Role of almitrine bismesylate in managing refractory hypoxemia in COVID19 acute respiratory distress syndrome

To the Editor,

In the ongoing COVID19 pandemic due to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), clinicians have been using several permutations and combinations to deal with COVID19 Acute Respiratory Distress Syndrome (ARDS). As there is no evidence based anti-viral or a vaccine available at this moment, management is purely supportive based on existing evidence. Clinicians all over the world have used non-invasive/invasive ventilation with lung protective strategies using high FiO2 and positive end expiratory pressure (PEEP), corticosteroids, inhaled nitric oxide (NO), extra-corporeal membrane oxygenation (ECMO), anticoagulants, antivirals, hydroxy-chloroquine sulphate, inflammatory inhibitors, serotherapy with variable results.[1] Researchers are still searching and experimenting various pharmacological agents in variety of doses which could improve intrapulmonary shunting leading to refractory hypoxia in COVID19 ARDS. One such drug is almitrine bismesylate.

Almitrine is a respiratory stimulant and acts as an agonist of peripheral chemoreceptors situated on the carotid bodies. It is a selective pulmonary vasoconstrictor which is mediated by calcium and in various doses has been shown to facilitate pulmonary vasoconstriction which eventually diverts increased pulmonary blood flow from areas of lung which are diseased or injured and thus cannot contribute to oxygenation. Roch *et al*. had demonstrated in a small cohort that a dose of 4-16 μg/kg/min infusion has shown to improve PaO2/FiO2 (P/F) ratio which is used to assess improvement in oxygenation.[2]

Almitrine has seen resurgence in clinical use during the recent COVID19 pandemic owing to its unique mechanism of action on pulmonary vasculature. Losser *et al*. recruited 17 intubated COVID19 ARDS patients who were administered 4–12 μg/kg/min infusion and found that there was statistically significant improvement in oxygenation from baseline in patients after almitrine infusion.[3] Barthélémy *et al*. analyzed the data from 19 mechanically ventilated patients with advanced settings, paralyzed with prone ventilation in almost all patients. Almitrine infusion was administered at 2 μg/kg/min which showed improvement in P/F ratio but did not improve overall patient outcomes.[4] Huette *et al*. managed a 57-year-old female who developed acute cor pulmonale secondary to COVID19 ARDS, diagnosed by transesophageal echocardiography.[5] She was ventilated as per ARDS protocol but hypoxemia was refractory. Almitrine infusion at 4 μg/kg/min was initiated which improved oxygenation and also right ventricular function.

Contrary to this, the findings of Cardinale *et al*. were contradictory. The authors used almitrine along with inhaled NO in 20 COVID19 ARDS patients with P/F ratio of less than 120 and were sedated, paralyzed, and mechanically ventilated.[6] They found that almitrine alone or with NO could not improve oxygenation in moderate to severe ARDS. They also mentioned that loss of HPV could not be the only mechanism of intrapulmonary shunting. In all above-mentioned scenarios, the sample size was small, patient characteristics and ICU management was not standardized and there was no control group. The timing of starting almitrine infusion was not uniform. Well-designed, adequately powered studies with a control arm would be necessary to know the dose, timing of starting and duration of infusion in critically ill COVID19 ARDS patients. Till then, almitrine bismesylate can be used as a rescue drug and titrated to manage refractory hypoxemia.

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Conflicts of interest

There are no conflicts of interest.

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