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The overlap syndrome of chronic obstructive pulmonary disease and obstructive sleep apnoea

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Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnoea (OSA) are the two most common chronic respiratory disorders in the adult population. The prevalence of COPD in Poland is estimated at 10% [1, 2] and that of OSA is similarly high. The prevalence of OSA in an epidemiological study in a representative sample of Warsaw inhabitants was 7.5% [3]. In 1985, Flenley referred to the coexistence of these two conditions in a single patient as the "overlap syndrome". Although this term is increasingly used to refer to the coexistence of other disease entities (e.g. asthma and COPD), it was originally attributed to the association of OSA and other respiratory disorders (COPD, cystic fibrosis, interstitial lung diseases) [4].

The prevalence of the overlap syndrome of COPD and OSA assessed in two population studies in patients over the age of 40 was 1% [2, 5]. This value refers to patients with an apnoea/hypopnoea index (AHI) exceeding 5 and suffering from excessive daytime somnolence. If we merely consider breathing disturbances during sleep (independently of daytime somnolence) the prevalence of the overlap syndrome in the adult population reaches 3–4% [2, 6]. Both conditions are believed to be associated with a different major risk factor (smoking in COPD and obesity in OSA) and their frequent coexistence is thought to be of random nature.

The overlap syndrome is characterised by the occurrence of obstructive apnoeic and hypopnoeic episodes caused by obstruction of the upper respiratory tract (oropharynx) in a patient with COPD. The diagnosis requires the presence of excessive daytime somnolence and demonstration of episodes of sleep apnoea or hypopnoea occurring more frequently than every 12 minutes and lasting at least 10 seconds each with subsequent arterial blood hypoxaemia or waking.

Already in the 1970s it was observed that most episodes of nocturnal hypoxaemia in patients with COPD occurred during the rapid eye movement (REM) phase of sleep. During these episodes partial pressure of oxygen in the arterial blood fell as low as 26 mmHg. Patients were often more hypoxic during sleep than during exercise. There were reports of an association of nocturnal hypoxaemia, particularly hypoxaemia occurring in the REM phase of sleep, with hypoventilation, ventilation and perfusion (V/Q) mismatch, with increasing airway resistance and relaxation accompanied by relaxation of intercostal muscles resulting in a reduced chest mobility. The reduced muscular activity depended on the effect of the REM phase of sleep and on muscular atrophy and dysfunction in the course of COPD.

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Patients with the overlap syndrome are at an increased risk of nocturnal oxygen desaturation compared to COPD patients with the same level of bronchial obstruction. They develop complete respiratory failure with increased carbon dioxide retention more frequently. In patients suffering from OSA with hypercapnia during waking hours the ventilatory response to chemoreceptor stimulation is considerably impaired, in proportion to the severity of bronchial obstruction [7]. Hypercapnia in combination with initially intermittent (nocturnal) but subsequently permanent hypoxaemia leads at an accelerated rate to pulmonary hypertension, right-sided heart failure and other sequelae of pulmonary heart disease. The overlap syndrome of COPD and OSA along with the clinical presentation of the most severe cases with alveolar hypoventilation, carbon dioxide retention and morbid obesity is the topic of an original paper by Prof. Anna Brzecka published in the current issue of *Pneumonologia i Alergologia Polska* [8].

Although it was initially postulated that intermittent nocturnal hypoxia in patients with OSA which causes momentary blood pressure increases in the pulmonary circulation might lead to permanent pulmonary hypertension with time, this hypothesis was not confirmed in a subsequent study. It was demonstrated that OSA patients with pulmonary heart disease (about 12% of the patients) also showed signs of hypoxia during the day, whose development required coexistence of COPD. It was finally shown that patients with the overlap syndrome, but not patients with OSA alone, are characterised by an increased risk of pulmonary hypertension, right-sided heart failure and carbon dioxide retention. The above sequelae develop much more rapidly in patients with the overlap syndrome compared to patients with pure COPD [9].

In addition to the increased susceptibility for the development of pulmonary heart disease, deaths during sleep have also been observed in the overlap syndrome. The deaths have been most common in patients with accompanying hypoxaemia and carbon dioxide retention [10].

The management of patients with the overlap syndrome requires continuous positive airway pressure (CPAP) delivered by nasal mask or other devices for non-invasive ventilation support during sleep/waking hours with biphasic positive airway pressure (BiPAP) being the most common one. Not infrequently, due to chronic hypoxaemia, patients with the overlap syndrome also require home oxygen therapy. The oxygen catheter is usually connected to an appropriate port in the nasal mask. There are more advanced models of devices for non-invasive ventilatory support in which oxygen is connected directly to the ventilator and oxygen concentration (FiO_2) is established very precisely.

In advanced forms of the overlap syndrome, when patients with home oxygen therapy clinics receiving oxygen treatment for at least 6 months were recruited for the study, OSA was observed in 15.8% of them. Because some of the patients with the overlap syndrome refused treatment with CPAP it was possible to observe both groups of patients during a longer follow-up. Five-year survival in patients receiving oxygen therapy and CPAP (mean pressure: 9.8 cm H_2O) was 71% compared to 26% in the group receiving oxygen therapy only. After adjustments for multiple other confounders were made it was established that the risk of death in patients receiving oxygen therapy and CPAP was 5-fold lower than in the group receiving oxygen therapy only [11].

In the recent years there has been a discussion over the presence of chronic systemic inflammatory syndrome (CSIS) accompanying heart diseases, metabolic syndrome and smoking, and diagnosed on the basis of elevated C-reactive protein (CRP). The signs of chronic inflammation are seen in COPD [12] and OSA alike [13], which is why criteria that take into account both of these conditions have been proposed [14]. The common pathophysiologic mechanisms found in COPD and OSA include elevated levels of CRP, interleukin-6 (IL-6), nuclear factor κB (NF-κB) and cytokine derivatives (tumour necrosis factor alfa [TNF-α], interleukin-8 [IL-8]), formation of free oxygen radicals as a result of oxidative stress and the similarity of circulating inflammatory cells (CD8+ T cells) [6, 12, 13]. Although there is a regularly increasing body of information on the pathophysiologic mechanisms of CSIS, the detailed investigation of the relationships between the individual conditions, especially in the overlap syndrome, requires many studies.

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