Hypertonic Saline and PEP: Is It Worth a Try?

Cystic fibrosis (CF) is a recessive genetic disease that requires aggressive therapies to slow the disease progression. CF is a complex disorder that primarily affects the digestive system and the lungs. A major characteristic of CF is lung disease, which is responsible for the majority of CF-related deaths.

CF is caused by an absent or deficient CF transmembrane regulator, which is a protein responsible for chloride secretion. This ion-transport abnormality causes a progressive loss of lung function, with a cascading pathophysiology that creates a vicious cycle in which the airways suffer dehydration, mucus retention, obstruction, inflammation, and infection. Current CF respiratory therapies aim to break the cycle and treat the symptoms.

The Cystic Fibrosis Foundation is committed to finding a cure for CF—a therapy that actually targets the basic genetic defect, and the Foundation's CF Therapeutics Development Network has several clinical trials underway.¹ However, the mantra in CF research and care is to leave no stone unturned. In other words, any and all possible therapeutic approaches to fight this disease are considered for research and discovery, including medications already available on the market. Investigating and hopefully discovering the usefulness of medications already available is referred to as the “low-hanging fruit.”

Hypertonic saline is one of the low-hanging fruits studied in CF. In Australia it was noticed that surfers with CF had better outcomes than non-surfers. The hypothesis was that the salty mist inhaled during surfing helps clear the airways through osmosis—that the inhaled salt allowed more water into the airways and increased the airway surface liquid. This hypothesis prompted investigation, and studies did indeed show improved mucociliary transport.^{2,3} To date, the largest study of hypertonic saline in CF, by Elkins et al,⁴ was a multicenter study in patients with CF who inhaled 7% hypertonic saline twice daily. The therapy significantly decreased the incidence of pulmonary exacerbations and moderately improved pulmonary function. As a result of those studies, inhaled hypertonic saline therapy is now recommended by the Cystic Fibrosis Foundation as a maintenance therapy for patients with CF who are ≥ 6 years old, and there is a study in process with children younger than 6 years.⁵

Unfortunately, not everyone can tolerate hypertonic saline therapy. Some patients experience substantial bron-

chospasm, and in those patients hypertonic saline is not recommended. Furthermore, in those who can tolerate it there is the concern that inhaling 4 mL of hypertonic saline twice daily adds an additional 30 min of therapy to an already time-consuming daily treatment regimen. With respect to hypertonic saline therapy, it boils down to the question of toleration and/or adherence, which is why the data from O'Connell and colleagues⁶ in this issue of the Journal are so intriguing. They studied a positive expiratory pressure (PEP) nebulizer to deliver hypertonic saline to 4 patients who previously could not tolerate hypertonic saline via a traditional nebulizer, due to bronchospasm, bad taste, and intolerable cough. All 4 patients tolerated and adhered to hypertonic saline via PEP nebulizer, and there was a trend toward fewer pulmonary exacerbations and longer time between exacerbations. These results are impressive.

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O'Connell and colleagues thought outside the box. The study, albeit a small case series, is motivating and thought provoking. The patients appear to have benefited from the PEP therapy, with bronchodilation, reduced bronchospasm, and improved aerosol deposition. Interestingly, in an editorial on hypertonic saline therapy, Ratjen mentioned concern about inhaled hypertonic saline not reaching the small airways where the mucus plugging is causing obstruction.⁷ Perhaps PEP therapy with hypertonic saline is the answer! Why not try this technique the next time you challenge a patient who previously showed a 15% decline in pulmonary function, or hated the taste, or could not tolerate the excessive cough after taking hypertonic saline via nebulizer alone? It seems more than worthy of a try, in light of the potential benefits of hypertonic saline therapy. Furthermore, what if one was to actually *perform* PEP therapy while taking the hypertonic saline? Perhaps combining the therapies will boost adherence, as well as benefit.

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Ms O'Malley has disclosed relationships, with Pari, Pharmaxis, and Gilead.

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