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Original Article

Antibiotic therapy and Effects of Respiratory Physiotherapy Techniques Cystic Fibrosis Patients Treated for Acute Lung Exacerbation: an Experimental Study

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ABSTRACT

Introduction: Intravenous antibiotics in combination with intensive respiratory physiotherapy were evaluated for acute lung exacerbations in chronic infections of *Pseudomonas aeruginosa* in cystic fibrosis patients. Forced expiratory technique (FET) was assessed during hospital stay and discharge. The aim of this study was 1) to evaluate the immediate effects of FET and of 2) Intravenous antibiotics in combination with daily respiratory physiotherapy (IA+RPT) on parameters of lung function, body anthropometry and clinical scores of cystic fibrosis patients with acute lung exacerbation with chronic infection by *Pseudomonas aeruginosa*, during hospital stay and at hospital discharge after clearing the infection.
Patients and method: Eighteen patients between 7–28 years old were included in a prospective non-controlled clinical study. Body anthropometry values, Cystic Fibrosis Clinical Score (CFCS) exacerbation, Cystic Fibrosis Foundation Score (CFFS), and severity scores (SS) were evaluated before and after admission. Oxygen saturation (SpO_2), heart (HR) and respiratory rate (RR) were evaluated before and after FET.
Results: CFCS (32.4+7.2) and CFFS (6.4+1.7) had decreased at hospital discharge for 18.9+3.3 and 0.3+0.5, respectively ($p < 0.001$). IA+ RPT reduced RR means ($p = 0.003$) and increased SpO_2 ($p = 0.006$), forced expiration volume at 1 min (FEV_1) ($p = 0.021$) and nutritional values ($p = 0.002$). During admission, FET immediately improved HR ($p = 0.028$), RR ($p = 0.001$) and SpO_2 ($p = 0.015$), despite significant maximum voluntary ventilation reduction ($p = 0.028$); after the infection was treated the FET did not significantly alter parameters.
Conclusion: IA+RPT improved clinical conditions of cystic fibrosis patients. FET improved cardiorespiratory variables of patients at risk for infection.

Efectos de la antibioterapia y la técnica fisioterápica respiratoria en pacientes con fibrosis quística tratados por exacerbación pulmonar aguda: estudio experimental

Palabras clave:
Fibrosis quística
Pediátrico
Fisioterapia torácica
Pseudomonas aeruginosa

RESUMEN

Introducción: Se evaluó el tratamiento con antibióticos intravenosos en combinación con la fisioterapia respiratoria intensiva para las exacerbaciones pulmonares agudas de las infecciones crónicas por *Pseudomonas aeruginosa* en pacientes con fibrosis quística. Durante la hospitalización y el alta se evaluó la técnica de espiración forzada (TEF). El objetivo de este estudio fue 1) valorar los efectos inmediatos de la TEF y de 2) los antibióticos intravenosos combinados con la fisioterapia respiratoria diaria (AI+FTR) sobre los parámetros

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de función pulmonar, antropometría corporal y puntuaciones clínicas de pacientes con fibrosis quística y exacerbaciones pulmonares agudas de una infección crónica por *Pseudomonas aeruginosa* en la hospitalización y el momento del alta hospitalaria tras remisión de la infección.

Pacientes y métodos: En un estudio clínico prospectivo, no controlado, se incluyeron 18 pacientes, de 7-28 años de edad. Antes y después de la hospitalización se evaluaron los valores antropométricos corporales, exacerbación de la puntuación Cystic Fibrosis Clinical Score, Cystic Fibrosis Foundation Score y puntuaciones de gravedad (PG). Antes y después de la TEF, se evaluaron la saturación de oxígeno (SpO_2), FC y FR.

Resultados: En el momento del alta hospitalaria, la Cystic Fibrosis Clinical Score (32,4 + 7,2) y Cystic Fibrosis Foundation Score (6,4 + 1,7) habían disminuido 18,9 + 3,3 y 0,3 + 0,5, respectivamente ($p < 0,001$). La AI+FTR redujo la FR media ($p = 0,003$) y aumentó la SpO_2 ($p = 0,006$), el volumen espiratorio forzado en el primer segundo ($p = 0,021$) y los valores nutricionales ($p = 0,002$). En el momento de la hospitalización, la TEF mejoró de inmediato la FC ($p = 0,028$), FR ($p = 0,001$) y la SpO_2 ($p = 0,015$), a pesar de un reducción significativa de la ventilación voluntaria máxima ($p = 0,028$); tras la remisión de la infección, la TEF no alteró significativamente los parámetros.

Conclusión: La AI+FTR mejoró el estado clínico de los pacientes con fibrosis quística. La TEF mejoró las variables cardiorrespiratorias de los pacientes con riesgo de infección.

Introduction

Over the last 3 decades, there have been many advances in the diagnosis and treatment of cystic fibrosis (CF). These developments have been associated with effective multidisciplinary treatment and aggressive therapeutic interventions, and have improved median life expectancy and quality of life of patients,[1] although lung infection continues to play a leading role in the high rates of morbidity and mortality.[2]

In Brazil, the colonisation of and chronic infection by *Pseudomonas aeruginosa (P. aeruginosa)* has an earlier incidence than in developed countries. The infection is evidenced by the exacerbation of clinical symptoms such as fever, increased coughing, increased sputum, dyspnea, loss of appetite, weight loss, absenteeism from school and work, and decreased exercise tolerance.[2-4]

Patients experiencing an acute lung exacerbation of chronic infection by *Pseudomonas aeruginosa* (APECIP) are characterised by a fast decline in lung function and poorer prognosis, which depends on the number of episodes and the time elapsed between them.[2,5,6]

In most regional reference cystic fibrosis units there are protocols for intravenous antibiotic therapy (IAT) for APECIP. Many of these units have published studies that describe the improvement of respiratory symptoms, lung function parameters, quality of life and inflammatory markers after IAT.[2,5-8] In a few studies carried out in patients with APECIP, other therapeutic interventions combined with IAT were evaluated, such as respiratory physiotherapy (RPT).[8-10]

RPT contributes to the clearance of bronchopulmonary secretions of CF patients with lung disease, with improved lung ventilation and quality of life. There is no "gold standard" for the treatment of CF. Different techniques may be combined but there is no evidence regarding which of these strategies is the most effective one. The decision will depend on the age of the patient and their capacity to perform the manoeuvers.[8] The benefits of using conventional techniques (percussion, vibration and postural drainage), physical activity, instruments such as the Flutter® device and the positive expiratory pressure (PEP) mask have been reported.[8-12] The forced expiration technique (FET) promotes relative independence for the patient, thus making it a recommendable technique.[11,12] The principle of this treatment is based on the combination of one or two non-violent forced expirations (or "huffs") with periods of controlled breathing to prevent airflow obstruction. This is followed by the induction of productive, non-exhausting coughing to eliminate secretions that have been transported to the upper respiratory tract due to migration within equal pressure points. There are some studies that have investigated the effect of this technique on unstable airways in the presence of APECIP before and after IAT.

To date, after the combination of IAT and RPT, the examinations and parameters recommended for the treatment of cystic fibrosis lung disease include: spirometry, oxygen saturation, blood gas analysis, plethysmography, microbial culture, volume and mucus rheology, nutrition, hospitalisation, questionnaires, imaging techniques, evaluation scores and clinical variables.[9-14] The effectiveness of IAT on APECIP has been demonstrated[8]. However, there have been no markers presented of the effects of RPT with a significant enough response to increase the benefits of this procedure to the fullest extent possible.[10-12,15]

The aim of this study was to evaluate the immediate effects of daily FET and IAT+RPT on the parameters of lung function, nutrition and clinical scores of CF patients with acute lung exacerbation of chronic infection by *P. aeruginosa* on admission to hospital and on discharge from hospital after infection remission.

Patients and Methods

Design

Prospective, uncontrolled study conducted on patients with cystic fibrosis.

Participants

Patients with cystic fibrosis came from the cystic fibrosis reference unit of the Paediatric Department Center for Research in Paediatrics (CIPED)/Pulmonary Physiology Laboratory of the University of Campinas (Universidade Estadual de Campinas/UNICAMP), hospitalised with APECIP for a period of 3 years.

Individuals were included in the study if they were diagnosed with CF based on clinical evidence, two sweat tests and genetic testing,[15] and if they presented with APECIP.

According to the European consensus criteria, chronic infection by *P. aeruginosa* was established by the presence of the bacteria in a minimum of three cultures, during a period of 6 months, with direct/indirect signs of infection and tissue injury.[2]

APECIP was established by several values obtained during the application of the Cystic Fibrosis Clinical Score (CFCS) and the Cystic Fibrosis Foundation Score systems (CFFS).[13,14,16,17] Both systems evaluate the signs and symptoms of acute lung exacerbation (table 1). The CFCS is a 5-point scale with a maximum score corresponding to the worst clinical state, which can reach 50 points.[16] The CFFS consists of 11 clinical features and the presence of more than 5 of these involves a lung exacerbation.[17]

Table 1
Cystic Fibrosis Clinical Score (CFCS) and Cystic Fibrosis Foundation Score (CFFS)

CFCS			CFFS 11 clinical signs of exacerbation	
Subjective criteria	Objective criteria	Points	1	Increased coughing;
			2	Increased sputum production and/or change in sputum appearance
Cough	Fever	01–05	3	Fever (>38°C for at least 4 hrs in a 24-hr period) or on more than one occasion in the previous week;
Sputum	Weight:	01–05	4	Loss of weight and anorexia
			5	School or work absenteeism (due to illness) in the previous week
Appetite	Respiratory frequency/retraction	01–05	6	Decreased exercise tolerance;
Dyspnea	Decrease in respiratory/wheezing noises	01–05	7	Increase in RF and/or respiratory work;
			8	New finding in chest examination (e.g. crepitations, wheezing, rales);
Energy	Rales	01–05	9	New finding in chest x-ray;
5–25	5–25	25–50	10	Decreased forced expiratory volume in one second from baseline study in the last 3 months;
Total = subjective+objective criteria points			11	Decreased haemoglobin saturation (according to oximetry) from baseline in the last 3 months >10%

Table based on original articles of Kanga J, Kuhn R, Craigmyle L, Haverstock D, Church D, Cystic Fibrosis Clinical Score: a new scoring system to evaluate acute pulmonary exacerbation, Clin Ther, 1999; 21(8): 1343–56,et al, (1999) and Ramsey BW, Boat TF. Outcome measures for clinical trials in Cystic Fibrosis, Summary of a Cystic fibrosis Foundation Consensus Conference. J Pediatr. 1994; 124(2): 177–92.

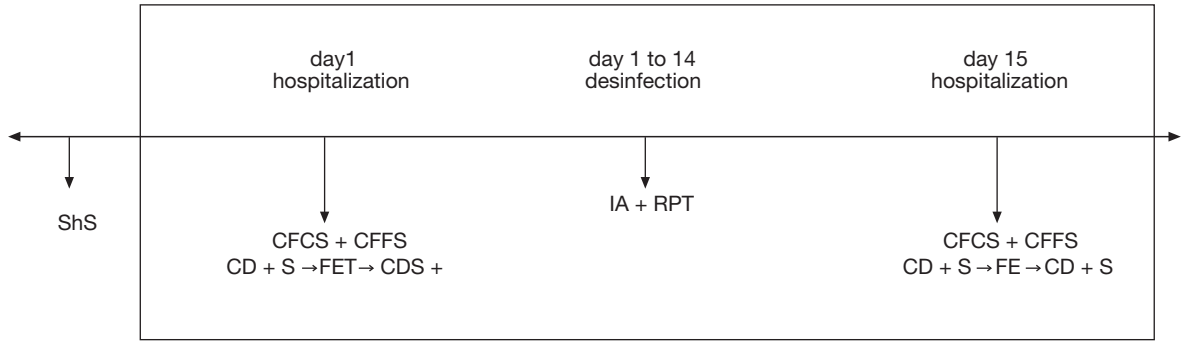

Figure 1. Study plan.

1. Day 1 of hospitalisation
2. Daya 1-14 of resolution of infection
3. Day 15 of hospitalisation
4. ShS
5. CFCS + CFFS
6. Spirometry + clinical data
   Forced expiration technique
   Spirometry + clinical data
7. IAT + respiratory physiotherapy
8. CFCS + CFFS
9. Spirometry + clinical data
   Forced expiration technique
   Spirometry + clinical data

CFCS = Cystic Fibrosis Clinical Score; CFFS = Cystic Fibrosis Foundation Score; FET: Forced expiration technique; ShS = Shwachman Score.

Intervention

Following confirmation of APECIP, patients were referred for hospitalisation for a period of 14 days and received IAT according to the sensitivity detected by the antibiogram.[2,8] RPT techniques were applied twice a day for 30 minutes, a systematic procedure for this service, standardised according to the *Clinical Guidelines for Physiotherapy Management of Cystic Fibrosis Trust*[11] Patients 7-12 years of age underwent Flutter® and percussion. For those over 12 years of age, Active Cycle of Breathing Techniques (ACBT) were used in addition to the two previously mentioned techniques.

All patients received intravenous ceftazidime (150 mg/kg/day) and amikacin (30 mg/kg/day). In the presence of *Staphylococcus aureus*, oxaciclina (200 mg/kg/day) was added to the treatment.[2] During hospitalisation, other therapeutic procedures were maintained such as the inhalation of a bronchodilator three times a day, administration of dornase alpha and nutritional support measures.

Variables Analysed

As defined in the study plan (fig. 1), we analysed the spirometric and other parameters (body anthropometry values, clinical parameters and scores) on the first and last day.

The clinical parameters were analysed immediately after the CFCS and CFFS. To obtain these parameters, the patient remained in a prone position with a rest period of 20 minutes and then 10 minutes

in an upright position, in order to homogenise the baseline values for evaluating respiratory frequency (RF), heart rate (HR), and oxygen saturation of haemoglobin (SpO_2). For these last two parameters, we used an oximeter manufactured by OxiPuls Med (Fundação Adib Jatene, São Paulo, Brazil). After obtaining these parameters, spirometry was performed according to the guidelines set by the *American Thoracic Society.*[18] A MedGraphic System spirometer, model CPFS/D (Medical Graphics Corporation, St. Paul, MN, USA) was used and the patient's weight, height, sex, age and ethnicity were recorded prior to the examination. The patients performed the tests in a sitting position and the best of three recordings was used with the tests taking a minimum of 6 seconds using the same technique. We examined the percentages of the predictable variable values: forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), slow vital capacity (SVC), maximum voluntary ventilation, forced expiratory flow ($FEF_{25-75\%}$), peak expiratory flow (PEF), inhalation capacity and expiratory reserve volume (ERV). After spirometry, the patients underwent the physiotherapy procedure with FET. The FET was described by Webber as a combination of one or more "huffs" (a prolonged, forced expiration keeping the glottis open) and periods of controlled breathing (diaphragmatic breathing). Low speed expiration was used with low lung volumes in order to contribute to the drainage of secretions from the distal airways.[9,19]

In this study, the patient remained seated, breathed deeply and controlled the exhalation for 20 minutes. The physiotherapist's hands followed the patient's breathing over each of the 8 regions (basilar lung segment, medial segment, right lung apex, left lung apex, frontal/sternum chest region, basilar segment, medial segment and then repeating the frontal chest region) while the patient performed 5 forced expiratory manoeuvers with the glottis open: "huffs" in conjunction with four manoeuvers. On the fifth "huff" the patient was asked to cough with help from the physiotherapist. Following this, the patient breathed 5 times with the diaphragm (controlled breathing). Once these manoeuvers were finished, the patient rested until further evaluation.

The spirometric and clinical data were recorded on 4 separate moments: at the time of hospitalisation, for IAT (before FET_1 and after FET_1); and when they were discharged from the hospital, after IAT+RPT (before FET_2 and after FET_2).

One patient was excluded from the study due to difficulties in performing FET and spirometry.

The severity of CF was classified according to the Shwachman Score (ShS),[16,17] during the visits leading up to hospitalisation.

Data Analysis

To process the data, we used SPSS version 11. For comparison of variables of the times studied, we used the Wilcoxon test. To verify the correlation between the variation of CFCS and age, anthropometric body parameters and lung function at the time of hospitalisation, we used the Spearman correlation coefficient. We used a probability value of $p \leq 0.05$ for all statistical calculations.

The study was approved by the research committee of the University of Campinas in Brazil (number 182/2001) and all patients and their legal guardians signed an informed consent form.

Results

The study included 18 patients, 10 of whom were male (55.6%), from 7-28 years of age (16.1 ± 6.3). The ShS score ranged from 30 to 75 (53.6 ± 12). In three patients the condition/disease was classified as *good*, five as *moderate*, nine as *mild* and one as *severe* (30 points).

After the IAT+RPT period, there was a decrease in mean RF ($p = 0.003$) and an increase in SpO_2 ($p = 0.006$), FEV_1 ($p = 0.021$) and PEF ($p = 0.006$). No significant differences were observed between the predictable values of FVC ($p = 0.080$) and $FEF_{25-75\%}$ ($p = 0.247$) (table 2).

During the IAT+RPT period, the average weight increased from 36.1 to 37.1 kg ($p = 0.002$) and the BMI increased from 15.4 ± 2.6 to 15.8 ± 2.5 ($p = 0.002$) (table 3).

The CFCS exacerbation score was 32.4 ± 7.2 (22.0 to 49.0) and, at the time of hospital discharge was 18.9 ± 3.3 (12.0 a 24.0) ($p < 0.001$). The mean difference between both periods was 13.5 ± 6.3 (table 3). There was a significant reduction in the CFFS score ($p < 0.001$).

There was no correlation between the CFCS variation and age ($p = 0.550$): ($p = 0.686$), BMI ($p = 0.459$), SpO_2 ($p = 0.231$), FEV_1 ($p = 0.160$), FVC ($p = 0.438$) and ShS ($p = 0.337$).

At the time of hospitalisation, a statistically significant increase in SpO_2 ($p = 0.015$) and a reduction in RF and HR ($p = 0.001$ y $p = 0.028$) was noted in patients undergoing FET. Nevertheless, there was a significant reduction in maximum voluntary ventilation from 53.5% of the predictive value to 50.2 % ($p = 0.028$) (table 4).

The immediate effect of FET on spirometric and cardiorespiratory parameters at the time of hospital discharge is listed on table 5. Immediately following the FET, there was a significant reduction in the PEF values ($p = 0.009$) and no other variables changed.

Discussion

In the present study, we analysed the effect of FET in patients with cystic fibrosis, before and after APECIP treatment, revealing the effectiveness of this technique at the time of hospitalisation. This study also confirms the positive effects of the combination of IAT and RPT for these cases.

The treatment of APECIP raises important issues: the exact moment for initiating treatment, the medication that should be prescribed, whether therapeutic combinations should be administered, and whether these should be administered systematically before starting APECIP.

In our hospital, patients with this process are hospitalised and undergo a combination of IAT+RPT for 14 days. This study demonstrated that the treatment substantially improved lung function, body anthropometry parameters, cardiorespiratory parameters and lung exacerbation scores.

The mean values for the spirometric variables of the patients studied (FEV_1: 44.7% y FVC: 61.7%) demonstrated mild involvement at the time of inclusion. Compared with other studies that have evaluated the effects of IAT+RPT, this present study's patient sample showed signs of more severe disease.

The significant improvement of FEV_1 and PEF indicates that IAT+RPT treatment was effective in clearing the airways of patients

Table 2
Mean and standard deviation of the HR, RF, SpO_2 and lung function parameters in hospitalisation and following discharge from hospital after intravenous antibiotics and respiratory physiotherapy

	Hospitalisation		Discharge		
	Mean	SD	Mean	SD	P value
HR (bpm)	109.0	22.5	99.6	20.6	0.055
RF (rpm)	27.6	8.1	22.5	5.0	0.003
SpO_2 (%)	92.4	4.9	94.6	2.3	0.006
FEV_1 (%)	44.7	21.6	50.0	22.6	0.021
FVC (%)	61.7	21.3	67.3	24.5	0.080
$FEF_{25-75\%}$ (%)	26.3	20.4	31.1	22.0	0.247
PEF (%)	56.2	25.8	66.0	26.0	0.006
IC (%)	63.3	21.2	68.1	21.7	0.129
SVC (%)	62.4	20.7	67.6	21.4	0.098
MVV (%)	53.5	29.4	59.3	26.8	0.065
ERV (%)	62.8	31.1	68.9	45.5	0.586

ERV: expiratory reserve volume; $FEF_{25-75\%}$: forced expiratory flow 25-75%; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; IC: inhalation capacity; MVV: maximum voluntary ventilation; p: probability of the Wilcoxon test; PEF: peak expiratory flow; SpO_2: oxygen saturation; SVC: slow vital capacity; (%), predictable percentage.

Table 3
Mean and standard deviation of body weight and BMC and exacerbation scores in hospitalisation and following discharge from hospital after intravenous antibiotics and respiratory physiotherapy

	Hospitalisation		Discharge		
	Mean	SD	Mean	SD	P value
Weight (kg)	36.1	12.8	37.1	13.3	0.002
BMI (kg/m^2)	15.4	2.6	15.8	2.5	0.002
CFFS	6.4	1.7	0.3	0.5	< 0.001
CFCS	32.4	7.2	18.9	3.3	< 0.001

CFCS: Cystic Fibrosis Clinical Score; CFFS: Cystic Fibrosis Foundation Score; p: probability of the Wilcoxon test; (%):predictable percentage.

Table 4
Mean and standard deviation of the HR, RF, SpO_2 values and lung function parameters before (before TEF_1) and after TEF (after TEF_2) in hospitalisation for intravenous antibiotics and respiratory physiotherapy

	Before FET_1		After FET_1		
	Mean	SD	Mean	SD	P value
HR (bpm)	109.0	22.5	103.6	18.8	0.028
RF (rpm)	27.6	8.1	24.7	7.0	0.001
SpO_2 (%)	92.4	4.9	93.6	4.7	0.015
FEV_1 (%)	44.7	21.6	44.9	20.5	0.861
FVC (%)	61.7	21.3	62.1	24.0	0.795
$FEF_{25-75\%}$ (%)	26.3	20.4	25.6	19.6	0.627
PEF (%)	56.2	25.8	55.2	24.5	0.494
IC (%)	63.3	21.2	65.4	18.3	0.236
SVC (%)	62.4	20.7	65.0	27.8	0.550
MVV (%)	53.5	29.4	50.2	27.4	0.028
ERV (%)	62.8	31.1	67.9	77.3	0.149

ERV: expiratory reserve volume; $FEF_{25-75\%}$:forced expiratory flow 25-75%; FEV_1: forced expiratory volume in one second; FVC: forced vital capacity; IC: inhalation capacity; MVV: maximum voluntary ventilation; p: probability of the Wilcoxon test; PEF: peak expiratory flow; SpO_2: oxygen saturation; SVC: slow vital capacity; (%):predictive percentage.

Table 5
Mean and standard deviation of the HR, RF, SpO2 values and lung function parameters before (before TEF2) and after TEF (after TEF2) in hospital discharge after intravenous antibiotics and respiratory physiotherapy

	Before FET_2		After FET_2		
	Mean	SD	Mean	SD	P value
HR (bpm)	99.6	20.6	100.2	18.1	0.679
RF (rpm)	22.5	5.0	22.3	5.6	0.562
SpO_2 (%)	94.6	2.3	95.4	2.4	0.066
FEV_1 (%)	50.0	22.6	50.0	22.2	0.694
FVC (%)	67.3	24.5	66.4	24.4	0.466
$FEF_{25-75\%}$ (%)	31.1	22.0	31.2	22.0	0.702
PEF (%)	66.0	26.0	62.7	25.6	0.009
IC (%)	68.1	21.7	72.3	24.8	0.083
SCV (%)	67.6	21.4	71.8	24.0	0.079
MVV (%)	59.3	26.8	58.4	26.9	0.317
ERV (%)	68.9	45.5	72.9	41.4	0.542

ERV: expiratory reserve volume; $FEF_{25-75\%}$: forced expiratory flow 25-75%; FEV_1: forced expiratory volume in one second; FRC: forced vital capacity; IC: inhalation capacity; MVV: maximum voluntary ventilation; p: probability of the Wilcoxon test; PEF: peak expiratory flow; SpO_2: oxygen saturation; SVC: slow vital capacity; (%), predictable percentage.

with APECIP although the individual effect of IAT and of RPT on spirometry could not be determined.

Several studies have reported an improvement in lung function with IAT.[2,4,7,8,22,23] Although spirometry is often used for this measurement, in completed studies, it is suggested that FEV_1 is the main indicator.[7,12,15,21] Its reproducibility, high correlation with mortality, contribution to the indication for lung transplantation and applicability in the research of the effects of different treatments, represent some of the arguments for using this parameter.[15,16,18] It has also been shown that other methods, such as the forced oscillation technique, are alternatives for evaluating lung function after IAT for APECIP[21].

IAT reduces inflammation and inflammatory airway obstruction in patients with cystic fibrosis.[2,8,15] The authors suggest that the effectiveness of IAT is enhanced when combined with intensified RPT during hospitalisation,[20,23,24] preferably before the administration of antibiotics. However, the isolated effects of IAT and RPT have never been evaluated in this situation. An ethical screening test is being carried out on a model to examine the separate roles of IAT and RPT. A CF patient admitted for treatment of a lung exacerbation requires the services provided mainly by the respiratory therapist, which include the administration of nebulised drugs (antibiotics, dornase alpha, bronchodilators, hypertonic saline solution, implementation of the RPT, supplemental oxygen supply and initiation of non-invasive and invasive mechanical ventilation support). As a result, an important aspect of hospitalisation is the interaction between therapist and patient. Following the recommendation of the CF lung guides, information and training are provided to patients and their families.[15]

Recently, Prasad et al and Homnick described the difficulty in isolating the effects of RPT and the effects of a multidisciplinary therapeutic strategy (nutrition and inhalation therapy).[1,19] This is even more difficult during hospitalisation for the resolution of infection since factors such as rest and IAT are involved.[8,24,25]

An individual study with methodological implications tried to isolate the effect of RPT in the therapeutic approach for APECIP. Oberwalder et al (1991) performed lung function tests immediately after the positive expiratory pressure manoeuvers of the airways with TEF at 4 different times: at the time of hospitalisation and on the 5th, 10th and 15th days. They observed a progressive increase in lung function parameters after physiotherapy, which they attributed to the cumulative effect of the therapy during hospitalisation.[24]

Lung volume changes have been clinically relevant in the assessment of patients with chronic obstructive lung disease after the bronchodilator test, as compared to FEV_1 and FVC.[26] Given this basis, the evaluation of volumes determined for slow vital capacity by spirometry may constitute an alternative to assessing the effect of RPT in cystic fibrosis since the methods used are controversial.[9,10-12] In this study, the association of IAT+RPT, as with the isolated FET, did not result in an improvement in parameters related to lung volume measurements (inhalation capacity and FVC), although there was a decrease in RF with IAT combined with RPT and after FET during hospitalisation. The increase in lung volume favours the reduction of inspiratory cycles, which ensures adequate ventilation and maintains gas exchange. As a result, it is hypothesized that an improvement in volume could be related to an improvement in RF and SpO_2.

We found a decrease in HR and RF and an increase in SpO_2 immediately after FET and also after IAT+RPT, which highlights the positive effect of respiratory physiotherapy on cardiorespiratory parameters. The same result was documented in a study that used Active Cycle of Breathing Techniques where the main component was FET.[20]

The use of SpO_2 measurements as a marker of the effect of RPT is considered to be accessible, easy to apply and low cost. However, unlike in the present study, few investigations have obtained consistent results using this parameter.[19] The result of this study may be related to the severity of the patients' clinical state as well as the choice of a determined RPT with fewer side effects. The fact that FET does not trigger hypoxia, bronchospasms and gastroesophageal reflux, as happens with the application of conventional techniques, contributes to the indication of this method primarily in individuals with APECIP.

Although currently there is no marker with a sensitivity and specificity appropriate for assessing the effects of RPT,[10,12,25] the

assessment of RF, HR and SpO_2 appears to constitute an appropriate marker for airway clearing techniques such as FET. We note that the three parameters behave similarly, suggesting that the technique's clearing effect favours an improvement in ventilation and oxygenation, with a corresponding decrease in respiratory effort.

After IAT+RPT, there was also a significant change in the CFCS and CFFS exacerbation scores. The application of these clinical scores in cystic fibrosis has been adopted for several reasons: assessment of disease severity, prediction of its development, identification of lung exacerbations and monitoring of the response to the treatment. In this study, the changes were highly significant since the values of both scores showed an improvement in the patients' clinical and general state after hospitalisation. The study supports the view that a consensus needs to be reached on treatment guidelines for cystic fibrosis.[2,3,15,26]

During the correlation analysis we did not find any variables that correlated with an improvement in CFCS. This indicates that, independent of age, disease severity, expiratory flow values and body anthropometric parameters at the time of hospitalisation, an improvement was obtained in all patients with IAT+RPT.

Many studies have investigated the effects of an improvement in nutrition on lung function and vice versa. In the present study, in addition to the previously mentioned improvement in lung function, the combination of IAT+RPT favoured an increase in weight and BMI in the patient. Some authors have assessed the energy expenditure of patients with cystic fibrosis.[6,27,28] Few studies have identified a substantial influence of respiratory state on nutritional components, especially in situations of acute lung exacerbation. IAT seems to moderate patients' baseline energy expenditure,[6,8,28] which would explain the improvement in weight and BMI identified in this study. The change in body weight was related to the treatment of nutritional support provided during hospitalisation.

There was no immediate improvement in spirometric values in either of the two times that FET was applied. There was a significant reduction in maximum voluntary ventilation in patients with APECIP after undergoing FET. This reduction was due to the fact that the manoeuver required muscular effort and the technique was performed in a situation of bronchial obstruction, dyspnea and shortly after coughing as a consequence of the physiotherapy procedures. In addition to the substantial exhaustion of the patient, the reduction of this variable may also be associated with a dynamic hyperinflation immediately after FET. This event occurs during exercise/effort when the limitation of airflow produces high lung respiration volumes, which increase elastic work and favour hyperinflation. A few studies that have compared the effects of conventional RPT and FET on FEV_1 have found either a greater clearing effect of the airways with conventional treatments or no difference between the techniques.[7,12] A better expectoration and improvement in the FEV_1 values was observed with the application of TEF associated with postural drainage.[9,10-12,25] In these studies, the application of FET was not standardised, a control group was not included and there were problems with the methodology, which has raised continuous criticism in recently published articles and reviews.

FET was introduced into physiotherapy with the objective of minimising the characteristic stress induced by conventional techniques and obtaining a clearing of bronchial secretions.[9,11] The technique is indicated for cases of acute exacerbations. Over the last ten years, the inclusion of FET in the RPT has been recognised as an important advance in physiotherapy treatment.[9-11] Furthermore, for treatment of patients with bronchiectasis, as with cystic fibrosis, Vendrell et al recommend the application of RPT in self-treatment, which facilitates long-term adherence to the use of the technique.

In APECIP, the airways are inflamed, or blocked, with epithelial desquamation, instability and hyperreactivity. During the forced expiration manoeuver, as in the spirometry manoeuver, coughing and RPT, these features of the airways may be exacerbated, which enhances the tendency to collapse.[29,30] As a result, the application of FET would not accompany positive spirometry results even though its effects on clearing are made evident through a substantial improvement in the cardiorespiratory parameters evaluated.

Since FET is a technique for airway clearance, the implementation of this manoeuver after the resolution of infection reduced PEF, which we attribute to the absence of secretions in the airways and the effort induced by the forced expiratory spirometry manoeuver.[30]

The difficulty in providing an adequate sample size in studies assessing the effects of RPT in cystic fibrosis has been documented.[25] The authors of the present study acknowledge the limitations of the sample although recent studies on RPT and IAT[5,21] have described a similar casuistry (16 and 14, respectively). At present, with the well-defined knowledge and guidelines established for APECIP, many multicentric studies can now be done with a calculated sample size to verify the described hypothesis with greater statistical precision. Another limitation of the present study was that recurrence was not considered an evaluation parameter, neither was the severity of exacerbation episodes in CF patients undergoing the treatment protocol presented in the study. The authors suggest that this is a future goal for studies on IAT and RPT given the clinical relevance of the number and quality of hospitalisations in the development of therapeutic methods for treating the disease.

Although respiratory physiotherapy is a treatment adjunct to other therapeutic interventions in cystic fibrosis, as is IAT, the technique and ideal standardisations are still controversial as are the most appropriate parameters for the evaluation of its effects and the most appropriate moment for its application.

Conclusion

The present study showed the effect of IAT+RPT on the scores and on the cardiorespiratory, nutritional and spirometric parameters, as well as showed clinical improvement in patients with APECIP. The positive effect of FET was observed at the time of hospitalisation, which was probably due to the important obstructive component in this situation.

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