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## Letter to the Editor

## Authors' response: metabolic and drug-based approach of obstructive sleep apnea (OSA) patients with COVID-19



Dear Editor,

We have read with the great interest a letter to editor by Machado et al. [1] which commented on our publications regarding obstructive sleep apnea (OSA) and coronavirus disease 2019 (COVID-19) outcomes [2]. We agree with the statements from Machado et al. in their letter which highlighted the relationship between hypoxemia and cytokine storm (CS), therefore suggesting the use of continuous positive airway pressure (CPAP) as a non-invasive ventilation (NIV) during the early course from COVID-19 [1]. However, we also must not forget the metabolic aspects from OSA.

Most patients with OSA have other comorbid conditions, especially obesity, diabetes, and dyslipidemia which also contributed to the severity and mortality outcomes from COVID-19, through the dysregulation of renin-angiotensin system (RAS) and elevations of angiotensin-converting enzyme (ACE) activity [2]. One of the drugs commonly taken by those groups of patients is metformin. Metformin helps in controlling blood glucose levels, lowering low density lipoprotein cholesterol (LDL-C) levels, increasing high density lipoprotein cholesterol (HDL-C), and also has weight-reducing effects [3]. In case of COVID-19, metformin can phosphorylate ACE2 which results in the decreased binding between ACE2 and SARS-CoV-2 receptor binding domain (RBD), thus reducing SARS-CoV-2 infectivity [4]. Moreover, metformin can also inhibit inflammatory response which could contribute to the CS through activation of AMP-activated protein kinase (AMPK) [4]. Therefore, the use of metformin drugs in patients with OSA, particularly in those who also have obesity, diabetes, and dyslipidemia is highly encouraged.

Besides the use of CPAP to prevent hypoxemia for patients with OSA during the early course of COVID-19, the use of anti-inflammatory drugs, such as ivermectin, which is given during the late course of the disease before multi-organ failure happened is also strongly suggested for further controlling the CS. Ivermectin can reduce the levels of IL-1, IL-6, and TNF- $\alpha$ , cytokines which are commonly elevated in severe COVID-19 patients, and also suppress the translocation of lipopolysaccharide (LPS)-induced nuclear factor-kappa B (NF- $\kappa$ B) translocation, therefore preventing the clinical deterioration and reducing the mortality rate from COVID-19 [5]. Together with SARS-CoV-2 vaccine prioritization for people with OSA, this approach we offered may help in reducing the burden from COVID-19 in those groups of people.

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## Conflict of interest

None.

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