Risk of propofol use for sedation in COVID-19 patients

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Dear Editor,

The spread of coronavirus disease (COVID-19) has led to an increasing number of severe cases, with many patients needing ventilation. In such cases, continuous sedation is required, and based on recent literature, ICU mortality is around 20–30% [1].

Sedatives currently used in clinical practice include midazolam, propofol, and dexmedetomidine. Propofol has several properties that make it a potentially superior choice for sedation of intubated ICU patients. Sedation with propofol can be rapidly commenced and terminated, even after prolonged administration, allowing for greater control over the level of sedation and faster weaning from mechanical ventilation. However, propofol has several drawbacks that should be considered, especially in COVID-19 patients.

In 2015, Schläpfer *et al.* [2] conducted a study using a rat sepsis model. They reported that all rats anaesthetised with propofol died within 24 hours, unlike those treated with other anaesthetics. If the infusion rate or the total dose is too high, intravenously infused lipid emulsions might inhibit the function of the reticuloendothelial system, resulting in immunosuppression [3]. Intravenously administered lipid emulsions bind to serum proteins, thereby forming lipoproteins. If the dose is too high, the fat droplets that do not form lipoproteins are treated by the body's immune system as foreign substances and are phagocytosed by reticuloendothelial cells. This response might lead to a diminished immune reaction to other foreign substances such as bacteria and viruses.

When propofol was introduced in the United States, surgical-site infection (SSI) cases increased nationwide. In June 1990, the Centers for Disease Control and Prevention reported that propofol use increases the risk for SSIs because of bacterial contamination of lipid emulsions [4]. A recent study reported that the number of SSI cases in patients undergoing gastroenterological surgery was significantly higher with propofol use than with sevoflurane use. Therefore, it was concluded that surgical contamination was not the cause of the SSIs [5]. Following the switch in the treatment from inhaled sevoflurane anaesthesia to total intravenous propofol anaesthesia at our hospital, clinicians noticed a sudden and significant increase in the number of SSIs in patients who underwent open-heart surgery. After experiencing difficulties in infection control for 2–3 years, the results were presented at the Annual Meeting of the Japanese Association for Thoracic Surgery in 2014 [6]. The COVID-19 pandemic puts these findings in a new light.

With COVID-19 becoming more widespread and severe, an increasing number of patients are experiencing thromboembolic disorders such as deep vein thrombosis, lower limb ischaemia, and pulmonary microembolism [7]. Infection, thromboembolism, acute respiratory distress syndrome, and myocardial damage can also occur as adverse drug reactions with lipid emulsions. These adverse drug reactions resemble the currently reported complications of COVID-19 that could make the disease more severe. In the absence of a revolutionary drug treatment for COVID-19, patients

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placed on ventilator support might require long-term sedation. Under these circumstances, the total dose of the administered sedative will be far higher than that used for intraoperative anaesthesia. Propofol infusion syndrome is a rare syndrome that affects patients undergoing long-term treatment with a high dose of this anaesthetic and sedative drug (> 4 mg kg^{-1} h^{-1} for more than 24 hours). It can lead to cardiac failure, myopathy, metabolic acidosis, and kidney failure, and is often fatal [8, 9]. Therefore, these complications must also be considered when treating COVID-19 patients.

The extent of propofol use in different countries is unknown. Differences in propofol use among individual cases are also conceivable. Can the abnormally high fatality rate in severe COVID-19 cases be partially explained by excessive administration of lipid emulsions?

As COVID-19 spreads, more patients are experiencing thromboembolic disorders [7], which can also occur as adverse drug reactions with lipid emulsions. These adverse drug reactions resemble many of the complications of COVID-19 and further complicate cases. Patients placed on ventilator support might require long-term sedation and a potentially high dose of anaesthesia over time. Therefore, the immunosuppressive risk associated with propofol use due to its lipid emulsion content should be considered when choosing sedatives for such patients.

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