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EDITORIAL

Does asthma cause sleep disorders . . . or the other way around?☆

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In the present issue of the Jornal de Pediatria, the paper by Estanislau et al.[1] assesses the association between the hours of sleep and the suffering from asthma in adolescents. The study was designed considering that the independent variable in the regression analyses is sleep, while the dependent one is asthma. The authors conclude that asthma prevalence is significantly higher in individuals who sleep less hours. It is a study which has the great strength of including 59,442 adolescents in the analyses. Still, there is an important issue when considering the results: it is a crossover study, which does not allow the knowledge of whether asthma precedes sleep disturbance or the other way around. Casual relationship in epidemiology need three conditions: association, direction and temporal relationship.[2] The authors find an interesting association, but does the lack of sleep have a causal relationship to asthma?

It is perfectly known that asthma presents frequently nocturnal symptoms which are associated with a bad quality of sleep, usually including arousing, parasomnias and breathing difficulties, apart for a lower quality of life of parents when the patients are children.[3]

There is an interesting question that one might ask to oneself, and this is whether asthmatic condition associates an altered sleep architecture or a consequence of a higher prevalence of obstructive sleep apnea syndrome (OSA), which is the most frequent sleep disorder in childhood. On the other hand, could asthma be the cause of the sleep disorder or vice-versa? It is even possible to consider a bi-directional association and thus asthma would be a risk factor for OSA in some children while OSA might be a risk factor for asthma in other. OSA is considered a disorder in which by –ideally– polysomnography an abnormal number of apnea episodes of obstructive origin are detected during normal sleep. However, respiratory sleep disorder (RSD) is a wider term and includes any respiratory disorder during sleep and not only OSA. In children, the assessment of RSD is frequently performed by means of questionnaires.

Is there an altered sleep architecture in asthmatic children and adolescents?

As it has been already said previously, asthma has nocturnal symptoms which may alter the normal sleep architecture as compared with the healthy population. In fact, the study by Khassawneh et al.[4] found significant differences in the aforementioned architecture as assessed by polysomnography in a selected group of 85 asthmatic adolescents with low risk of OSA, as evaluated by the Pediatric Sleep Ques-

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tionnaire. Those patients had less sleep time, less sleep time in REM phase, less sleep latency and less SatO2 nadir. They had also more time awake after they initially slept (wake after sleep onset — WASO), higher arousal index both spontaneous and due to respiratory causes and, finally, higher apnea/hypopnea index (AHI). In fact, 29% of participants had patterns compatible with OSA in spite of having low risk scores. But even in asthmatic patients with normal AHI, that is, without OSA, those sleep values are significantly altered as compared to normal values; except, of course, for the arousal index from respiratory causes and the AHI. It is also of interest that sleep disturbances were not related to asthma control.

Is asthma a risk factor of OSA or RSD?

The association between asthma and OSA in children has been studied widely. There is even a systematic Review and meta-analysis[5] which includes 17 studies with a total of 45,155 children (53% male) of a mean age of 8.6 ± 2.5 years. The authors found a higher risk of OSA among asthmatic patients (OR 1.91; 95%CI: 1.04–2.13) independently of the diagnostic method (polygraph or polysomnography). Some years later, the same authors performed a new systematic review with the aim of unravelling the relationship between asthma and SRD, with special focus on the impact of treatment.[6] This study selected 32 previous ones and include 143,343 children (51% male) with a mean age of 8.4 ± 2.5 years: the man conclusion is that asthmatic children have higher likelihood of suffering from OSA.

Finally, the same group made a systematic search in the attempt to demonstrate asthma causes RSD considering the whole nine criteria for associations: strength of the association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experimentality and analogy. This concludes that temporality criteria cannot be demonstrated, as there are no cohort studies showing that asthma precedes OSA. Therefore, directionality (asthma causing OSA) cannot be established.[7]

Thus, the current knowledge seems to indicate that asthmatic children have a higher prevalence of OSA, being asthma a potential risk factor for RSD.

Is RSD risk factors for asthma?

This is the direction of the study by Estanislau et al.[1] and other studies, from which it is worth mentioning one published in 2015 by Li et al.[8] for in one hand they assess this association by a cross-sectional study by means of questionnaires in a big population of 20,672 children (response rate 91.9% and age range 5–12 years); and on the other, they include a meta-analysis of 12 previous studies including 38,766 children. In the cross-sectional study the find that both snoring (OR = 1.28, 95%CI: 1.01–1.62) and OSA (OR = 1.92; 95%CI: 1.34–2.76) are statistically significant asthma predictors. The meta-analysis also showed that RSD is a risk factor for asthma (OR = 1.55; 95%CI: 1.44–1.66) both considering cross-sectional studies (OR = 1.56, 95%CI: 1.45–1.68) and cohort studies (OR = 1.46; 95%CI: 1.16–1.75).

The review by Sánchez et al.[6] also shows that RSD is associated to more severe cases of asthma and that OSA treatment (tonsillectomy) was associated to a significant improvement of asthma. On the other hand, Ross et al.[9] studied 108 asthmatic children that were followed prospectively over one year that had been managed according to international guidelines and observed that asthma grave was found in 55% of children with RSD but only in 20% of children without SRD (OR = 3.63; 95%CI: 1.26–10.4) after adjusting for obesity, gender and ethnicity.

More recently, the study by Oka et al.[10] showed in a numerous population of 27,935 children between 6 and 17 years of age admitted to hospital due to an asthma attack, that in 1.4% of them in which OSA coexisted, non-invasive ventilation was more frequently needed (OR = 1.2; 95%CI: 1.16–1–24) to manage the attack; and that hospital stays were longer (OR = 1.2; 95%CI 1.16–1–24).

In a systematic review on the effect of tonsillectomy on asthma control Kohli et al.[11] found that the procedure might be of help, although it is cautioned that there are few studies and that their design is not the most adequate.

According to the previous evidence, it could be concluded that SRD and OSA are risk factors for asthma, end even of an increased severity of the condition.

Is it plausible a bidirectionality in the relationship between asthma and SRD?

The authors can certainly find arguments to try and understand this relationship: certain comorbidities are frequent in both conditions and could contribute in both directions. Obesity is a factor related to asthma[12] and with SRD.[13] Gastroesophageal reflux is also related to asthma[14] and it has also been demonstrated that more than 40% of children with OSA due to tonsillar hypertrophy have abnormal esophageal pHmetry.[15] Finally, the prevalence of allergic rhinitis among asthmatics is very high[16] and it is also associated with SRD.[17]

On the other hand, asthma and OSA are conditions which share inflammatory characteristics with interrelationships between them[18,19] and it has been described that OSA may contribute to airway remodeling in severe cases of asthma.[19]

The clinical implications of the associations between SRD and asthma are obvious because asthma is aggravated and further disturbs the quality of life of patients. Pediatricians must be aware of this comorbidity that is so frequent.

Conflicts of interest

The authors declare no conflicts of interest.

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