Halotherapy in Patients with Cystic Fibrosis: A Pilot Study

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Abstract

Objectives: Cystic fibrosis (CF) is a complex genetic disorder characterized by dehydration of the respiratory epithelial surface resulting in impaired mucociliary clearance [1,2]. Thick, sticky secretions obstruct the lower airways and sinuses, providing an environment for chronic infection. A significant proportion of CF patients experience sinus symptoms and almost all have radiographic findings of chronic sinusitis. Increasing the volume of airway surface liquid improves mucus clearance in patients with CF [2,3]. Inhaled hypertonic saline is one method used in patients older than 6 years to rehydrate the Airways [3]. In clinical trials hypertonic saline inhalation improved pulmonary function [2,4], and respiratory symptoms, reduced pulmonary exacerbations [4,5] and reduced absenteeism from school or work [5]. Halotherapy (HT; “halos” means salt in Greek) aims to deliver salt particles into the upper and lower airways, and appears to be a promising alternative method.

Introduction

Cystic fibrosis (CF) is a complex genetic disorder characterized by dehydration of the respiratory epithelial surface resulting in impaired mucociliary clearance [1,2]. Thick, sticky secretions obstruct the lower airways and sinuses, providing an environment for chronic infection. A significant proportion of CF patients experience sinus symptoms and almost all have radiographic findings of chronic sinusitis. Increasing the volume of airway surface liquid improves mucus clearance in patients with CF [2,3]. Inhaled hypertonic saline is one method used in patients older than 6 years to rehydrate the airways [3]. In clinical trials hypertonic saline inhalation improved pulmonary function [2,4], and respiratory symptoms, reduced pulmonary exacerbations [4,5] and reduced absenteeism from school or work [5]. Halotherapy (HT; “halos” means salt in Greek) aims to deliver salt particles into the upper and lower airways, and appears to be a promising alternative method.

For centuries, especially in Eastern Europe, people have visited natural salt caves for the healing properties of the air. Halotherapy (HT) simulates conditions in a natural salt cave by dispersing salt particles in a controlled air medium. While similar in principles to hypertonic saline, HT differs in that it delivers dry aerosol microparticles (1-5μm) of salt rather than a wet solution [6]. Typically, a person visits a facility that provides HT services for a period of 30-60 minutes, where they read or perform relaxing activities while undergoing halotherapy. Breathing through the nose and mouth allows treatment effect to target the upper and lower airways.

While considered spa treatment, Halotherapy’s effectiveness was evaluated in multiple clinical trials. HT was studied in 139 patients with respiratory diseases, among whom 5 had CF. Improvements in flow-volume loop parameters and decreased bronchial resistance measured by plethysmography were reported after 10-20 sessions. The CF patients were reported to have similar response with the treatment [7]. Another recent study showed an increase in lung function and sputum production in 6 CF subjects after only 5 halotherapy sessions [7].

As a pilot work to assess feasibility, evaluate effectiveness, and gather clinical data to better estimate sample size for an experimental study, we used a pre- and post- test study design to assess the effect of HT on the pulmonary and sinus symptoms, dyspnea, and quality of life in CF patients.

Methods

This open-label study was performed at the Salt Room® Orlando, which provided the facilities for HT. Patients from a single CF care center (Central Florida Pulmonary Group, Orlando, FL, USA) were enrolled in the study between January and June of 2012. Study endpoints were measured twice: before the first and after the last HT
The average duration of follow up was 3 weeks. FEV1 and FVC continued on their standard regimen of treatment for CF.

Participants who had received antibiotics or corticosteroids for the treatment of a pulmonary exacerbation within 30 days, had taken hypertonic saline within two weeks, or had used HT previously were all excluded from the study. Patients were screened for eligibility in the study protocol, including all 9 sessions of HT. Two additional patients met the inclusion criteria but they developed respiratory exacerbations before starting the treatment and were excluded from the analysis. Every participant completed medical history and physical exam, performed spirometry, returned for a baseline visit within one week of screening. At the baseline visit patients provided written consent, or assent. Eligible participants, based on the available clinical information, were clinically stable on their medical regimen for at least a month prior to enrollment, forced vital capacity (FVC) > 40% of predicted value, forced expiratory volume in one second (FEV1) between 30% and 85% of predicted value, and a score of 10 or above on the rhinologic domain of the Sino-Nasal-Outcome Test-20 (SNOT 20), which is a validated patient-outcome reported measure with four sub-domain: psychological function, rhinological symptoms, sleep function, and ear and/or facial symptoms [8]. Participants who had received antibiotics or corticosteroids for the treatment of a pulmonary exacerbation within 30 days, had taken hypertonic saline within two weeks, or had used HT previously were all excluded from the study. Patients were screened for eligibility in the clinic, prior to enrollment. Eligible participants, based on the available clinical information, returned for a baseline visit within one week of screening. At the baseline visit patients provided written consent, had a medical history and physical exam, performed spirometry, and answered questionnaires, including the Borg dyspnea index test, Cystic Fibrosis Questionnaire-Revised (CFQ-R), and the Sino-Nasal Outcome Test (SNOT-20).

### Results

Between January and June of 2012, twelve participants completed the study protocol, including all 9 sessions of HT. Two additional patients met the inclusion criteria but they developed respiratory exacerbations before starting the treatment and were excluded from the analysis. Every participant completed medical history and physical exam, spirometry test, and sets of questionnaires (Borg, CFQ-R, SNOT-20). During the course of the study the participants continued on their standard regimen of treatment for CF.

The baseline characteristics of the participants are shown in Table 1. The average duration of follow up was 3 weeks. FEV1 and FVC did not change significantly (p value of 0.49 and 0.87, respectively).

### Table 1: Baseline Characteristics of the 12 Patients

| Age | Female | FEV1 (L)(% predicted) | FVC (L) | FEV1/FVC | SNOT 20 | Borg Dyspnea Score |
|-----|--------|-----------------------|---------|----------|---------|-------------------|
| 35.11 | 8 (66.7%) | 1.841.7 +/-0.75 (56.17) | 2.8183 +/-0.98 | 65.3% +/-12.73% | 1.48 +/-0.65 | 2.17 +/-1.09 |

All values except gender are stated +/- SD

### Table 2: Effect of Halotherapy on Lung Function, SNOT, and Borg Score

| FEV1 | FVC | SNOT 20 | Borg Score |
|------|-----|---------|------------|
| -0.0192 (95% CI -0.0781 to 0.0398, P=0.49) | -0.0100 (95% CI -0.1202 to 0.0142, P=0.87) | -0.62(95% CI -1.03 to -0.2, P=0.007)* | -0.79(95% CI -1.64 to 0.05, P=0.065) |

Dyspnea index (Figure 2); the mean score decreased by 0.79 (95% CI -1.03 to -0.2, P=0.007). Among the CFQ-R Table 3 domains health perception domain, to 100, the best score (good health). Asterisks indicate P<0.05 for the comparison between before- and after- treatment.

### Table 3: Effect of Halotherapy on CF-Q-R**

| Physical | Vitality | Emotion | Role | Treatment Burden | Eating | Weight | Digest |
|----------|----------|---------|------|-----------------|--------|--------|--------|
| 8.33 (95% CI 4.09 to 12.57, P = 0.001)* | 6.25 (95% CI -2.97 to 15.47, P = 0.16) | 3.95 (95% CI -1.98 to 9.90, P = 0.176) | 0 (correlation and t test can't be computed since values were unchanged) | 1.85 (95% CI -9.72 to 13.42, P = 0.73) | 10.18 (95% CI 3.19 to 17.15, P = 0.008)* | 5.092 (95% CI 1.95 to 12.14, P = 0.14) | 4.62 (95% CI -11.03 to 1.77, P = 0.14) | 0.00 (95% CI -6.81 to 6.81, P = 1.0) | 5.55 (95% CI -10.54 to 21.65, P = 0.46) | 9.25 (95% CI -2.94 to 21.46, P = 0.124) | 10.18 (95% CI 4.39 to 15.97, P = 0.002)* |

* Statistically significant difference

** For each domain in the CFQ-R a higher score indicated improvement. Highest possible =100.
change did not reach significance (p=0.124). All the other domains showed no significant change (Figure 3). There were no reports of chest tightness or wheezing as a direct result of the HT.

Discussion

This pilot study of HT is the first to include assessment of pulmonary function, dyspnea scores, sinus symptoms, and quality of life exclusively in patients with CF. Hypertonic saline has long been used successfully in CF, and HT is thought to work similarly in clearing the thick mucus secretions. A potential advantage of HT is the osmotic effects of salt particles both in the nose and sinuses as well as the lower airways. Hypertonic saline inhalation functions mainly in the lower airways, and may also be used via lavage or nebulization to the sinuses, but this is a separate procedure. Hypertonic saline can provoke bronchospasm in susceptible individuals; none of the participants in our study reported such symptoms.

The symptomatic improvement in the sinus symptoms may relate to the ability of the salt particles from HT to reach a target in the sinuses and stimulate mucus clearance. In this study, we enrolled only participants with significant baseline sinus symptoms (score >10 on the SNOT-20 rhinosinusitis domain). HT may not have similar effects on patients with absent or minimal sinus symptoms.

The improvement in some of the CFQ-R domains must be interpreted with caution as the study population was relatively small. The improvement in physical activity score may infer improved exercise capacity, which helps preserve pulmonary function [10]. The improvement was also significant in the health perception and digestive domains. One could speculate that the digestive domain may be influenced by better sinus function by improving olfactory sensation, and therefore appetite.

Our study had some limitations. Since this was an open-label study, we could not evaluate whether the improvement in the reported symptoms were due to subjective effects or objective physical benefits. While there were clear trends toward improvement in dyspnea perception, our pilot study was not powered enough to detect the change. The improvement in sinus symptoms was based on patient report, but was not validated by objective measures like sinus imaging. While the study was too short to evaluate outcomes like reduction in antibiotics or surgery, our initial findings suggest that a more detailed and longer-term study may be worthwhile to evaluate those important outcomes. Longer-term studies are also necessary to evaluate the effect of HT on pulmonary exacerbations and lung function. Examining the quantity or rheologic characteristics of sputum might also be considered in further studies, as well as the effects of HT on bacterial colonization.

In conclusion, this exploratory study has demonstrated that HT may have some benefit in CF patients with symptomatic sinus disease. Longer studies, using particularly a randomized controlled study design, are necessary to better evaluate the effects of HT on other outcomes and on patients with asymptomatic sinus disease.

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Conflict of interest

Daniel Layish MD sits on the Board of Directors of the Salt Therapy Association and serves as Medical Advisor for the Salt Room® Orlando. Dr. Geller is currently employed by AbbVie, Inc in North Chicago, IL.

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