Hospital versus home treatment of respiratory exacerbations in cystic fibrosis

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Summary

Background: Treatment of respiratory exacerbations in Cystic Fibrosis (CF) is important in slowing disease progression. The treatment may be given either at home or at the hospital. The aim of our study was to compare both treatment settings.

Material/Methods: We retrospectively analyzed data of 139 treatments in 54 CF patients (age range 12–47 y) treated for respiratory exacerbations at the hospital (n=84) and/or at home (n=55). Primary outcomes were improvement in pulmonary function tests (PFTs), weight gain and duration of treatment in relation to treatment setting. Secondary outcomes were these same parameters, but in relation to different clinical preconditions and CF-related complications.

Results: Mean improvement in FEV1 (% predicted) was similar between the hospital and home treatments (14.3±34.4% *vs.* 14.3±20.2%, respectively; NS), yet treatment duration was significantly shorter at the hospital (9.7±6.7 *vs.* 16.3±9.1 days, respectively; P<0.02), especially for patients colonized with Pseudomonas aeruginosa (11.1±5.5 *vs.* 18.0±11.0 days, respectively; p<0.01). At the hospital, a subgroup of patients with CF-related complications improved their FEV1 significantly more than those at home (13.1±19.4% *vs.* 1.9±14.9%, respectively; P<0.02), particularly patients with CF-related diabetes mellitus (CFRDM) (11.4±18.7% *vs.* 1.7±14.6%, respectively; P<0.05). Patients tended to gain more weight at the hospital compared to home treatment (1.36±4.6 kg and 0.49±3.6 kg respectively; P=0.06).

Conclusions: Hospital treatment for acute respiratory exacerbations in CF may be superior to home treatment, as indicated by a shorter duration of hospitalization, better improvement in FEV1 in patients with CF-related complications, CFRDM in particular and a trend toward better weight gain.

key words: Cystic Fibrosis • exacerbation • home treatmant • hospital treatment

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BACKGROUND

Cystic fibrosis (CF) is a life-limiting autosomal recessive genetic disorder. Significant pulmonary disease occurs in the majority of CF patients, manifested as a progressive cough, increased dyspnea and decline in lung function caused by acute and chronic infection and inflammation in the airways [1]. With advances in therapy and a multidisciplinary approach, life expectancy has increased dramatically from a median of several years to a projected median survival of over 50 years of age for individuals born in 2000 [2]. Several factors may contribute to the increase in survival of CF patients, including early diagnosis of CF followed by early preventive treatment and close clinical follow-up, aggressive treatment of malnutrition and the enhanced use of antibiotics and physiotherapy both as intermittent routine treatment and as treatment for respiratory exacerbations, the vast majority of which are caused by bacterial pathogens. Furthermore, frequent intravenous (IV) antibiotics treatment at the hospital and vigorous eradication treatment for first isolation of *Pseudomonas aeruginosa* were also shown by the Scandinavian centers to be beneficial [3–7]. Intravenous antibiotics are usually the treatment of choice in such exacerbations and may be given either as home treatment or in a hospital setting. Several studies have compared both treatment settings, but to date no conclusion as to which is superior has been established in the literature [8–11]. In most studies, inspection of improvement in pulmonary function test (PFTs) indices during the interventions had shown large variation, indicating that some of the patients vastly improved or deteriorated, while other patients did not. Furthermore, the effect of the treatment settings in different clinical preconditions such as gender, chronic colonization of *Pseudomonas aeruginosa* and CF-related complications and the probability of a patient to improve his lung function at a specific treatment setting were not fully explored. Moreover, it has been shown in previous studies by Sanders et al that about 25% of the patients treated for pulmonary exacerbations fail to recover to baseline PFTs, especially female patients, undernourished patients, and patients with persistent infection with *Pseudomonas aeruginosa, Burkholderia capacia complex* or *methicillin-resistant Staphylococcus aureus* [12,13].

The aim of this study was to investigate the likelihood of a CF patient to improve in a specific treatment setting and to investigate whether home or hospital setting results were influenced by clinical preconditions.

MATERIAL AND METHODS

Subjects

The study population consisted of patients with proven CF by clinical characteristics and identified CFTR alteration mutation and/or pathological sweat chloride test (above 60 mmol/L). Patients were aged 12 to 47 years, and all were part of the National CF Center, Edmond and Lily Safra Children's Hospital, Tel Hashomer, Israel.

Study design

We retrospectively obtained all data of hospital and home treatments between the years 2007–2009 from records of the CF patients. Inclusion criteria were the necessity of home or hospital treatment due to acute respiratory exacerbation. Respiratory exacerbations were defined according to the Cystic Fibrosis guidelines [14]. Excluded were patients after lung transplantation. Location of treatment was based on physician's assessment of patient clinical status. Patients who needed supplemental oxygen, IV fluid resuscitation and supplemental caloric intake such as total parental nutrition (TPN) or patients who were unlikely to manage home treatment were hospitalized. Several patients were hospitalized at their own preference. Patients who had changed location of treatment during treatment were excluded. All patients, whether treated at home or in the hospital, received at least 2 anti-pseudomonal antibiotics based on the sensitivities of the most recent sputum culture. Where aminoglycosides were prescribed, doses were adjusted according to blood levels and kidney function test. Nebulized antipseudomonal antibiotics such as Tobi or Colistin were continued. Patients colonized with *Staphylococcus aureus* were also treated with anti-Staphylococcal antibiotics during the acute episode. Patients treated at the hospital routinely received physiotherapy twice a day, were put on a high-calorie diet, were treated by a multidisciplinary team according to need, and performed forced spirometry twice a week. Patients treated at home usually performed physiotherapy 3 to 5 times a week provided by community physiotherapists or family members, and performed forced spirometry and had a physician follow-up once or twice weekly. Patients completed their treatment when clinical and PFTs improvement was achieved as decided by the treating physician, and treatment length ranged from 10 days to 5 weeks.

The study was approved by the appropriate ethical committees related to the institution in which it was performed.

Spirometry

Forced spirometry was performed according to the Report Working Party Standardization of Lung Function Tests ERS/ATS guidelines [15,16] prior to start of treatment, during treatment and within a week post-treatment regardless of the treatment site. All curves were stored, and the best curve with the maximal forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) were analyzed for the study.

Analysis of data

The effects of the treatment site were primarily judged by changes in FEV1 pre- and post-treatment. In addition, the effects of treatment site were related to other clinical preconditions such as CF alteration mutations, gender, body mass index (BMI), baseline FEV1 (%predicted), chronic colonization of *Pseudomonas aeruginosa, Mycobacterium abscessus* and *Methicillin-resistant Staphylococcus aureus* (MRSA), CF-related complications such as pancreatic insufficiency (PI), CF-related diabetes mellitus (CFRDM), distal intestinal obstruction syndrome (DIOS), liver and kidney disease, pancreatitis and Allergic Bronchopulmonary Aspergillosis (ABPA). All patients with these clinical preconditions were assigned to sub-groups accordingly. The effect of treatment site on weight gain, duration of treatment, time to next exacerbation and the cost of the treatment were also inspected.

Table 1. Anthropometric data, bacterial colonization, CF related complications and baseline spirometry indices of patients divided to home and hospital treatments.

	Home (N=55)	Hospital (N=84)	P value
Gender (male/female)	38/17	48/36	0.2112
Age (yrs)	27.8±6.9	26.7±8.2	0.4124
Weight (kg)	55.2±7.5	51.6±8.0	**0.0419***
Height (cm)	168±8.3	163±9	**0.0376***
Body mass Index (BMI)	19.8±2.3	19.4±2.3	0.4846
P. aeruginosa colonization positive	30 (55%)	40 (48%)	0.4890
CF related complications positive	38 (69%)	75 (89%)	**0.0038***
* CFRDM – positive	20 (36%)	36 (43%)	0.4831
** PI – positive	15 (27%)	64 (76%)	**0.0001***
Baseline Spirometry (%predicted)			
FVC	66.5±18.0	58.9±18.3	**0.0173***
FEV1	47.7±15.2	41.8±16.0	**0.0319***
PEF	65.3±18.0	53.5±17.8	**0.0020***
FEF 25-75	25.8±16.2	23.0±18.8	0.3666

* CFRDM – Cystic Fibrosis related Diabetes mellitus; ** PI – pancreatic insufficiency.

Statistical analysis

The change in spirometry indices in relation to treatment setting (groups) and the effects of the clinical preconditions were compared using paired and unpaired t-tests, as appropriate. Patients having FEV1<40% predicted were considered to have severe lung disease. A change of ≥10% from baseline FEV1 was considered clinically significant. The odds ratio of a patient to improve his FEV1 in relation to home or hospital setting and in relation to clinical preconditions was analyzed using chi-square or Fisher test. P<0.05 was considered significant. We used the GraphPad Software statistical package.

RESULTS

Data were analyzed from 54 patients, 12 to 47 years of age who underwent 1 or up to 3 treatments at home or at the hospital. Twenty-four (44%) patients received only hospital treatments, 12 (22%) received only home treatments, and 18 (33%) received both treatments during the enrolment period. A total of 139 treatments were conducted, of which 84 (60%) were at the hospital and 55 (40%) were at home.

The anthropometric data, bacterial colonization, CF-related complications and lung function indices prior to intervention are presented in Table 1. There were significant differences between the home and hospital groups concerning height and weight, but no difference in calculated Body Mass Index (BMI). In the hospital group more patients had CF-related complications compared to the home group, in particular, pancreatic insufficiency (PI) (75 (89%) *vs.*

38 (69%), respectively; P<0.01 and for PI 64 (76%) *vs.* 15 (27%), respectively; P<0.01). The percent of patients suffering from severe lung disease differed between settings: n=44 (52%) at the hospital and n=13 (24%) at home, as reflected by the different spirometry indices outlined in Table 1

Mean duration of treatment was 9.7±6.7 days for the hospital site and 16.3±9.1 days for the home site (P<0.02). Specifically, treatment duration in patients colonized with *Pseudomonas aeruginosa* was significantly shorter at the hospital than at home (11.1±5.5 *vs.* 18.0±11.0 days, respectively; P<0.01), as well as in patients without CF-related complications (11.9±6.6 *vs.* 18.5±12 days, respectively; P<0.01). In other analyzed clinical preconditions, duration of treatment was similar in both treatment sites. In that respect, the cost of stay at the hospital was $540 USD/day, with an approximate treatment cost of $5200 USD/admission. Cost of home treatment was $140 USD/day with an approximate total treatment cost of $2300 USD.

The effect of treatment site on lung function for the entire group is presented in Table 2. There was no significant difference in mean percent change in spirometry indices in relation to treatment site. The effect of treatment site on changes in FEV1 in relation to the main clinical preconditions is presented in Table 3. Looking at hospital versus home treatments, patients having CF-related complications improved their FEV1 significantly more at the hospital compared to at home (13.1%±19.4 *vs.* 1.9%±14.9, respectively; P<0.01), especially patients suffering from CFRDM (11.4%±18.7 *vs.* 1.7%±14.6, respectively; P<0.05) and patients with PI (14.4%±19.6 *vs.* 4.1±22.5, respectively; P<0.01). At the

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Table 2. Mean percent change in spirometry indices in each of the treatment setting. There was no statistical difference between the groups.

% change ±SD	Home treatments n=55	Hospital treatments N=84	P value
FVC	12.2±17.5	8.8±16.9	0.2574
FEV1	14.3±34.4	14.26±20.2	0.9989
PEF	14.1±27.5	9.0±19.3	0.2010
FEF25–75	8.1±22.6	16.0±25.2	0.0620

Table 3. The percent change in FEV1 from baseline level for each of the treatments sites and in relation to the different clinical preconditions. The significance between home and hospital sites is presented horizontally. The significance between with or without clinical precondition is presented vertically.

FEV1 % change – mean ±SD	Home	Hospital	P value
Pseudomonas (Yes)	17.1±29.3	**21.4±21.0**	0.3155
Pseudomonas (No)	10.9±40	**7.4±29%**	0.5511
P value	0.3558	**0.0001**	
CF-related complications (Yes)	**1.9±14.9**	**13.1±19.4**	**0.0004**
CF-related complications (No)	**24.6±42.1**	17.4±22.4	0.3454
P value	**0.0003**	0.1854	
* CFRDM (Yes)	**1.7±14.6**	**11.4±18.7**	**0.0014**
* CFRDM (No)	**17.0±30.8**	16.3±21.2	0.8741
P value	**0.0012**	0.1140	
** PI (Yes)	**4.1±22.5**	**14.4±19.6**	**0.0004**
** PI (No)	**14.1±28.2**	13.3±22.6	0.8537
P value	**0.0422**	0.7613	

* CFRDM – Cystic Fibrosis related Diabetes Mellitus; ** PI – Pancreatic Insufficiency.

hospital, Patients colonized with *Pseudomonas aeruginosa* improved their FEV1 significantly more compared to patients not colonized with *Pseudomonas aeruginosa* (21.4%±21 *vs.* 7.4%±29, respectively; P<0.02).When looking at the home site only, those having CF-related complications improved FEV1 less than those free of complications (1.9%±14.9 *vs.* 24.6%±42.1, respectively; P<0.02), especially patients suffering from CFRDM, who improved their FEV1significantly less than patients without CFDRM (1.7%±14.6 *vs.* 17%±30.8, respectively; P<0.02).

Changes in FEV1 were not influenced by the treatment site in relation to sex, CFTR alteration mutation, chronic colonization of *MRSA* or *Mycobacterium abscessus.*

The odds ratio of a patient to improve or deteriorate their FEV1 in different treatment sites in relation to clinical preconditions is presented in Table 4. The odds to improve FEV1 (more than 10% baseline) at the hospital for patients with CF-related complications, especially CFRDM, were 3 times higher than the odds ratio to improve at home (0.96 *vs.* 0.32 and 0.79 *vs.* 0.25, respectively). The odds to deteriorate FEV1 (more than 10% baseline) at home compared

to at the hospital were higher for the entire study group (0.18 *vs.* 0.09) and for male patients (0.26 *vs.* 0.06). Patients not colonized with *Pseudomonas aeruginosa* deteriorated at the hospital significantly more than those colonized with *Pseudomonas aeruginosa* (0.32 *vs.* 0.05). Age, baseline PFTs prior to treatment, CFTR alteration mutation and pancreatic insufficiency did not affect the changes in FEV1 in either of the sites.

Other findings: Patients treated at the hospital improved their weight by 1.36±4.6 kg compared to patients treated at home who improved their weight by 0.49±3.6 kg (P=0.06). Time to next admission did not differ between the 2 groups.

DISCUSSION

In the present study we investigated the preferable treatment site, hospital versus home, during respiratory exacerbations in our CF population in relation to hospitalization duration, change in PFTs as a representative for clinical improvement, and the odds ratio of a patient to improve or deteriorate PFTs in either of the settings. We found that while for the entire group mean improvement in PFTs was similar

Table 4. The odds ratio to show a significant change in FEV1 (> or <10%) from baseline values in relation to treatment site and clinical preconditus.

	Improve		Deteriorate	
	Home	**Hospital**	**Home**	**Hospital**
Study group	0.61	0.96	**0.18***	**0.09***
Gender				
Male	0.47	0.89	**0.26***	**0.06***
Female	1.13	1.13	0.06	0.12
Pseudomonas				
Yes	0.67	1.70	0.07	**0.05***
No	0.59	0.56	0.14	**0.32***
CF related complications				
Yes	**0.32***	**0.96***	0.11	0.09
No	0.79	1.00	0.18	0.00
CFRDM**				
Yes	**0.25***	**0.79***	0.11	0.06
No	0.96	1.13	0.16	0.12

* Significant P<0.05; ** CFRDM – Cystic Fibrosis related Diabetes mellitus.

in both sites, the improvement was achieved within a shorter duration of treatment when carried out at the hospital. We further found that the hospital site was most beneficial to the specific subgroup of patients with CF-related complications, especially CFRDM. The improvement in PFT was accompanied by a trend toward better improvement in weight gain at the hospital. Although all patients improved their lung functions in both treatment settings, we noticed that there was a greater risk for deterioration of lung functions at home for all patients and especially for males. On the contrary, patients not colonized with *Pseudomonas aeruginosa* appear to deteriorate more at the hospital.

Pulmonary exacerbations are a major source of morbidity for cystic fibrosis patients and are likely to contribute to lung function decline. Therefore, determining the optimal approach to exacerbation therapy is an important issue for which there has been little objective data. Each of the treatments sites has advantages and disadvantages.

Hospital site: hospital treatment provides the patient a comprehensive supportive multidisciplinary care with physiotherapy twice a day physiotherapy and diet monitoring in our center. Furthermore, patients with co-morbidity are monitored and treated by specialized consultants. This may explain why patients with CF-related complications, CFRDM in particular, significantly improve PFTs more at the hospital and were significantly more likely to do so. A significant portion of our adult patients have CF-related complications. Naturally these patients are no longer living with their parents who used to support them during exacerbations at an earlier age. In consequence, their ability to treat themselves, especially to monitor their glucose blood level due to CFRDM, may be compromised compared to monitoring and treatment given at the hospital. Nezer et al. [17]

showed that even non-diabetic CF patients tend to lose their glucose blood level balance during acute pulmonary exacerbations. In their pilot study they showed that these patients may benefit from glucose blood level monitoring and may improve PFTs after being treated with insulin when required. Indeed, the efforts of a CF endocrinologist and a specialized dietitian and customized food may explain both the better weight gain and the better control of CFRDM, and in consequence the better PFTs achieved in our hospitalized patients. Patients colonized with *Pseudomonas aeruginosa* also showed a trend of better improvement in PFTs at the hospital as compared to those treated at home.

The duration of hospital treatments was significantly shorter as compared to the home site. We suggest that comprehensive and aggressive treatment given at the hospital may explain this. This significantly shorter duration yielded similar improvement in PFTs compared to the longer duration of home treatment. Cochrane review by Balaguer and Gonzalez de Dios found that maximal recovery of lung function occurs within the first 8 days of therapy with intravenous antibiotics at the hospital [18]. Nazer et al. demonstrated that even patients with different disease severity levels improved more and in a shorter time when treated at the hospital [19]. The disadvantage of hospital treatment is the possibility of cross-infections, stopping one's daily routine and the cost of admission, which is significantly higher than the cost of home treatment. Thornton et al in the United Kingdom showed hospital treatment to be more expensive than home treatment [20]. We believe that the difference in costs is similar in most parts of the world, but should not be a factor when evaluating the best option for the patient.

Home site: There is a large worldwide drive for treating exacerbation in CF patients at home. The Cystic Fibrosis

pulmonary guidelines from 2009 concluded against delivery of intravenous antibiotic treatment in a non-hospital setting unless resources and equipment are equivalent to those in the hospital setting [14]. Home treatment is characterized by self-care management and is considered to enable the patient to maintain daily routine and quality of life (QOL). The latter was not proved to be beneficial. Wolter et al showed no significant improvement of emotional well-being after home treatment compared to hospital treatment, and even better QOL after hospital treatment [21]. More recently, Esmond et al. showed the same results with no differences in QOL between the 2 treatment sites [22], which might be explained by the anxiety accompanying an unfamiliar self-administered home treatment.

We have shown that for the entire study group and especially for male patients the odds ratio of deterioration of more the 10% from baseline FEV1 at home were much higher compared to the odds ratio to deteriorate after treatment at the hospital. We suggest that both the aggressive comprehensive treatment at the hospital as well as a poorer adherence during home treatment may contribute to this finding. We found that at home our patients often (but this has not been thoroughly investigated) encounter technical problems managing venous access, forget treatments, are unable to fit them into a busy schedule or are under pressure to return to daily routine before treatment is finished and improvement is accomplished. Phillips showed that up to 84% of adult patients had drugs left over post-treatment [23] and Bosworth and Nielson found decreased frequency and probably quality of chest physiotherapy when patients were treated at home [24]. Indeed, adherence during home treatment without medical staff supervision is probably harder to maintain and should be considered when prescribing home treatment.

Conclusions

In conclusion, our results suggest that hospital treatment for acute respiratory exacerbations in CF may be superior to home treatment, as indicated by a shorter duration of hospitalization, better improvement in FEV1 in patients with CF-related complications (CFRDM in particular) and a trend toward better weight gain.

Our study is limited as a single center retrospective study and reflects the national center's experience and should promote further studies on this issue. This study provides further insights into the advantages or disadvantages of treating subgroups of patients at the hospital versus home treatment for respiratory exacerbation. Before the widespread use of home treatment, larger randomized studies need to take place to confirm its efficacy.

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