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Positive Expiratory Pressure (PEP) versus Conventional Chest Physiotherapy in Pediatric Patients with Acute Exacerbation of Cystic Fibrosis

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Abstract

Background

Pulmonary involvement is the main cause of mortality in cystic fibrosis (CF). Airway clearance techniques are non-pharmacological complement options for CF patients. The aim of this study was to evaluate the short-term outcome of airway cleaning treatment in patients with cystic fibrosis in a children's hospital.

Materials and Methods

This clinical trial study conducted on 40 CF patients referring to the specialized lung clinic of Tabriz Pediatric Center in Tabriz, Iran from April 2016 to April 2017. Patients were randomly divided into two equal case (PEP), and control (conventional) groups. The basic spirometry parameters were measured on the European Respiratory Society criteria. After therapeutic intervention, the patients were followed for the next six months and the number of hospital admissions were recorded.

Results

The mean of FEV1, FEV1/FVC and FEF25%-75% in the control group after treatment were 62.60±20.39, 86.70±19.39 and 55.20±32.78, respectively. Comparison of the control group means of FEV1, FEV1/FVC, and FEF25%-75% in the case group after intervention (57.52±14.62, 76.80±21.83 and 59.8±28.71, respectively) showed significant differences ($p<0.05$). The number of re-hospitalization during the following six months in the case and the control groups were 1.4±1.23 and 2.00±0.64, respectively, which was significantly different ($p = 0.00$).

Conclusion

The patients undergoing treatment (PEP and control groups) showed better spirometry results. In the PEP group, the number of re-hospitalizations was significantly lower than the control group.

Key Words: Cystic fibrosis, Lung injury, Pediatrics, Positive expiratory pressure.

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1- INTRODUCTION

Cystic fibrosis (CF) is an autosomal recessive disease due to the mutation in the CFTR gene (1, 2). This disease affects the exocrine glands and causes various manifestations including: pulmonary and digestive dysfunction, pancreatic insufficiency and causes frequent respiratory infections and premature death (1, 3). Chronic pulmonary infections are the cause of mortality in 80% of cases (1). Also, the risk of malignancy in gastrointestinal organs and hepatobiliary is more common in CF patients (4). The recent medical advantages in diagnosing and treating these patients have led to a significant increase in the life expectancy and quality of life of these patients (5). However, the median longevity of patients known to be around 40 years (1). Early diagnosis and timely treatment can lead to better clinical outcomes for these patients (6). The pulmonary diseases are the main cause of mortality in CF patients (7).

The mucus retention a result of impaired clearing of the airway sticky secretions is a major manifestation of pulmonary disease (7). Accordingly, many treatments have been devoted to airway purification (1, 7). Meanwhile, the airway clearance techniques (ACT) have been introduced as the most important treatment in this regard (8). ACT methods include conventional chest physiotherapy (CCPT) or postural drainage and percussion (PD and P), active cycles of respiration technique (ACBT), autogenic drainage (AD), Positive expiratory pressure (PEP), Flutter, high-frequency chest wall oscillation (HFCWO), and non-invasive ventilation (NIV) in the form of BIPAP (9). The goal of ACT physiotherapy is to move and drain large amounts of pulmonary secretions(7). By improving pulmonary function, we can reduce the progression of pulmonary disease and thus improving the quality of life for these patients (10).

ACT is a non-pharmacological complement therapy in CF (11); however, due to time-consuming and patient collaboration; routine use of these methods is difficult and depends entirely on patient compliance (12). In some studies, up to 108 minutes of daily ACT has been reported in adults ACT patients (11). For this reason, many studies have highlighted the compilation and poor collaboration of patients with the use of ACT methods (11). However, cooperation in the continuation of the treatment of chronic illness, such as CF, is of great importance, as it may be necessary to prevent the need for an increase in the dosage of used drugs, exacerbation of the disease and the need for frequent admissions (13, 14). We aimed to evaluate the effectiveness of ACT in the short term in CF patients in Tabriz Children's Hospital, Iran.

2- MATERIALS AND METHODS

2-1. Method

The subjects were 40 children (according the following formula) referring to the lung clinic of Tabriz Pediatric Center in Tabriz, Iran with CF exacerbation between April 2016 and April 2017, were included in this randomized clinical trial (IRCT20131012014988N3).

$$n = \frac{(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2 \times (S_1^{\,2} + S_2^2)}{(\mu_1 - \mu_2)^2} \approx 20$$

The patients were randomly divided into two equal case (PEP) and control (conventional) groups. The control group was treated with antibiotics (third generation cephalosporin according to protocol for treatment of CF exacerbation at Tabriz Children's Hospital) and CCPT (9). The case group received antibiotic therapy and CCPT in addition to use of the mouthpiece PEP device (on days 2, 4 and 6 after admission for 30 minutes). In this treatment, the mouthpiece of the PEP

device should be positioned well into the mouth. Patient inspires with a slightly larger than tidal volume breath through the mouthpiece and slightly active expiration is then performed through the mouthpiece. Spirometry was performed on the days of admission and discharge to evaluate the forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC and forced expiratory flow (FEF; 25%, 50%, 75%), and FEF 25%-75%. The spirometry findings of each individual were measured based on the ERS criteria according to the age, gender, height and weight of the patient. The patients were followed during the next six months and the frequency of exacerbation of disease and number of hospital admissions were compared. This study was approved by the Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1396.827), and signed informed consent forms were obtained from all patients or their parents before inclusion in the study. The inclusion criteria were 5-14 years of age with a confirmed CF diagnosis and a base line FEV1 of 20% to 70%. Children were excluded if they had coexistent heart disease and severe exacerbation requiring intensive care or mechanical ventilation.

2-2. Statistical Analysis

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS), version 22.0. The data were analyzed by descriptive statistics (mean, standard deviation and frequency-percent); while for comparing the two interventional methods and the difference in mean of this study, student t test and ANOVA test were used. A P-value < 0.05 was considered statistically significant.

3- RESULTS

In this study, 40 patients aged 5 to 14 years with CF exacerbation were studied. Amongst all 40 patients, 25(62.5%) were male and 15(37.5%) female. Mean age was 9±2.16 years. The patients 'demographic information are presented in **Table.1**. Improvement of vital sign of patients after treatment are demonstrated in **Table.2**. There was no significant difference between body temperature, and Respiratory rate after treatment between groups (P>0.05). However, children receiving PEP had significantly more improvement in the heart rate, and SPO2 results (P<0.05). According to the **Table.3** the Blood Gas analysis parameters were better after the intervention in both groups but these changes were not statistically significant between groups (P>0.05 for each parameter).

The mean of FEV_1, FEV_1/FVC, and FEF25-75% in conventional group before the treatment were 51.20±22.19, 71.86±18.27, and 40.00±33.66, respectively; and in the PEP groups were 47.80±30.89, 70.40±20.93, and 40.20±49.80, respectively. There was no significant difference between the two groups for the all basic spirometry parameters (P<0.05 respectively) (**Table.4**).

Comparing the spirometry findings after treatment in each group, there was a significant improvement in all parameters in both groups, but the mean of FEV1, FEV_1/FVC, FEF25%, and FEF25-75% after the intervention changed significantly in the PEP group (P<0.05 for each parameter-**Table.4**). Also, the Re-Hospitalization during the 6 months in the PEP group and the Conventional group were 1.4±1.23 times and 2.00±0.64 times, respectively, which this difference was statistically significant (P = 0.00).

Table-1: The baseline characteristics of patients

Parameter	Frequency, (n=40 cases) (percent % or Mean±SD)
Age (Year)	9±2.16
Gender Girl Boy	 37.5% 62.5%
Weight (Kg)	20.52±3.20
Height (Cm)	123.9±19.33
Groups PEP CONVENTIONAL	 50% 50%
HR (Beats/Min)	102.40±10.90
SaO2 (%)	85.40 ± 3.90
BT (ºC)	36.98±0.57
RR (per Min)	41.50 ± 13.75
HG	13.39±1.37
RBC	4.95±0.42
WBC	152.30±53.38
PLT	408.70±152.25
CRP - + ++ +++	 20 8 8 4
ESR	45.20±19.57

SD: Standard deviation; PEP: Positive Expiratory Pressure; HR: Heart Rate; SaO2:O2 saturation; BT: Blood Temperature; RR; Respiratory Rate; HG: Hemoglobin; RBC: Red Blood Cell; WBC: White blood cell; PLT: platelet; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate.

Table-2: The vital sign results of patients for each group before and after treatment

Parameters	PEP, (n=20)	Conventional, (n=20)	P-value
HR before	102.6±14.48	102.20±8.21	0.3
HR after	103.2±17.22	112.40±10.59	0.03
SaO2 before	87.6±4.72	83.20±1.64	0.22
SaO2 after	91.60±3.71	88.60±3.20	0.00
BT before	37.00±0.39	36.90±0.72	0.40
BT after	37.00±0.08	36.80±0.57	0.09
RR before	38.80±16.66	44.20±12.85	0.18
RR after	26.60±8.53	29.00±5.56	0.25

(Data are presented as Mean±SD); PEP: Positive Expiratory Pressure; HR: Heart Rate; SaO2:O2 saturation; BT: Blood Temperature; RR; Respiratory Rate.

Table-3: The Blood Gas analysis results of patients for each group before and after treatment

Parameters	PEP, (n=20)	Conventional, (n=20)	P-value
PH before	7.38±0.03	7.38±004	0.40
PH after	7.39±0.49	7.39±0.11	0.84
PCO2 before	41.46±4.67	39.10±6.83	0.36
PCO2 after	37.5±4.15	37.88±8.18	0.4
HCO3 before	23.84±1.02	22.50±4.14	0.26
HCO3 after	24.34±1.94	23.16±3.69	0.17
PO2 before	48.9±8.46	62.20±22.19	0.35
PO2 after	57.52±14.62	54.54±11.97	0.40

(Data are presented as Mean±SD); PEP: Positive Expiratory Pressure; PCO2: Pressure of co2, PO2: Pressure of o2.

Table-4: The spirometry results of patients for each group before and after treatment

Parameters	PEP, (n=20)	Conventional, (n=20)	P-value
FEV1 before	47.8±30.89	51.20±22.19	0.40
FEV1 after	57.52±14.62	62.60±20.39	0.02
FVC before	53.8 ±23.79	66.60±27.70	0.40
FVC after	62.80±26.83	71.40±30.40	0.30
FEV_1/FVC before	70.40±20.93	71.86±18.27	0.36
FEV_1/FVC after	76.8±21.83	86.70±19.39	0.01
FEF25% before	36.8±24.59	60.00±39.33	0.40
FEF25% after	52.6±30.92	62.40±36.51	0.00
FEF50% before	45.00±41.89	50.60±27.70	0.34
FEF50% after	43.40±26.07	43.20±27.70	0.98
FEF75% before	47.2±43.01	68.00±46.99	0.30
FEF75% after	49.4±32.11	62.60±46.40	0.26
FEF25-75% before	40.20±49.80	40.00±33.66	0.36
FEF25-75% after	59.8±28.71	55.20±32.78	0.00
PEF before	56.34±44.10	77.40±61.30	0.36
PEF after	56.00±34.76	77.20±47.29	0.08
Re-Hospitalization during the 6 month	1.4±1.23	2.00±0.64	0.00

(Data are presented as Mean±SD); SD: Standard deviation; FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; FEV1/FVC: Forced expiratory volume in 1 second/ Forced vital capacity ratio; FEF25%: Forced expiratory flow at 25% of expired vital capacity; FEF50%: Forced expiratory flow at 50% of expired vital capacity; FEF75%: Forced expiratory flow at 75% of expired vital capacity; PEF: Peak expiratory flow; FEF(25-75%): Forced expiratory flow between 25% and 75% of expired vital capacity.

4- DISCUSSION

The aim of this study was to evaluate the short-term outcome of airway cleaning treatment in patients with cystic fibrosis in a children's hospital. Comparing the spirometry findings after treatment in each group, there was a significant improvement in all parameters in both groups, but the mean of FEV1, FEV_1/FVC, FEF25%, and FEF25-75% after the intervention changed significantly in the PEP group ($P<0.05$ for each parameter). The number of re-hospitalization during the following six months in the case and the control groups were 1.4±1.23 and 2.00±0.64, respectively, which was significantly different ($p = 0.00$). Cystic fibrosis is a complex and fatal genetic disorder (1, 3). Although CF affects the pulmonary and gastrointestinal systems (9), 85% of deaths are due to pulmonary involvement (15). The destruction of the airway surface fluid, chronic inflammation and infection cause accumulation of secretions and affects the airway system (4). ACT treatment is considered to be the most important tool in the management of pulmonary involvement in CF cases (16). The International Physiotherapy Group/Cystic Fibrosis (IPG/CF) has introduced a number of ACTs that have been shown by controlled clinical studies to be acceptable. These include active respiration cycle, PEP, oscillating PEP, AD and PD and P (17). The current study was undertaken to evaluate the effectiveness of PEP and CCPT as the ACTson the short-term outcome of CF patients admitted to Tabriz Children's Hospital in 2016 and 2017. The spirometry findings after treatment in both groups demonstrated significant improvement in all parameters.There was no significant difference between body temperature, and respiratory rate after treatment betweengroups. However, children receiving PEP had significantly greater improvement in heart rate and SPO_2 results. Recent studies have shown that ACT has the short-term benefits of increasing the movement of mucus accumulated in the airways and improving

the symptoms of the disease (18, 19). It has been observed that ACT could effectively improve patientvital signs such as O_2 saturation (SaO_2), and heart rate. Main et al. (20) examined the effect of using CCPT on CF patients and found that there was no statistically significant difference in comparison with other methods for improvement in pulmonary function. There also was no significant difference in the number of hospital admissions between the CCPT group and other treatments. In conformity with previous studies, the results of the current study found no significant improvement in patient outcome. Review articles, systematic reviews and recent clinical trials comparing CCPT with other therapies have reported that this treatment method is less considered by specialists and researchers and that new therapies such as PEP or non- invasive ventilation (NIV) had better outcomes in improving the pulmonary status of CF patients.

In a recent systematic review (1), the effectiveness of the CCPT method was compared with other ACT approaches. That study FEV1, FVC and FEF25%-75% between CCPT and other methods (ACBT, AD, PEP and HFCC). The frequency of exacerbation of the disease, the number and duration of hospitalizations, quality of life and mortality of the patients have been investigated and it has been reported that CCPT has no significant effect on the patient readmissions. Similar to previous reports, the readmission rate during the current six-month study period for the case and control group were 1.4±1.23 and 2.00±0.64 times, respectively, which is a significant difference. There was no statistical superiority in CCPT for pulmonary function in comparison with other methods (20, 21). Most patients considered PEP and autogenic drainage as superior to CCPT, and considered it easier to perform. For the number of hospital admission days, none of the methods were superior to another and no difference was reported in this regard. There also were no significant differences in the number of hospital admissions. However, in contrast with those results of the current study, the readmission time was significantly lower in the PEP group than the conventional group. In another systematic overview (5), the efficacy of PEP was investigated in comparison with other methods. In that study, FEV1 was not significantly different over the three months of the study. However, longer-term studies have had different outcomes and more studies are recommended in this regard. The frequency of exacerbation in patients undergoing PEP (for one year) was significantly lower than other methods. In most studies (22-24), PEP has been reported to be the preferred methodology for participants preferred, which conforms to the results in the current study. The patients and parents mentioned that they were more comfortable with PEP than CCPTas a treatment. In confirmation of previous studies regarding the efficacy of physiotherapy interventions, the current study found that most vital signs and spirometry parameters had improved in both groups; comparison of the conventional group and PEP group showed significant improvements in this regard. In the PEP group, SPO_2, FEV1, FEV1/FVC, FEF25% and FEF25%-75% had significantly different results when compared to the primary results.

4-1. Limitations of the study

The main limitation of our study was the lack of a physiotherapy center for cystic fibrosis patients in the hospital.

5- CONCLUSION

In conclusion, after treatment (PEP and control group) significantly improved respiratory function in children with cystic fibrosis. In the PEP group, the number of re-hospitalizations was significantly lower than in the control group.

6- ABBREVIATION

FEV1: Forced expiratory volume in 1 second,
FVC: Forced vital capacity,
FEV1/FVC: Forced expiratory volume in 1 second/ Forced vital capacity ratio,
FEF 25%: Forced expiratory flow at 25% of expired vital capacity,
FEF 50%: Forced expiratory flow at 50% of expired vital capacity,
FEF 75%: Forced expiratory flow at 75% of expired vital capacity,
NIV: Non- invasive ventilation,
PCO2: Pressure of co2,
PO2: Pressure of o2,
HR: Heart Rate,
BT: Blood Temperature,
RR: Respiratory Rate,
PEF: Peak expiratory flow,
ERS: European Respiratory Society,
SaO_2: O_2 saturation,
FEF (25-75%): Forced expiratory flow between 25% and 75% of expired vital capacity.

7- CONFLICT OF INTEREST: None.

8- ACKNOWLEDGMENT

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