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Sleep Medicine 3 (2002) 449–450

SLEEP MEDICINE

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Journal search and commentary

Elevated plasma C-reactive protein and increased cardiovascular/cerebrovascular risk in sleep apnea patients
Article reviewed: Elevated C-reactive protein in patients with obstructive sleep apnea (a brief rapid communication)[☆]

Mark H. Sanders

University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Objective

To determine if patients with obstructive sleep apnea–hypopnea (OSAH) have an elevated C-reactive protein (CRP).

Study population

Data were obtained from 18 males and four females with untreated OSAH. The control population consisted of 15 males and five females in whom OSAH was excluded and who, as a group, were matched to the OSAH population with regard to age and body mass index (BMI).

Methods

Study participants with OSAH underwent a split-night polysomnogram (PSG) paradigm. Venous blood was sampled between 20:00 and 22:00 h prior to PSG evaluation of the individuals identified to have OSAH. Neither the timing of the venous sampling nor the relationship to PSG are specified in the control population. CRP was quantified by latex particle enhanced immunoturbidimetric assay.

Parametric and non-parametric statistics were employed, depending on the distribution of the data. Analysis of variance was employed to test the independent association between CRP and Apnea + Hypopnea Index (AHI), adjusting for age, gender, BMI, smoking, alcohol intake, LDL and HDL.

Results

The AHI of the OSAH and Control populations were 60 ± 5 and 3 ± 1, respectively (mean $\pm$ SEM). There were no significant differences between the two groups with respect to gender, age, BMI, ratio of non-smokers to smokers, number of alcoholic beverages consumed per week, heart rate, mean blood pressure, HDL, LDL, awake oxyhemoglobin saturation (SpO_2, $96 \pm 0.4\%$ and $97 \pm 0.04\%$, OSAH vs. Controls), or Arousal Indices (51 ± 5 and 16 ± 5, OSAH vs. Controls). The nadir of SpO_2 during sleep in the OSAH patients was $79 \pm 1.6\%$. Plasma CRP was significantly higher in the OSAH patients compared with the Control group (median (range): 0.33 (0.9–2.73) vs. 0.09 (0.2–0.9); $P < 0.0003$). There was a significant, linear relationship between plasma CRP levels and AHI in the OSAH patients ($r = 0.55$, $P < 0.01$). A 'multivariate' analysis indicated that plasma CRP levels were independently associated with severity of OSAH as reflected by the AHI (adjusted for age, gender, BMI, smoking, alcohol intake, LDL and HDL; $F = 6.8$, $P = 0.032$).

Conclusion

The investigators concluded that patients with OSAH have an increased plasma CRP compared with a matched control population without OSAH. Furthermore, the level of CRP measured in the OSAH patients fell within a range that is associated with an increased risk for cardiovascular disease. Finally, the investigators concluded that the CRP levels were correlated with the AHI. They speculated that CRP may provide a mechanism for assessing cardiovascular/cerebrovascular risk in OSAH patients and a target to guide therapeutic decision-making.

[☆] Shamsuzzaman ASM, Winnicki M, Lanfranchi P, Wolk R, et al. Circulation 2002;105:2462–2464.

PII: S1389-9457(02)00106-5

Comments

This report by Shamsuzzaman and coworkers, was published as a *Brief Rapid Communication* in *Circulation*, highlighting the perceived significance of the observations. It is increasingly recognized that OSAH is associated with oxidative stress and systemic inflammation. In addition, there is an accumulating library of information supporting an increased risk for adverse cardiovascular and cerebrovascular consequences in association with, if not as a result of, OSAH. That oxidative stress and inflammatory mediators have been implicated in the pathogenesis of endothelial cell dysfunction and atherosclerosis makes it appealing to consider these processes as a fundamental link between OSAH and vascular disorders. CRP may well be an important mediator and marker for this pathologic biologic bridge. Like interleukin (IL)-6, which participates in its regulation, CRP has been shown to be elevated under conditions of hypoxia (e.g. altitude). Furthermore, if the similarity to IL-6 is more expansive, CRP may also be increased in conjunction with sleep deprivation. Obviously, both hypoxemia and sleep deprivation frequently accompany OSAH and may therefore participate in the genesis of inflammatory processes. Although Shamsuzzaman et al. noted a significant linear relationship between the CRP level and the AHI, only about 30% of the variance in AHI was explained by the CRP level. Almost certainly, there are other operative factors that remain to be evaluated. Conspicuously absent from the report are data relating CRP to parameters of overnight oxygenation. In addition, it is to be noted that the study was not a case-controlled study. Evidence for insulin resistance in conjunction with OSAH indicates that this metabolic perturbation, a possible contributor to an inflammatory process, must also be carefully considered. These issues notwithstanding, it is important to remember that this report is a *Brief Rapid Communication* and with it comes the promise of exciting new basic science and clinical insights.