Pharmacokinetic Design of Closed Circle Sevoflurane Inhalational Sedation for COVID-19 Patients

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Introduction: During the COVID-19 pandemic the capacity for conventional ventilation and sedation has been challenged. Anesthesia providers have been conscripted to manage anesthesia machines and supplies of intravenous sedatives have been exhausted. Inhalational sedation has been proposed as a solution for these challenges[1], however, the methods employed may not be applicable to anesthesia machines available in ad hoc settings, and may require constant involvement of anesthesia providers in hazardous settings. The proposed system is comprised of the following features:

1) A closed circle system with the vaporizer set to a subhypnotic concentration
2) A liquid bolus calculated to achieve a peak concentration predicted to achieve a BIS of 50
3) Delivery of the bolus when patient response to command is observed by the ICU nurse

Methods: The Kennedy sevoflurane model[2] was implemented in state-space form and the Cortinez pharmacodynamic model [3]were implemented in MATLAB. Simplex minimization was employed to solve for the liquid bolus and vaporizer setting resulting in a BIS nadir of 50 and peak of 60 at 2 hour intervals.
Results: Stable cycles with periods of over 1 hour could be consistently produced.

Conclusions: Clinical validation will be required to determine the utility of this approach.

References: 1. Jerath A, Ferguson ND, Cuthbertson B. Inhalational volatile-based sedation for COVID-19 pneumonia and ARDS. *Intensive Care Med*. 2020;46(8):1563-1566

2. Kennedy RR, Baker AB. The effect of cardiac output changes on end-expired volatile anaesthetic concentrations--a theoretical study. Anaesthesia.2001 Nov;56(11):1034-40

3. Cortínez LI, Anderson BJ. Modeling the pharmacokinetics and pharmacodynamics of sevoflurane using compartment models in children and adults. Paediatr Anaesth. 2018 Oct;28(10):834-840.