Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Propofol and sedation in patients with coronavirus disease

To the Editor,

Currently, coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a pandemic. I read the interesting article "Neuroleptic malignant syndrome in patients with COVID-19" recently published in the *American Journal of Emergency Medicine* [1]. Intravenous anesthetic propofol has been widely used for sedation in intensive care units. This case report described continuous infusions of propofol for the sedation of patients with COVID-19. The exact amount of propofol, which is administered by bolus followed by continuous infusion, was not described in this report [1]. However, the use of propofol in the patient with COVID-19 should be cautioned due to the following rationale. Recently, it was reported that SARS-CoV-2 uses angiotensin-converting enzyme 2 (ACE2) as a cell entry receptor, indicating that ACE2 is important for SARS-CoV-2 for the cell entry and transmission [2]. Angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II, which causes vasoconstriction and is involved in endothelial dysfunction. However, ACE2 degrades angiotensin II to angiotensin (1–7), which causes vasodilation via activating the MAS receptor [3]. The actions of ACE2 and ACE are antagonistic [3]. ACE2 is highly expressed in the lung, kidney, endothelium, and heart [3-5]. Propofol (1.78, 3.56, and 7.12 μg/ml) used in clinically relevant concentration increased ACE2 mRNA level of the human pulmonary artery endothelial cells in a time-dependent and concentration-dependent manner [4]. Propofol increased ACE2 protein level and ACE2 activity in the cell membrane of the human pulmonary artery endothelial cells [4]. In addition, propofol increased ACE2 expression in the human umbilical vein endothelial cells [5]. These reports suggest that the propofol-induced increase in ACE2 expression may contribute to the high-risk factors of COVID-19 [2,4,5]. Inhibition of the renin-angiotensin-aldosterone system using an ACE inhibitor or angiotensin II receptor blocker increases ACE2 expression levels – a functional receptor of SARS-CoV-2 [3]. Thus, using ACE inhibitors or angiotensin II receptor blocker for the treatment of hypertension may also contribute to risk factors of COVID-19 [3]. Comorbidities of patients with COVID-19 include hypertension, diabetes, and coronary heart disease [3]. Hence, the increased ACE2 expression induced by administrating ACE inhibitor or angiotensin II receptor blocker used to treat hypertension and diabetic renal disease may contribute as a high risk factor of COVID-19 [2,3]. Propofol used for sedation sometimes causes hypotension as a side effect [6]. Furthermore, as propofol may induce an increased ACE2 expression leading to angiotensin (1–7) production and subsequent vasodilation, propofol-induced hypotension may be aggravated in the patient with COVID-19 [4,6]. Considering the factors mentioned above, the use of propofol in patients with COVID-19 should be avoided when possible in favor of alternative sedative agents, including midazolam and dexmedetomidine. Thus, further studies regarding the risks of propofol use in the patients with COVID-19 are needed.

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