

## **Cystic Fibrosis, Adult Patient with Mechanical Ventilation and its Application of Exogenous Surfactant!**

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**Received:** May 24, 2019; **Published:** June 28, 2019

### **Abstract**

Cystic fibrosis is defined conceptually as a pathology that is caused by mutations specifically in the gene that encodes the CFTR protein (cystic fibrosis transmembrane conductance regulator). The authors describe the experience of a clinical case with a female patient diagnosed with Cystic Fibrosis, with a positive culture by *Inquilinus Limosus* who had 18 days of intubation, and within their treatment was given exogenous surfactant to try to improve their ventilatory status. In this case, the decrease in exhaled CO<sub>2</sub>, the fall in the plateau pressure and the resistance of the airway were evidenced.

**Keywords:** *Cystic Fibrosis; Exogenous Pulmonary Surfactant; Adult Patient*

### **Abbreviations**

CFTR: Cystic Fibrosis Transmembrane Conductance Regulator; CF: Cystic Fibrosis; ENAC: Respiratory Epithelial Sodium Channel; SP-A: Surfactant Protein A; SP-B: Surfactant Protein B; SP-C: Surfactant Protein C; SP-D: Surfactant Protein D; CD14: Cellular receptor called CD14 present in the alveola macrophage; CO<sub>2</sub>: Carbon Dioxide; CmH<sub>2</sub>O: Centimeters of Water; MmHg: Milimeters of Mercury; ARDS: Adult Respiratory Distress Syndrome

### **Introduction**

Cystic fibrosis known by its initials (CF) is defined conceptually as a pathology that is caused by mutations specifically in the gene that encodes the CFTR protein (cystic fibrosis transmembrane conductance regulator) [1]. CFTR is widely described as an anionic channel of the cell membrane which affects ions and fluids in exocrine tissues, determining their quantity, and interacts with a respiratory epithelial channel (ENaC), affecting other cellular proteins [2].

When two defective CF gene alleles of both parents are genetically transmitted, it results in CF and when there is CFTR dysfunction in sweat glands there will be an increase in salt in the sweat and poor secretion of chloride and bicarbonate in the respiratory tract, causing secretions that eventually result in obstruction of the mucosa, chronic infection and inflammation, altering the mucociliary clearance [2].

The mucociliary clearance, of all the existing mechanisms in the respiratory system is one of the most important, its function being to protect the deeper respiratory tracts of the inhaled particles, such as allergens, pathogens or other contaminants. The respiratory epithelium contains hair-like structures called cilia, which are protected by a protective layer of mucus. In addition, superior to this is another liquid layer on the surface of the airway, in which finally foreign particles and microorganisms are trapped. Dehydration in the periciliary fluid causes a decrease in mucociliary clearance, this situation together with mucus hypersecretion of inadequate consistency further compromises the true function of the respiratory system [3].

These altered mechanisms consequently produce chronic colonizations of the respiratory tract with bacteria that eventually lead to repeated infections of the lower respiratory tract, resulting in inflammation and remodeling of tissues. As a treatment for these infections, oral, inhaled and systemic antibiotics are prescribed, producing a colonization, but with resistant organisms, representing a further predictor of premature death in conjunction with a rapid decrease in lung function [4].

Existing all these proinflammatory responses present new therapeutic intentions that could promote improvements in these patients, within these proposals are the exogenous cathelicidins, which are still under investigation for a possible therapeutic effect due to their antibacterial activity and an immunomodulatory activity, and an additional capacity modulating the inflammatory responses of the host, such as the production of inflammatory cytokines and the migration of immune cells. In addition, the benefits of exogenous surfactant are being observed, in order to facilitate pulmonary delivery of therapeutic agents, being a possible delivery vehicle, due to its ability to improve the distribution of therapeutic agents to the peripheral lung regions, in addition to the already known immunomodulatory properties of the surfactant, lubrication of the ciliary layer and maintain pulmonary recruitment. Its use has been repeatedly investigated in patients with Acute Respiratory Distress Syndrome and in premature newborns with surfactant deficiency resulting in the administration of exogenous surfactant is safe and well tolerated in a spectrum of pulmonary diseases, however, it is necessary to have with more conclusive studies [4].

### Clinical Case

Female patient of 31 years of age, attended in a class A hospital of the Costa Rican Social Security, with a diagnosis of Cystic Fibrosis with CFTR dysfunction, who had domiciliary management with antibiotic therapy, in addition to therapies with instrumental mechanisms for bronchial cleaning between they vibrator vest, Acapella and aerosoloterapia.

The patient is admitted for an infectious disease, in spite of antibiotic therapy, therapy with instrumental mechanisms, vibrating vest and manual therapy, the patient continues with a torpid evolution, and it was necessary to start with the administration of high-flow oxygen therapy by means of High-flow nasal cannula, subsequently, its condition does not improve and it was necessary to perform an endotracheal intubation, a culture of bronchial secretion was performed and a positive culture report was received by *Inquilinus Limosus* (first reported in Costa Rica, this crop was reported).

After 18 days of intubation an extubation attempt was made which was unsuccessful, and for this reason the tracheostomy was scheduled. During a general visit, the case is discussed and it is decided to postpone the completion of the tracheostomy and initiate with the application of exogenous pulmonary surfactant intratracheally and nebulization with it.

A surfactant preparation of 100 mgs was made in 10 cc of physiological serum, and it was administered every 8 hours for 72 hrs. It should be noted that the procedure was performed in the following order:

- Bronchial lavage was performed with surfactant with the same dilution.
- He was administered 14 cc of intratracheal surfactant dilution through the endotracheal tube.
- Finally, it was nebulized with surfactant.

The evolution of the patient was very satisfactory after the placement of surfactant, allowing the decrease in mechanical ventilator parameters, their CO<sub>2</sub> levels reported in volumetric capnography decreased from 57 mmHg to 53 mmHg and finally to 43 mmHg, the

resistance of the pathway airway fell from 51 cmH<sub>2</sub>O/L/sec, to 19 cmH<sub>2</sub>O/L/sec, the plateau pressures progressively decreased from day 1 of application until day 3 of extubation from 26 cmH<sub>2</sub>O to 18 cmH<sub>2</sub>O on the day of extubation, finally achieved successful extubation after 3 days of the application of Exogenous Pulmonary Surfactant.

**Discussion**

In the results obtained in this clinical case, it can be observed how the application of pulmonary surfactant could improve oxygenation and alveolar ventilation, as well as the mechanisms of bronchial cleansing in patients with Cystic Fibrosis, with respect to this case it was possible to observe a decrease in the measurement of CO<sub>2</sub>, reflecting an improvement in alveolar ventilation, and at the level of ventilatory mechanics, improvements were observed in the plateau pressure, and airway resistance, which represents the use of lower airway pressures, improvement in the pulmonary volume, and decreased secretions in the airway, as well as a decrease in inflammation in the bronchial tree [5].

The surfactant in addition to being recognized for its function of decreasing the surface tension in the liquid air interface, also is for developing a very important function, this being to prepare a defense against infection and inflammation, specifically surfactant protein B and C (SP-B and SP-C), which in conjunction with SP-A and SP-D, have immunomodulatory properties, SP-A and SP-D, have structural similarity to the family of collectins (they have an immune role), SP-B, inhibits the production of nitric oxide in alveolar macrophages and SP-C interacts with CD14, therefore it is a molecule that interacts in a recognition pattern which makes it possible to extend its use immunological to other organisms that invade the lung, these properties suggest that in this clinical case, in addition to the antibiotic therapy used, the use of surfactant could have potentiated it by its immunomodulatory function [6].

Improvement parameters from day 1 to day 3			
	Carbon dioxide	Airway Resistance	Plateau pressure
Day 1	57	51	26
Day 2	53	32	22
Day 3	43	19	18

**Table 1:** Parameters of ventilatory mechanics and CO<sub>2</sub> measured in the evolution day 1 to day 3

Exogenous surfactant is being associated with treatments for CF, being shown to have bactericidal activity against pathogens, in addition to regulating inflammation, this provides strong evidence as a therapeutic agent for the treatment of respiratory infections associated with CF and other infections. pulmonary bacteria [4].

Gunasekara L., *et al.* explain that in CF there is clearly an altered function of the pulmonary surfactant in the airways of patients, thus altering their lung function [7].

Raghavendran K., *et al.* report that the pulmonary surfactant dysfunction could be reversed or decreased, increasing the concentration of surfactant, and both respiratory function and lung mechanics have shown improvements after the administration of exogenous surfactant in multiple studies with animals with of respiratory distress in vivo, in this clinical case it was possible to demonstrate improvement in the level of airway resistances, plateau pressure and its decrease in CO<sub>2</sub> levels that reflect an improvement in ventilation after the application of surfactant. In this same review, the authors conclude that more studies should be done with other forms of preparations that could demonstrate even more benefits in lung diseases in adult patients and ARDS [8-10].

The dose that was decided upon was applied according to that applied by Rodríguez V., *et al.* in which they used the exogenous surfactant dilution in the preparation of 100 mgs diluted in 10 cc of physiological saline, which they used in the treatment of pulmonary atelectasis It was also used in the same dilution by Barrese Y., *et al.* (2015) in the treatment with pulmonary surfactant in respiratory distress syndrome in adults [11,12].

## Conclusion

In conclusion, the use of pulmonary surfactant in this clinical case could be one of the causes that contributed to a satisfactory evolution of the patient and could be an emergent therapy in the management of patients with CF, however, they warrant more reviews of cases and experimental studies to be able to generate more evidence in this type of therapy.

## Conflict of Interest

The authors declare that they have no conflict of interest with the publication of this study. The previous case report was analyzed and approved by the Scientific Ethics Committee.

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Volume 8 Issue 7 July 2019

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