BJA

British Journal of Anaesthesia, xxx (xxx): xxx (xxxx)

CORRESPONDENCE

Propofol and SARS-CoV-2 infection

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Keywords: antiviral; drug repurposing; outcome; propofol; SARS-CoV-2

Editor—Specific antiviral drugs for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remain to be developed, and the effectiveness of vaccines or other therapeutic agents against the virus is an active area of research. Recent proposals have advanced a list of potential agents for repurposing to treat coronavirus disease 2019 (COVID-19). It is not known whether anaesthetic agents and sedatives modulate this infection or disease progression.

The angiotensin converting enzyme 2 (ACE2)/Ang(1–7)/Mas receptor axis exerts anti-inflammatory actions,[1] and data suggest that propofol could upregulate ACE2.[2,3] In human pulmonary artery endothelial cells, Cao and colleagues[2] reported that propofol produced concentration-dependent (10–50 μM) and time-dependent (6–30 h) upregulation of ACE2 mRNA with an associated increase in cell membrane ACE2 activity. In this regard plasma propofol concentrations are important to consider; during general anaesthesia, levels of 2–5 μg ml^{-1} (about 10–30 μM) are reported, but these represent total concentration, and free concentrations are substantially lower because of protein binding.[4] However, the relative importance of total or free is not known. Using relatively high concentrations of propofol (50 and 100 μM) in human umbilical vein endothelial cells, Zhang and colleagues[3] found increased expression of ACE2/Ang(1–7)/Mas receptors and phosphorylation of endothelial nitric oxide synthase to inhibit angiotensin 2-induced apoptosis. ACE2 is widely expressed in human cells and tissues and is a target cell receptor for internalisation of SARS-CoV-2.[5] Continuous infusion of propofol has the potential to increase tissue concentrations and then upregulate ACE2. It is therefore possible that propofol could enhance internalisation of SARS-CoV-2 to precipitate and exacerbate development and persistence of COVID-19.

However, propofol may have beneficial effects against SARS-CoV-2. Clinically relevant (total) concentrations of propofol displaced the binding of (+)[^{3}H]SKF-10047 (a selective σ1 receptor agonist) with a propofol K_i of 10.2 μM (K_i: a 'measure' of binding affinity). Propofol may be a σ1 receptor antagonist.[6] In their repurposing paper, Gordon and colleagues[7] identified two sets of pharmacological agents displaying antiviral activity: inhibitors of mRNA translation and predicted regulators of σ1 and σ2 receptors. As σ1 and σ2 receptor antagonists suppress SARS-CoV-2, σ1 antagonist effects (by propofol) may provide a beneficial action against COVID-19. In addition, as propofol has both antioxidant and anti-inflammatory actions,[8] it may reduce SARS-CoV-2-induced systemic inflammation and thereby provide organ protection.

Propofol is commonly used as a general anaesthetic agent in the operating theatre and a sedative for critically ill patients including those with COVID-19 in the ICU. However, we do not know whether propofol worsens or improves COVID-19 by upregulation of ACE2 or by σ1 antagonistic, antioxidant and anti-inflammatory effects, respectively. As many COVID-19 patients have already been treated in intensive care and undergone surgery under general anaesthesia, outcomes data are likely to exist. It would be instructive to determine the effects of anaesthetic protocol (general *vs* regional anaesthesia, TIVA *vs* inhalation anaesthesia) and agents on outcomes in COVID-19 patients. Based on the results of such retrospective analyses, further prospective RCTs could be planned.

Declarations of interest

KH declares no conflicts of interest. DG Lambert is Chairman of *BJA*.

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doi: 10.1016/j.bja.2020.08.032