Obstructive Sleep Apnea, Cpap and Covid-19: A Brief Review

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Summary. Obstructive sleep apnea (OSA) is a broadly diffused curable chronic low-grade inflammatory disease sharing impressive clinical and pathogenetic features with Covid-19. Moreover, a potential role of OSA as a detrimental factor for Covid-19 severity has been hypothesized. Continuous positive airway pressure (CPAP) is the mainstay treatment for moderate-severe OSA, but the beneficial effects of ventilation strongly depend on medical expertise and on the patient's adherence and compliance. Although several papers have analyzed the overlaps and outcomes of OSA and Covid-19, limited attention has been dedicated to ventilatory adherence and management of OSA cohorts exposed to Covid-19. We briefly review the literature data, pointing out the main risks and benefits of CPAP for OSA patients in the pandemic setting. (www.actabiomedica.it)

Key words: obstructive sleep apnea syndrome, Covid-19, inflammation, non-invasive ventilation, CPAP

Introduction

The entire world is fighting against a novel coronavirus called Sars-Cov2 responsible for bilateral infiltrative pneumonia, which may lead to severe respiratory insufficiency1. The WHO named the disease Covid-19. Demonstrated risk factors for Covid-19 include obesity, diabetes, hypertension, older age and male sex2. Attention has been focused also on the potential role of obstructive sleep apnea (OSA) as a detrimental factor for disease severity. To date, Pubmed search strategy based on keywords ((sleep apnea) AND (covid)) OR ((OSA) AND (covid)), offers 73 articles, mainly composed of letters to editor, recommendations and brief reviews, with only a limited amount of original articles of variable sample sizes, in many cases sharing information collected through phone calls or indirect patient evaluation. Most of the cited papers analyze the clinical commonalities between OSA and Covid-19; indeed an impressive overlap between the canonical characteristics of Sars-Cov2 and OSA is often recognizable (Fig.1). The prototypical subject affected by severe Covid-19 is an obese middle-aged/elderly male suffering from a metabolic syndrome: similar features are major risk factors for OSA development.

Pathophysiology of increased risk in OSA patients

Variable underlying mechanisms are responsible for higher rates of disease complication in patients affected by OSA, a risk factor for community-acquired pneumonia and viral infections. OSA is also linked to pneumonia severity, it can predispose to increased aspiration and may compromise the efficacy of the defensive cough reflex3. During influenza epidemics,
particular, non-invasive ventilation, e.g., continuous positive airway pressure (CPAP) is the mainstay for treatment of moderate-to-severe OSA patients. CPAP promotes variable cardiovascular protective effects, reduces hypercoagulability decreasing platelet activation, clot strength, hematocrit and lowering blood viscosity. It also increases functional residual capacity thereby improving gas exchange. Furthermore, benefits on arterial stiffness and reduction of serum inflammatory markers including IL-2, IL-4, IL-6, MCP-1, PDGF, and VEGF α can be appreciated in severe OSA patients using non-invasive ventilation for at least 4-hours/night. Reduced mRNA expression of markers related to tissue hypoxia and macrophage infiltration, such as ATF4, CHOP, ERO-1, CD68, CD36, IL-6, PDGF β have also been described. Accordingly, CPAP reduces incidence of acute vascular events and improves post-stroke functional outcome among OSA patients adherent to treatment (Fig.2). Beneficial effects of CPAP in OSA patients are recognizable since the very beginning of therapy, but strongly depend on patient’s adherence and compliance to therapy. Solid data confirmed the importance of regular follow-up to guarantee treatment efficacy: a minimum of 4-h/night is mandatory for at least 70% of nights, with best results when CPAP is used for at least 6-hours/night.

**Safe use of CPAP devices**

Current available recommendations from international societies underline risks related to the utilization of PAP devices in terms of increased virus transmission through aerosol and droplets generation with possible environmental contamination. In the current pandemic background, clinical trends postpone OSA diagnosis and PAP titration rather than starting therapy immediately and keeping adequate follow-up plans. However, relevant scientific contributions demonstrate that filters protect from viral diffusion: using a well-fitted oronasal mask results in a negligible dispersion of aerosol at pressures from 5 to even up to 20 cmH20. Set-up anti-viral filters prevent bacteria and viruses from entering the CPAP tubes and masks, protecting the patients’ airway without influencing...
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Importance of adherence to therapy

To the best of our knowledge, the published material exploring the epidemiological link between OSA and Covid-19 neglects the role of chronic non-invasive ventilation nor tries to stratify results according to patients’ adherence to treatment. In a pathology with manifold dynamics including patients’ compliance, available information regarding efficacy and adherence to treatment is mandatory to understand the relationship between OSA and Covid-19. Accordingly, exploring whether well-performed therapy lowers the risk for complications related to Covid-19 in OSA

Table 1. Everyday hygiene advisories for CPAP users

| Advisories                                      |
|------------------------------------------------|
| Apply a viral/bacterial filter on the machine  |
| Change machine viral/bacterial filter at least after 24 h of utilization |
| Clean masks and tubes with hand-hot soap water |
| Wash your hands with soap and water before and after handling the CPAP device |
| Ensure well-fitting of oro-nasal mask to minimize air leaks |
| Prefer the utilization of a non-vented mask     |
patients becomes a topical issue. Unfortunately, adherence to therapy in OSA samples has slightly decreased in the last months: in a telephone survey performed in New York City around 11% of OSA patients declared that they had ceased to use their PAP device, reflecting the difficulties for sleep clinicians to maintain adequate connection to outpatients\(^{17}\). Updated data from other countries, exploring patients’ compliance during the pandemic, are desirable. It is known that CPAP discontinuation may lead to relapses including lethargy, headache, confusion and dyspnoea\(^{18}\). Therefore, control of PAP devices can allow timely identification of changes in breathing patterns, which may be useful for an early identification of latent viral infections, integrating available screening procedures\(^{19}\).

**Conclusion and perspectives**

Given the multiple and immediate beneficial role of CPAP in reducing risks for infectious complications, chronic inflammation and thrombophilia in OSA patients and considering the relative safety of PAP when adequate precautions are satisfied, we suggest that involved specialists should work on diagnosis of high-risk cases using safe procedures (gloves, full face shields and others personal protective equipment), starting therapy in newly diagnosed patients with appropriate PAP devices and masks (well-fitting non-vented masks and antiviral filters should be preferred), encouraging regular follow-up (warranting routinely machine hygiene) and promoting adherence with either telemedicine or direct contacts if necessary. Even if each country will deal with changing situations, constantly adjusting to emergencies and unpredictable necessities, there is urgent need for harmonized protocols to guide OSA management during this era of pandemic.\(^{20}\) To shed light on the OSA and Covid-19 interaction, wide-sample studies analyzing the significance of well-conducted chronic ventilation therapy shall be carefully explored, focusing on CPAP adherence and efficacy, since the importance of patients compliance and the existence of a dose-response relationship between CPAP and health state benefits is a pivotal issue\(^{21}\). Should these premises be confirmed, enhanced screening programs to guarantee prompt OSA management and protocols of behavioral intervention and/or patient coaching to encourage stronger adherence to therapy may reduce the need for intensive care support during the present and future infective outbreaks, upgrading health care standards.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

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