Published in final edited form as:

Pediatr Pulmonol. 2013 August ; 48(8): . doi:10.1002/ppul.22665.

INCREASED ADHERENCE TO CFF PRACTICE GUIDELINES FOR PULMONARY MEDICATIONS CORRELATES WITH IMPROVED FEV1

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Abstract

BACKGROUND—CFF practice guidelines recommend patients age 6 use dornasealfa and hypertonic saline daily, and those age 6 colonized with *P. aeruginosa* use inhaled tobramycin and oral azithromycin to improve lung function and reduce pulmonary exacerbations. A decline in FEV1 was noted in our 2008 CF Center Report. We hypothesized that increasing adherence to prescribing guidelines for these pulmonary medications would improve mean FEV1.

METHODS—This was a quality improvement project completed at a US CF center. CFF practice guidelines were reviewed with the center physicians. Patients were identified that were eligible to receive recommended therapies and it was determined whether they were prescribed the therapies. Baseline FEV1 data was collected. Adherence rates and FEV1 were followed quarterly for 1 year. Providers received a quarterly report card with adherence rates, mean FEV1 compared to colleagues, and a list of eligible patients that were not prescribed recommended therapies.

RESULTS—92 patients were included. At baseline, the overall adherence rate was 59%. Overall adherence increased quarterly ($p < 0.001$). Each quarter there was improvement in adherence to prescribing for each medication ($p < 0.001$). Except in quarter 1, FEV1 increased quarterly ($p = 0.092$). There was moderate correlation ($r = 0.533$) between improved adherence and improved FEV1.

CONCLUSIONS—Educating clinicians about guidelines, providing feedback on adherence to guidelines, and monitoring prescribing patterns improves prescribing adherence. FEV1 showed improvement after months of sustained adherence, trending towards significance. Longer follow-up is necessary to determine if improved prescribing adherence translates into improved FEV1 or slows rate of decline in FEV1.

Keywords

cystic fibrosis; dornasealfa; hypertonic saline; tobramycin; azithromycin; guidelines; adherence

Introduction

Cystic Fibrosis (CF) is an inherited disease that impacts multiple organs. Abnormalities in the cystic fibrosis transmembrane conductance regulator (CFTR) cause abnormal sodium absorption and chloride secretion. These abnormalities result in the formation of thick mucus plugs that clog the airways, decrease mucociliary clearance, and provide a nidus for bacterial infection. Chronic infection results in a neutrophil-dominated inflammatory response.^{1,2} Over time the inflammation remodels the airways and causes progressive destruction, decline in lung function, and respiratory failure.²

Over the last 20 years there has been a considerable increase in life expectancy for patients with CF.³ This increase has been attributed to many contributing factors, including: antibiotics, anti-inflammatories, mucolytics, and consistent care at a CF Center.^{4–18} Respiratory complications are the largest source of morbidity and mortality for CF patients, so many therapies are aimed at maintaining and improving lung function in patients with CF. The Cystic Fibrosis Foundation (CFF) pulmonary guidelines recommend that all patients age 6 should use dornasealfa and hypertonic saline on a daily basis, and those age 6 colonized with *Pseudomonas aeruginosa* should use inhaled tobramycin (TOBI) and oral azithromycin to improve lung function and reduce pulmonary exacerbations.¹⁹

The CFF provides an annual report to each CF center summarizing how each center compares on a national level for specific measures. Measures and outcomes are outlined on an annual basis by the CFF. Centers enter site-specific data in the CF Patient Registry, which is then analyzed and compared with the other CF accredited centers. This comparative data set is reported back to the center. Forced expiratory volume in one second (FEV1) data is reported in several age groupings: 6–12 years, 13–17 years, 18–29 years, and >30 years. FEV1 is monitored closely in patients with CF as it is associated with morbidity and mortality. Preservation of FEV1 is one of the goals of the pulmonary therapies used to treat CF. A decline was noted in mean FEV1 in the 6–17 and 13–17 year age groups in the 2008 CF Center Patient Registry Report for the CF Center at Children's Hospitals and Clinics of Minnesota. The mean FEV1 decreased from 99.7 to 97.3 in the 6–17 age group, and 100.2 to 92.5 in the 13–17 age group. Although this is a small decrease, there was concern about progression of the decline and potential long-term impact on morbidity and mortality for our patients. Concomitantly it was recognized that physician adherence to the pulmonary medication guidelines, although in some cases higher than the national average, had room for improvement (only 85.7% of eligible patients were on azithromycin, 82.3% on TOBI, 78.2% on dornasealfa, and 29.5% on hypertonic saline; compared to the national averages of 65.9%, 68.1%, 78.3%, and 42.7%, respectively).^{20,21} The objective of this study was to use a simple intervention to increase provider prescribing adherence to the CFF pulmonary medication guidelines. We hypothesized that increasing clinician adherence to the guidelines for these four pulmonary medications would improve the mean FEV1 in the 13–17 year olds and would stabilize FEV1, in hopes of preventing further decline in the 6–17 year olds.

Materials and Methods

This was a quality improvement project which used the Plan, Do, Study, Act process.^{22,23,24} The study was approved by the Institutional Review Board at Children's Hospitals and Clinics of Minnesota (CHCM) and was completed at CHCM (University of Minnesota CF affiliate).

At the start of the study, CFF pulmonary guidelines were reviewed with the CF Center physicians.¹⁹ Each physician received a copy of the guidelines along with a one-page

summary of the recommendations for dornasealfa, hypertonic saline, TOBI, and azithromycin. A CF Action Plan was created that included the four targeted pulmonary medications, airway clearance strategies, nutrition/dietary recommendations, and other CF medications (Figure 1). The CF Action Plan is completed by physicians at each visit and is given to patients and their families. Our goal, by listing all the medications on one document, was to prompt providers to remember to prescribe the recommended therapies.

The CF Patient Registry was used to identify patients who, based on CFF pulmonary guidelines, were eligible to receive dornasealfa, hypertonic saline, TOBI, and azithromycin, and to collect baseline FEV1 data. Patients' charts were reviewed to determine whether they were prescribed the recommended therapies. Prescribing adherence rates and FEV1 were followed quarterly for one year. Providers received a quarterly report card with prescribing adherence rates and mean FEV1 compared to their colleagues, as well as a list of eligible patients that were not on recommended therapies (Figure 2).

Statistical analysis

Chi-square compared prescribing adherence rates between physicians and quarters. Two-sample t-test compared mean FEV1 between patients who were prescribed medications and patients who were not. ANOVA compared mean FEV1 by quarter. Pearson correlation coefficient described the relationship between overall adherence rate and FEV1. All statistical analyses were conducted using the Statistical Program for Social Sciences version 15.0 software (SPSS).

Results

127 patients with CF were seen at CHCM in 2008. 92 patients were included who were eligible to receive dornasealfa, hypertonic saline, TOBI, and/or azithromycin. According to the 2008 CF Patient Registry report (baseline), the overall clinician prescribing adherence rate to CFF guidelines was 59%. Each quarter there was improvement in adherence to prescribing for all medications ($p<0.001$, $p<0.001$, $p=0.001$, and $p=0.003$ for dornasealfa, hypertonic saline, TOBI and azithromycin, respectively) (Figure 3). The overall clinician adherence rate increased quarterly (Figure 4) ($p<0.001$). For the 6–17 year olds, mean FEV1 was 97% at baseline. For the 13–17 year olds, mean FEV1 was 93% at baseline. Each quarter following the intervention, FEV1 increased ($p=0.092$) (Figure 4). There was a moderate correlation ($r=0.533$) between improved adherence and improved mean FEV1 (Figure 4). Patients who were prescribed hypertonic saline and TOBI had a significantly higher mean FEV1 ($p=0.018$ and $p=0.011$, respectively).

Discussion

This study followed the steps outlined by Garber, et al., for improving guideline adherence. Baseline practices were measured, guidelines were disseminated, staff and patients were educated, implementation of practices was monitored, and patient outcomes were measured.²⁵ The results are similar to those of McPhail, et al., who found that educating physicians about prescribing guidelines, providing feedback on prescribing adherence failures, and monitoring prescribing patterns over time improves prescribing adherence.²⁶ As the authors advocate, prescribing guidelines alone do not improve patient outcomes. Physicians must be aware of the guidelines, accept the recommendations, and subsequently implement the guidelines. The results of Garber and McPhail are echoed in the work by Glauser, et al., who note that one time dissemination of guidelines is not sufficient for changing clinician behavior. System changes are necessary for providers to adapt to guidelines.²⁷

A simple intervention, demonstrated by this study, increased provider adherence to guidelines and, unlike the work of McPhail and colleagues, demonstrated a trend for improvement in patient outcomes. It showed that increased provider adherence to prescribing guidelines moderately correlates with improved FEV1.²⁶ Improvement in FEV1 is the expected goal for use of the four pulmonary medications: dornasealfa, hypertonic saline, TOBI, and oral azithromycin. Dornasealfa and hypertonic saline are aimed at decreasing the viscosity of airway secretions, thus improving airway secretion clearance.^{10,28} TOBI is used to eradicate and suppress chronic infection/colonization of *Pseudomonas aeruginosa* which is associated with a more rapid decline in lung function.²⁹ Azithromycin, both by its anti-inflammatory effect and anti-microbial effect has been shown to improve FEV1 and decrease frequency of pulmonary exacerbations of CF.^{6,8, 31}

This study shows a trend of improvement in FEV1 when compared to baseline but did not reach statistical significance. This may be due to several reasons: (1) our baseline adherence rate to prescribing guidelines was already above the national average. There was room for improvement in all areas, but for three of the four medications we were already above or near 80%, (2) our baseline FEV1 was 93% predicted, a decline compared to the previous years, but still within normal and above the national average of 89%, and (3) pulmonary medications may maintain lung function and/or prevent pulmonary exacerbations, rather than actually improve lung function, therefore it may take longer than a year (the length of this study) to see a statistically significant improvement.

Prior to this intervention, it was custom to rely on the physicians to educate themselves about practice guidelines. There was not a system in place to disseminate new information. This intervention has demonstrated that the practice needs to take an active role in disseminating new information to providers, and clarifying expectations as to how they relate to new guidelines.

This study has several limitations. It was performed at a single CF center with eight CF providers and one CF nurse. Presumably it is easier to implement this type of intervention in a smaller practice setting. Consequently, the results are similar to those of McPhail, et al.²⁶ This study relied heavily on the data entered in the CF Patient Registry. If data was missing or contradictory, every attempt was made to obtain accurate prescribing information. There may have been times when the database did not reflect the most up-to-date information.

Conclusions

Educating clinicians about prescribing guidelines, providing feedback on adherence to guidelines, and monitoring prescribing patterns over time improve prescribing adherence. Mean FEV1 shows improvement after several months of sustained adherence and trended towards statistical significance. Longer follow-up is necessary to determine if improved prescribing adherence translates into improved mean FEV1 or a slower rate of decline in FEV1.

Abbreviations

CF	cystic fibrosis
CFTR	cystic fibrosis transmembrane conductance regulator
CFF	Cystic Fibrosis Foundation
TOBI	inhaled tobramycin
FEV1	forced expiratory volume in 1 second

CHCM	Children's Hospitals and Clinics of Minnesota
ANOVA	Analysis of variance

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CF ACTION PLAN

Your FEV1 today = ____ L ____ %predicted Personal Best= ____ L ____ %predicted, Date: ____

AIRWAY CLEARANCE:

- **This is the most important thing you can do to keep your lungs healthy!**
- Your plan includes:
 - **EXERCISE:** 30 minutes 5 days per week
 - **Vest therapy:**
8, 9, 10 at a pressure of 10 and 18, 19, 20 at a pressure of 6 for 5 min each
 - ____ minutes, at least 2 times **each day!** (If coughing more than usual, increase this to 3-4 times each day!)
 - Don't forget to take 3 deep breaths OR cough 3 times between each frequency!
 - **Nebulized medications:**
 - ☐ Albuterol 2 puffs OR 2.5 mg nebulized at beginning of airway clearance
 - ☐ Pulmozyme 2.5 mg nebulized ____ times a day with Vest
 - ☐ Hypertonic Saline ____%, ____mL nebulized ____ times a day with vest
 - ☐ TOBI ____mg nebulized 2 times a day, every other month, at the end of vest treatment
 - ☐ _____

MEDICATIONS:

In addition to your nebulized medications your medications include:

- ☐ Enzymes: _____
- ☐ Antacid: _____
- ☐ Vitamins: _____
 - ☐ Vitamin D3 _____
- ☐ Zithromax (azithromycin): ____ mg every MWF
- ☐ _____
- ☐ _____

Medication changes made today include:

NUTRITION/DIET:

- **Nutrition is extremely important in keeping your lungs healthy!**
- Choose food high in calories, fat, & protein.
- Eat plenty of high-calcium foods.
- Eat foods high in salt/sodium and use the salt shaker.
- If prescribed, take your enzymes at every meal and snack.

Today's weight: ____ pounds, height ____

Goal weight: ____ pounds

Today's BMI %: ____; Goal is 50% or higher

Your personalized nutrition plan includes:

- ☐ Nutritional Supplements: _____
- ☐ Calorie Boosters: _____
- ☐ _____

Stop the spread of germs:

- Avoid contact with people who are sick.
- Use hand sanitizer or wash your hands!
- Keep up to date with immunizations, including annual flu shot every fall.
- Disinfect your nebulizer as instructed!!
- Stay at least 3 feet away from other people with CF.

When sick, increase vest and nebs to 3-4 times daily. If not better within 48 hrs, be sure to call!

UPCOMING TESTS/VISIT:

Yearly labs due: _____

OGTT due: _____

Next visit: _____

IMPORTANT CONTACT INFORMATION:

Office hours: M-F 8:30-4:30 (after 4:30 you will be connected with the pediatric pulmonologist on call)

Phone number: 612-813-3300 or toll free 1-888-242-3327

Figure 1.

CF Action Plan – Provided to all CF patients. Included targeted therapies to remind physicians of pulmonary medication guideline recommendations.

Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung Health

Pulmozyme

For patients with CF, 6 years of age and older who are asymptomatic, or have mild, moderate, or severe lung disease, the CFF strongly recommends the chronic use of dornase alfa to improve lung function and reduce exacerbations.

Hypertonic saline

For patients with CF, 6 years of age and older, the CFF recommends the chronic use of inhaled hypertonic saline to improve lung function and to reduce exacerbations.

TOBI

For patients with CF, age 6 years and older who are asymptomatic, or have mild, moderate, or severe lung disease with *Pseudomonas aeruginosa* persistently present in cultures of the airways the CFF recommends the chronic use of inhaled tobramycin to reduce exacerbations.

Azithromycin

For patients with CF, 6 years of age and older, and with *Pseudomonas aeruginosa* persistently present in cultures of the airways, the Cystic Fibrosis Foundation recommends the chronic use of azithromycin to improve lung function and to reduce exacerbations.

Flume et al. AJRCCM 2007;176(10): 957.

CRCCS Provider Adherence to CFF Pulmonary Guidelines:

Provider	Pulmozyme	Hypertonic Saline	TOBI*	Azithromycin	% Overall Adherence	Mean FEV1 (%predicted)
All	71%	41%	64%	68%	61%	90%
1	100%	100%	100%	100%	100%	86%
2	60%	40%	100%	100%	75%	77%
3	81%	70%	55%	64%	68%	95%
4	100%	40%	50%	75%	66%	85%
5	92%	18%	67%	83%	65%	93%
6	67%	29%	60%	100%	64%	90%
7	41%	24%	75%	50%	48%	89%
8	64%	29%	50%	50%	48%	84%

Highlighted patients are currently not taking 1 or more of the recommended CF pulmonary meds.

Provider 2	Pulmozyme	Hypertonic Saline	TOBI	Azithromycin
John Doe	X		X	X

Figure 2.

Example of the quarterly report card that each provider received. Compares prescribing adherence rates between providers and identifies patients not on recommended therapies.

Figure 3.
Change in prescribing adherence rates for pulmonary medications

Figure 4.
Change in prescribing adherence rate versus change in FEV1 (% predicted) by quarter