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CARTA AL EDITOR

Lung surfactant: its role against the new Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

Surfactante pulmonar: posible intervención frente al nuevo Síndrome Respiratorio Agudo Severo Coronavirus 2 (SARS-CoV-2)

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Dear Editor:

As it is known, the first patients with symptoms of Coronavirus 19 (COVID-19) disease appeared in Wuhan, China, in December 2019. Since then, the disease has spread rapidly and progressively, affecting 184 countries. More than 3.5 million confirmed cases have been reported with a fatality rate over 7 %.(1) The most common symptoms of Coronavirus infection include fever, dry cough, fatigue, sore throat, and shortness of breath. In the most severe cases, it can manifest

itself as pneumonia, Severe Acute Respiratory Syndrome, kidney failure and even death.[2]

The prevalence of severe hypoxic respiratory failure in patients with COVID-19 is 19 %.[3] Reports from China show that 4 % to 13 % of patients with COVID-19 need non-invasive mechanical ventilation and 2.3 % to 12 % require invasive mechanical ventilation.[4,5,6] The incidence of hypoxic respiratory failure in patients with COVID-19 continues to be researched. About 14 % of infected patients develop the disease in its most severe form, requiring oxygen therapy, 5 % are admitted to the Intensive Care Units and require invasive mechanical ventilation.[3]

The Acute Respiratory Distress Syndrome (ARDS) has been described as the leading cause of mortality from COVID-19.[7,8] Hoffmann, *et al.* explained that Coronavirus 2 of the Severe Acute Respiratory Syndrome (SARS-CoV-2) penetrates the cell and uses as a receptor the angiotensin-converting enzyme 2 (ACE2), which is a membrane exopeptidase, present in organs such as the kidney, lungs and heart.[9] Pulmonary ACE2 is located in type II pneumocytes, which are cells that produce and secrete lung surfactant. If the virus replicates in these cells and destroys them, the production of the endogenous surfactant in patients is affected and the cascade that ends with ARDS is triggered. In a histological analysis of postmortem lung tissues from patients who died from COVID-19, Carsana *et al.* found characteristics of the exudative and proliferative phases of diffuse alveolar disease such as: capillary congestion, pneumocyte necrosis and hyperplasia, hyaline membrane, interstitial edema, reactive atypia, platelet thrombus formation, and fibrin,[10] evidencing a clinical picture of ARDS.

To face the sepsis developed by COVID-19, the expert panel makes recommendations regarding the management of patients with ARDS related to the invasive mechanical ventilation, which includes the use of high values of positive pressure at the end of expiration, mechanical ventilation in the prone position, alveolar recruitment maneuvers, inhaled nitric oxide, and the use of extracorporeal membrane oxygenation.[11] However, no reference is made to therapeutics aimed at mitigating the alveolar collapse resulting from the endogenous surfactant deterioration where strategies such as the use of exogenous lung surfactant may contribute to improving alveolar oxygenation and acute hypoxemic respiratory failure.

We believe that timely administration of a proven exogenous lung surfactant may provide benefits to SARS-CoV-2 patients, as is the case with other ARDS etiologies.

The exogenous lung surfactant from porcine origin (Surfacen), produced and registered in Cuba since 1995, has a composition of phospholipids (95 %), mainly dipalmitoylphosphatidylcholine (DPPC) and hydrophobic proteins (SP-B and SP-C) that constitute 1.5 % and other lipids (3.5 %). This drug was evaluated in non-clinical studies, where it demonstrated a significant improvement in the pulmonary gas exchange, its anti-inflammatory, antibacterial and antileishmanial effect and it prevented the anatomopathological lesions, typical of the Respiratory Distress

Syndrome.[12,13,14,15]

The suggestion to apply Surfacen therapy in ARDS, in children and adults, was supported by its pharmacological and biophysical properties, which are essential to try to reverse or, at least, attenuate the complex process of inflammatory and oxidant character that comprises its physiopathology.[16]

The clinical trials conducted with this lung surfactant demonstrated its efficacy in improving oxygenation, ventilatory and radiographic variables, and clinical course. It also contributed to reducing mortality in preterm infants and children with ARDS, with a safety profile similar to that of other lung surfactants currently on the market.[17]

The treatment scheme used in children and adults with ARDS, which combines repeated low doses (100 mg every 8 hours for 3 days) of Surfacen with conventional oxygenation and mechanical ventilation treatment, determined the favorable evolution of the patients.[17] The justification for using low doses as a treatment scheme for ARDS is based on the fact that there is no consensus on the optimal dose and that using amounts similar to those used in newborns requires the intrapulmonary administration of a volume of liquid, which would cause the alveolus to flood, affect gas exchange and obstruct the airways.

The scientific evidences regarding the use of this drug in Cuba allowed registering its use in adults with ARDS in 2010 and in children with this condition in 2014. In the national action protocol for the clinical management of SARS-CoV-2 patients in Cuba,[18] Surfacen is one of the drugs recommended for use. The first dose (100 mg) should be administered at the time of the patient's intubation.

Based on this evidence, the authors believe that the timely administration of Surfacen could be part of a beneficial strategy in patients with SARS-CoV-2.

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Conflict of interest

The authors declare no conflict of interest.

Authorship contribution

EDC: Literature review, compilation of information, structure and writing of the article.
VSRM: Literature review, revision and contributions to the article focused on intensive care medicine.
NMOM: Original idea of the article and management of the team.
All authors participated in the discussion of the results, read, reviewed, and approved the final text.