MODERN METHODS FOR ASSESSMENT OF LUNG FUNCTION IN EARLY CHILDHOOD (3-6 YEARS)

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Abstract

The study of lung functions by forced spirometry in childhood is a gold standard. International guidelines indicate that lung function testing is possible in children from 3 years old, but the challenge is the lack of cooperation. This requires the introduction of other functional tests that do not need cooperation and at the same time provide reliable information.

Indications: The main indications for the study of lung functions in childhood are related to diagnosis, monitoring of the disease, evaluation of applied treatment and future prognosis.

Examination methods: The lack of cooperation of the examined child, the inability to sedate, the age from 3 to 6 years, require an adapted approach and application of research methods that combine safety, ease of performance and provide reliable information. Functional tests include multiple breath washout methods by inhaling inert gas, which assess the course of diseases as cystic fibrosis, without requiring coordinated assistance, but provide information on the homogeneity of the airflow; forced oscillation method, which obtains information about changes in both the large and small airways; the measurement of nitric oxide in the exhaled air as an inflamometer for eosinophilic bronchial inflammation, etc.

Conclusion: Modern methods for assessing lung function play an important role in the diagnosis and treatment of respiratory diseases in early childhood, although they are rarely widely used. The study at this age is challenging, but it provides valuable information in young children under 6 years of age with cystic fibrosis, bronchopulmonary dysplasia and recurrent wheezing.

Keywords: *children, young age, pulmonary function testing*

Introduction

Lung function testing in young children is an important objective measurement that provides information about possible changes linked to respiratory diseases [1]. The age span between 3 and 6 years is especially challenging because children are too old to be sedated but at the same time too young to cooperate and perform a repeatable and reliable spirometry test. Small airway diseases are also very common among this paediatric population but the gold standard in lung function – forced spirometry – often does not provide enough information about this part of the bronchial tree. New methods are introduced and try to reveal all these possible pathologic changes in lung functions since they have a long-term detrimental effect later in life. Most reliable pulmonary function test in children need to be easy to perform, safe, objective, sensitive and specific and stable over time to follow-up conditions that start early in life like cystic fibrosis and asthma. In the last years promising new methods are feasible and leave the labs to be applied in clinical practice [1,2,3]. The methods of multiple breath washout, forced oscillation techniques and fraction of exhaled nitric oxide are just a few of them but they provide specific information and may be applied together with standard spirometry.

Multiple breath washout method

The multiple breath washout methods were first described 60 years ago. They measure the distribution of ventilation in the lungs and its homogeneity, while also determining lung volumes,

e.g. FRC, when the inhaled inert mixture is washed out. This lung volume is measured when the airways open during quite breathing, and the most commonly used inert gases are helium (He), nitrogen (N2) and sulfur hexafluoride (SF6) [4,5]. They are not absorbed into the body and are not excreted in the lungs during the test and are not involved in gas exchange.

By measuring the homogeneity of the air distribution, even a minor peripheral obstruction can be detected, which would otherwise be missed by conventional tests. The MBW test, in addition to N2, can also be performed with sulfur hexafluoride - SF6, using air from the room, after a small amount of the inert gas has been inhaled until equilibrium is reached in the lungs (Fig.1). The residual volume obtained in this way may not be sufficiently informative in terms of hyperinflation, but the study of impaired ventilatory distribution may be important when peripheral airway diseases such as e.g. cystic fibrosis and bronchiolitis obliterans.

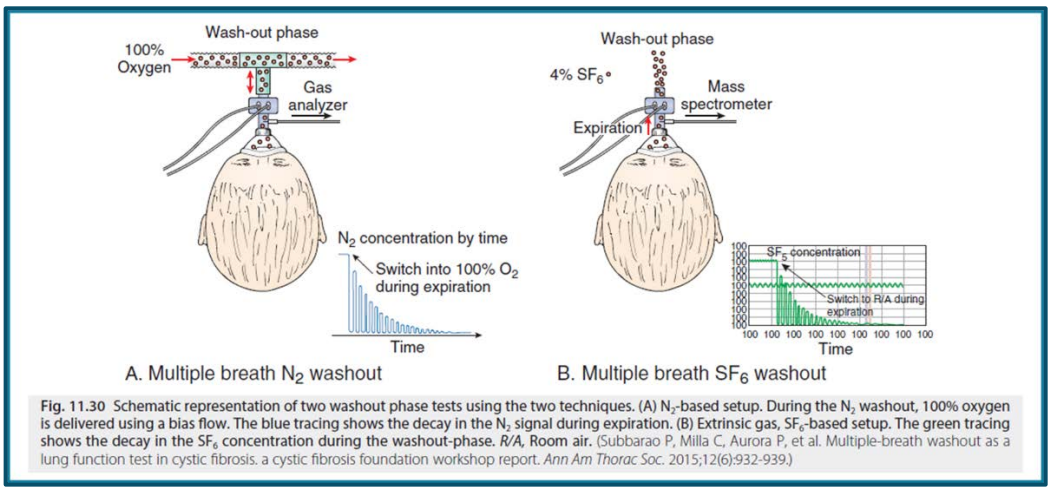

Fig. 11.30 Schematic representation of two washout phase tests using the two techniques. (A) N_2-based setup. During the N_2 washout, 100% oxygen is delivered using a bias flow. The blue tracing shows the decay in the N_2 signal during expiration. (B) Extrinsic gas, SF_6-based setup. The green tracing shows the decay in the SF_6 concentration during the washout-phase. *R/A*, Room air. (Subbarao P, Milla C, Aurora P, et al. Multiple-breath washout as a lung function test in cystic fibrosis. a cystic fibrosis foundation workshop report. *Ann Am Thorac Soc.* 2015;12(6):932-939.)

Figure 1 Schematic representation of different multiple breath washout methods[6]

This method is used due to the easy-to-carry procedure, the absence of complex breathing manoeuvres and relatively affordable equipment. Gas-dilution methods provide additional information to standard lung tests such as spirometry and are of utmost importance because they can be applied to a wide age range, especially young children, while increasing the possibility of early detection of lung damage [7].

The Lung Clearance Index (LCI) is most often used to describe ventilatory inhomogeneity, and as this index increases, i.e. more breathing cycles are needed to clear the inert gas from the lungs. At the same time, this index is relatively stable both during childhood and puberty, and its variability is relatively low and therefore suitable for monitoring lung diseases. During childhood, the LCI is independent of age, sex, weight and height. Appropriate reference values are published, and the upper limit of the norm is defined as the mean of LCI + 2 SD.

The Lung Clearance Index is highly sensitive compared to spirometry and in most patients with cystic fibrosis, it is the parameter that progresses with otherwise normal spirometry and values of the main lung parameters within reference limits [7,8].

Modern guidelines describe in detail the requirements for the equipment, the performing procedure, the analysis of the results obtained and the relevant recommendations in each of the mentioned aspects related to testing in childhood and adult patients.

The method of forced oscillation technique

For the first time in 1956, Arthur DuBois measured airway resistance using the forced oscillation technique (FOT). FOT is a method based on the mechanics of oscillations, leading to the vibration of the air flow from the mouth to the alveoli and contact tissues with a subsequent

assessment of the mechanical characteristics of the respiratory system, summarized by the term Impedance (Zrs) with its components – Resistance (Rrs) and Reactance (Xrs).

It can provide important objective information in children with diseases of the respiratory system: bronchial asthma, cystic fibrosis, bronchopulmonary dysplasia, interstitial lung disease [4,9,10]. Although not as widely available as spirometry, this method can be performed by young children and those who cannot perform "quality" spirometry.

Often, the small airways become involved in the onset of lung diseases. There are changes in the functions even before the clinical symptoms start and before there are changes in spirometry.

Unlike spirometry and FEV1, the term "forced" has nothing to do with the maneuver of FOT. Here only quite breathing is required, usually lasting 16-30 seconds. This is a non-invasive method that measures mostly airway resistance.

The device generates oscillations of small amplitude, superimposed on normal tidal breathing and therefore has the advantage over conventional techniques for studying lung function, as it does not require specific breathing manoeuvres. The generated vibrations have different frequencies, but the most significant information is obtained at relatively lower frequencies of 5 - 8 Hz.

The use of low frequencies depends on the patient's respiratory rate, and this is especially important in young children, where it is difficult to obtain reliable data at frequencies less than 6 Hz, since their respiratory rate is between 0.5 and 1 Hz. Vibrations of the cheeks and pharyngeal wall during the examination can compromise data from the survey.

Measurements are performed in a sitting position with the head slightly extended backwards. Flexion should be avoided. A clip should be placed on the nose. During the measurement, the examiner gently supports the patient's cheeks and mandible with the help of both hands (Fig. 2).

Data obtained at lower frequencies are of good sensitivity in diagnosing broncho-obstructive syndrome.

Airway resistance is calculated based on the change in pressure and airflow resulting from superimposed vibrations (oscillations). Resistance (Rrs) reflects the relationship between pressure and airflow. As the frequency of oscillations decreases, the resistance increases, reflecting the resistance of the peripheral airways. Reactance (Xrs) reflects the elastic properties of the respiratory system. At low frequencies, it is negative.

The point at which Xrs crosses zero is called the resonance frequency (Fres) and is a reflection of the frequency at which the elastic and inertial properties of the lung are balanced, i.e. it reflects the lung compliance. The area between the reactance curve and the abscissa is denoted as the reactance area – AX. This is the sum of the reactance at a frequency of 5Hz to Fres (Fig. 3).

Figure 2 FOT measurement in preschool Children

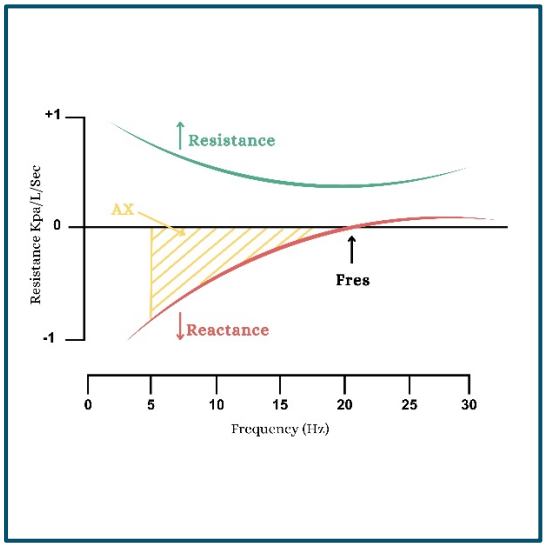

Figure 3 Graphic representation pf parameters

Studies have shown that Xrs and AX are more indicative of peripheral airway obstruction compared to resistance (Rrs). These two parameters clearly distinguish healthy children from those with diseases affecting the small respiratory tract.

Oscillometry is carried out with quite breathing, which makes it a suitable method for lung testing in preschool children and in clinical practice it can be used to identify children with asthma symptoms in whom early therapeutic intervention is indicated in order to prevent future deterioration of lung function and disease progression.

The methods of measurement of fraction of exhaled nitric oxide

Measurement of the fraction of nitric oxide in exhaled air (FeNO) is an important biomarker for an inflammatory process present in the respiratory system. The measurement of FeNO is a validated, accessible test, and its amount in the exhaled air is an indicator of the presence of eosinophilic inflammation in the respiratory tract [11,12]. There is a strong correlation with eosinophilic inflammation in the airways and given the strong association of the latter with a positive response to corticosteroid treatment, elevated FeNO levels predict steroid response in patients with nonspecific respiratory symptoms. Furthermore, the decrease in FeNO in corticosteroid therapy is dose-dependent, allowing for precise dosage adjustment.

The FeNO methodology is well validated and standardized for use in clinical practice. Detailed guidelines for the procedure have been developed, as well as reference values for children aged 4-17 years. In younger children and infants, the procedure is not standardized and is less used [11, 12, 13, 14].

Measurement of FeNO in exhaled air is one of the few functional methods that allow functional respiratory analysis in early childhood. This makes it especially promising for pulmonary functional diagnostics in childhood.

Above the age of 4-5 years, the child is already able to cooperate, and this makes this non-invasive test possible and reliable. The examined child inhales room air and exhales into the device with a constant flow rate of 50 ml. per second until reaching a plateau for at least 2 seconds at an expiry of at least 4 seconds.

The application of FeNO is not only in the diagnosis, but also in the monitoring and follow-up of therapy in children with wheezing.

FeNO measurement is also an important indicator in asthma tracking. Measured FeNO levels often correlate with asthma control and contribute to a more complete characterization of asthma patients. In addition, FeNO in the course of the disease can identify patients who would benefit most from corticosteroid treatment compared to those who have non-eosinophilic inflammation.

The National Institute for Health and Care Excellence (NICE) recommends measuring FeNO as a diagnostic tool in combination with other diagnostic methods such as spirometry in children and adults who are moderately likely to develop asthma.

In preschoolers, FeNO can provide information and distinguish different phenotypes of wheezing, as well as predict the onset of asthma later in life, while in school-age children FeNO has diagnostic value in terms of asthma, but also high predictive value in atopy and respiratory symptoms.

It remains an open question whether FeNO can predict a decrease in lung function or a disturbance in lung growth, for which further studies are needed.

Conclusion

New methods for assessing pulmonary function play an important role in the diagnosis and treatment of respiratory diseases in early childhood, although they are rarely widely used. The study at this age is challenging, but it provides valuable information in young children under 6 years of age with cystic fibrosis, bronchopulmonary dysplasia and recurrent wheezing. Further research is needed to validate and standardize most of these reliable tests in the young preschool children.

Conflict of interest: None

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