



## Letter

## Sedating ventilated COVID-19 patients with inhalational anesthetic drugs

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Most patients with COVID-19 exhibit mild to moderate respiratory symptoms; however, some develop severe pneumonia and hypoxemia is a frequent cause of death. Severely ill COVID-19 patients often require endotracheal intubation and mechanical ventilation. The choice of drugs to sedate these patients differs widely depending on drug availability and clinical expertise. We suggest that care providers with the appropriate clinical expertise, consider the use of inhalational anesthetic drugs, such as sevoflurane and isoflurane for the following reasons.

Intensivists and anesthesiologists are teaming up to treat the sickest COVID-19 patients. They have reported that ventilated COVID-19 patients often require high doses of intravenous sedative drugs such as propofol, midazolam, ketamine and dexmedetomidine. Not surprisingly, there is a growing shortage of these drugs. Also, studies of patients with severe lung injury from causes other than COVID-19 have shown that inhalational anesthetic drugs improve oxygenation and lower mortality when compared with propofol or midazolam [1]. The severity of lung injury in COVID-19 patients correlates with levels of cytokines and viral load. Convincing preclinical data from others and us have shown that inhalational anesthetic drugs attenuate lung inflammation and dilate airways [2,3]. These effects are mediated by  $\gamma$ -aminobutyric acid type A (GABA<sub>A</sub>) receptors, which are expressed in different types of cells in the lung. Stimulating GABA<sub>A</sub> receptors in lung epithelial cells reduces the production of proinflammatory cytokines; whereas activating GABA<sub>A</sub> receptors in airway smooth muscle cells stimulates bronchodilation and improves oxygenation [2,3].

The use of inhalational anesthetic drugs for ventilated COVID-19 patients is both practical and cost effective in low- and high-income countries. These drugs allow sedation levels to be closely

and rapidly controlled [4]; and drug administration does not require electronic infusion pumps, which are in short supply. Conventionally, anesthetic drug delivery units and gas scavenging systems that reduce atmospheric pollution are not available in most critical care units. However, operating rooms which contain the equipment, are being converted into critical care units and anesthetic gas machines are being used as ICU ventilators during the surge of COVID-19 cases [5]. In non-operating room settings, less conventional devices including the AnaConDa system can be used to administer the drugs.

Care providers must exercise caution and consult with anesthesiologists when treating COVID-19 patients with inhalational anesthetics because of the adverse effects of the drugs [4]. They are contraindicated in patients with malignant hyperthermia and can cause cardiovascular instability and respiratory depression [4]. Whether long-term adverse effects result from prolonged drug treatment remains unknown. Finally, to mitigate adverse effects, the Anesthesia Patient Safety Foundation (APSF) has developed guidelines for sedating COVID-19 patients with inhalational anesthetic drugs and recommendations for repurposing anesthetic gas machines as ICU ventilators [5].

Clinical trials of COVID-19 patients are under development in Canada and elsewhere; however, until definitive data are available, care providers should consider the use of inhalational anesthetic drugs. These drugs reduce inflammation, dilate airways, and improve oxygenation and thus, may improve patient outcome.

## Author contributions

B.A.O., D.S.W. and W.Y.L. wrote the letter.

## Declaration of Competing Interest

B.A.O. is an inventor named on a Canadian patent (2852978), a US patent (9517265), and a pending US patent (62/268,137). D.S.W. and W.Y.L. have no competing interests.

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