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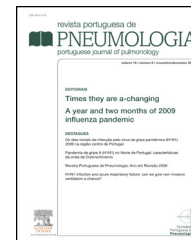
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## EDITORIAL

# Obstructive sleep apnoea syndrome is an under-recognized cause of uncontrolled asthma across the life cycle



Obstructive sleep apnoea syndrome (OSA) is a clinical syndrome marked by recurring episodes of upper airway obstruction that lead to markedly reduced (hypopnoea) or absent (apnoea) airflow at the nose/mouth. These episodes of impaired ventilation are usually accompanied by loud snoring and hypoxemia, and are typically terminated by brief arousals.<sup>1</sup> However, despite having significant breathing problems during sleep, most patients have no readily detectable respiratory abnormality while awake. OSA is a very common yet underdiagnosed disorder often occurring in a context of multimorbidity.<sup>2</sup>

The pathophysiological mechanisms involved in OSA are complex and not fully understood. Critical upper airway narrowing/collapse usually occurs in the oropharynx, between the nasal choanae and epiglottis, an area lacking rigid structural support. Patency of this vulnerable segment is dependent on the action of pharyngeal dilator and abductor muscles that are normally activated in a rhythmic fashion during each inspiration. Collapse of the upper airway occurs if the negative upper airway pressure generated by inspiratory pump muscles exceeds the dilating force of these upper airway muscles.<sup>3</sup>

A variety of factors contribute to upper airway narrowing in patients with OSA. Obesity contributes to OSA pathogenesis in multiple ways including altering upper airway anatomy and collapsibility, ventilatory control and increasing respiratory work load. OSA itself contributes to the development of obesity. Moreover, both OSA and obesity promote the activation of inflammatory pathways, which is likely a key mechanism in cardiovascular and metabolic disease processes.<sup>4</sup> Anatomical factors that predispose to upper airway narrowing should be sought in the physical examination of a patient suspected of having OSA, which, in addition to tonsillar hypertrophy, include retrognathia, micrognathia, and macroglossia.<sup>5</sup> However, the most common physical finding is a non-specific narrowing of the pharyngeal airway with reduced visualization of the posterior pharyngeal wall. The etiology of OSA in children differs

from adults in that adenotonsillar hypertrophy is the most common cause of the disorder although the increasing prevalence of obesity among children in recent years represents an important contributing factor in many cases.<sup>6</sup>

OSA is a unique physiologic stressor that contributes to the development or progression of many other disorders, particularly cardiovascular diseases and hypertension.<sup>7,8</sup> OSA is also associated with metabolic, and neurocognitive disease, increased cancer-related deaths,<sup>9</sup> and COPD.<sup>10</sup> Treatment with continuous positive airways pressure (CPAP) to reverse OSA-related symptoms and multimorbidities provides variable benefit in some but not all patients.

OSA is also frequent among subjects with asthma.<sup>11,12</sup> In population based studies, patients with asthma have a significantly higher risk of developing OSA than the general population.<sup>13</sup> The increased risk of OSA may be associated with the concomitant presence of rhinitis<sup>14,15</sup> or obesity.<sup>16</sup> The potential contribution of nasal obstruction to OSA has been debated. While many reports have shown a relationship between nasal obstruction and OSA,<sup>17,18</sup> other reports have failed to find a relationship.<sup>19,20</sup> The paper of Madama et al published in this journal raises two important issues in multimorbid asthma and OSA<sup>11</sup>:

1. Asthma in old age adults: Asthma is common in old age adults<sup>21</sup> and there are overlaps with other diseases such as COPD. The overall management of asthma in the elderly population is also complicated by specific features that the disease develops in the most advanced ages, and by the difficulties that the physician encounters when approaching the older asthmatic subjects.<sup>22</sup> OSA increases the prevalence in old age adults and those with obesity. The overlap between asthma, OSA and obesity needs a careful attention<sup>23</sup> since the treatment differs from asthma alone. This syndrome is usually not considered in guidelines.<sup>24</sup> AIRWAYS ICPs will approach this problem in depth in order to provide some recommendations for this new overlap syndrome in old age

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adults.<sup>11</sup> The initiative AIRWAYS ICPs (Integrated care pathways for airway diseases)<sup>25</sup> has launched a collaboration to develop practical multisectoral care pathways (ICPs) to reduce the burden of chronic respiratory diseases, their mortality and multimorbidity. AIRWAYS-ICPs proposes a feasible, achievable and manageable pathway from science to guidelines and policies using existing networks and stakeholders committed to the Action Plan B3 of the European Innovation Partnership on Active and Healthy Aging (EIP on AHA)<sup>26</sup> and the WHO Global Alliance against Chronic Respiratory Diseases (GARD).<sup>27,28</sup> It is implemented in European countries and regions, as part of the EIP on AHA, and is scaled up globally with GARD. The Renovated Action Plan of the EIP on AHA has a synergy on chronic respiratory diseases in old age people, an under-recognized societal problem.

- Uncontrolled asthma: The risk of OSA is associated with poor asthma control. Patients with inhaled steroid treatment have a higher risk for OSA than those without steroid treatment.<sup>13</sup> In the SARP-II (Severe Asthma Research Program), OSA risk is associated with a neutrophilic airway inflammation in asthma, which suggests that OSA may be an important contributor to the neutrophilic asthma.<sup>29</sup> Unrecognized OSA may be a reason for poor asthma control, particularly among older patients. In one study, CPAP use attenuated the likelihood of severe asthma in older subjects by 91%.<sup>23</sup> Sleep disordered breathing are also increased in asthmatic children and the prevalence of sleep disordered breathing increased with increasing asthma severity.<sup>30</sup> Overall, recent studies indicate that OSA and asthma are closely associated in pathogenesis, symptoms, and therapies, and there is a coexistence of OSA in difficult-to-control asthmatic patients.<sup>31</sup> Thus, as proposed by Madama et al.,<sup>11</sup> in asthmatic patients with uncontrolled disease, asthma suggestive of OSA should be investigated (e.g. daytime sleepiness, snoring, choking or gasping during sleep, recurrent awakenings) and polysomnography readily performed if needed. OSA should therefore be considered in patients with severe asthma either as a differential diagnosis<sup>32</sup> or as a multimorbidity that prevents asthma control. Guidelines should consider this new overlap syndrome since the treatment of OSA was shown to improve asthma control in these patients.

In patients with asthma, OSA should be investigated whenever there is inadequate control of symptoms of nocturnal asthma despite the treatment recommended by guidelines having been administered. There is evidence in the literature that the use of CPAP contributes to asthma control in asthma patients with OSA and uncontrolled asthma.<sup>24</sup>

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