Evaluation of the Forced Oscillation Technique and the Extended RIC Model in the Analysis of Individuals with Work-Related Asthma

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Abstract

The main objective of this study was to evaluate the performance of the Forced Oscillation Technique (FOT) and the extended RIC (eRIC) model in the analysis of respiratory mechanical alterations in individuals with work-related asthma (WRA). Twenty-nine individuals were evaluated: 17 healthy and 12 with WRA. Considering the resistive properties of the respiratory system, we observed increases in resistance of the peripheral airways (RpeRIC, $p < 0.009$) and a reduction in WRA homogeneity ($p < 0.02$). The use of a bronchodilator resulted in improvement of the total (R0, $p < 0.05$) and mean (Rm, $p < 0.01$) resistance. Regarding reactance, in the WRA group, the mean values were more negative (Xm, $p < 0.03$), while the resonance frequency increased (Fr, $p < 0.0001$), with decreases in dynamic compliance (C, $p < 0.05$, CeRIC, $p < 0.01$) and inertance (IeRIC, $p < 0.02$). We can conclude that FOT associated with the eRIC model may represent an alternative for longitudinal evaluation in WRA patients and can contribute to early disease identification.

Keywords

Forced oscillation technique • Respiratory mechanics • Diagnosis • Occupational asthma

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1 Introduction

Asthma is a chronic treatable disease of the airways that affects all age groups and presents high prevalence, morbidity and mortality worldwide [1]. It is estimated that 10–15% of the asthma cases that begin in adulthood are directly caused by occupational factors, while another 10% result from worsening pre-existing asthma due to working environment conditions [2]. Work-related asthma (WRA) is characterized by obstructed and hyperreactive airways due to the work environment conditions and not to stimuli from outside the workplace [3, 4].

The functional evaluation of asthma, through spirometry, establishes the diagnosis, documents the severity of the airflow obstruction and monitors the course of the disease and the changes resulting from the treatment [5]. However, this technique requires high patient cooperation in the performance of forced respiratory manoeuvres, which may limit its use in children, the elderly or individuals with altered cognition [6]. In addition, the forced manoeuvre puts the bronchi under stress, which can alter the bronchial tone and lead the individual to exhaustion by repetition [7]. Whole-body plethysmography allows the measurement of pulmonary volumes, capacities and resistance [8] but requires high cooperation manoeuvres, much like spirometry.

The Forced Oscillation Technique (FOT), a simple and non-invasive application methodology, has as its main advantages the need for little cooperation and the realization during spontaneous breathing. It can contribute with new parameters for analysis [9]. Recent studies suggest that this technique can be applied in the detection of early respiratory changes in smokers [10], patients with sarcoidosis [11], silicosis [12] and conventional asthma [13]. Thus, it is possible to infer that FOT can contribute to the early diagnosis of patients with occupational diseases [14] and to the longitudinal evaluation of these volunteers. However, we found only one study in the literature that analysed changes

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in respiratory mechanics associated with work-related asthma through FOT [15].

2 Objectives

In this context, the objectives of this study were [1] to compare the resistive and reactive properties of the respiratory system of healthy individuals and individuals with work-related asthma, [2] to determine the best parameters to diagnose the mentioned alterations and [3] to analyse the changes resulting from the bronchodilator test in these patients.

3 Materials and Methods

The present study is a controlled observational study developed at the Biomedical Instrumentation Laboratory of the State University of Rio de Janeiro. The study was approved by the Research Ethics Committee of the Pedro Ernesto University Hospital (protocol 456–CEP/HUPE). All individuals signed a consent form. There were no conflicts of interest.

3.1 Volunteers

Twenty-nine individuals were analysed. The control group (CG) consisted of 17 individuals with normal spirometry and no history of previous lung disease. Twelve individuals were included in the WRA asthma group. For both groups, the exclusion criteria were tuberculosis, trauma or thoracic surgery, respiratory infections in the last 30 days, chemotherapeutic and/or radiotherapeutic treatment and inability to perform the tests.

The CG was submitted to spirometry and FOT tests. In the WRA group, the sequence of the tests performed was as follows: interview, Asthma Control Test (ACT) questionnaire and respiratory function tests (FOT, spirometry and plethysmography, in this order).

The use of bronchodilator medication (400 μg salbutamol sulphate spray) was performed immediately after the first set of pulmonary function tests and the second cycle of measurements 15 min later. The WRA group measurements were analysed for two moments: pre-bronchodilator (WRA Pre-BD) and post-bronchodilator (WRA Post-BD). A questionnaire [16] was also applied to evaluate the control of asthma in the 30 days prior to the pulmonary function tests.

3.2 Forced Oscillation Technique

The FOT system applies sinusoidal pressure signals with frequencies that are multiples of 2 Hz in the range of 4–32 Hz, using a device developed in our laboratory [17]. During the examination, the subject remains seated, breathing through a mouthpiece, using a nasal clip and holding their cheeks to reduce the shunt effect of the upper airways. Three consecutive tests of 16 s each are performed, obtaining the mean as the final result. The minimum coherence function considered for acceptance is 0.9.

The results associated with the resistive impedance component were analysed using a linear regression between 4 and 16 Hz to obtain the resistance at the intercept (R0), associated with the total resistance of the respiratory system. The mean resistance between 4 and 16 Hz (Rm), related to the airway resistance, was also assessed, as was the slope of the resistance curve, associated with the non-homogeneity of the respiratory system.

The results related to the reactive component were described by the mean reactance (Xm), associated with the homogeneity of ventilation, the dynamic compliance (Cdin), associated with the elastic properties of the respiratory system, and the impedance modulus of the respiratory system at 4 Hz (Z4), associated with the total mechanical load of the respiratory system.

An electrical model was used to obtain more details about the respiratory mechanics in WRA [18] (Fig. 1). This model employs resistance (R), related to the resistance of the central airways; inertance (I), associated with the inertia associated with the displacement of air mass within the system; dynamic compliance of the respiratory system (C); and peripheral resistance (Rp), describing the resistance presented by the small airways of the respiratory system. The total resistance (Rt), the sum of the values of R and Rp, was also calculated.

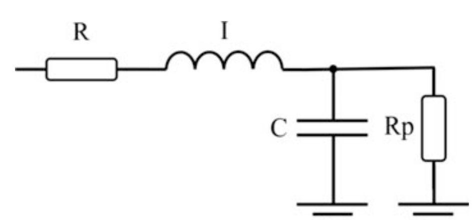

Fig. 1 Electrical representation of a two-compartment model used to analyze respiratory impedance. Resistance, inductance and capacitance are the analogs of mechanical resistance, inertance and compliance, respectively. R is analogous to central airway resistance and Rp describes peripheral resistance, I is associated with lung inertance and C with alveolar compliance

3.3 Data Processing, Presentation and Statistical Analysis

A commercial software package (Origin® 8.0, Microcal Software Inc., Northampton, MA, USA) was used to compare the differences between the groups. First, the Shapiro Wilk test was applied to analyse the distribution of each sample. Considering the non-normal distribution, non-parametric tests were applied. For the comparison of two different groups (control and WRA preDB and control and WRAposBD), the Mann-Whitney test was applied. For the comparison of the same group in different situations (preBd and postBD), the Wilcoxon test was applied.

4 Results

Considering the absence of statistical significance between the biometric parameters analysed, the sample was considered homogeneous (Table 1). The results obtained from the spirometric parameters presented reduced mean values in the presence of asthma. For resistance and TGV measurements, there was improvement after the use of the bronchodilator, with increases in the mean values. Similar results were obtained for Gaw, with improvement of the mean values after bronchodilator use (Table 2). Table 3 shows the sample characteristics according to the disease severity considering Raw measured by plethysmography.

R0 was significantly reduced in the WRA group after use of the bronchodilator (Fig. 2a; $p < 0.05$). A similar result was observed in Rm (Fig. 2b; $p < 0.01$). S showed a reduction in homogeneity in the WRA Pre-BD group ($p < 0.02$) and improvement in the Post-BD group ($p < 0.05$) (Fig. 2c). In the reactive parameters, Xm (Fig. 2d) presented more negative values in the presence of WRA Pre-BD ($p < 0.03$) and Post-BD ($p < 0.01$) and with improved homogeneity in the presence of the bronchodilator ($p < 0.05$). A similar result was observed in Fr (Fig. 2e). Compliance (Fig. 2f) was reduced in the WRA Pre-BD group ($p < 0.05$) and did not show significant change after bronchodilator use.

There were no changes comparing the impedance at 4 Hz between the control group and WRA pre or post bronchodilator. This parameter was reduced after bronchodilator use in the WRA group ($p < 0.02$).

The changes observed from the eRIC model are described in Fig. 3. A significant change in R (Fig. 3a) was observed in the comparison between the Pre-BD and Post-BD groups ($p < 0.005$). For Rp (Fig. 3b), there were increased mean

Table 1 Anthropometric characteristics of the groups studied

	Control (n = 17)	Work-related asthma (n = 12)
Age (years)	48.1 ± 11.6	48.1 ± 12.9
Weight (kg)	72.1 ± 10.2	78.7 ± 14.1
Height (cm)	166.1 ± 6.5	164.5 ± 7.2
BMI (kg/m^2)	26.2 ± 4.1	27.3 ± 6.1

BMI body mass index

Table 2 Spirometric and plethysmographic measurements of the groups studied

	Control (n = 17)	Work-related asthma (n = 12)	
		Pre-BD	Post-BD
FEV_1 (L)	3.1 ± 0.7	2.3 ± 0.5	2.4 ± 0.6
FEV_1 (%)	99.8 ± 12.6	75.6 ± 16.3	79.6 ± 18.2
FVC (L)	3.8 ± 0.8	3.1 ± 0.7	3.2 ± 0.8
FVC (%)	100.1 ± 13.2	83.1 ± 15.0	84.2 ± 17.9
FEV_1/FVC	83.3 ± 4.2	74.9 ± 9.5	77.6 ± 6.9
FEF 25–75%	3.5 ± 0.9	2.1 ± 1.0	2.3 ± 0.8
FEF/CVF	0.8 ± 0.2	0.6 ± 0.3	0.7 ± 0.2
Raw (cmH_2O/L/s)		8.0 ± 6.1	5.2 ± 4.4
sGaw (L/s/cmH_2O)		0.11 ± 0.09	0.15 ± 0.11
TGV (L)		4.1 ± 5.8	3.5 ± 5.1

FEV_1—forced expiratory volume in one second; FVC—forced vital capacity; FEV_1/FVC—relation between FEV_1 and FVC; FEF 25–75%—forced expiratory flow between 25 and 75%; FEF/CVF—ratio of FEF 25–75% and FVC; Raw—airway resistance; sGaw—specific airway conductance; TGV—thoracic gas volume; n = number of patients evaluated. Pre-BD—pre-bronchodilator; PostBD—post-bronchodilator

Table 3 Classification according to resistance measure

Volunteers	Raw	Severity
4 (34%)	<2.5	Normal
1 (8%)	2.5–4.4	Light
1 (8%)	4.5–8.0	Moderate
6 (50%)	>8.0	Severe

Raw—airway resistance

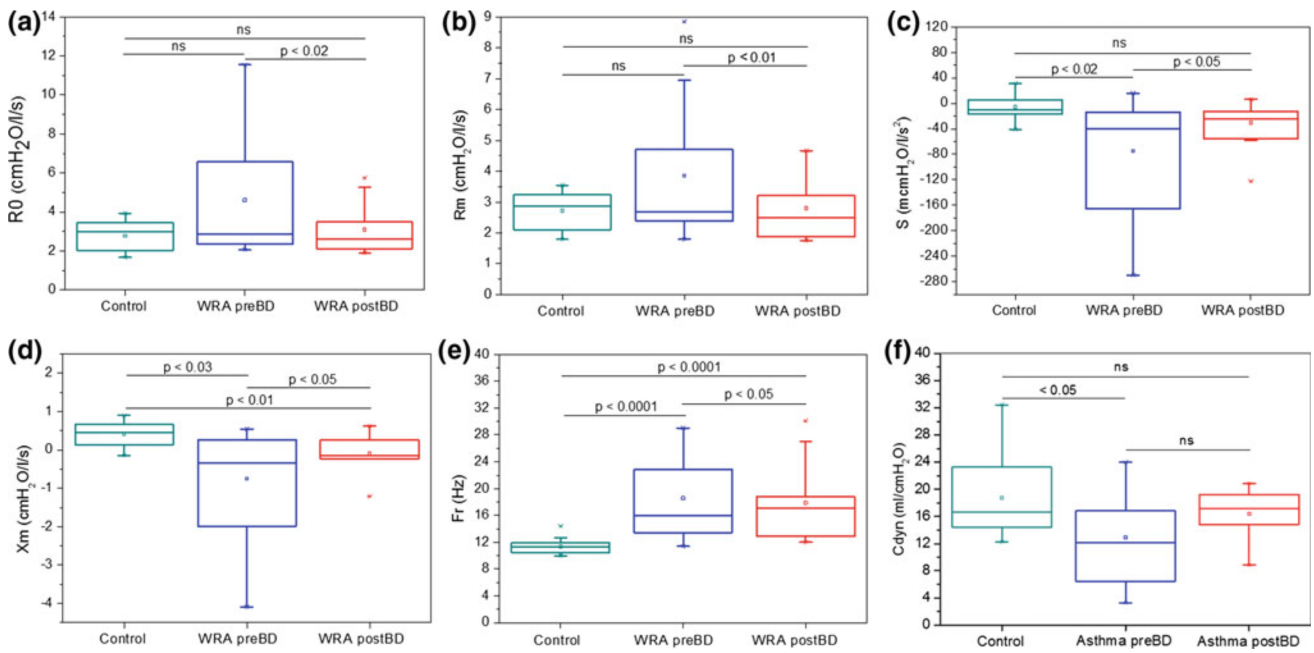

Fig. 2 Comparative analysis of the classical parameters obtained from the control group and worked-related asthma group. Respiratory system resistance (R0; **a**), mean resistance (Rm, **b**) and slope of respiratory resistance (S; **c**), mean respiratory reactance (Xm; **d**), resonant frequency (Fr, **e**) and dynamic compliance (Cdyn; **f**). WRA: work related asthma

values in the Pre-BD ($p < 0.009$) and Post-BD ($p < 0.002$) asthmatics groups. In C (Fig. 3c), the mean values were reduced in the Pre-BD ($p < 0.01$) and Post-BD ($p < 0.02$) WRA groups. Similar behaviour was observed for I (Fig. 3 d), with significant reductions in the Pre-BD ($p < 0.02$) and Post-BD ($p < 0.02$) WRA groups. There were no significant changes in Rt (Fig. 3e).

The Asthma Control Test showed that 50% of the individuals in the WRA group presented score values lower than 18 [16] and therefore were classified as uncontrolled asthma, while 50% were considered as controlled asthma.

5 Discussion

The results from the spirometric and plethysmographic parameters (Table 2) were compatible with the mentioned changes and are in agreement with data previously described in the literature [19].

In the asthmatics group, 50% of the individuals presented values lower than 18 in the ACT and therefore were classified as uncontrolled asthma, while 50% were considered as controlled asthma. This finding can explain the fact that 6 individuals (50%) with WRA presented high Raw and were classified as severe obstruction by plethysmography (Table 3).

R0 is associated with the total resistance of the respiratory system, including airways, the pulmonary parenchyma and the thoracic cage; Rm describes changes in central airways [20]. In the presence of WRA, the airway obstruction and possible irreversible structural changes (airway remodelling) [5, 21] caused by chronic inflammation may lead to deterioration of pulmonary function. However, in the present study, as described in Fig. 2a, b, there were no significant changes in total and mean resistance comparing the CG and the WRA groups, likely due to the great heterogeneity of the asthmatics group studied. In contrast to our results, a previous study [15] showed that R0 was the best parameter to

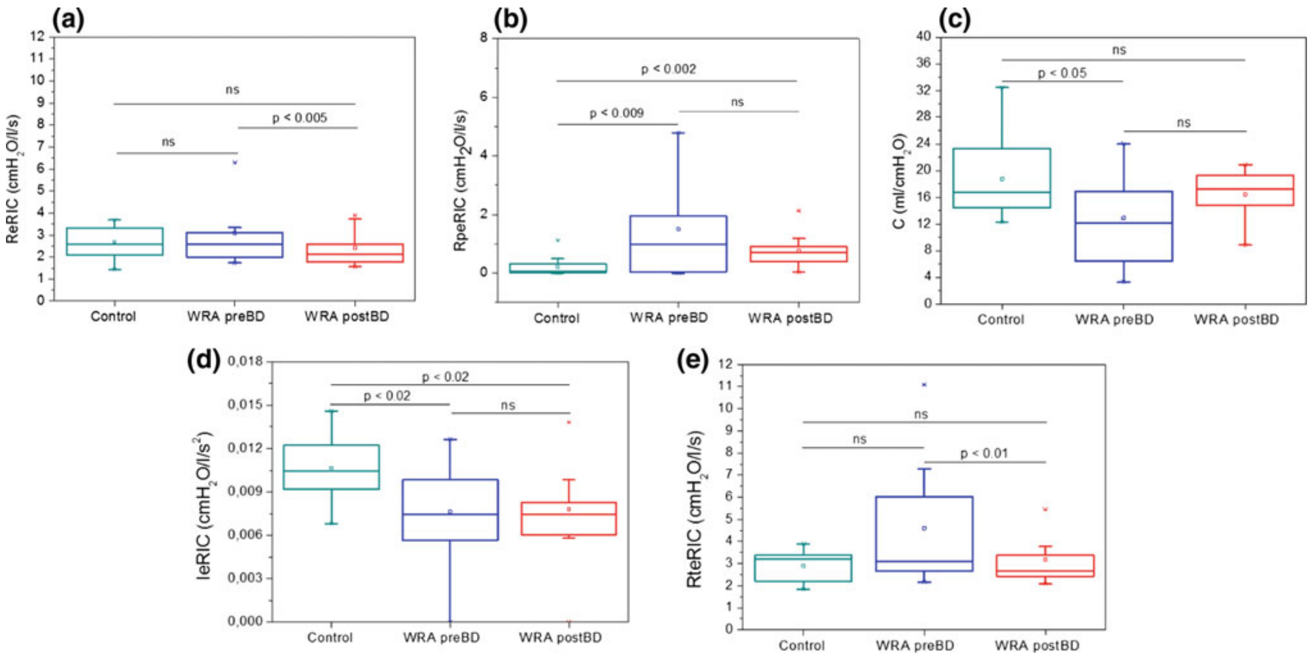

Fig. 3 Influence of work-related asthma and bronchodilator use on parameter values estimated from the compartmental model analysis. Central airway resistance (ReRIC; **a**), peripheral resistance (RpeRIC; **b**), alveolar compliance (CeRIC; **c**), lung inertance (IeRIC; **d**) and total resistance (RteRIC; **e**). WRA: work related asthma

discriminate volunteers with occupational asthma when compared with non-asthmatic patients. However, comparing the pre- and post-BD WRA groups, the FOT was able to identify the improvements in both R0 and Rm after bronchodilator use. Similar results were found in a study with 29 asthmatic adults [7].

The slope of the resistance curve is associated with intrapulmonary gas distribution, and thus, with ventilation homogeneity [22, 23]. In the present study, we observed a decrease in respiratory system homogeneity in the presence of WRA ($p < 0.02$), with a significant improvement after bronchodilator use ($p < 0.05$), in agreement with what was described in previous studies with asthmatics and patients with cystic fibrosis [7, 24, 25]. The alteration of homogeneity may be associated with an inflammatory process with reduction of bronchial lumen either by the presence of bronchospasm or secretion [26]. In agreement with these results, Cavalcanti et al. showed that the use of the bronchodilator led to an increase in the mean values of S in asthmatic volunteers ($p < 0.05$), which may reflect a reduction in respiratory system impedance and an improvement in homogeneity [26].

In normal individuals, the low-frequency reactance is negative due to the system's compliance, showing an increasing value up to zero at approximately 8 Hz (resonance frequency) [9]. More negative values of Xm were observed in the presence of Pre-BD ($p < 0.03$) and post-BD ($p < 0.01$) WRA, with improvements after bronchodilator use ($p < 0.05$). These results may be related to the increase in the resistance of the peripheral airways that occurs in asthma, as was observed by Souza et al. when studying asthmatic children [27]. More negative values of Xm were reflected in the increase of resonance frequency (Fig. 2e).

There is a much greater influence of upper airway impedance in asthmatic individuals than that observed in normal individuals, in addition to the presence of pulmonary remodelling caused by the frequent inflammatory processes, the increased airway resistance and loss of the elastic support of the pulmonary parenchyma [28]. In our study, the impedance at 4 Hz was reduced after bronchodilator use in the WRA group ($p < 0.02$), reflecting the reduction of the total mechanical load of the respiratory system; however, there was no significant difference in the comparison between the control group and the WRA group.

In a study with asthmatic adults with different levels of obstruction [29], significant changes were observed in all parameters in the eRIC model, in contrast to our findings, where there were no significant changes in ReRIC and RteRIC when comparing the CG and WRA groups (Fig. 3). However, we noticed a reduction in ReRIC ($p < 0.005$) after bronchodilator use in the asthmatic group. RpeRIC was increased in the presence of asthma. This fact is compatible with the pathophysiology of this disease, as it is notorious for causing changes in the peripheral airways resulting from frequent bronchoconstriction reactions [28]. Considering that the disease begins in the peripheral airways, we can speculate that the modifications found in the RpeRIC may reflect early modifications in the airways. There were significant reductions in IeRIC and CeRIC ($p < 0.002$ and $p < 0.01$, respectively), reflecting the pathophysiology of asthma, including intermittent and reversible bronchial narrowing caused by bronchial smooth muscle contraction, mucosal oedema and mucosal hypersecretion [30].

6 Conclusions

This study indicates that FOT may be useful in the identification of respiratory system modifications in volunteers with WRA. Considering that asthma begins in the peripheral airways, the main finding refers to the modifications found in the RpeRIC, which may reflect early modifications in the airways of these individuals. FOT associated with the eRIC model may constitute a simple and easily applied methodology that can be an adequate alternative for both the longitudinal evaluation of these patients and the early identification of the disease.

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