

FORCED OSCILLATION TECHNIQUE IN THE ASSESSMENT AND MANAGEMENT OF ASTHMATIC CHILDREN: A NARRATIVE REVIEW

INTRODUCTION

Asthma is the chronic disease with most incidence among children (1). The symptoms are frequently presented within the first years of life and the diagnosis is based on each patient's clinical history (2). The measurements of pulmonary function are an important part of asthma evaluation, since they help build a diagnosis through the analysis of bronchial reversibility and detect poor prognosis in disease control (1).

Spirometry is the main method used to document characterized alterations of pulmonary function in asthma patients. However, its accuracy can be compromised regarding children, since acceptability and reproducibility of the exam both depend on focus and prolonged effort (3). Another diagnostic method to characterize the functional alterations of asthma include the airway resistance measures, which can be obtained through oscillometry, light switch technique and plethysmography (4).

Oscillometry is considered a modern tool that allows for the measurement of the respiratory system's impedance (Z_{rs}). A Z_{rs} includes all the forces that oppose the movement of air, being composed by resistance (R_{rs} , frictional forces) and reactance (X_{rs} , elastic and inertial forces). These components of Z_{rs} can be calculated by mathematical transformations of the relation between pressure and flow in the frequency's domain (5).

The Forced oscillations technique (FOT) allows for the evaluation of Z_{rs} through R_{rs} and X_{rs} , from a tidal volume respiratory maneuver (6). The advantage of this noninvasive pathway of analysis makes this an appropriate method particularly for poorly cooperative patients and, therefore, an important element regarding pulmonary evaluation in children (7).

Although there are differences among the measurement processes, spirometry and FOT are methods which present complementary and non-interchangeable information (3). By observing the FOT results it becomes clear that more studies are needed to clarify unprecedented results contributing with the diagnostics in pneumology. That being said, the objective of this study was to review the clinical utility of this method in the pulmonary evaluation of children with asthma.

METHODOLOGY

This study consists of a narrative literature review, built up from 4 steps: the establishment of the time period

to be studied, the choosing of a database to be analyzed, the characterization of the keywords that were used and the selection of relevant studies.

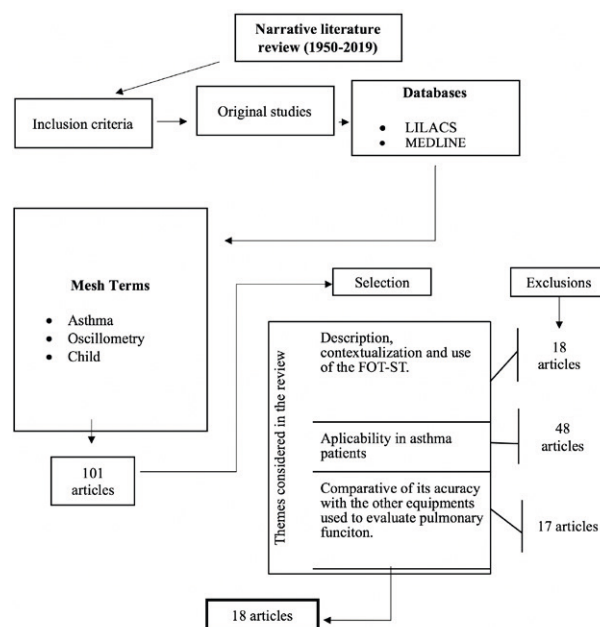
The inclusion criteria were the following: studies from 1950 to 2019, with a sample population between 3 and 18 years of age, asthma sufferers and that used oscillometry as a form of evaluation.

The bibliographical search was done between November of 2019 and January of 2020, in the following databases: *Medical Literature Analysis and Retrieval System Online (MEDLINE)* and *Latin-American and Caribbean Health Science Literature (LILACS)*. The following Mesh terms were used as search parameters: "asthma", "oscillometry" and "child" crossed using the AND and OR Boolean connectors.

The articles included in this review were summarized by author, equipment used in the evaluation, sample, objective and main results. Briefly described in table 1 for an effortless visualization of each selected work.

This study excludes narrative review studies, integrative, systematic and meta-analysis and operational directives. As to the ethical aspects, an ethics committee submission was not required since the data utilized was from articles indexed in databases. The flowchart 1 presents the methodological criteria.

Figure 1. Methodologic flowchart.



Correspondence author:

Marcos Brum A., Endereço: Av. Ipiranga, 6681 - Partenon - Porto Alegre/RS – 90610-000, E-mail: marcos.antunes@edu.pucrs.br, Contato: 55 51 33203000, ramal 2221.

RESULTS

From the search in the database 101 articles were found, after reading the abstracts and doing an integral review, 18 articles that contemplate the methodological characteristics specified for this study (Table 1). The researches of Dubois et al. (3), 1956, and Heijkenskjöld Rentzhog et al. (8), 2013, present mixed samples (children and adults), however, the first study is considered to be the precursor on evaluation through FOT and the second is a study of great relevance to the analysis of bronchial reversibility markers, therefore, even if there are also data from adults in those studies, the results obtained from children's evaluations still justify their addition in the table.

Based on the presented results, (13) (72%) studies created multi frequencies evaluations, with an amplitude between 5 and 35 Hz. From these, 9 (69%) added complementary exams being spirometry, the most frequent one (1-4,6,10,13,14, 8).

As to the clinical outcomes, five articles (28%) approached bronchial alterations, five (28%) investigated possible discrepancies between the sensibilities of the measurements among different equipments, as well as its association in the establishment of a diagnosis and, eight articles (44%) produced evaluations regarding pulmonary impedance.

Eleven studies were case-control type studies (61%), in which the FOT presented enough sensitivity to observe pulmonary alterations and witness asthma's physio pathological aspects, in which healthy children, regarding a respiratory perspective, presented significantly higher average R_{rs} and X_{rs} components. The observed alterations in the R_{rs} values demonstrate that the technique is effective to evidence bronchial reversibility post BD use (7,9,15,15).

DISCUSSION

FORCED OSCILLATION TECHNIQUE

The FOT was proposed in 1956 from the elaboration of a method that allowed to evaluate mechanical properties of the respiratory system. The characterization of respiratory impedance is based on the analysis of its components: resistance (R_{rs}) and reactance (X_{rs}). These values are obtained by overlapping pressure fluctuations on ventilation during the evaluation period (8). One of the main advantages of this method is the ease with which the maneuvers can be performed, in such a way that the subject being analyzed only has to breath at a normal rate for the impedance data to be collected (9).

PULMONARY IMPEDANCE

The Z_{rs} demonstrate the total mechanical charge offered by the respiratory system, as well as its resistive, elastic and interactive properties. The impedance is composed by the R_{rs} and the X_{rs} , being determined in multi frequency oscillations (1,17). The R_{rs} describes the total energy dispersion, encompassing the sum of the product of the Newtonian resistances related to the airways, the pulmonary tissue and the thoracic wall, as well as the resistance that results from the redistribution of the gas (8). The X_{rs} describes the accu-

mulation of energy in the respiratory system, the potential energy is associated with the respiratory complacency (C_{rs}), while the kinetic energy is described by the respiratory inductance (I_{rs}) (9). The I_{rs} is related to the energy involved in the acceleration and deceleration of the fluid (air) in the airways as well as in the pulmonary tissue (1).

The measurement of impedance by the FOT is based on the response to oscillations of pressure applied in the airways. These impulses are generated by a speaker and induce a oscillatory flow in which the amplitude of the wave is inversely proportional to the mechanical impedance of the respiratory system (Z_{rs}) (15). Higher frequencies represent the impedance of central regions, while the lower frequencies describe peripheral and central areas of the respiratory system (17).

This tool's different evaluation methods present specific benefits. The analysis by monofrequenced waves are tuned for the immediate evaluation of the breathing process, since it allows to observe the alterations presented in the airways during a respiratory cycle. This method of evaluation contemplates resistive and elastic properties of the respiratory system (5,7,13,15,17).

The studies in which a multi frequency evaluation was used represent the majority of the analyzed studies (71%), this type of analysis can be characterized as a slow one, since it represents the average behaviour of the respiratory system through various ventilatory cycles, generating even more detailed results. The indexes obtained from this analysis contemplate R_{rs} and X_{rs} in various frequencies, allowing the evaluation of indexes associated to the total resistance, the non-homogeneity and the respiratory system's dynamic complacency (1-4,6,8,9,12,15,16,18).

APPLICABILITY IN ASTHMA SUFFERER

Although it was created in the 1950's, the FOT's first studies regarding asthma in children were only available in the year 1970. The initial studies showed that children with asthma presented an increase of the total respiratory system's resistance because of the reduction of the airway gauge. This characteristic is best described by measurements that use low frequency, which include central and peripheral airways (1,3,7).

The respiratory system's total complacency is also altered in asthma patients, a factor that is associated with the increase of peripheral airway resistance as pointed out before. However, this modification is also accompanied by the group of anatomopathological alterations caused by the bronchial remodeling, a factor that hinders the elasticity of the airways and causes excessive bronchial lean muscle constriction (14).

The heterogeneity of the ventilation, commonly altered in obstructive pulmonary diseases, also reduces the respiratory complacency by aerial imprisonment, affecting the respiratory reactance observed by the FOT (1,10,19).

The R_{rs} and the X_{rs} are indirect markers of bronchial obstruction and have a good sensitivity for a peripheral airway evaluation (12,17). The resistance reduction after the inhalation of a bronchodilator has a good sensitivity and excellent specificity for asthma in children (11,21).

Table 1. Summarizing the results.

Authors	Equipment in the evaluation	Sample	Objective	Results
*Dubois et al., 1956 (8)	FOT 2-15 cps.	10 individuals.	Observe the respiratory impedance in response to airflow.	Characterization of airways as a resistance and capacitance system.
Wanner et al., 1977 (7)	FOT in 10 Hz, spirometry and pletismography, pre e post BD.	13 children between 7 and 13 years, with medical history of asthma.	Demonstrate bronchodilator effect.	It takes 2 minutes after administering the bronchodilator for the effect to peak.
Lebecque et al., 1987 (6)	FOT between 6-26 Hz, spirometry and histamine challenge test.	31 children between 7 and 17 years, being 19 of them females.	Analyze R_{rs} and VEF1 correlation during the histamine challenge test.	The FOT has the capacity to evaluate the reactivity of airways caused by the histamine challenge test.
Marchal et al., 1994(9)	FOT between 6-32 Hz. Pre and post BD.	35 children between 2,5 years and 17 years with asthma, being 23 with light asthma and 12 with moderate or grave asthma.	To compare standard techniques and head generators in the evaluation of pulmonary response to broncomotor agents	The head generator enhances the FOT's sensitivity in the evaluation of broncomotor response in children.
Mazurek et al., 1995 (10)	FOT between 10-20 Hz with spirometry pre and post BD.	75 children between 5.5 and 15 years, 53 with asthma, 40 males.	Evaluate the use of head generator in the bronchodilator evaluation in children.	The head generator has a higher capacity to demonstrate the obstruction's reversibility
Thamrin et al., 2007(11)	FOT between 4-48 Hz and reactance between 6, 8 and 10 Hz. Pre and post BD.	288 children, with ages between 3.5 and 6.6 years, of which 210 were patients with respiratory diseases.	To characterize the FOT's bronchodilator response in healthy subjects and to compare it with different groups of respiratory diseases.	Recommends the delimitation – 40% and 65% as a positive BD response for reactance and resistance respectively.
Meraz et al., 2007 (12)	IOS between 5H-15 Hz.	40 children aging between 2 and 5 years, with asthma.	To characterize pulmonary function's sensitive oscillometry parameters and establish estimates for constriction and non-constriction.	The study demonstrated success in differentiating between constricted and non-constricted airways.
Souza et al., 2009 (1)	Spirometry and FOT between 4-32 Hz.	40 children, 20 controls and 20 asthma patients. Aging between $8,2 \pm 2,0$ and $8,0 \pm 2,1$, respectively.	To investigate alterations in the resistive and reactive properties of the respiratory system in asthma patients and to evaluate the FOT's contribution to the diagnosis of asthma.	The FOT properly described the pathophysiology alterations of asthma, demonstrating potential for evaluating pulmonary mechanics in asthma patients.
Harrison et al., 2010 (2)	FOT between 6-9 Hz and pletismography, pre and post BD.	59 children who presented wheezing 24 healthy controls, aging between 3 and 6 years.	To detect abnormalities both in the pulmonary function and the bronchodilation in preschoolers, using the FOT and specific airway resistance measures.	Neither technique could identify suppressed pulmonary function nor reversibility to the bronchodilator in children with asthma wheezing.

Pétak et al., 2012 (4)	FOT between 4-24Hz and spirometry, applied after histamine test and aerosolized methacholine.	20 asthma patients, between 5 and 18 years old.	To compare the sensitivity between FOT and spirometry in the detection of hyper-reactivity in asthmatics.	Both presented capability of evaluating bronchoconstriction and can be considered for the detection of hyper-reactivity in asthmatics.
Shulze et al., 2012 (13)	Spirometry and FOT in 5Hz, pre and post administration of methacholine.	48 children with bronchitis, between 3 and 6 years, with recurrent wheezing and multiple coughing episodes, for longer than 6 weeks.	To evaluate the association between IOS spirometry indexes in a short methacholine challenge protocol.	A short protocol for the methacholine challenge is viable in children. IOS detected 70-80% of patients that were also detected by the correspondent spirometry exam.
Murakami et al., 2014 (14)	Spirometry, Forced inhalation of NO ₂ and FOT between 5-35Hz, pre and post BD.	132 children, aging between 10,86±4,78 years, 98 asthmatics, and 88 males.	To evaluate bronchial alterations using FOT.	The alterations presented both in reactance and resistance on the FOT reflect the bronchial reversibility.
Robinson et al., 2014 (5)	FOT with 6 Hz, tripled for each different test.	60 asthmatic children, aging between 10,4±1,22.	To determine the relationship between FOT variations and severity of asthma and control of symptoms in children and to compare measures from asthmatics with non-asthmatics.	The FOT can be used as a objective monitoring tool for pediatric asthma and this topic needs more studies.
Ioan et al., 2015 (15)	FOT in 8Hz, pre and post BD, with standard generator and head generator.	85 children, 58 asthmatics, aging between 8,1±1,5.	To test the artifact in the FOT's capacity to diagnose asthma in children.	In asthmatic children, the upper airway artifact significantly affects the FOT measures.
Czövek et al., 2016 (16)	FOT between 4-26 Hz.	101 children, 26 asthmatics.	To find keywords of Zrs in breathing that accurately indicate airway obstruction during VC breathing.	The new FP ΔR measure detects airway obstruction with great sensitivity and specificity, making it an adequate tool for FP testing in children.
*Heijkenskjöld Rentzhog et al., 2017 (3)	Spirometry, FOT between 5-19 Hz.	294 individuals, of these 234 pneumopathy sufferers, aging between 13 and 39 years.	To analyze the association between FP variables, obtained from spirometry and FOT, diagnosis and asthma control.	Resistance measures of FOT and spirometry presented similar levels of sensitivity in asthma diagnosis.
Starzewska-Dymek et al., 2018 (17)	FOT in 8 Hz, pre and post BD.	53 children with controlled asthma, 53 with not controlled asthma and early onset 45 healthy controls, aging between 2 and 6 years.	To evaluate X _{rs} and R _s parameters in healthy children groups with controlled and not controlled asthma.	R _s and X _{rs} obtained by FOT discriminate patients with asthma from healthy children.
Sol et al., 2019 (18)	Spirometry and IOS between 5-20Hz.	819 children, aging between 4 and 18 years, with 600 asthmatics.	To identify the difference between inhalation measures and exhalation measures obtained using IOS among children with and without asthma.	The inhalation/exhalation analysis differentiated children with asthma from controls, pointing out airway tightening in asthmatics during exhalation.

cps: cycles per second, Hz: Hertz, BD: Bronchodilator, IOS: Impulse oscillation, FOT: Forced Oscillation technique, VEF₁: Forced Expiratory Volume in the first second, R_{rs}: Respiratory resistance, X_{rs}: Respiratory reactance, *: Mixed sampling studies.

FOT AND SPIROMETRY IN ASTHMA

The spirometry test is the most used in the evaluation of obstructive airway disorders, however, it presents restrictions for age ranges lower than 6 years, even though the *American Thoracic Society (ATS)* and *European Respiratory Society (ERS)* have both established a more flexible acceptability and reproducibility for this group (1). In this scenario, the capacity with which the FOT allows for an evaluation of the respiratory system's mechanical particularities from a non-invasive and with tidal volume perspective is of great clinical importance. Research demonstrates the capacity of this technique to be used in children aging less than 2 years, which can anticipate the diagnosis of respiratory diseases, allowing for the elaboration of adequate strategies sooner. The FOT presents an equivalent capacity of the spirometry to characterize the pulmonary function, be it in children with asthma or without it. In peripheral airway disorders the FOT presented higher analytical power, even though the variables obtained by the spirometry, such as the VEF₁, presents greater efficiency to demonstrate information about the diagnosis and control levels (4).

CONCLUSIONS

The FOT has a high sensitivity for evaluating the respiratory system, making it a promising tool for assessing pulmonary function in children with asthma. Part of its success is due to the simplicity of the method, being it non-invasive, easily applicable and for requiring almost no cooperation from the subject. In children with asthma this technique has shown greater accuracy for evaluation of smaller gauged peripheral airways, serving as a complementary method to the spirometry and to enrich the diagnosis, allowing for a better understanding of the disease and its progression.

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