CRP levels.

Results

Inflammatory biomarkers, obesity and OSA severity

A significantly higher correlation was found for BMI than visceral fat volume with CRP and IL-6 levels (bootstrap analysis). Oxygen desaturation index, hypoxia time and minimum SaO₂ significantly correlated with IL-6 and CRP levels, but apnea hypopnea index did not. When stratified by BMI category, OSA severity was associated with IL-6 and CRP levels in obese subjects only (Figure 5).

Response surface modeling for IL-6 and CRP

A multiple linear regression model with interaction terms showed an independent association of OSA severity with IL-6 levels and an interaction between OSA severity and BMI, i.e., degree of obesity altered the relationship between OSA and IL-6 levels (Figure 6). An independent association of OSA severity with CRP levels was found for minimum SaO₂ only, not the other OSA severity indices. A similar interaction of minimum SaO₂ and BMI on CRP levels was found for males and postmenopausal women.

Models with visceral fat explained much less of biomarker variance than models with BMI.

Conclusion

• OSA severity is an independent predictor of levels of IL-6 and CRP but interacts with obesity such that this association is found only in obese subjects.

• In nonobese subjects, there is no association of IL-6 and CRP levels with OSA severity.

• BMI, a total fat measure, predicts IL-6 and leptin levels better than visceral fat.

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