

EDITORIAL





Exploring the bidirectional relationship between asthma and obstructive sleep apnea in Brazilian pediatric patients: one more piece to the Puzzle



Luana Nosetti D ª, David Gozal D Þ,*

^a Insubria University, F. Del Ponte Hospital, Department of Pediatrics, Pediatric Sleep Disorders Center, Varese, Italy ^b University of Missouri School of Medicine, Department of Child Health, Child Health Research Institute, Columbia, MO, USA

Obstructive sleep apnea (OSA) and asthma are two common respiratory disorders in children and adults, and as such, they can be concurrently present in the same patients. Both OSA and asthma share many common risk factors including obesity, prematurity, environmental exposures, a history of early-life lower respiratory tract infections, gastroesophageal reflux disease, and allergic rhinitis.^{1,2} Both asthma and OSA share pathogenic mechanisms which include systemic and localized activation and propagation of inflammatory pathways.³ Consequently, it is anticipated that there will be a bidirectional link between asthma and OSA. Under the driving assumption of the united airway hypothesis,⁴ emerging evidence further suggests that the two diseases may complicate the clinical course of each other. On the one hand, OSA could modify the extent and severity of asthmatic airway inflammation and thereby facilitate the emergence of poorer asthma control. On the other hand, asthma increases the collapsibility of the upper airway and increases vagal tone, contributing to the development and worsening of OSA, along with inflammatory mediators in the lower airways promoting the proliferation of upper airway lymphoid tissues.^{5,6} One of the corollaries of such interactions is that adenotonsillectomy, the first line of treatment of OSA in children, results in improved asthma control in patients suffering from both diseases.^{5,7} However, when the converse approach is examined, there is limited evidence on how anti-asthma medications affect OSA severity in the same patients.

See paper by Fumo dos Santos et al. in pages 443-448.

* Corresponding author.

E-mail: gozald@health.missouri.edu (D. Gozal).

With this information as a background, Fumo-dos-Santos and colleagues⁸ performed a cross-sectional study in a tertiary Pediatric Pulmonary Clinic in Brazil to investigate the prevalence of OSA in asthmatic children and explore whether sex, puberty status, and asthma severity and control (based on GINA criteria and a questionnaire display any predictive capacity regarding the presence of OSA. The investigators evaluated 80 asthmatic children (age 7-18 years, 51.3% female) and included a home polygraphy type III study in 76 subjects. The presence of OSA was detected in 61.2%, but no significant associations emerged. Such absence of any meaningful relationships between OSA severity and asthma severity (assessed by either pulmonary function or disease activity) should not be surprising. In the largest study to date involving thousands of children, Bhattacharjee and colleagues showed that adenotonsillectomy led to a reduction in the use of breakthrough medication and hospital admission among asthmatic children whose clinical characteristics essentially became similar to those of asthmatic children who did not have OSA.⁷ Thus, considering the high lability, i.e., day-to-day, or night-to-night variability of each of two diseases in any given patient in addition to the wide spectrum of disease severity for each affected child, it is predictable that the interactions between the two conditions may not necessarily display significant associations in a cross-sectional study that included relatively few subjects. A point of interest was the socioeconomic distribution of the participants. Socioeconomic status was based on the Criterio Brasil Classification. Most of the subjects enrolled belonged to the middle class, with scant representation by both the upper and lowerclass. In light of the social determinants of both asthma and OSA,^{9,10} expansion of the

https://doi.org/10.1016/j.jped.2023.05.004

0021-7557/© 2023 Published by Elsevier Editora Ltda. on behalf of Sociedade Brasileira de Pediatria. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

socioeconomic spectrum to include a more balanced cohort representation would have been of great interest.

What can we learn after reading this paper? First, and most importantly, OSA is frequently present among asthmatic children. Varying prevalence has been reported in other studies based on different criteria used to assess asthma or to define OSA severity (questionnaires, spirometry, polysomnography, portable polygraphy), but the findings have been quite consistent. Second, sex was not a risk factor for OSA in contrast with many other studies in which both OSA and asthma tend to occur more frequently in boys than in girls, particularly in younger age groups, probably because of their relatively reduced airway size until reaching maturity.² Conversely, asthma prevalence increases in females during puberty. Third, usually asthma is associated with more severe OSA, and the presence of OSA is associated with severe asthma. The cross-sectional nature of this study precludes any inferences as to the clinical outcomes.

Thus. Fumo dos Santos and colleagues⁸ are to be commended for this study, obviously carried out in a limited resource setting while aiming to concurrently obtain quantitative and objective measures of lung function and respiration during sleep. Notwithstanding such efforts, the jury is still out as to whether two diseases of the airway are to be viewed as worse than each in isolation.

Conflicts of interest

The authors declare no conflicts of interest.

References

- Sánchez T, Gozal D, Smith DL, Foncea C, Betancur C, Brockmann PE. Association between air pollution and sleep disordered breathing in children. Pediatr Pulmonol. 2019;54:544–50.
- **2.** Garza N, Witmans M, Salud M, Lagera PG, Co VA, Tablizo MA. The association between asthma and OSA in children. Children. 2022;9:1430.
- 3. Wang R, Mihaicuta S, Tiotiu A, Corlateanu A, Ioan IC, Bikov A. Asthma and obstructive sleep apnoea in adults and children - an up-to-date review. Sleep Med Rev. 2022;61:101564.
- 4. Tiotiu A, Novakova P, Baiardini I, Bikov A, Chong-Neto H, de-Sousa JC, et al. Manifesto on united airways diseases (UAD): an Interasma (global asthma association - GAA) document. J Asthma. 2022;59:639–54.
- Sánchez T, Castro-Rodríguez JA, Brockmann PE. Sleep-disordered breathing in children with asthma: a systematic review on the impact of treatment. J Asthma Allergy. 2016;9:83–91.
- **6.** Dayyat E, Serpero LD, Kheirandish-Gozal L, Goldman JL, Snow A, Bhattacharjee R, et al. Leukotriene pathways and in vitro adenotonsillar cell proliferation in children with obstructive sleep apnea. Chest. 2009;135:1142–9.
- 7. Bhattacharjee R, Choi BH, Gozal D, Mokhlesi B. Association of adenotonsillectomy with asthma outcomes in children: a longitudinal database analysis. PLoS Med. 2014;11:e1001753.
- Fumo dos Santos C, Smith AK, Togeiro SM, Tufik S, Moreira GA. Obstructive sleep apnea in asthmatic children: a cross-sectional study about prevalence and risk factors. J Pediatr. 2023;99(5): 443–8.
- **9.** Park JW, Hamoda MM, Almeida FR, Wang Z, Wensley D, Alalola B, et al. Socioeconomic inequalities in pediatric obstructive sleep apnea. J Clin Sleep Med. 2022;18:637–45.
- Kozyrskyj AL, Kendall GE, Jacoby P, Sly PD, Zubrick SR. Association between socioeconomic status and the development of asthma: analyses of income trajectories. Am J Public Health. 2010;100:540–6.