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ORIGINAL ARTICLE

EFFECTS OF POSITIVE AIRWAY PRESSURE ON PULMONARY FUNCTION PARAMETERS

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KEYWORDS: Cystic fibrosis; Pulmonary function.

Background: Few studies have assessed the immediate effects of positive airway pressure, such as the Expiratory Positive Airway Pressure (EPAP) and Flutter devices, on pulmonary function.

Objective: The objective of this study was to assess the immediate changes in pulmonary function after using the EPAP and Flutter devices in patients with cystic fibrosis.

Methods: Fourteen patients aged 18±3 years with varied mixed severity of pulmonary disease were enrolled. EPAP (15cmH_2O) and Flutter were used for 15 minutes, randomly, within a week interval. The helium dilution test was used to measure the functional residual capacity, total lung capacity and residual volume. Statistical analysis was performed using two-way ANOVA, and $p<0.05$ was considered significant.

Results: There were no significant changes in pulmonary tests with either EPAP or Flutter ($p>0.05$ for all comparisons).

Conclusions: Therefore, in the assessed patients, the use of Flutter and EPAP did not promote significant short-term changes in pulmonary function.

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INTRODUCTION

In patients with cystic fibrosis (CF), the malfunction of the cystic fibrosis transmembrane regulator protein, creates an abnormal airway environment, leading to the production of thick and tenacious mucus, mucociliary dysfunction, pulmonary infections and airway obstruction[1-7].

Airway clearance techniques are important components in the management of these patients[1,5,8-10]. The clearance therapy most widely used is called conventional physiotherapy and includes postural drainage, a time-consuming and demanding intervention that requires the assistance of another person. Some patients also experience discomfort with these techniques[1,3,5,8,10-14]. EPAP (expiratory positive airway pressure) and Flutter, were introduced to provide airway clearance while promoting treatment adherence, patient independence and minimization of the discomfort caused by conventional physiotherapy[8,10,12,14-17]. EPAP is a device that uses a threshold resistor capable of generating positive expiratory pressure opposite to expiratory flow, in a constant manner and at predetermined levels, which maintains the expiratory pressure even when the flow is interrupted[18]. Flutter, on the other hand, is a system including a weighted ball in a calibrated orifice of expiratory limb[19], which provides variable positive expiratory pressure in the airways that is associated with high-frequency oscillations[14]. It is believed that high-frequency oscillations cause vibrations in the airway wall, promoting mucus detachment and airway clearance[14].

Only two studies have reported the use of EPAP as treatment for CF patients, and in only one of them the device was compared with Flutter. Van der Schans et al*.* [20] assessed pulmonary function while patients underwent EPAP with two pressure levels (5 cmH_2O and 15 cmH_2O), and Padman et al*.*[13] assessed pulmonary function after 1 month of EPAP and Flutter treatment. In the study by Van der Schans et al*.* [20], there was an increase in total lung capacity (TLC) and functional residual capacity (FRC) for the two pressure levels. Comparing the two levels, the use of EPAP with 15 cmH_2O led to a significant increase in TLC and FRC, which returned to baseline values as soon as the positive pressure was interrupted. In the study by Padman et al*.* [13], there was no alteration in pulmonary function one month after the use of EPAP, Flutter or conventional physiotherapy.

The objective of this study was to assess pulmonary function parameters, mainly functional residual capacity and residual volume, in CF patients using the two positive expiratory pressure devices (EPAP and Flutter).

METHODS

Sample

This was a crossover study conducted in the Cystic Fibrosis Clinic and the Pulmonary Function Laboratory of the Federal University of Minas Gerais (UFMG), in partnership with the Laboratory of Research and Assessment of Cardiopulmonary Performance of the Physiotherapy Department of UFMG. All subjects had more than 60 mEq/L of chloride in the sweat test, obtained from pilocarpine iontophoresis [21]. The inclusion criteria were: age higher than 12 years, clinically stable, not hospitalized in the past month due to pulmonary exacerbation, not a regular user of EPAP or Flutter, and no recent history of pneumothorax and hemoptysis. Exclusion criteria included: inability to perform pulmonary function tests [22], use of supplemental oxygen, pneumothorax and hemoptysis during data collection period, presence of variation in systemic arterial blood pressure above 10 mmHg (diastolic) and 20 mmHg (systolic) during intervention, and oxygen saturation < 88% before or during intervention. The study was approved by the Institutional Ethics Committee. Informed consent was obtained from each subject or parent/legal guardian (when appropriate).

Measurements

The following variables were registered by spirometry: forced vital capacity (FVC) forced expiratory volume in 1 s (FEV_1), and forced expiratory flow between 25% and 75% of forced vital capacity (FEF_{25-75}) were recorded as well as measurement of pulmonary static volumes by closed circuit helium dilution with multiple breaths: TLC, FRC, residual volume (RV) and RV/TLC [22], were performed using Collins Pulmonary Testing System (Braintree, MA, USA). At least three maneuvers of forced expiration were performed to measure FVC, FEV_1, FEV_1/FVC and FEF_{25-75}. The dynamic volumes were reported as the percentage of the predicted value according to Knudson [23]. Two tests with FRC variation below 10% were performed. The static volumes measured using the helium dilution method were reported as absolute values. Spirometry and helium dilution tests were performed before and 15 minutes after intervention. Classification of pulmonary function was performed according to the guidelines of the pulmonary function tests [22].

FRC, RV, TLC and RV/TLC were considered primary outcomes; FEV_1, FVC, FEV_1/FVC, and FEF_{25-75} were considered secondary outcomes. Transcutaneous oxygen saturation (SpO_2) and heart rate were monitored during interventions (Dixtal, Oxypleth, Biomédica, Manaus, Brazil). Each patient visited the Pulmonary Function Laboratory twice with a week interval [4,8,11]. The order in which each device was used was randomized by MatLab software (Natick, USA).

Intervention

Flutter

The Flutter is a pipe-shaped device consisting of a mouthpiece, a plastic cone holding, a steel ball and a perforated hood. When the patient expires through the device, the ball moves up and down, creating a repeated opening/closing cycle during the expiration. The protocol used was similar to the one reported by Konstan et al*.* [24] and McIlwaine et al*.* [14]: the patient remained seated with support for the upper limbs, and the device position was selected for comfort and for maximum vibration and minimum obstruction. Slow and deep inspirations through the nose were performed, with a pause of 2-3 seconds after inspiration. Expiration was then performed through the mouthpiece to reach the expiratory RV (not maximum expiration). The patient was told to keep his or her cheeks as deflated as possible, and the procedure was repeated 10 times. Afterwards, the patient was asked to perform the expiratory forced technique (Huff) twice [8,25]. Spontaneous coughing was neither stimulated nor discouraged. The total intervention time was 15 minutes, and the intervention was supervised by one investigator. The device used was the Flutter VRP1 (Scandipharm, Birmingham, LA, USA).

EPAP

EPAP has a unidirectional valve through which the patient breathes in, and a threshold resistor, through which he or she breathes out and allows a pressure ranging from 5 to 20 cmH_2O. This device can be used through a facemask or a mouth piece with nasal clip [18]. The same protocol used for Flutter was adopted. The pressure level was 15 cmH_2O, based on results reported by Van der Schans et al*.* [20] The device used was manufactured by Vital Signs Inc. (Totowa, NJ, USA).

The following parameters were monitored before and after intervention: systemic arterial blood pressure, respiratory and heart rate, breath sounds, transcutaneous oxygen saturation and signs of increased effort. During intervention, systemic arterial blood pressure was measured every 5 minutes. Heart rate and SpO_2 were monitored continuously.

Statistical analysis

Data were presented as means and standard deviations. Data distribution analysis was performed using Shapiro-Wilk's test, and normal distribution was observed for the following variables: FRC, RV, RV/TLC, FRC, FEV_1, FEV_1/FR and SpO_2. For variables with non-normal distribution (TLC and FEF_{25-75}), data were transformed using radical or logarithmic calculations depending on variance or standard deviation.

For the comparison of pulmonary static volumes, dynamic volumes and SpO_2 before and after interventions, two-way analysis of variance (ANOVA) was used [26]. Paired comparison was not performed because there was no significant difference in the variance analysis. In all statistical tests, the significance level α was fixed at 0.05. SPSS (13.0, Chicago, IL, USA) was used as a database as well to perform statistical analyses.

RESULTS

Among the 14 patients studied, nine were males and five were females. Six presented normal spirometric values, and eight showed some dysfunction. Table 1 presents patients' demographic and anthropometric data, as well as a classification of their pulmonary function and colonization.

Table 1: Descriptive characteristics, pulmonary function classification, and pulmonary colonization for studied patients.

Patient	Gender	Age (years)	BMI (kg/m^2)	Pulmonary function classification	Pulmonary colonization
1	M	17	21.39	Normal	*S. aureus*
2	M	18	19.45	Normal	None
3	M	18	19.27	Mild obstruction	*S. aureus*
4	F	19	18.85	Normal	None
5	F	17	13.83	Combined moderate obstruction and restriction	*P. aeruginosa*
6	F	15	23.65	Mild obstruction	None
7	M	21	18.89	Normal	None
8	M	17	22.05	Mild obstruction	None
9	M	17	20.75	Normal	None
10	F	16	20.62	Normal	*S. aureus*
11	M	25	18.18	Combined mild obstruction and restriction	*P. aeruginosa*
12	M	25	27.00	Mild obstruction	None
13	F	17	17.81	Moderate obstruction	*P. aeruginosa*
14	M	12	13.96	Severe obstruction with FVC reduction	*P. aeruginosa*

M refers to male, F to female and BMI to body mass index.

Table 2 shows the measures of pulmonary static volumes. Again there-was no significant difference in any of the variables (TLC: p=0.935 [F=0.007]; FRC: p=0.988 [F=0.0002]; RV: p=0.927 [F=0.009]; RV/TLC: p=0.935 [F=0.007]). The same result was observed for spirometric variables. There was a slight increase in TLC, FRC, RV, and RV/TLC after Flutter, but the increase was not statistically significant.

Table 2: Changes in static volume values with each therapy according to pulmonary function classification.

	EPAP		**%**	**Flutter®**		**%**	***p***
	Before	**After**		**Before**	**After**		
TLC (L)	5.40±1.20	5.29±1.23	**↓ 2.0**	5.32±1.18	5.19 ±1.23	**↓2.44**	NS
FRC (L)	2.66±0.59	2.59± 0.59	**↓2.6**	2.61±0.57	2.57±0.67	**↓1.53**	NS
RV (L)	1.37±0.46	1.23 ±0.42	**↓10.2**	1.35±0.42	1.30±0.48	**↓3.70**	NS
RV/TLC	28.5 ±9.75	25 ±8.01	**↓ 12.3**	26.5±7.99	25.5±8.26	**↓3.77**	NS

EPAP refers to expiratory positive airway pressure, TLC to total lung capacity, FRC to functional residual capacity, RV to residual volume, L to liters, % to percent change after therapy, ↑ to increase, ↓ to decrease, NS to without significant differences (ANOVA two-way).

Table 3 presents spirometric values before and after each intervention, as well as SpO_2 values. Spirometric values were analyzed using ANOVA, and there were no significant differences (FVC: p=0.10 [F=0.005], FEV_1: p=0.66 [F=0.002], FEF_{25-75}: p=0.46 [F=0.005] and FEV_1/FVC: p=0.758 [F=1.665]). There was no significant difference between the variables before and after the use of both devices, either separately or in combination. Moreover, there was no significant difference in SpO_2 values before and after each intervention, as well as after the use of the two devices (p=0.585 [F:0.302]).

Table 3: Pulmonary function and transcutaneous oxygen saturation (SpO_2) for each therapy.

	EPAP		Flutter®		*p* value
	Before	**After**	**Before**	**After**	
FVC (% predicted)	92.69 ± 17.55	90.86 ± 18.68	93.79 ± 15.98	93.86 ± 14.58	NS
FEV_1 (% predicted)	92.69 ± 28.76	85.21 ± 24.72	93.92 ± 26.64	86.79 ± 19.71	NS
FEF_{25-75} (% predicted)	75.38 ± 33.89	72.07 ± 36.37	70.00 ± 31.77	69.93 ± 31.15	NS
FEV_1/FVC	83.77 ± 13.18	83.64 ± 13.06	83.64 ± 10.67	83.77 ± 10.27	NS
SpO_2 (%)	96.21 ± 1.25	97.00 ± 1.36	95.86 ± 1.79	96.93 ± 1.94	NS

Data are presented as mean ± standard deviation. EPAP refers to expiratory positive airway pressure, FVC to forced vital capacity, FEV_1 to forced expiratory volume in the first second, $FEF_{25-75\%}$ to forced expiratory flow between 25-75% of FVC, FEV_1/FVC to Tiffeneau index, SpO_2 to transcutaneous oxygen saturation, NS to without significant differences (ANOVA two-way).

Table 4 presents data comparing the six patients with normal pulmonary tests and the eight patients with impaired pulmonary function. As shown, there were no statistically significant differences.

Table 4: Comparison between patients with normal pulmonary static volumes and the patients with impaired ventilation, in percent of changes.

	Normal (n=6)		Obstruction or restriction (n=8)	
	EPAP (%) NS	Flutter®(%) NS	EPAP (%) NS	Flutter®(%) NS
TLC (L)	**↑ 0.67**	**↓ 0.50**	**↑ 0.34**	**↓ 1.20**
FRC (L)	**↓ 1.94**	**↓ 1.09**	**↓ 0.61**	**↓ 3.56**
RV (L)	**↑ 1.17**	**↓ 1.43**	**↓ 2.96**	**↓ 4.70**
RV/TLC	**↑ 1.23**	**↓ 2.48**	**↓ 4.50**	**↓ 3.54**

EPAP refers to expiratory positive airway pressure, TLC to total lung capacity, FRC to functional residual capacity, RV to residual volume, L to liters, % to percent change after therapy, ↑ to increase, ↓ to decrease, NS to without significant differences (ANOVA two-way).

DISCUSSION

In the present study neither EPAP nor Flutter significantly changed FRC, RV and TLC. This equivalence was observed before and after each intervention, as well as after undergoing both interventions: after EPAP and Flutter.

All patients performed the interventions with one week interval, which decreased the possibility of superimposing the effects of one device over another, thus influencing the results. Other authors have adopted similar intervals in their studies [4,8,11].

In the present study, the initial spirometry values showed no significant differences, showing the similarity of the patients' initial pulmonary function.

The choice of pulmonary static volumes as dependent variables in the present study was based on the premise that external positive expiratory pressure allows the transmission of positive expiratory pressure to the airways, keeping them open during expiration [8], promoting more homogeneous pulmonary ventilation [27].

Pulmonary static volumes did not show significant changes when pre-intervention and post-intervention data were compared. This corroborates with the results from another study. Padman et al. [13] assessed the efficacy of three treatments during one month: conventional physiotherapy, EPAP, and Flutter. Fifteen patients with mild to moderate pulmonary disease aged five to 17 years were recruited to the study. Pulmonary function tests were performed before and after each treatment. There were no significant changes in the pulmonary function tests after each intervention.

Newhouse et al. [4] compared Flutter, intrapulmonary percussive ventilation, and conventional chest physiotherapy in patients with CF having an FEV_1 61% of the predicted value. Eight patients, with mean age of 17 years, performed pulmonary function tests before and one and four hours after intervention. There were no significant changes in pulmonary function tests and pulmonary static volumes. Van der Schans et al. [20] assessed EPAP with 5 and 15 cmH_2O. Eight clinically stable patients with mean age of 17 years participated in the study.

Different pulmonary function parameters were assessed, among them FEV_1, TLC, RV and FRC. Thoracic gas volume (TGV) in TLC and FRC was measured (TGV_{TLC}, TGV_{FRC}) before and after the use of EPAP. The patient breathed for 2 minutes with EPAP and rested for 2 minutes. TGV_{TLC} and TGV_{FRC} were measured during both periods. This maneuver was repeated four times. During EPAP with 5 and 15 cmH2O, there was a significant increase in TGV_{TLC} and TGV_{FRC}. There was a significant increase in both parameters for EPAP with 15 cmH_2O when compared with EPAP with five cmH_2O. However, after two minutes of intervention, the values returned to the initial levels.

Homnick et al. [5] compared Flutter with conventional physiotherapy in 22 patients with age ranging from 8 to 44 years. Body plethysmography was performed within 24 hours of hospitalization and on the day preceding discharge. There was a significant decrease in RV and RV/TLC after the interventions preceding discharge. It is possible that the observed improvements were at least partially due to other interventions (antibiotics, bronchodilators) used to treat exacerbations.

The unique study comparing the long-term effects of positive expiratory pressure (6-9 months) with conventional physiotherapy and PEP mask usage reported a decrease only in RV [28]. Therefore, positive expiratory pressure may have long-term benefits not apparent in short-term assessments. Additionally, disease severity is a consideration. This is a limitation of the present study, because only one patient had marked ventilatory impairment. It is possible that interventions in patients with more compromised pulmonary function yield different results, as observed in patients with pulmonary disease exacerbation. However, a comparative analysis between patients with unaltered pulmonary function and those with ventilatory dysfunction did not show significant differences.

A decrease in ventilation mismatch and better gas exchange and oxygenation are to be expected following the use of such positive expiratory pressure devices as EPAP and Flutter. In this study, significant changes were not observed in SpO_2 before and after the use of these devices, corroborates with similar studies [4,11,13]. This is possibly due to initial SpO_2 values that were never less than 95% and therefore within the normal range.

In conclusion, the assessment of the short-term effects of EPAP and Flutter on pulmonary function in adolescents and adults with CF showed that neither devices significantly affected pulmonary static volume and pulmonary function. Therefore, it is important to recommend any one of these devices based on pulmonary function classification, clinical stability and patient age.

CONFLICT OF INTEREST

None to declare.

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