The Use of Home Spirometry in Pediatric Cystic Fibrosis Patients: Results of a Feasibility Study

Aarti Shakkottai, MD[1], and Samya Z. Nasr, MD, CPI[1]

Abstract

Medication adherence is poor among pediatric cystic fibrosis (CF) patients, with adolescents having one of the lowest adherence rates. We wanted to identify an adherence intervention that would be acceptable to CF adolescents and assess its feasibility. We surveyed 40 adolescents with CF and asked about barriers to and motivators for their own adherence and to generate ideas for potential adherence interventions. Since most of the respondents chose frequent spirometry at home and medication reminders for interventions, we selected 5 subjects, 10 to 14 years of age, with CF to test the feasibility of home spirometry and medication reminders in pediatric CF patients. This article summarizes the results of both the survey and the feasibility pilot study.

Introduction

Cystic fibrosis (CF) is a chronic, life-shortening illness that affects approximately 1 in 3400 live births within the United States.[1] It is a multisystem disease that results in recurrent pulmonary exacerbations, a steady decline in lung function over time, fat malabsorption, protein-calorie malnutrition, and deficiencies in fat soluble vitamins.[1] CF, like other chronic illnesses, carries a heavy treatment burden. It involves the use of multiple medications several times a day, airway clearance, and dietary requirements.[2] With advancing age and disease severity, there is an increase in treatment complexity and consequently treatment burden, which ultimately results in poor adherence.[2] This has been associated with frequent pulmonary exacerbations, lower lung function, numerous hospitalizations, greater health care costs, and early mortality.[2-5]

Adolescents and young adults generally have lower rates of adherence.[2,3] Prescription refill data reveal adherence rates of 46% to pancreatic enzymes, 60% to multivitamins, and 65% to dornase alfa, a nebulized mucolytic agent.[3] Adolescents also experience the greatest decline in their lung function.[6] Poor nutritional status and, specifically, a body mass index (BMI) less than the 50th percentile is a risk factor for worsening lung function.[7] Good nutritional status has been shown to positively correlate with both lung function and medication adherence.[3]

Several factors have been reported to negatively influence treatment adherence among CF patients including forgetfulness, time pressures, competing priorities, and a perceived lack of usefulness of the prescribed treatment.[8-12] Awareness of the impact of nonadherence on health outcomes is a strong adherence motivator among adolescents with CF.[9,12] Feedback from pulmonary function studies (PFTs) has been shown to improve treatment adherence among adolescents and young adults with CF.[9] Home spirometry with the goal of obtaining more frequent PFT measurements has been trialed in both pediatric and adult patients with CF for early detection of pulmonary exacerbations but not specifically for improving treatment adherence.[13,14] Medication reminders have been used to promote self-management skills and

[1]University of Michigan Health System, Ann Arbor, MI, USA

Corresponding Author:
Samya Z. Nasr, Department of Pediatrics and Communicable Diseases, University of Michigan Health System, 1500 E Medical Center Drive, SPC 5212, Ann Arbor, MI 48109-5212, USA.
Email: snasr@umich.edu

ultimately adherence among children and adolescents with CF.[9,15] Few studies have evaluated the feasibility or desirability of specific adherence interventions in adolescents with CF.

In order to develop an intervention that would be appealing to and potentially useful in promoting treatment adherence in this patient population, we surveyed adolescents and young adults in our Pediatric CF Center. The purpose of the study was to elicit their opinions about interventions that would best encourage them in improving their adherence. Based on the responses from the survey, we also conducted a pilot study to assess the feasibility of a portable personal spirometer device that also provided medication reminders among pediatric CF patients.

Methods

We conducted a survey of CF patients aged 12 to 21 years from our Pediatric CF Center to gauge their opinions regarding the utility of various adherence interventions. Surveys were administered in-person during clinic visits, on the pediatric inpatient wards, or via telephone. Surveys were conducted over a span of 4 months. All participants had a confirmed diagnosis of CF with a sweat chloride measurement ≥60 mEq/L and/or 2 disease-causing mutations.

The survey consisted of 2 parts. The first part was focused on eliciting the participants' views on their own adherence to medications. Participants were asked about the number of medications they were taking on a daily basis and the frequency at which they taking them. They were asked to rate their adherence on a scale of 0 to 4, with 0 indicating nonadherence and 4 representing 100% adherence. Participants were also asked about potential adherence barriers and motivators. They were provided with a few examples that they could either circle yes or no as it applied to them, or they could specify any other motivators and barriers to adherence. In the second part of the survey, subjects were asked to generate ideas for potential adherence interventions. A few choices such as home spirometry and medication reminders were provided in addition to the opportunity to specify any other suggestions for improving adherence.

The second part of the study was designed to evaluate the feasibility of home spirometry and medication reminders, the 2 top adherence intervention ideas from the survey. Five subjects aged 10 to 14 years with CF were recruited for this pilot study. The Spiro PD (PMD Healthcare, Allentown, PA) personal spirometer was chosen for monitoring PFTs at home. It is an Food and Drug Administration–approved device that allows its users to measure their PFTs up to once a day, store and track values on the device, and download the results onto a computer as a PDF. It generates flow-volume loops and volume-time curves and reports the forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and forced expiratory flow 25th to 75th percentile (FEF25-75) as a percent predicted based on age, gender, height, and ethnicity using the NHANES III (Third National Health and Nutrition Examination Survey) reference values. It also provides reminders for up to 25 different medications.

Three of the 5 subjects were randomly selected to receive the Spiro PD for measuring their PFTs once a week at home for 3 months. The other 2 subjects were followed to assess their adherence to medications without the intervention. Subjects were trained on the proper use of their device at enrollment by a respiratory therapist (RT) who also contacted them once a week via telephone to record their PFT result and address any questions about the device. Devices were programmed to provide daily medication reminders for inhaled hypertonic saline, dornase alfa, and CF multivitamins. We chose these medications for their convenient once or twice daily dosing.

We evaluated treatment adherence using medication possession ratios (MPRs) for inhaled hypertonic saline, dornase alfa, and CF multivitamins. An MPR is calculated by dividing the total days of medication supplied by the number of days within that period. Adherence during the course of the study was compared to that in the 3 months prior to enrollment. Health outcome parameters including PFTs, BMI percentile, and frequency of pulmonary exacerbations were obtained on all participants at baseline and end of study through review of their medical records. These are routinely assessed in all CF patients during their quarterly clinic visits. In addition, we assessed our participants' perceptions of treatment burden at baseline and at end of study based on their responses to the Cystic Fibrosis Questionnaire–Revised (CFQ-R), a validated health-related quality of life measure for CF patients.[16-18] The pilot study was approved by the University of Michigan Institutional Review Board. It was also registered with http://www.clinicaltrials.gov.

Results

Forty participants completed the questionnaires. Table 1 summarizes the respondents' demographics. Participants reported taking an average of 12.30 (SD 7.61, range 4-40) medications daily. Twenty-seven participants (67.50%) reported having 2 or more barriers to their adherence with forgetfulness being the most common.

Table 1. Demographic Characteristics of the Survey Respondents.

Characteristics	Respondents (N = 40), Mean (SD)
Age (years)	16.45 (2.77)
Gender (% female)	57.50
BMI (percentile)	41.74 (26.52)
FEV1 (% predicted)	79.43 (23.40)
FEF25-75 (% predicted)	65.48 (35.19)
Sweat chloride (mmol/L)	91.88 (28.60)
% delF508 homozygous	40.00
% delF508 heterozygous	55.00

Abbreviations: BMI, body mass index; FEV1, forced expiratory volume in 1 second; FEF25-75, forced expiratory flow 25th to 75th percentile.
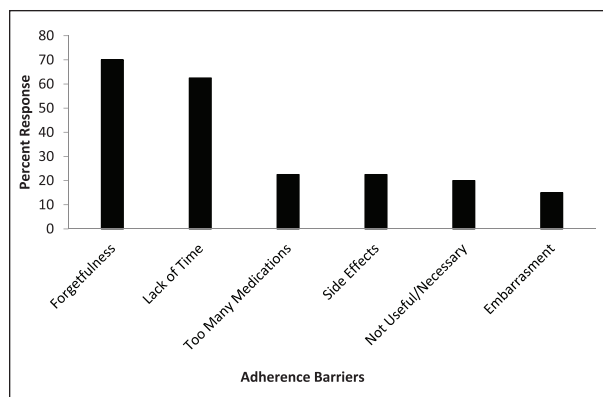

Figure 1. Barriers to adherence as reported by the survey respondents.

Figure 2. Motivators for adherence as reported by the survey respondents.
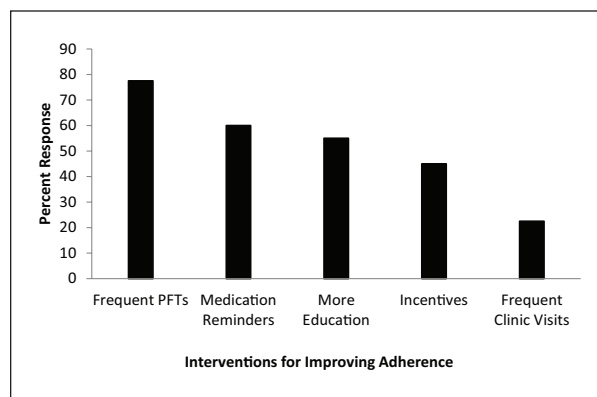
Figure 3. Interventions for improving adherence suggested by our survey respondents.

Table 2. Baseline Characteristics of the Participants in the Pilot Study.

Characteristics	Intervention Group (N = 3), Mean (SD)	Control Group (N = 2), Mean (SD)
Age (years)	11.50 (0.64)	11.93 (1.29)
FEV1 (% predicted)	74.33 (16.65)	93.00 (1.41)
BMI (percentile)	64.33 (19.14)	41.50 (16.26)
Sweat chloride (mmol/L)	100.00 (5.66)	95.00 (1.41)
% homozygous delF508	66.66	50.00
% heterozygous delF508	33.33	50.00

Abbreviations: FEV1, forced expiratory volume in 1 second; BMI, body mass index.

Figure 1 shows the various adherence barriers. On a scale of 0 to 4, with 0 being 0% and 4 being 100% adherence, mean self-reported adherence was 3.33 to oral medications, 3.27 to airway clearance regimen, and 3.36 to inhaled medications. Mean overall adherence was 2.96 among those with 2 or more self-reported barriers as compared to 3.54 among those with 1 or no reported barriers.

Thirty-seven respondents (92.50%) identified 2 or more factors that positively influenced their adherence to medications. Figure 2 shows the different adherence motivators listed by the respondents. Twenty-nine respondents (72.50%) reported encouragement from parents, other family members, and friends as an adherence facilitator. Frequent monitoring of PFTs as an adherence intervention was endorsed by 31 respondents (77.50%), with 29 of them supporting home spirometry. Twenty-two out of the 24 respondents that chose medicati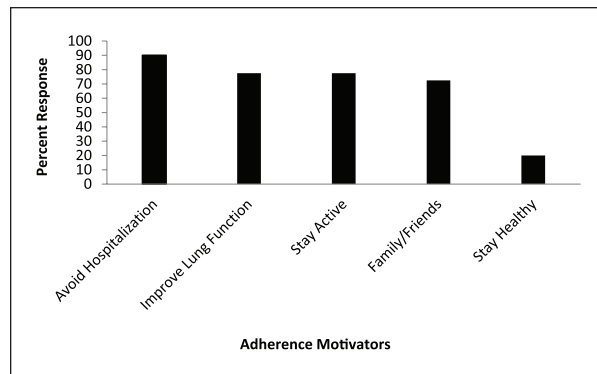on reminders as an intervention recommended implementing them either as a text message or smartphone application. All of the intervention ideas are shown in Figure 3.

The baseline demographics of the 5 subjects that participated in the home spirometry feasibility study are summarized in Table 2. The intervention group had a

Table 3. Health Outcome and Quality of Life Measures in the Intervention and Control Groups at Baseline and End of Study.

Characteristics	Intervention Group (N = 3)		Control Group (N = 2)	
	Baseline, Mean (SD)	3 Months, Mean (SD)	Baseline, Mean (SD)	3 Months, Mean (SD)
FEV1 (% predicted)	74.33 (16.65)	77.00 (6.56)	93.00 (1.41)	91.50 (16.26)
FEF25-75 (% predicted)	71.33 (32.87)	76.33 (8.02)	98.00 (48.08)	83.00 (52.33)
BMI (percentile)	64.33 (19.14)	64.00 (21.28)	41.50 (16.26)	47.00 (8.49)
No. PE (in 3 months) total	2	2	1	1
Treatment burden score (child CFQ-R)	74.33 (6.35)	81.67 (16.80)	78.00 (31.11)	72.50 (23.33)
Treatment burden score (parent CFQ-R)	59.33 (17.24)	67.00 (19.05)	61.00 (24.04)	66.50 (31.82)

Abbreviations: FEV1, forced expiratory volume in 1 second; FEF25-75, forced expiratory flow 25th to 75th percentile; BMI, body mass index; CFQ-R, Cystic Fibrosis Questionnaire–Revised.

lower mean FEV1 and FEF25-75 percent predicted but a higher mean BMI percentile compared to the control group. Average training time was 30 minutes. Mean percent adherence to the weekly spirometry was 94.67%. Average use of the medication reminder feature was 50.23%, largely due to alarms not being audible enough and/or finding it too cumbersome to repeatedly change alarm times to suit changing schedules. Subjects appreciated the opportunity to review their PFTs during the weekly telephone calls.

Mean FEV1 percent predicted over the 3-month study period as reported on the Spiro PD was 75.77%. Mean FEV1 percent predicted from clinic for this same time period was 75.67%. Mean FEF25-75 percent predicted on the Spiro PD was 46.89%, while that obtained in clinic was 73.83%. Table 3 summarizes the changes in PFTs, BMI, and treatment burden scores observed during the course of the study in the 2 groups. The intervention group maintained their BMI and had an increase in their PFTs. There were individuals in both groups that experienced pulmonary exacerbations over the course of the study but none of them required hospitalization. Furthermore, there was no change in the average number of pulmonary exacerbations in either group. Parent and child CFQ-R treatment burden scores improved in the intervention group.

Figure 4 illustrates the mean MPR for dornase alfa, inhaled hypertonic saline, and CF multivitamins in the 2 groups at baseline and at end of study. The intervention group had a mean composite MPR of 1.11 at baseline compared to 0.99 in the control group. The mean composite MPR at the end of the study was 1.16 in the intervention group and 1.03 in the control group.

Discussion

We surveyed adolescents with CF to identify an adherence intervention that would be acceptable to them. The
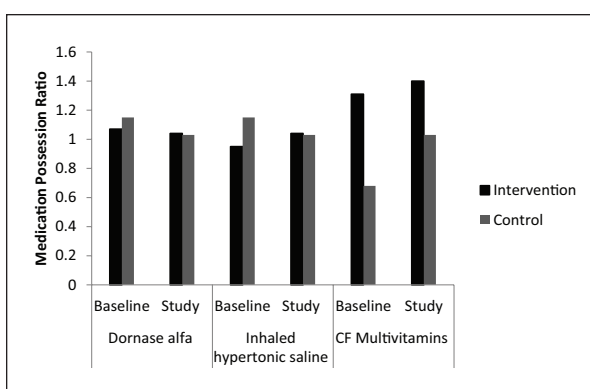

Figure 4. Mean medication possession ratios for inhaled hypertonic saline, dornase alfa, and CF multivitamins in the intervention and control groups at baseline and end of study.

first part of the survey questioned participants about their own adherence and the factors that positively or negatively influence it. Majority reported having at least 2 barriers to their adherence with forgetfulness and a lack of time being the most common. These 2 adherence barriers have been frequently reported by CF patients and their caregivers.[8-10,12] Survey respondents also cited doubts about the necessity or usefulness of some of the treatments as being a barrier to their adherence. The lack of significant symptoms, especially after being poorly adherent to a prescribed treatment, has often been reported as a reason for continued nonadherence.[9,12] Self-reported adherence to inhaled medications was better than that to oral medications, possibly because of a greater likelihood of experiencing symptoms when missing them. In addition, prescription refill data show better adherence to inhaled medications as compared to oral medications among CF patients of all age groups.[3] Self-reported adherence was lower among respondents with more barriers, which is also consistent with previous reports.[10]

The tangible feedback of PFTs was a strong adherence motivator among the survey participants. This finding has been previously reported among adolescents with CF.[9] Knowing the effects of their nonadherence on their health has been reported as an adherence facilitator by many adolescents and perhaps PFTs could help provide that feedback.[12] Reminders by parents or caregivers or those provided electronically such as through a text message have been shown to encourage self-management and ultimately improve adherence among adolescents with CF.[9,12,15] Medication reminders were identified as an adherence motivator and also a potential adherence intervention by majority of the survey participants.

We selected the Spiro PD device for measuring PFTs at home since it also provides medications reminders. While there was excellent correlation between the FEV1 percent predicted generated on the device with that obtained in clinic, there were significant discrepancies in the FEF25-75 percent predicted values. This may have been secondary to the small sample size, in addition to the intervention group having moderate lung disease. There is literature that indicates that the FEF25-75 can be variable in patients with moderate or severe lung disease.[19,20]

This was a pilot study to evaluate the feasibility of using the Spiro PD device. The small sample size and short study duration made it difficult to appreciate any significant changes in adherence or health outcome parameters. The slightly higher incidence of pulmonary exacerbations in the intervention group is consistent with their lower baseline lung function. The higher perception of treatment burden among the intervention group at baseline is also consistent with their lower lung function as suggested by Quittner and colleagues.[18,21] The lower caregiver reported treatment burden scores as compared to the self-reported scores is also consistent with previous reports.[18]

The studies showed that adolescents with CF value the feedback from frequent PFT monitoring and that home spirometry could be successfully used in pediatric CF patients. A larger study is currently underway to evaluate the impact of performing frequent spirometry at home on treatment adherence, health outcomes, and quality of life over a longer period of time.

Authors' Note

Author Contributions

AS: Contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

SZN: Contributed to conception and design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

Funding

References

1. Cystic Fibrosis Foundation Patient Registry. 2014 Annual data report. Bethesda, MD. Cystic Fibrosis Foundation; 2015.
2. Sawicki GS, Goss CH. Tackling the increasing complexity of CF care. *Pediatr Pulmonol*. 2015;50(suppl 40):S74-S79.
3. Shakkottai A, Kidwell KM, Townsend M, Nasr SZ. A five-year retrospective analysis of adherence in cystic fibrosis. *Pediatr Pulmonol*. 2015;50:1224-1239.
4. Quittner AL, Zhang J, Marynchenko M, et al. Pulmonary medication adherence and health-care use in cystic fibrosis. *Chest*. 2014;146:142-151.
5. Eakin MN, Bilderback A, Boyle MP, Mogayzel PJ, Riekert KA. Longitudinal association between medication adherence and lung health in people with cystic fibrosis. *J Cyst Fibros*. 2011;10:258-264.
6. Rosenfeld M, VanDevanter DR, Ren CL, et al; Investigators of Coordinators of the Epidemiologic Study of Cystic Fibrosis. Decline in lung function does not predict future decline in lung function in cystic fibrosis patients. *Pediatr Pulmonol*. 2015;50:856-862.
7. Cogen J, Emerson J, Sanders DB; EPIC Study Group. Risk factors for lung function decline in a large cohort of young cystic fibrosis patients. *Pediatr Pulmonol*. 2015;50:763-770.
8. Dziuban EJ, Saab-Abazeed L, Chaudhry SR, Streetman DS, Nasr SZ. Identifying barriers to treatment adherence and related attitudinal patterns in adolescents with cystic fibrosis. *Pediatr Pulmonol*. 2010;45:450-458.
9. George M, Rand-Giovannetti D, Eakin MN, Borrelli B, Zettler M, Riekert KA. Perceptions of barriers and facilitators: self-management decisions by older adolescents and adults with CF. *J Cyst Fibros*. 2010;9:425-432.
10. Bregnballe V, Schiøtz PO, Boisen KA, Pressler T, Thastum M. Barriers to adherence in adolescents and young adults with cystic fibrosis: a questionnaire study

in young patients and their parents. *Patient Prefer Adherence*. 2011;5:507-515.

11. Goodfellow NA, Hawwa AF, Reid AJ, Horne R, Shields MD, McElnay JC. Adherence to treatment in children and adolescents with cystic fibrosis: a cross-sectional, multi-method study investigating the influence of beliefs about treatment and parental depressive symptoms. *BMC Pulm Med*. 2015;15:43.

12. Sawicki GS, Heller KS, Demars N, Robinson WM. Motivating adherence among adolescents with cystic fibrosis: youth and parent perspectives. *Pediatr Pulmonol*. 2015;50:127-136.

13. Finkelstein SM, Wielinski CL, Kujawa SJ, Loewenson R, Warwick WJ. The impact of home monitoring and daily diary recording on patient status in cystic fibrosis. *Pediatr Pulmonol*. 1992;12:3-10.

14. Lechtzin N, West N, Allgood S, et al. Rationale and design of a randomized trial of home electronic symptom and lung function monitoring to detect cystic fibrosis pulmonary exacerbations: the early intervention in cystic fibrosis exacerbation (eICE) trial. *Contemp Clin Trials*. 2013;36:460-469.

15. Johnson KB, Culpepper D, Scott P, Gordon JS, Harris C. The utility of providing automated medication dose reminders to young children on chronic medication. *J Telemed Telecare*. 2011;17:387-391.

16. Modi AC, Quittner AL. Validation of a disease-specific measure of health-related quality of life for children with cystic fibrosis. *J Pediatr Psychol*. 2003;28:535-545.

17. Quittner AL, Buu A, Messer MA, Modi AC, Watrous M. Development and validation of the Cystic Fibrosis Questionnaire in the United States: a health-related quality-of-life measure for cystic fibrosis. *Chest*. 2005;128:2347-2354.

18. Quittner AL, Sawicki GS, McMullen A, et al. Psychometric evaluation of the Cystic Fibrosis Questionnaire-Revised in a national sample. *Qual Life Res*. 2012;21:1267-1278.

19. Quanjer PH, Weiner DJ, Pretto JJ, Brazzale DJ, Boros PW. Measurement of FEF25-75% and FEF75% does not contribute to clinical decision making. *Eur Respir J*. 2014;43:1051-1058.

20. Lukic KZ, Coates AL. Does the FEF25-75 or the FEF75 have any value in assessing lung disease in children with cystic fibrosis or asthma? *Pediatr Pulmonol*. 2015;50:863-868.

21. Habib AR, Manji J, Wilcox PG, et al. A systematic review of factors associated with health-related quality of life in adolescents and adults with cystic fibrosis. *Ann Am Thorac Soc*. 2015;12:420-428.