

COVID-19 CORRESPONDENCE

Propofol and SARS-CoV-2 infection

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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 colleagues² 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 $\mu\text{g ml}^{-1}$ (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 colleagues³ 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 (+)[³H]SKF-10047 (a selective σ_1 receptor agonist) with a propofol K_i of 10.2 μM (K_i : a 'measure' of binding affinity). Propofol may be a σ_1 receptor antagonist.⁶ In their repurposing paper, Gordon and colleagues⁷ identified two sets of pharmacological agents displaying antiviral activity: inhibitors of mRNA translation and predicted regulators of σ_1 and σ_2 receptors. As σ_1 and σ_2 receptor antagonists suppress SARS-CoV-2, σ_1 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 σ_1 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.

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COVID-19 and occupational skin hazards for anaesthetists

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Editor—Anaesthesiologists are expected to adhere strictly to the WHO '5 Moments for Hand Hygiene' during patient care, including tracheal intubation and extubation.¹ These moments include before and after touching a patient or their surroundings, before aseptic procedures, and after patient bodily fluid exposure. Thus, the hazards of frequent hand hygiene are an important consideration for anaesthesiologists.

The presence of a pandemic further highlights these risks; in particular, the coronavirus disease 2019 (COVID-19) pandemic has reinforced awareness regarding hazards exacerbated by hand hygiene practices and use of personal protective equipment (PPE). The Centers for Disease Prevention and Control (CDC) recommends hand decontamination between each step of donning and doffing PPE.² These practices increase exposure to a variety of irritants and allergens that can have deleterious effects on the skin and the individual. Anaesthesiologists who have suffered from irritant or allergic contact dermatitis can be subject to incapacitating personal and professional losses as this ailment may prevent them from providing direct patient care.¹

Survey evidence before COVID-19 suggests that contact dermatitis affects ~4% of healthcare workers and comprises

70–90% of skin diseases among them.^{3,4} Risk stratification is based on several factors. Those who have a history of atopy are at higher risk of developing contact dermatitis.³ Although Black and Hispanic populations may have a higher incidence of severe atopic dermatitis, studies on skin barrier function in different racial or ethnic groups have not shown consistent differences in epidermal structure or the development of contact dermatitis with exposure to irritants.^{5,6} Extrinsic risk factors for contact dermatitis include prolonged glove use and hand washing. Thus, the prevalence of dermatitis is expected to increase during a pandemic as a result of excessive precautionary measures.^{3,4} Hand hygiene techniques have a broad spectrum of potential adverse effects, ranging from cutaneous xerosis (abnormally dry skin) to severe allergic or irritant reactions. Acutely, contact dermatitis may present with skin erythema, oozing, scaling, crusting, or vesicles (Fig. 1). If chronic, contact dermatitis can lead to lichenification and fissures.⁴ About 80% of contact dermatitis is irritant in nature and the remainder true type IV hypersensitivity reactions. Soaps and detergents are a common cause of irritant contact dermatitis.⁴

Hand cleansing, while important in maintaining provider and patient safety, may be excessive during a pandemic and