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COMMENTARY

An inflammatory relationship

Commentary on Kheirandish-Gozal L, Capdevila OS, Tauman R, Gozal D. Plasma C-reactive protein in nonobese children with obstructive sleep apnea before and after adenotonsillectomy. *J Clin Sleep Med*. 2006;2(3):301–304. doi:10.5664/jcsm.26589

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Our neurology attending physician during pediatric residency was fond of reminding us that an association does not prove causation; "true-true and unrelated" was one of his favorite sayings. The study published in 2006 by Kheirandish-Gozal et al[1] was a step toward establishing the relationship between pediatric OSA and systemic inflammation by studying children with OSA and measuring inflammatory markers before and after adenotonsillectomy (AT). A chronic inflammatory state has been proposed as 1 of the mechanisms by which OSA contributes to the development of cardiovascular disease. The authors referenced a previous cross-sectional study[2] showing a correlation between OSA severity measures and C-reactive protein as the impetus for their 2006 study that was designed to include measurements before and after intervention. They reported a significant decrease in C-reactive protein levels with treatment of OSA by AT and found a correlation between AHI, a measure of OSA severity, and C-reactive protein levels before the intervention.[1] This study has been cited scores of times by members of this same research team and by many others in subsequent studies directed at characterizing the comorbidities of pediatric OSA related to systemic inflammation.

Not surprisingly, there have been some conflicting results; when humans are used as a research model for human disease there are many variables, and not all can be accounted for by even the most meticulous research design. For example, obesity is a major confounding factor in adult and pediatric studies. Kheirandish-Gozal and coworkers have posited that some of these differences in findings could be explained by genetics and environmental exposures.[3] The Childhood Adenotonsillectomy Trial,[4] a large randomized controlled study of pediatric OSA comparing outcomes of AT vs watchful waiting, found no difference in C-reactive protein levels within either group after intervention or between treatment arms. The Childhood Adenotonsillectomy Trial authors did note that children with severe hypoxemia were not included in the study.[4]

AT results in the removal of tissue, which is subject to infection and inflammation, so evaluation before and after alternative OSA treatments is another tempting research design. Such studies have been performed in adults, with some showing decreases in inflammatory markers with successful CPAP treatment,[5] but there are notable exceptions,[6] including a recent study by Campos-Rodriguez[7] that failed to show a reduction in systemic inflammation by successful CPAP treatment in a cohort of adult women with OSA. Definitive studies evaluating changes in inflammation with CPAP therapy in pediatrics are needed; younger individuals have had less opportunity to be affected by multiple comorbidities, thus simplifying the interpretation of results. Kheirandish-Gozal and Gozal[3] noted that there is much to learn about which inflammatory markers will yield the most clinically relevant information in directing treatment and understanding risk.

Given that children are increasingly affected by the obesity epidemic, many will not be adequately treated by AT alone. Many young people with obesity will become adults experiencing life-limiting cardiovascular and metabolic diseases and searching for modifiable risk factors. CPAP decreases sleep disruption and hypoxemia, and this treatment may interrupt the cascade of events contributing to autonomic dysfunction, endothelial damage, metabolic disease, and cognitive impairment, some of which may be mediated by inflammation. Yet children and teens struggle to be adherent to CPAP, even under the best of circumstances. Perhaps in the future we will order an "OSA inflammatory panel" in addition to polysomnography, including a treatment plan designed to reduce inflammation alongside adenotonsillectomy and PAP.

CITATION

Davidson Ward SL. An inflammatory relationship. *J Clin Sleep Med*. 2020;16(suppl_1):3S–4S.

REFERENCES

1. Kheirandish-Gozal L, Capdevila OS, Tauman R, Gozal D. Plasma C-reactive protein in nonobese children with obstructive sleep apnea before and after adenotonsillectomy. *J Clin Sleep Med*. 2006;2(3):301–304.
2. Tauman R, Ivanenko A, O'Brien LM, Gozal D. Plasma C-reactive protein levels among children with sleep-disordered breathing. *Pediatrics*. 2004;113(6):e564–e569.
3. Kheirandish-Gozal L, Gozal D. Pediatric OSA syndrome morbidity biomarkers: The hunt is finally on! *Chest*. 2017;151(2):500–506.

4. Quante M, Wang R, Weng J, et al. The effect of adenotonsillectomy for childhood sleep apnea on cardiometabolic measures. *Sleep*. 2015;38(9):1395–1403.
5. Xie X, Pan L, Ren D, Du C, Guo Y. Effects of continuous positive airway pressure therapy on systemic inflammation in obstructive sleep apnea: a meta-analysis. *Sleep Med.* 2013;14(11):1139–1150.
6. Jullian-Desayes I, Joyeux-Faure M, Tamisier R, et al. Impact of obstructive sleep apnea treatment by continuous positive airway pressure on cardiometabolic biomarkers: a systematic review from sham CPAP randomized controlled trials. *Sleep Med Rev.* 2015;21:23–38.
7. Campos-Rodriguez F, Asensio-Cruz MI, Cordero-Guevara J, et al. Effect of continuous positive airway pressure on inflammatory, antioxidant, and depression biomarkers in women with obstructive sleep apnea: a randomized controlled trial. *Sleep*. 2019;42(10):zsz145.

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DISCLOSURE STATEMENT

The author reports no conflicts of interest.