Adherence to Airway Clearance Therapies by Adult Cystic Fibrosis Patients

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BACKGROUND: Airway clearance therapy (ACT) is critical in cystic fibrosis (CF). OBJECTIVES: To determine rates of self-reported adherence to ACT by patients treated in an adult CF program, to identify patient characteristics associated with poor adherence, to typify adherence according to ACT technique, and to indicate reasons for poor adherence. METHODS: Our cross-sectional study included CF subjects age 16 years and older. Enrollees were evaluated via general structured questionnaire, adherence questionnaire, clinical assessment, spirometry, and S_{pO_2} values. Each was stratified by self-reporting protocol as high, moderate, or poor adherence to ACT. Concordance between physiotherapist recommended ACT technique and self-reported subject adherence was subjected to agreement analysis. RESULTS: Of the 63 subjects studied, 38 (60%) qualified as high adherence, 12 (19%) as moderate adherence, and 13 (21%) as poor adherence. Logistic regression identified education level (less than high school) as an independent factor associated with poor adherence (odds ratio 10.2, 95% CI 1.23–84.7, $P = .03$). Positive expiratory pressure ($\kappa = 0.87$) and flutter device ($\kappa = 0.63$) usage both corresponded with a high level of agreement, while active cycle of breathing technique ($\kappa = 0.40$) and autogenic drainage ($\kappa = 0.39$) each showed moderate agreement. Agreement was low for percussion and postural drainage ($\kappa = 0.23$). Reasons given most frequently for poor adherence to ACT were "not enough time to do ACT" (28%), "cannot be bothered" (16%), and "do not enjoy ACT technique" (8%). Many (32%) provided no reason. CONCLUSIONS: Study outcomes showed a high rate of ACT adherence in adult CF subjects. Lower level of education was the most important factor in poor adherence to ACT. Self-reported adherence and treatment recommendations were in best agreement with positive expiratory pressure and flutter device techniques. *Key words: cystic fibrosis; Shwachman-Kulczycki score; lung function; adherence to treatment; disease severity; airway clearance therapy*
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Introduction

Cystic fibrosis (CF) is a multisystem disease leading to substantial chronic sinopulmonary disease, pancreatic exocrine dysfunction, excessive sweat chloride, and male infertility. Its incidence is estimated at one in 3,500 live

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births, making it the most common autosomal recessive inheritable condition. In recent years, medical and technologic advances have increased median survival worldwide, primarily through early diagnosis, input of specialists, better treatments, and organ transplantation.[1] However, standard methods are rigorous, requiring time-consuming regimens of patient self-care. Daily management routinely involves airway clearance therapies (ACTs), exercise, oral and inhaled respiratory medications, and oral supplementation (pancreatic enzymes, vitamins) to control malabsorption.[2,3]

While poor therapeutic adherence is typical and contributes substantially to CF treatment failures, the degree of inadequacy generally varies, depending on patient subset, therapeutic target, required treatment, and the definition of adherence. The relationship between adherence and progression of CF subsequently remains a matter of debate. It is likely that poor adherence, as with other chronic conditions, results in more acute episodes and hospital admissions and possibly contributes to premature death.[4] Reasons for adherence problems in CF have been explored in various studies,[2,5-7] acknowledging that daily management places high-level demand on adults with CF.[8]

ACT is an integral part of CF management that specifically calls for daily commitment. It is also the most time-consuming aspect of patient care, but it is considered critical for maintaining lung function. ACT is usually performed twice daily, but may be increased to 4 times per day if necessary. Although techniques and time intervals for ACT may vary, the aim is to promote expectoration, keeping airways clear; yet there are few studies exploring adherence rates with ACT. To understand better ACT nonadherence would be useful in subsequent attempts to search for the causes of this attitude, in order to develop strategies to improve adherence to treatment.[4,9,10]

Our objectives were to examine self-reported rates of adherence to ACT by patients in an adult CF program, to ascertain patient characteristics associated with poor adherence, and to exemplify adherence according to ACT technique. Reasons for poor adherence were also detailed.

QUICK LOOK

Current knowledge

Daily management of cystic fibrosis (CF) includes airway clearance therapies, which require daily commitment to time-consuming regimens. While the relationship of adherence to airway clearance therapies and progression of CF is a matter of debate, adherence to airway clearance therapies appears to reduce exacerbations and hospitalizations.

What this paper contributes to our knowledge

There was a high rate of airway clearance therapy adherence in adult CF patients. A lower level of education was the most important characteristic associated with poor adherence. Patients with less severe disease also had lower adherence rates. Treatment recommendations and self-reported patient adherence were in best agreement when positive expiratory pressure and flutter devices were used.

Methods

Study Design

This was a single center, cross-sectional study of prospectively collected data, approved by the ethics and research committee of the Hospital de Clínicas de Porto Alegre. All subjects ≥ 18 years of age, or legal guardians of minors, granted informed consent.

Patient Population

The subject cohort was drawn from the adult CF program at Hospital de Clínicas de Porto Alegre, Porto Alegre, Rio Grande do Sul, Brazil. Eligible patients were 16 years of age or older, with a diagnosis of CF according to consensus criteria,[11-13] and were clinically stable (ie, no exacerbation, therapeutic modification, or hospitalization in past 30 d). Failure to complete any of the study questionnaires and refusal of consent were grounds for exclusion.

Measures and Procedures

After a scheduled out-patient consultation, all subjects were individually interviewed by a research member, using a structured questionnaire, to weigh the following variables: age, age at diagnosis, sex, race, marital status, education level, socioeconomic status, and employability.

The present work is based on the assumption that self-reported adherence is a reasonable substitute for objective data regarding adherence. Adherence was assessed via questionnaire (see the supplementary materials at http://www.rcjournal.com) adapted from previous studies.[7,14] For example, response choices for frequency of chest physiotherapy were "every day or almost every day," "about 3–5 days a week," or "less than 3 days a week" (poor adherence). Reasons for nonadherence were also solicited, as were therapeutic duration, daily repetitions, and nature of routine chest physiotherapy. Questionnaires were completed anonymously, emphasizing the importance of confidentiality.

Subjects were again interviewed outside the out-patient area by a physiotherapist (not directly involved in patient treatment) and were asked to demonstrate their ACT tech-

nique. If performance was correct in all steps, the technique was rated as "adequate." If at least one step was incorrect, the rating was judged "inadequate." All ACT recommendations were made by the same physiotherapist overseeing patient treatment,[9,10] documenting the duration, daily repetitions, and nature of chest physiotherapy advised (see the supplementary materials at http://www.rcjournal.com). All clinical scores in the out-patient setting were assigned by the same senior member of the CF team according to the Shwachman-Kulczycki scoring system for CF severity.[15]

A computerized spirometer (Jaeger 4.31a, Jaeger/CareFusion, Würzburg, Germany) was employed for pulmonary function testing. FEV_1, FVC, and FEV_1/FVC were measured 3 times, with the best effort reported in absolute values and percent-of-predicted values for age, stature, and sex.[16] S_{pO_2} at rest was recorded (NPB-40, Nellcor Puritan Bennett, Pleasanton, California).

For statistical purposes, subjects were stratified by self-reported adherence to ACT: high adherence ("every day or almost every day"), moderate adherence ("about 3–5 days a week"), and poor adherence ("less than 3 days a week").

Statistical Analysis

Data analysis was facilitated by statistics software (SPSS 18.0, SPSS, Chicago, Illinois). Quantitative results were expressed as mean ± SD or as median and interquartile range, and qualitative outcomes as numbers of cases (% of all cases). Quantitative data with normal distribution were subjected to one-way analysis of variance with Tukey post-hoc test. For continuous data with non-normal distribution, Kruskal-Wallis and post-hoc Z test were used. Chi-square test was applied to all qualitative data, as well as the Yates correction or Fisher exact test, as required. Concordance between ACT technique (physiotherapist recommended) and self-reported subject adherence to the advised regimen was evaluated by κ analysis, weighted κ analysis, and intraclass correlation coefficient.

Multivariate analyses were generated through logistic regression, with method forward conditional. On this basis, the odds ratio was the odds ratio for poor adherence to ACT. Selected variables with a P value $< .10$ were introduced in the binary logistic regression, controlled by sex and age. All statistical tests used were 2-tailed. The level of significance was set at $P < .05$.

Results

Sixty-three of 71 patients participating in the adult CF program were eligible for study (8 refusals). Mean subject age was 23.1 ± 6.3 years, with 32 females and 31 males. All subjects were white.

General characteristics of the CF subjects are summarized by self-reported adherence level (Table 1), including 38 (60%) with high adherence, 12 (19%) with moderate adherence, and 13 (21%) with poor adherence. Assigned subsets did not differ significantly in age, age at diagnosis, sex, body mass index, marital status, income level (per annum), education level, or employability ($P > .05$), although a significant association between self-reported adherence status and education level ($P = .02$) was found. By comparison, the poor adherence group contained a higher proportion of high school non-graduates with > 8 years of schooling and a lower proportion of more educated subjects. Overall, 58.3% of subjects with advanced education achieved moderate adherence.

Clinical and functional lung parameters are summarized, stratified by self-reported adherence level, in Table 2. Shwachman-Kulczycki clinical score, percent-of-predicted FEV_1, and FEV_1/FVC (%) were significantly lower with high adherence (70.0, 53.9%, and 66.0%, respectively) versus poor adherence (80.0, 71.8%, and 76.4%, respectively, all $P < .05$), but did not differ significantly from moderate adherence level (82.5, 68.2%, and 71.2%, respectively, all $P > .05$). For the 3 groups, percent-of-predicted FVC ($P = .12$) and S_{pO_2} at rest ($P = .054$) did not differ significantly.

Variables of education level (less than high school vs high school and beyond), Shwachman-Kulczycki clinical score, FEV_1 (% predicted), and S_{pO_2} at rest, adjusted by sex and age, were introduced into the forward conditional regression model, with education level (less than high school) emerging as an independent factor associated with poor adherence (odds ratio 10.2, 95% CI 1.23–84.7, $P = .03$).

Specifics of ACT technique according to self-reported adherence were compiled (Table 3). The duration of the ACT was significantly longer for high adherence subjects (45 min) than for those of moderate and poor adherence (30 min each, $P = .009$). The daily number of ACT sessions was also significantly greater at high adherence (3.0 sessions) than at moderate and poor levels (2.0 sessions each, $P < .001$). Between groups, no significant differences were observed for the number of exercise sessions per week ($P = .85$) or the adequacy of ACT technique using autogenic drainage ($P = .89$), active cycle of breathing ($P = .52$), positive expiratory pressure ($P = .50$), flutter devices ($P = .17$), and percussion and postural drainage ($P = .95$).

Treatment recommendations (by physiotherapist) called for active cycle of breathing in 50 subjects (79.4%), autogenic drainage in 14 (22.2%), positive expiratory pressure in 16 (25.4%), flutter device usage in 6 (9.5%), and postural drainage in 28 (44.4%). Subsequent analysis showed that agreement between recommended treatment and self-reported subject adherence was very high, with positive expiratory pressure ($\kappa = 0.87$), while agreement was high with flutter devices ($\kappa = 0.63$), moderate with

Table 1. General Characteristics of Cystic Fibrosis Subjects According to Self-Reported Airway Clearance Therapy Adherence Classification*

	High Adherence (n = 38)	Moderate Adherence (n = 12)	Poor Adherence (n = 13)	P
Age, mean ± SD, y	24.3 ± 7.9	23.8 ± 5.8	20.5 ± 3.1	.24
Age at diagnosis, median (IQR), y	5.0 (1.0–11.5)	11.0 (7.5–21.3)	10.5 (1.1–17.0)	.27
Male/female, no. (%)	20/18	6/6	5/8	.67
Body mass index, mean ± SD, kg/m^2	21.0 ± 1.6	21.1 ± 3.2	20.5 ± 2.8	.79
Education Level, no. (%)				
≤ 8 years of school	5 (13.2)	1 (8.3)	0 (0.0)	.02
> 8 years of school and < high school	17 (44.8)	4 (33.3)	12 (92.3)†	
Higher education (≥ high school)	16 (42.1)	7 (58.3)	1 (7.7)†	
Marital Status, no. (%)				
Never married	32 (84.2)	8 (66.7)	9 (69.2)	.36
Married/partner	4 (10.5)	4 (33.3)	3 (23.1)	
Separated/divorced	2 (5.3)	0 (0.0)	1 (1.6)	
Income Per Annum, no. (%)				
< A$8,300	23 (60.5)	8 (66.7)	10 (76.9)	.67
A$8,300–27,660	7 (18.4)	3 (25.0)	2 (15.4)	
> A$27,660	8 (21.1)	1 (8.3)	1 (7.7)	
Study, no. (% yes)	14 (36.8)	6 (50.0)	6 (46.2)	.67
Job Availability, no. (%)				
Yes	13 (34.2)	7 (58.3)	6 (46.2)	.37
Part-time	3 (7.9)	1 (8.3)	2 (15.4)	
Full-time	10 (26.3)	6 (50.0)	4 (30.8)	

* One-way analysis of variance or Kruskal-Wallis test for continuous variables; chi-square test for categorical variables.
† Standard adjusted residual > 1.96 or < –1.96 (implies percentages significantly different).

Table 2. Clinical and Lung Function Characteristics of Subjects According to Self-Reported Airway Clearance Therapy Adherence Classification*

	High Adherence (n = 38)	Moderate Adherence (n = 12)	Poor Adherence (n = 13)	P
Schwachman-Kulczycki clinical score, median (IQR)	70.0 (65.0–81.3)^A	82.5 (70.0–93.8)^{AB}	80 (75.0–87.5)^B	.020
FEV_1, mean ± SD, % predicted	53.9 ± 26.3^A	68.2 ± 32.4^{AB}	71.8 ± 27.8^B	.038
FVC, % mean ± SD, % predicted	68.1 ± 24.8	78.7 ± 23.4	82.6 ± 18.9	.12
FEV_1/FVC, mean ± SD, %	66.0 ± 11.4^A	71.2 ± 18.2^{AB}	76.4 ± 10.9^B	.040
S_{pO_2} at rest, mean ± SD, %	95.3 ± 4.1	97.6 ± 1.2	97.2 ± 1.2	.054

* One-way analysis of variance with Tukey post-hoc test or Kruskal-Wallis with post-hoc Z test for continuous variables. In the post-hoc test, the letters A and B indicate that the means or medians are significantly different: A differs from B, and AB does not differ from A or B.

active cycle of breathing (κ = 0.40) and autogenic drainage (κ = 0.39) techniques, and low with percussion and postural drainage (κ = 0.23). In addition, concordance was high with frequency of exercise (sessions/week, intraclass correlation coefficient = 0.62), moderate with frequency of ACT (sessions/d, intraclass correlation coefficient = 0.42), but low with duration of ACT (minutes, intraclass correlation coefficient = 0.33).

Reasons stated for poor adherence with ACT are shown in Table 4. Seven subjects (28%) reported "not enough time to do ACT," while 4 (16%) responded with "cannot be bothered," and 2 (8%) with "do not enjoy ACT technique." Other reasons given by one subject (4%) each, included "do not believe that it does any good," "cannot find any motivation," "do plenty of exercise instead of ACT," and "feeling depressed." Eight subjects (32%) offered no explanation at all.

Discussion

Relatively high rates of adherence to ACT were achieved by subjects participating in an adult CF program at a large

Table 3. Evaluation of Airway Clearance Therapy Technique According to Self-Reported Adherence Classification*

	High Adherence (n = 38)	Moderate Adherence (n = 12)	Poor Adherence (n = 13)	P
Duration of ACT, median (IQR) min	45 (30–60.0)[A]	30 (30.0–45.0)[B]	30 (0.0–45.0)[B]	.009
ACT sessions per day, median (IQR), no.	3 (1.0–3.0)[A]	2 (1.0–2.0)[B]	2 (1.0–4.0)[B]	< .001
Exercise sessions/week, median (IQR) no.	3 (2.0–5.0)	2.5 (2.0–4.5)	3 (2.0–4.5)	.85
ACT Evaluation, no. (%)				
Autogenic Drainage				
Adequate	4 (10.5)	2 (16.7)	1 (7.7)	.89
Inadequate	3 (7.9)	1 (8.3)	2 (15.4)	
Not performing	31 (81.6)	9 (75.0)	10 (76.9)	
Active Cycle of Breathing				
Adequate	17 (44.7)	5 (41.7)	4 (30.8)	.52
Inadequate	7 (18.4)	3 (25.0)	1 (7.7)	
Not performing	14 (36.8)	4 (33.3)	8 (61.5)	
Positive Expiratory Pressure				
Adequate	11 (28.9)	2 (16.7)	2 (15.4)	.50
Inadequate	0 (0)	0 (0)	0 (0)	
Not performing	27 (71.1)	10 (83.3)	11 (84.6)	
Flutter Device				
Adequate	5 (13.2)	0 (0)	0 (0)	.17
Inadequate	0 (0)	0 (0)	0 (0)	
Not performing	33 (86.8)	12 (100)	13 (100)	
Percussion and Postural Drainage				
Adequate	4 (10.5)	1 (8.3)	1 (7.7)	.95
Inadequate	0 (0)	0 (0)	0 (0)	
Not performing	34 (89.5)	11 (91.7)	12 (92.3)	

ACT = airway clearance therapy
* Kruskal-Wallis with post-hoc Z test for continuous variables: the medians were significantly different if letters A and B are different (chi-square test for categorical variables).

Table 4. Reasons for Poor Adherence With Chest Physiotherapy

	No. (%) (n = 25)
Not enough time	7 (28)
Cannot be bothered	4 (16)
Do not enjoy the chest physiotherapy technique	2 (8)
Do not believe that it does any good	1 (4)
Cannot find any motivation	1 (4)
Do plenty of exercise instead	1 (4)
Feeling depressed	1 (4)
Cannot find any reason	8 (32)

tertiary care and university affiliated hospital in Porto Alegre, Brazil. Although a majority of those studied (60%) reported daily or near-daily ACT (high adherence), a substantial number (40%) engaged in ACT only about 3–5 days per week (moderate adherence) or < 3 days per week (poor adherence). A longitudinal study investigating adherence to ACT using daily telephone diary by 153 adolescents with CF did not fare as well, resulting in low, medium, and high levels of adherence at 14%, 49%, and 37%, respectively.[17] Patients with moderate-to-poor adherence are thus the logical target for therapeutic aid.

Of particular note, the reported number and duration of daily sessions for ACT were significantly greater in the high adherence subset, as opposed to moderate and poor adherence levels. Although patients with more severe disease would receive more challenging ACT recommendations in number and duration of daily sessions, the adherence classification was based on self-reported frequency of chest physiotherapy in a week ("every day or almost every day," "about 3–5 days a week," or "less than 3 days a week"). Shwachman-Kulczycki clinical score, percent-of-predicted FEV_1, and FEV_1/FVC (%) variables were significantly lower for subjects with high versus poor adherence (all $P < .05$), but did not differ from adherence at the moderate level (all $P > .05$). Apparently, patients with lesser pulmonary disease are apt to disregard the need for ACT, realizing its importance only when medical complications arise and further irreversible lung damage has already occurred. Healthcare professionals must therefore bolster efforts, finding strategies to enhance adherence when patient adherence is inadequate.

A smaller study ($n = 38$) by Dalcin et al[14] evaluated the global score of self-reported adherence to the chief therapeutic recommendations for CF patients. A total of 31 patients (81.6%) demonstrated a higher degree of adherence, with 7 (18.4%) displaying moderate/poor adherence. Interestingly, no statistically significant difference between groups was observed relative to Shwachman-Kulczycki clinical score and indices of pulmonary function (FEV_1, FVC, and FEV_1/FVC) (all $P > .05$).

In our study, agreement between ACT recommendations (by physiotherapist) and self-reported subject adherence was very high for the use of positive expiratory pressure. Agreement was also high for flutter devices and moderate for active cycle of breathing and autogenic drainage techniques, but it was low for percussion and postural drainage. As such, Modi et al[17] showed that adolescents with CF were more likely to attain moderate adherence with flutter device usage, compared with percussion and postural drainage and high-frequency chest wall oscillation (Vest therapy). Flutter and positive expiratory pressure devices can be implemented successfully and independently by CF patients once techniques have been mastered. However, a flutter device requires active patient participation at the risk of boredom or disinterest during the full prescribed duration of therapy. This underscores the importance of incorporating patient preference when rendering decisions on ACT technique, given the current lack of evidence for any method superiority.

Reasons most frequently offered by our subjects for poor adherence with ACT were "not enough time to do ACT" (28%), "cannot be bothered" (16%), and "do not enjoy ACT technique" (8%), although nearly one third (32%) gave no reason whatsoever. According to Dodd and Webb,[18] who investigated treatment nonadherence in adults with CF, the major reasons were related to health ("I feel well without treatment," "I'm not as serious as others") and time ("not enough time," "I am too busy," and "I forget"). Another publication, by Bucks et al,[19] focused on the interrelationships of illness perceptions, emotional representations, treatment beliefs, and reported adherence in 38 adolescents with CF. From their view, adherence to chest physiotherapy was rooted in a patient's perceived need for treatment relative to the potential for adverse effects. Subjects, in fact, expressed strong doubts about the necessity of chest physiotherapy. Our study identified patient characteristics specifically linked with poor adherence and typified adherence patterns for each mode of ACT, perhaps explaining therapeutic shortfalls.

In univariate analysis, we identified several factors associated with the degree of adherence: education level, Shwachman-Kulczycki clinical score, FEV_1 (% of predicted), and S_{pO_2} at rest. By multivariate analysis, low education level (less than high school) was the most important factor, independently correlating with poor adherence to treatment. While many of the subjects we recruited were below 18 years of age and had yet to start or finish high school, age- and sex-controlled results were unchanged. Then again, advanced education did not guarantee high adherence to ACT. Despite enabling scheduling and planning skills for better adherence, at some point the benefits derived from higher education cease to significantly influence adherence.

With respect to potential limitations, the cross-sectional design of this study was insufficient to define the temporal relationship between adherence to ACT and declines in health or lung function of CF patients. Our patient sampling was also small. In this work, ACT adherence evaluation was based on the subject self-reporting adherence. Self-reporting often overestimates adherence when compared with objective measures.[18] Although objective measures are more efficient, they are not always feasible for evaluation of adherence. Subjective self-report techniques are easy to use and seem to allow, albeit with less sensitivity, the identification of a group of patients presenting nonadherence to treatment. Still, the poor adherence rate cited here is comparable to that of prospective, longitudinal research comparing various ACT techniques,[20] and with self-reporting, a wide range of behaviors often surfaces as patients identify and describe specific barriers to adherence.[21,22]

Conclusions

In conclusion, this study revealed a high rate of ACT adherence in adult CF subjects. Lower level of education was the most important characteristic associated with poor adherence to ACT. Treatment recommendations and self-reported subject adherence were in best agreement when positive expiratory pressure and flutter devices were used. Healthcare professionals should consider these outcomes as potentially applicable to their own clinical practices.

REFERENCES

1. Boyle MP. Adult cystic fibrosis. JAMA 2007;298(15):1787-1793.
2. Abbott J, Dodd M, Bilton D, Webb AK. Treatment compliance in adults with cystic fibrosis. Thorax 1994;49(2):115-120.
3. Yankaskas JR, Knowles MR. Cystic fibrosis in adults. Philadelphia: Lippincott-Raven; 1999.
4. Myers LB, Horn SA. Adherence to chest physiotherapy in adults with cystic fibrosis. J Health Psychol 2006;11(6):915-926.
5. Passero MA, Remor B, Salomon J. Patient-reported compliance with cystic fibrosis therapy. Clin Pediatr (Phila) 1981;20(4):264-268.
6. Geiss SK, Hobbs SA, Hammersley-Maercklein G, Kramer JC, Henley M. Psychosocial factors related to perceived compliance with cystic fibrosis treatment. J Clin Psychol 1992;48(1):99-103.
7. Conway SP, Pond MN, Hamnett T, Watson A. Compliance with treatment in adult patients with cystic fibrosis. Thorax 1996;51(1):29-33.

8. Bernard RS, Cohen LL. Increasing adherence to cystic fibrosis treatment: a systematic review of behavioral techniques. Pediatr Pulmonol 2004;37(1):8-16.
9. Flume PA, Robinson KA, O'Sullivan BP, Finder JD, Vender RL, Willey-Courand DB, et al. Cystic fibrosis pulmonary guidelines: airway clearance therapies. Respir Care 2009;54(4):522-37.
10. McCool FD, Rosen MJ. Nonpharmacologic airway clearance therapies: ACCP evidence-based clinical practice guidelines. Chest 2006; 129(1 Suppl):250S-259S.
11. Rosenstein BJ. What is a cystic fibrosis diagnosis? Clin Chest Med 1998;19(3):423-441.
12. Rosenstein BJ, Cutting GR. The diagnosis of cystic fibrosis: a consensus statement. Cystic Fibrosis Foundation Consensus Panel. J Pediatr 1998;132(4):589-595.
13. Stern RC. The diagnosis of cystic fibrosis. N Engl J Med 1997; 336(7):487-491.
14. Dalcin PT, Rampon G, Pasin LR, Ramon GM, Abrahao CL, Oliveira VZ. Adherence to treatment in patients with cystic fibrosis. J Bras Pneumol 2007;33(6):663-670.
15. Shwachman H, Kulczycki LL. Long-term study of one hundred five patients with cystic fibrosis; studies made over a five- to fourteen-year period. AMA J Dis Child 1958;96(1):6-15.
16. Pereira CA, Sato T, Rodrigues SC. New reference values for forced spirometry in white adults in Brazil. J Bras Pneumol 2007;33(4): 397-406.
17. Modi AC, Cassedy AE, Quittner AL, Accurso F, Sontag M, Koenig JM, et al. Trajectories of adherence to airway clearance therapy for patients with cystic fibrosis. J Pediatr Psychol 2010;35(9):1028-1037.
18. Dodd ME, Webb AK. Understanding non-compliance with treatment in adults with cystic fibrosis. J R Soc Med 2000;93(Suppl 38):2-8.
19. Bucks RS, Hawkins K, Skinner TC, Horn S, Seddon P, Horne R. Adherence to treatment in adolescents with cystic fibrosis: the role of illness perceptions and treatment beliefs. J Pediatr Psychol 2009; 34(8):893-902.
20. Sontag MK, Quittner AL, Modi AC, Koenig JM, Giles D, Oermann CM, et al. Lessons learned from a randomized trial of airway secretion clearance techniques in cystic fibrosis. Pediatr Pulmonol 2010; 45(3):291-300.
21. Kettler LJ, Sawyer SM, Winefield HR, Greville HW. Determinants of adherence in adults with cystic fibrosis. Thorax 2002;57(5):459-464.
22. Oermann CM, Swank PR, Sockrider MM. Validation of an instrument measuring patient satisfaction with chest physiotherapy techniques in cystic fibrosis. Chest 2000;118(1):92-97.