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Application of the forced oscillation technique in diagnosing and monitoring of asthma in preschool children

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Abstract

The measurement of lung function in preschool children for the diagnosis of asthma is not routinely used. The need to perform forced expiratory manoeuvres requires active cooperation and thus limits the application of spirometry in this age group. The forced oscillation technique (FOT) is a simple and noninvasive method of assessing the mechanical properties of the respiratory system during tidal breathing. It is used in young patients and requires minimal cooperation. It provides an objective assessment of the respiratory system in a group of patients in whom we have not yet had appropriate diagnostic tools. In recent years, due to the availability of new technical solutions, FOT has been increasingly used and has a chance to become a valuable tool in diagnosing and monitoring of treatment in preschool children.

This article presents the possibility of the clinical application of FOT in diagnosing and monitoring of early childhood asthma.

Key words: asthma, preschool children, forced oscillation technique, pulmonary function tests

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Introduction

Asthma is the most common chronic childhood disease [1]. In almost half of the patients, the first symptoms of asthma appear in childhood [2]. The occurrence of wheezing is common in the first years of life, and it is estimated that approximately 50% of children experience at least one episode of wheezing before 6 years of age [3, 4]. The challenge is the early identification in this group of children in whom the presence of wheezing in early childhood will be associated with the onset of asthma.

Cohort studies have shown that preschool children who exhibit wheezing have worse spirometric parameters at the age of 6 [5]. The FEV_1 and FEV_1/FVC deficits found in adolescents and young adults who had had wheezing symptoms in childhood were determined to appear when the children were approximately four years of age or even earlier, suggesting early remodelling and irreversible long-term effects on pulmonary function and growth [6–8].

Bearing in mind the above observations, one has to agree that the assessing and monitoring of respiratory functions in young children is extremely important.

The aims of lung function tests, such as objectifying the diagnosis, assessing the severity, monitoring the disease and evaluating the effectiveness of therapeutic interventions, have become vital in this age group [9].

Pulmonary function tests for a number of reasons do not find widespread use among preschool children. The need for active cooperation and performing forced expiratory manoeuvres are the main obstacle here and limit the amount of correctly performed spirometry in the group of young children.

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To diagnose asthma, it is necessary to demonstrate reversible bronchial obstruction and/or non-specific bronchial hyperresponsiveness. International policies agree on the need to demonstrate the airflow limitation in the respiratory system and its reversibility to confirm asthma in both adults and children [10, 11]. Due to the difficulty in performing spirometry in young children (under 5 years of age), the assessment of airflow limitation is problematic. The identification of asthma in this age group is often a history-based clinical diagnosis, thorough differential diagnosis and response to the included treatment (therapeutic trial). The occurrence of symptoms of bronchial obstruction (at least three such episodes or one severe episode requiring hospital treatment and/or systemic glucocorticosteroids), which disappear after administration of short-acting $ß_2$-agonists (SABA) and clinical improvement after 8–12 weeks of treatment with an inhaled glucocorticosteroid and, if necessary, a short-acting bronchodilator, recurrence of symptoms after discontinuation of treatment, and no other causes of obstruction make it possible to diagnose asthma in the group of children under 5 years of age.

Spirometry is the gold standard and the method of choice in the diagnosis of obstructive airway diseases. It is also the most commonly performed pulmonary function test in pulmonary diagnostics in adults and children > 6 years of age. For children from 2 to 5 years of age, modified acceptability criteria for spirometry have been published [9]. In a joint review of the American Thoracic (ATS) and the European Respiratory Society (ERS), separate criteria for the acceptability and repeatability of spirometry have been adopted for this age group. The need for active and good cooperation during the test, the necessity of correct performance of the forced breathing manoeuvres, and thus the difficulty in meeting the criteria of acceptability and repeatability even under the modified ATS/ERS criteria cause that it has a limited application in preschool children and is not a routine diagnostic test. Not without significance is the fact, which is emphasised in the GINA position, that in children under the age of 5, spirometry is not always a reliable diagnostic tool. In many children with uncontrolled asthma, a spirometry test shows normal respiratory lung function in the period between exacerbations of the disease [10].

What are the characteristics that should be met by an ideal pulmonary function test in preschool children? According to the ATS/ERS recommendations, this should be a method that will be used in monitoring lung function from birth up to old age, simple to perform, safe, reproducible, accepted by the patient, sensitive in recognising changes in the respiratory system occurring with age and that will allow us to distinguish between a healthy and ill person [9].

Methods of measurement of respiratory resistance

In pulmonary diagnostics of young children, methods based on measurements performed during tidal breathing may be used, and therefore, there is no need for breathing manoeuvres. Such tests include, among others, measurement of respiratory resistance (Rrs) by forced oscillation technique (FOT), measurement of respiratory resistance by the interrupter technique (Rint, resistance by interrupter technique) or by whole-body plethysmography (Raw, airway resistance).

Increased respiratory resistance is one of the factors influencing the airflow limitation characteristic of obstructive diseases. The assessment of respiratory resistance, whose increased values appear earlier than clinical symptoms and disturbances in airflow (measured by spirometry), may, therefore, have clinical significance.

Theoretical aspects of FOT

The forced oscillation technique is a simple and noninvasive method for measuring the mechanical properties of the respiratory system during tidal breathing. The advantage of the procedure is that there is no need to perform forced expiratory manoeuvres, and hence minimal effort and only passive cooperation of the subject is required. The simplicity of the test allows it to be used successfully in 2-year-old children [12]. Among healthy children aged 2–7, 80% were able to perform the test correctly [13].

FOT employs external sound waves (pressure waves) being emitted by a loudspeaker and superimposes them on spontaneous breathing into the respiratory system without interfering with the respiratory cycle. Depending on the wave frequency used, we obtain information about various areas of the respiratory system.

Higher frequences waves travel a shorter distance reaching the central airways, while lower frequencies waves penetrate deeper towards the small airways and lung parenchyma.

Parameters of FOT

During the test, the changes in pressure and airflow in the respiratory system are analysed, the relationship of which allows the measurement of respiratory impedance. Respiratory impedance consists of 2 parameters: resistance (Rrs) and reactance (Xrs), providing information on both of the mechanical properties of the airways and lung parenchyma.

Resistance represents the resistance of the respiratory system, and reactance describes its elastic properties and flows in the peripheral airways.

FOT, in contrast to body plethysmography, allows the measurement of the total resistance of the respiratory system, which consists of the resistance of the central airways, peripheral airways, as well as the resistance of the lung parenchyma and chest wall. Because the last two values are small and negligible, resistance values depend mainly on airway patency.

Resistance (Rrs**)** in healthy people is mostly independent of the wave frequency.

In the case of airway obstruction, the resistance increases**,** and the dependence on the frequency becomes apparent. In central airway obstruction, the resistance increases at all frequencies**.** In the case of an obstruction in the peripheral airways, the frequency dependence is visible; the resistance values for low frequencies increase and are within the normal range at higher frequencies (which do not go peripherally and do not reach peripheral airways).

Reactance (Xrs) depends mainly on the elastic properties of the respiratory system and the inertia of tissues and gases. It gives us information on how effectively the lung is ventilated in its distal areas. Xrs falls below predicted values at low oscillating frequencies under the following conditions: peripheral obstruction, tidal expiratory flow limitation, alveolar gas trapping, and/or the closing of alveolar units. It is a parameter that depends on the frequency. For low frequencies, it takes negative values, and for higher values, it is positive. The point at which Xrs assumes a value of 0 (the elastic properties and inertia of tissues and gases are in equilibrium) is called the resonant frequency (*Fres*).

In obstructive disorders, the resistance increases and the reactance decreases, which indicates a peripheral obstruction.

In interstitial diseases, the reactance at lower frequencies also becomes more negative.

In obstructive and restrictive diseases, the direction of change in Xrs is the same. FOT does not differentiate between these disorders. Figure 1 shows the most common patterns of results and the possibilities of their interpretation

The FOT parameters, resistance and reactance, are closely related to growth and age. The resistance decreases, and the reactance increases with the growth of subjects, which reflects the development of the respiratory system, an increase in the cross-section of the airways and a rise in the number and size of the alveoli. The relationship between the parameters of FOT and growth is shown in Figure 2.

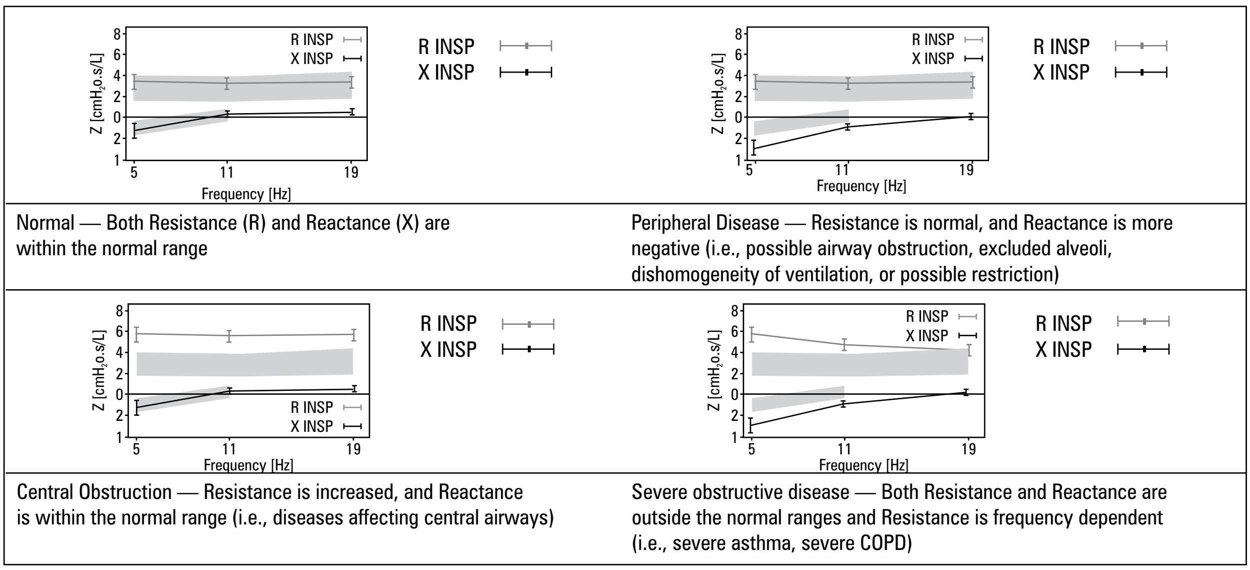


Figure 1. Interpretation of results; R INSP: inspiratory resistance; X INSP: inspiratory reactance; Z: impedance

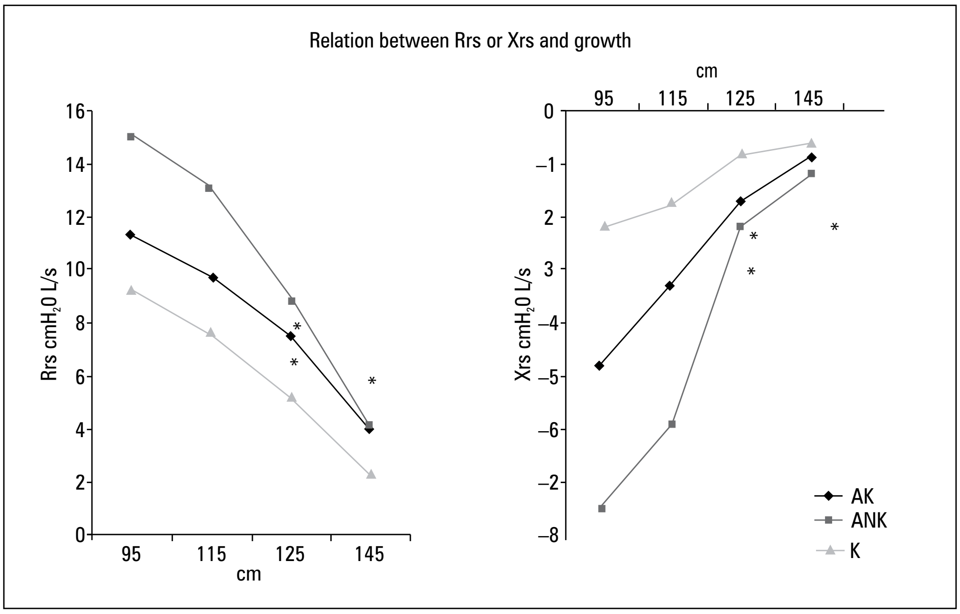


Figure 2. Graphs of the parameters of FOT (Rrs-resistance and Xrs-reactance) and growth; AK: controlled asthma; ANK: uncontrolled asthma; K: control group **(ref. 23)**

FOT is not a new method. It was introduced by Dubois and coworkers in 1956. Dubois described the classic method of FOT using sinusoidal acoustic waves of single frequencies introduced into the respiratory system during tidal breathing. Currently, new devices use 2 or 3 wave frequencies simultaneously (from 3–35 Hz). Less than 20 years later, a variant of the classic FOT method, impulse oscillometry (IOS) was introduced, which uses pressure impulses of waves at different frequencies (usually in the 4–32 Hz range) generated simultaneously. FOT/IOS differ in the methodology of the study.

FOT is a standardised method; procedures are based on recommendations by ATS/ERS [9, 14], and reference values are available [15]. The European Respiratory Society Task Force Report describes the principle of FOT and gives guidelines for the application and interpretation of the method also in the paediatric population [14]. The ATS/ERS Statement regarding pulmonary function testing in preschool children described clinical application of FOT in childhood asthma [9]. However, since these publications international statement of the FOT has not been updated to these days.

FOT methodology

The test is very simple to carry out. According to the ATS/ERS recommendations, the patient performs several tidal breathing cycles, which take approximately 8–16 s. For example, for some devices, 10 tidal breathing cycles through a disposable mouthpiece with an antibacterial filter is needed. During the test, the patient is in a sitting position with his head in a neutral position or with a slightly raised chin. The legs are based on the ground. The cheeks should be held (by means of their own hands or by the caregiver) so that they do not get vibrated during the examination. The software of some devices analyses the results of the test in real time. Breaths that are irregular or disturbed by coughing, crying, moving the tongue, leaking of the mouthpiece, closing the glottis or hyperventilating are automatically rejected and are not analysed. It is recommended to make 3 to 5 correct measurements. Coherence is an index of the correct performance and quality of the test (Fig. 3).

The repeatability of measurements in healthy preschool children ranges from 5–14% [9, 14, 16], and diurnal variation is higher in children with asthma but no more than 20% [14].

Reference range of FOT measurements

There are numerous reference data for FOT parameters for the paediatric population. After 2005, a dozen studies were published covering different groups of children from the age of 2 (including the population of Polish children in the study of Nowowiejska *et al.* [17]). These researches differ in the selection of ethnic groups, methodology, test protocols and devices; therefore, the use of the study outcomes should be cautious.

Figure 3. A preschool girl during the FOT examination. The patient in a sitting position during tidal breathing through a disposable mouthpiece. There is a clip on the nose, and the cheeks are held so that they do not get vibrated. The device performs real-time analysis

With regard to the fairly wide range of normal values (normal values may be different from each other even twice [18]), FOT has greater practical importance in comparing consecutive measurements at intervals and not only the assessment of single results [16, 18].

Clinical applications of FOT

The application of FOT is broad. In an official ATS/ERS statement on pulmonary function testing in preschool children, it is stressed that the FOT is a promising method in diagnosing and monitoring asthma in children [9].

Asthma is characterised by reversible bronchoconstriction, and FOT also allows to perform the reversibility bronchial test, which is frequently impossible to do in children due to poor cooperation [9]. The differences in Rrs and Xrs values between baseline measurement and after salbutamol are evaluated for bronchial reversibility tests [15].

In the group of young patients with whom it is impossible to perform spirometry, FOT is a helpful method improving the diagnosis of airway obstruction and assessing the severity of the disease. Rrs is very sensitive to the degree of obstruction of the airways. FOT as a method for measuring respiratory mechanics, allows the evaluation of both central and peripheral airways.

The main advantage of the FOT, unlike spirometry, is that it is a more sensitive tool for detecting obstruction in peripheral, small airways.

The pressure waves overcome different distances in the respiratory system, providing information about its various areas. Low frequencies (< 5 Hz) are more sensitive in assessing peripheral airways, while higher frequencies (> 8 Hz) reflect the condition of large, central airways [19].

FOT is a method that, due to its simplicity of performance, can be widely used in doctor's offices, in emergency departments or in hospitals at the patient's bedside. The method can be successfully carried out as part of the screening of children in nursery schools and schools. Among healthy children and patients in a stable condition, the study was able to effectively include over 80% of preschool children [12, 13]. Among subjects with asthma exacerbation admitted to the emergency department, the test was successfully performed among 20% of 3–year-olds and over 80% of 5-year-olds [20].

FOT in obstructive airway diseases in children

FOT makes it possible to distinguish children with asthma from healthy children by assessing the initial parameters of the FOT as well as the results of the assessment of reversibility of the airway obstruction test [7, 21–24].

Resistance and reactance are indirect determinants of bronchial obstruction, allowing to distinguish asthmatics from healthy children and are also sensitive parameters in the assessment of peripheral airways [25]. Some authors, however, did not show the usefulness of FOT in diagnosing asthma in children [26, 27]. Depending on the criteria used to recognise asthma (questionnaire and risk factors vs diagnostic and medical diagnosis), the impedance values differ. In studies conducted among children who were suspected of having asthma on the basis of only the questionnaires, impedance values did not differ from those found in healthy children [26, 27], but the lung function measured with the FOT was worse in children who had been diagnosed or suspected of having asthma during the study medical examination [21] as well as among children with asthma exacerbation, correlating well with their clinical condition [20].

In our paper, we have showed that FOT can distinguish children with asthma in the period without clinical symptoms from children from the control group [23].

In the Heijkenskjöld *et al*. [28] study, resistance assessment by FOT was not only equal to spirometry in the evaluation of patients with asthma but also, together with the assessment of reactance, provided additional information on the condition of peripheral airways, the state of which correlated with the degree of asthma control.

The resistance measured by FOT in the low frequency range varies significantly between healthy children and children with asthma, including those with normal spirometry [14]. It should be borne in mind that due to the different nature of the tests, forced inspiratory and expiratory manoeuvres during spirometry vs tidal breathing during FOT, one cannot expect that the results of these methods (despite the fact that both indicate bronchial obstruction) will closely correlate with each other. For this reason, they cannot be treated as equal methods.

Moreover, children with normal spirometry and with no reversibility of bronchial obstruction may have abnormalities measured by the FOT.

FOT in the identification of airway reactivity

Diagnosis of asthma is based on the demonstration of reversible bronchial obstruction and bronchial hyperresponsiveness. FOT is a sensitive diagnostic method in bronchomotor tests.

Reversibility

Studies have shown that the assessment of the degree of reversibility of bronchial obstruction is important because it may indicate the severity of asthma. Children with severe asthma demonstrated a greater reversibility of bronchial obstruction after bronchodilator in comparison to children with mild asthma [29].

In the assessment of bronchodilator response, different thresholds are given by individual researchers, and it is assumed that a reduction of Rs from 20 to 40% in relation to baseline values

Stimilus type: 8 Hz

Test type:	PRE	BD-POST
Measurement date:	20-07-2015 17:34	20-07-2015 18:03
Age [years]	5	5
Weight [kg]:	21	21
Height [cm],	118	118
BMI (kg/m^2):	15.1	15.1
Number of accepted breaths (%tot):	11 / 12 (84.6%)	12 / 15 (80.0%)
Equation for predicted values:	Calogero et al., Ped. Pulmon., July 2010[A]	Calogero et al., Ped. Pulmon., July 2010[A]
Mean Filter Impedance [cmH$_2$O/L/s]	0.61	0.61
Physician:	PAED	PAED

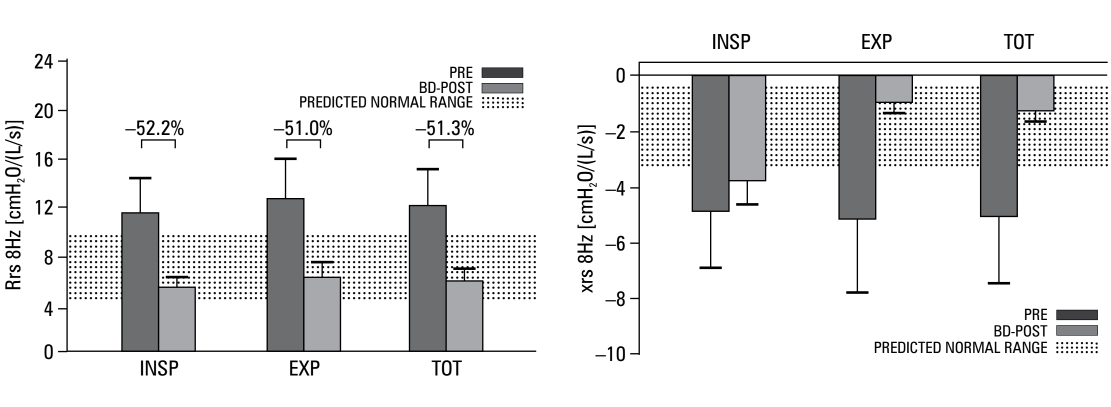


Figure 4. FOT — reversibility bronchial test; Rrs 8 Hz: resistance at 8 Hz; Xrs 8 Hz: reactance at 8 Hz; INSP: inspiratory component; EXP: expiratory component; TOT: total value; PRE: output values; BD: post-values after administration salbutamol, dotted field: normal range

after administration of short-acting ß$_2$-agonist indicates a positive response [9]. In the research conducted at our centre, we adopted a reduction in inspiratory Rrs (Rrs insp) for the frequency of 8 Hz by 32% in relation to the baseline values and by 65% for Xrs after bronchodilator (Fig. 4) [15].

In the study of Oostveen *et al.* [7], lung function measured by FOT in 4-year-old children with persistent wheeze was significantly worse, and the response after bronchodilator was higher in comparison with healthy children and children with early transient wheezes. Similar observations from the study by Marotta *et al.* [30] showed that the positive bronchodilator response determined by the FOT differentiates between 4-year-old healthy children and children at risk of developing bronchial asthma better than changes in FEV$_1$.

Our own research on a group of children from 2 to 6 years showed that the positive response after bronchodilator in FOT allows (with the presence of typical symptoms of asthma and exclusion of other causes of bronchial obstruction) the diagnosis of asthma [23].

The reversibility test assessed with the FOT is in agreement with FEV$_1$ [14, 20] and resistance measured by body plethysmography [14, 31].

Assessment of bronchial hyperresponsiveness

FOT is used in the evaluation of the airway hyperresponsiveness. The increase in Rrs in the bronchial challenge test (measured at the lowest wave frequency) by 35–40% in relation to the baseline value for children under 6 indicates a positive test result [9].

Significant changes in the parameters of FOT are achieved at lower doses of methacholine compared to spirometry, which makes the FOT study more sensitive [32].

Monitoring the course of the disease

FOT is a good tool in monitoring the course of asthma. Shi *et al.* [33] examined children with asthma, showing that oscillometric parameters distinguish children with good asthma control and lack of disease control. The sensitivity of spirometry and reversibility tests in this study proved to be low.

Our study showed that in children with uncontrolled asthma, resistance values were higher and reactance values were lower compared to children with good control of asthma and children in the control group [23].

FOT to assess risk factors for the loss of asthma control and impending asthma exacerbation

Oscillation parameters are also a good predictor of impending exacerbation of the disease. Shi *et al.* [34] compared the parameters of spirometry and impulse oscillometry in children with controlled asthma and children with the approaching exacerbation of asthma. There were no differences in spirometric parameters (small differences in FEV$_1$/FVC), while IOS parameters were significantly different in the both groups. IOS is an effective tool to assess the increased risk of impending loss of asthma symptom control. Similarly, the Genomen *et al.* [35] study showed that the oscillation method makes it possible to differentiate patients into groups with lower and higher risks of asthma exacerbation. Robinson *et al.* [36] revealed that the day-to-day variability of FOT parameters was higher in children with asthma than in the control group and was related to both the severity of asthma and the degree of symptoms control. The assessment of the small airways in asthma is important for determining further management, especially in the early stage of the disease when the signs are absent and spirometric parameters are in the norm [37–40].

In accordance with current guidelines, achieving and maintaining asthma control is the main goal of therapeutic management [10]. It is known that chronic inflammation in the peripheral airways (also present in patients with mild asthma) may be one of many factors hindering the achievement of disease control [41].

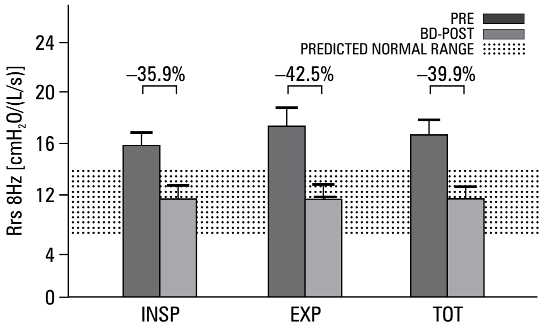
The assessment of the small airways is particularly important in children who, despite the presence of symptoms indicating a loss of asthma control, have parameters of lung function measured by spirometry within normal values. Therefore, in the absence of control of asthma symptoms, it is important to assess the peripheral airways [42], which is possible by means of the FOT. FOT proved to be a complementary method to spirometry providing additional information about peripheral airways [28] and has been suggested to be more sensitive in detecting airway obstruction because of no “deep inspiration” effect on bronchial tone required with a forced manoeuvre [30].

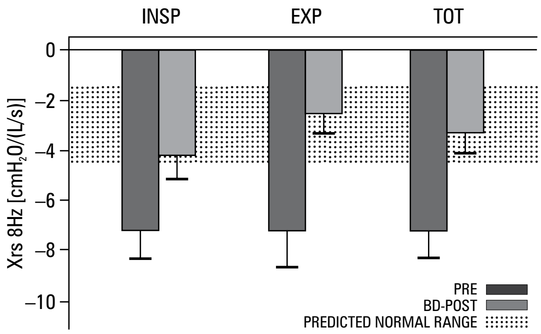
Evaluation of anti-inflammatory treatment

There are relatively few long-term studies assessing changes in FOT parameters during

Stimilus type: 8 Hz

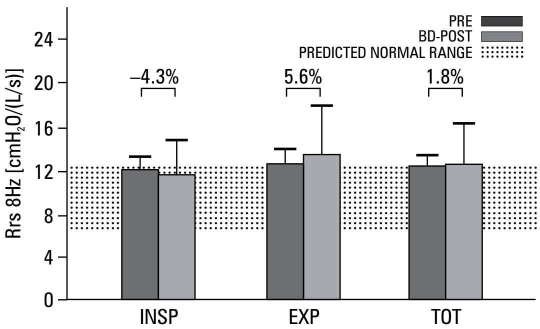
Test type:	PRE	BD-POST
Measurement date:	21-10-2015 17:36	21-10-2015 18:13
Age [years]	3	3
Weight [kg]:	14	14
Height [cm],	100	100
BMI (kg/m^2):	14.0	14.0
Number of accepted breaths (%tot):	8 / 11 (66.7%)	10 / 11 (90.0%)
Equation for predicted values:	Calogero et al., Ped. Pulmon., July 2010[A]	Calogero et al., Ped. Pulmon., July 2010[A]
Mean Filter Impedance [cmH_2O/L/s]	0.61	0.61
Physician:	PAED	PAED





Stimilus type: 8 Hz

Test type:	PRE	BD-POST
Measurement date:	13-01-2016 16:25	13-01-2016 16:44
Age [years]	3	3
Weight [kg]:	14	14
Height [cm],	100	100
BMI (kg/m^2)::	14.0	14.0
Number of accepted breaths (%tot):	8 / 11 (83.3%)	10 / 11 (83.0%)
Equation for predicted values:	Calogero et al., Ped. Pulmon., July 2010[A]	Calogero et al., Ped. Pulmon., July 2010[A]
Mean Filter Impedance [cmH_2O/L/s]	0.73	0.73
Physician:	PAED	PAED



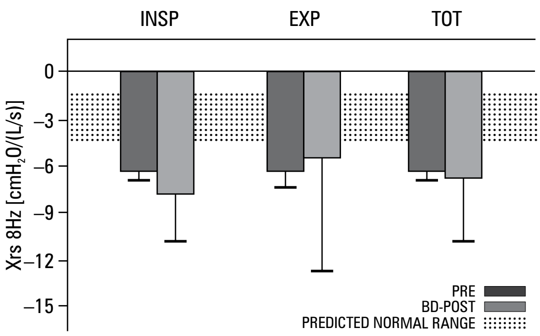


Figure 5. FOT — treatment monitoring. A 3-year-old girl with suspected early childhood asthma. Improvement of FOT parameters after 11 weeks of treatment with inhaled glucocorticosteroids; Rrs 8 Hz: resistance at 8 Hz; Xrs 8 Hz: reactance at 8 Hz; INSP: inspiratory component; EXP: expiratory component; TOT: total value; PRE: baseline values; BD-post: values after salbutamol administration; dotted field: range of normal values

asthma anti-inflammatory treatment in preschool children [43–45].

FOT in the assessment of the respiratory cycle

The advantage of this method is its ability to assess the entire respiratory cycle and thus both the inspiratory and expiratory phases. The practical dissimilarity is the difference between the inspiratory and expiratory phases. Observations indicate that the resistance in the expiratory phase is higher than in inspiratory, which is related to the constriction of the upper airways during expiration. This phenomenon intensifies with the increase of obstruction in the respiratory system. Children with asthma have excessively elevated resistance values in the exhalation phase compared to the inspiratory phase [22, 23, 46]. Due to the greater variability of the resistance in the exhalation phase, the parameter with the higher discriminative value for the assessment of bronchodilator response is the value of the inspiratory resistance.

Further research is required to assess the clinical significance of changes in reactance (Xrs) during the respiratory cycle and throughout bronchial reversibility tests in the diagnosis and monitoring of asthma in children.

Limitations of the FOT method

Due to the increasing availability of new FOT devices, the forced oscillation technique has a chance to become a method more commonly used in routine practice.

To implement FOT as a diagnostic tool, we should be aware of the method's limitations. Despite the simplicity during the study itself, there are artefacts resulting from poor testing technique (leaking around the mouthpiece, leaking nose clip, breathing irregularly, moving the tongue, coughing, crying, hyperventilating and glottal closure and incorrect position during the test). The person performing the test should pay special attention to its proper carrying out.

The poor cheek support is a common artefact during FOT measurement. Pressure oscillations are applied at the mouth and the impedance of extra-thoracic airway walls, including the cheek, tongue, mouthpiece and upper airway affect the results of measurements [14, 47]. If the cheeks are not held properly, resistance values reduce significantly (Rrs is therefore underestimated) [47]. The results of the measurements are affected by interference from the upper respiratory tract, especially at higher frequencies and when a respiratory obstruction is present. It is therefore important to properly hold the cheeks during the test so that they do not vibrate. Inaccurate cheek holding results in a significant lowering of the resistance value in patients with obstructive and interstitial diseases, with only a small effect on the measured values in healthy people [47].

It is known that the use of a bacterial filter adds a dead space volume, and resistance values measured with a bacterial filter may be slightly greater than those without a filter [48]. Modern devices allow to measure a filter's parameters before each patient's examination and provide a correction factor so measurements using different filters can be compared.

Tongue position can affect resistance values too, therefore, it's important to make sure it is not interfering with the airflow during the trial [48]. The special construction of the filter's mouthpiece is designed to reduce that effect.

Available normal FOT values are developed for different ethnic groups using various accessible devices and research protocols. They include at present a much smaller number of subjects compared to spirometry.

The reference values of FOT parameters of the inspiratory and expiratory phase for preschool children have not yet been established [49].

The standardisation and establishment of cut-off values for positive bronchial reversibility tests and bronchial challenge tests are needed. Further research requires determining the usefulness and role of Xrs and the differences between its inspiratory and expiratory components in children.

Summary

FOT is a promising method that should find its place and be widely used in paediatric-pulmonology-allergy practice. Due to its simplicity, non-invasiveness, and lack of the need for active cooperation, FOT should be applied in the diagnostic management of asthma in young children who cannot meet the requirements of proper spirometry. Particular importance is given to bronchomotor tests and repeated measurements over time to monitor response to treatment and to assess the course, the severity and the degree of disease control. FOT not only makes it possible to objectify the diagnosis in this age group but also reveals disorders in the peripheral, small airways to enable better control of asthma [50]. Compared to other methods of assessing respiratory resistance, FOT provides additional information using the reactance (Xrs), which supplies data about impaired flow in the peripheral airways and increased lung elastic properties. FOT is also a good tool to assess and monitor impaired lung function in the population of children who were preterm infants, from the first years of their lives [51]. Further work is needed to standardise the criteria for assessing the FOT results using various available devices.

Conflict of interest

The authors declare no conflict of interest.

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