Exogenous pulmonary surfactant as a potential adjuvant therapy in SARS-CoV-2 patients experiencing acute respiratory distress syndrome?

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Abstract

Given the rapidly evolving nature and case severity of the current pandemic, we present exogenous pulmonary surfactant therapy as a potential investigative route for intervention in cases of SARS-CoV-2 mediated acute respiratory distress syndrome. To the best of our knowledge, readily available bovine/porcine surfactant preparations are not currently being employed in hospitalized patients and could result in better overall outcomes and shorter average duration of ICU stay for inpatients. As hospitals in the United Kingdom and the United States face a wave of SARS-CoV-2 related admissions, it cannot be overstated that new approaches must be explored to reduce the health system burden.

Financial Support

The authors declare no financial support for this letter and no conflicts of interests.

Author Contributions

The manuscript was written through equal contributions of all authors. All authors have given approval to the final version of the manuscript.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is currently understood to enter cells by engaging the angiotensin-converting enzyme 2 (ACE2) receptor.[1] In the lungs, ACE2 is found on cell surfaces of airway epithelia and type 2 pneumocytes, which are responsible for the production and secretion of pulmonary surfactant. The virus uses these cells for fulminant replication, leading to their destruction and impaired surfactant production in the host. No therapeutic approach is presently directed at mitigating the resulting alveolar collapse mediated respiratory failure.

Exogenous pulmonary surfactant therapy, while widely used for the treatment of neonatal respiratory distress syndrome (NRDS), has not yet been implemented for treatment of SARS-CoV-2 associated respiratory failure, to the best of our knowledge, despite showing potential effectiveness in adult cases of acute respiratory distress syndrome (ARDS).[2] Multiple human studies indicate that surfactant instillation in large volumes significantly improves oxygenation indices and decreases mortality.[3] Paired trials pointing at improved oxygenation, but no difference in survival metrics, can partially be explained by low volumes of applied surfactant, inefficient administration techniques, or the heterogeneity of ARDS causation in the target populations.

Severe cases of SARS-CoV-2 typically involve the development of ARDS followed by septic shock or specific organ dysfunction (e.g., acute kidney injury, fulminant myocarditis), leading to death.[4] Existing critical-care, however, is limited to antibiotics/antivirals and oxygenation support (high-flow oxygen and noninvasive positive pressure ventilation) prior to intubation and mechanical ventilation for advanced disease. Thus, ARDS from rapid type-2 pneumocyte destruction appears to be an appropriate target for therapy to mitigate alveolar compromise and prevent progression of later-stage syndromes.

With current figures indicating that approximately 20% of patients with proven SARS-CoV-2 infections are hospitalized, of whom 25% require critical care, it cannot be overstated that reducing ICU length of stay is critical in decreasing overall mortality and health system burden.[5] There is a unique opportunity to approach this problem using readily available bovine/porcine surfactant preparations, at the appropriate doses, for compassionate-use exemption and rapid, immediate clinical trials.

In summary, we propose the exploration of surfactant therapy--via endotracheal aerosolization at 300mg/kg or similar--for use in conjunction with standard procedure in intubated patients.

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