Exercise for COPD: Take it Without a Grain of Salt

Hyperosmolar saline has been used for many years for sputum induction as an aid to diagnosing lower respiratory infections, especially tuberculosis.[1] More recently 7% saline has been used as a therapeutic aerosol to assist airways clearance in persons with cystic fibrosis (CF) and non-CF bronchiectasis. Studies have shown that the regular, twice daily inhalation of 7% saline aerosol is safe for persons with CF and helps promote mucus clearance, with improvement in pulmonary function and a decrease in respiratory tract exacerbations.[2,3] Long-term studies in CF have established the role of hyperosmolar saline as a therapeutic agent, and it is now recommended as part of the treatment regimen for this disease.

As a result of these encouraging findings, there has been a rush to consider using hyperosmolar saline for variety of other pulmonary diseases, including chronic obstructive pulmonary disease (COPD) and asthma. In contrast to CF, there are few data that show benefit of hyperosmolar saline therapy in these conditions, but compelling data showing an adverse response to the inhalation of 3% saline in persons with moderate to severe COPD.[4] Despite this, the relatively low cost of hyperosmolar saline and its safety profile when used to treat CF have led to its use for the treatment of COPD.

In contrast to the paucity of data related to the effectiveness of hyperosmolar saline, it is clear that structured exercise rehabilitation programs are of great benefit to patients with COPD. A Cochrane review concluded that exercise rehabilitation "relieves dyspnea and fatigue, improves emotional function, and enhances patients' sense of control over their condition. These improvements are moderately large and clinically important. Rehabilitation forms an important component of the management of COPD".[5] Exercise improves functional exercise capacity, as measured by shuttle walking or the standardized 6-min walk distance, it improves strength and nutritional status, and it promotes airway clearance. Although exercise programs are less expensive than even the cheapest of drugs, for exercise to be beneficial it requires a greater time and effort commitment on the part of patients.

In this issue of RESPIRATORY CARE, Valderramas and colleagues present results of a study where they asked the question, "If we enroll subjects with COPD in an exercise rehabilitation program, will they obtain additional benefit if they also inhale hypertonic saline?" The answer to this question was a resounding "No".[6] Although all subjects were enrolled in exercise rehabilitation and had significant improvement in 6-min-walk test distance and a decrease in dyspnea, the improvement, particularly in functional exercise capacity, was greater in those who inhaled iso-osmolar saline, as compared to 3% hyperosmolar saline.

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This is an important and well-designed study. This study was appropriately powered, and the duration of 8 weeks was sufficient to assess interventions. The use of functional exercise capacity as a primary outcome variable was very important. Functional exercise capacity is more sensitive to improvements in mucus clearance than pulmonary function or quantity of sputum expectorated. Along with dyspnea measurements and quality of life, these outcomes are probably the best suited to evaluate the effect of exercise training or of a potential expectorant medication such as hyperosmolar saline.[7] By adding saline to exercise training rather than using hyperosmolar saline as the only intervention, they highlighted the crucial importance of exercise rehabilitation. Furthermore, the results suggested that hyperosmolar aerosol *decreased* the benefits of exercise.

There are some limitations to the Valderramas et al study. The severity of COPD was not well categorized, and, although Valderramas et al state that the subjects had moderate to severe COPD according to the Global Initiative for Chronic Obstructive Lung Disease guidelines, it would have been useful to know if there were subjects who received more or less benefit based on a more precise assessment of their disease severity. Valderramas et al used 3% saline as their active intervention, and only gave this 3 times a week. This is in contrast to studies in CF and non-CF bronchiectasis, where 7% saline aerosol is usually administered several times each day. Still, 12% of the subjects had to withdraw from the study because of adverse effects related to the hyperosmolar saline. Thus, it would be very unlikely that more frequent and higher dosing of hyperosmolar saline would have provided more benefit, and may have produced even more adverse effects.

It is also possible that normal saline inhalation may not be inactive. Studies that have used saline as an active intervention to promote mucus clearance have been un-

derpowered, but, in general, there has been no definitive benefit shown.[7] There is also a concern with the aerosol generator used. If the aerosol truly had a particle size of 0.5 μm, it is possible that the particles were too small to effectively deposit within the conducting airways of these subjects. It would have been useful to have a better characterization of the aerosol generated and some indication of aerosol deposition.

Hypertonic saline is inexpensive, and, because of its established effectiveness in CF lung disease, it is sad but unlikely that the results of the Valderramas et al study will slow the trend of inappropriate use for the treatment of other lung diseases. It is easier for a patient to sit passively for 5–10 min inhaling an aerosol than it is to exercise vigorously for 60 min at least 3 times per week. Easier is not always better, and, based on these results, it is fair to say that inhaling hyperosmolar saline may be detrimental in persons with moderate to severe COPD. As clinicians and scientists, we must do all that we can to help our patients, but also must take care to do no harm. It is my hope that papers such as this will increase enthusiasm for the widespread use of exercise rehabilitation programs in COPD while limiting the use of unproven and potentially harmful therapies.

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