Lung Function Tests, Quality of Life and Telemedicine

Subjects: Respiratory System

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Asthma is a heterogeneous disease usually characterized by chronic airway inflammation and recognized as the most prevalent chronic illness among children. Despite this, the knowledge as to how asthma affects adolescents is still scarce. One of the main management problems of asthmatic adolescents is the poor adherence to pharmacological and non-pharmacological treatments.

asthma adolescent spirometry impulse oscillometry quality of life

1. Introduction

Asthma is a heterogeneous disease that is usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation [1]. This chronic respiratory disorder is recognized as a major non-communicable disease in the pediatric population. According to the WHO (2013), adolescence can be seen as "the period in human growth and development that occurs after childhood and before adulthood, from ages 10–19" [2]. The 2021 update of the Global Strategy for Asthma Management and Prevention highlights the impact of rapid physical, cognitive and social changes on the management of asthmatic adolescents [1]. While persons of all ages suffer from asthma, certain age groups and their accompanying developmental stage challenge the implications of the disease even more. As a result, asthmatic adolescents may also have low treatment adherence toward preventive strategies and therefore high morbidity [3].

Despite the growing establishment of a personalized medicine approach [4] and modern omics methods [5] in diagnosis and management of asthma, the assessment of respiratory function [1] and the impact on quality of life [6] (QoL) in a "delicate" phase of growth are still two crucial challenges in asthmatic adolescents.

In addition, the COVID-19 pandemic has prompted clinicians to expand and, at times, change their follow-up tools for asthmatic patients, exploring the contribution of telemedicine to manage asthmatic teenagers [7].

2. How to Explore Asthma in Adolescents: The Role of Lung Function Tests

Currently, the evaluation of respiratory function is primarily based on techniques such as spirometry, which includes forced vital capacity (FVC) and vital capacity (VC) maneuvers [8].

These spirometric maneuvers are used to diagnose, to predict the course of asthma and to estimate the risk of exacerbations [1]. In particular, the aforementioned spirometric investigations aim to characterize airways in terms of the presence and severity of airflow obstruction [8].

Asymptomatic asthmatic children may hide significant bronchial obstruction. Children with chronic airway obstruction may experience less breathlessness than children with acute obstruction [9]. In addition, poor perception of bronchial obstruction effects may place asthmatic adolescents in front of a greater risk of respiratory function decline and acute exacerbations [10]. Therefore, periodic evaluation of respiratory function is necessary to optimize the management of asthmatic children.

2.1. Flow-Volume Curves

The authors of the National Asthma Education and Prevention Program (NAEPP) guidelines recommend spirometry every 1–2 years for asthmatic children over 5 years of age [11].

The basics of spirometry apply to both pediatrics and adults, using the same principles for testing and equipment. Maximal expiratory flow-volume curves are considered the gold standard to assess respiratory function in asthmatic children [1]. In particular, periodic evaluation of pre- and post-bronchodilator forced expiratory volume in 1 second (FEV1) could help to identify children at risk of progressive respiratory function decline [12][13].

Furthermore, FEV1, in addition to being considered important to assess asthma severity [11][14], is an independent predictor of asthma exacerbations [15][16][17]; 1-year risk of asthma exacerbations is double in asthmatic children with a predicted baseline FEV1 <60% compared with children with normal values [17].

Recently, Hopp et al. updated data on lung function and bronchodilator response in asthmatic children, providing a plausible hierarchy of use of spirometric test results [18]. In particular, a 12% increase in FEV1 after bronchodilator, although considered an appropriate cut-off [19], could be potentially excessive in younger children. In fact, there is evidence that a threshold of more than 8% performed better than 12% in a study enrolling 1041 asthmatic children (mean age, 8.9 ± 2.1 years) from the Childhood Asthma Management Program [20]. More recently, Sottile et al. [21], studying 1146 white children aged 5 to 13 years from the ongoing CHildhood ASthma and Environment Research (CHASER) study (ClinicalTrials.gov ID: NCT02433275), showed that the probability of having asthma was almost nil when post-bronchodilator FEV1 change was less than or equal to 7.9%.

Although the pediatric population, the focus of this entry, is expected to meet the American Thoracic Society/European Respiratory Society recommended end of forced expiration (EOFE) criteria [8], younger children could complete forced expiration in only 2 or 3 s. Despite this, FVC change after pharmacological bronchodilation test and a reduced total exhalation time after bronchodilation could help to investigate the presence of air trapping. In fact, Sorkness et al. identified an air-trapping obstruction phenotype among asthmatic children aged 6 to 17 years adopting a FVC z score of less than −1.64 or a FVC increase of at least 10% after bronchodilator [22].

However, FEV1 as well as the FEV1/FVC ratio are poorly correlated with the severity of symptoms; hence, asthma management should not be based solely on reported symptoms [23].

Historically, forced expiratory flow between 25 and 75% of FVC (FEF25-75) has been used to evaluate flow from the small airways. More precisely, FEF25-75 should be considered a measurement of flow at lower lung volumes. As in adults, the variability of the FEF25-75 is greater than that of the FEV1 and FVC [24]. Nevertheless, some studies suggested that FEF25-75 could be a clue of the symptomatic state in children [25][26][27]. In 2010, Simon et al. [28] found that the sensitivity of FEF25-75 to 65% of predicted value, in identifying a 20% change in FEV1 after bronchodilator in children enrolled in PACT [29] and CLIC [30] trials, was 90%.

2.2. Impulse Oscillometry

The forced oscillation technique (FOT) was developed in 1956 to explore respiratory functions [31]. A modification of this method is impulse oscillometry (IOS) [32]. In the latter, a loudspeaker delivers a regular, square pressure wave at a constant frequency to the respiratory system using spectral analysis from which all other individual frequencies are derived.

Compared to spirometry, IOS is a much simpler technique for assessing airway impedance and reactivity. IOS is effortless, is performed in tidal breathing and does not require special cooperation from the patient. In addition, IOS makes it possible to distinguish central versus peripheral airway obstruction [33][34].

The main indicators of IOS are: (1) resistance at 5 Hz (R5), (2) resistance at 20 Hz (R20), (3) the difference between R5 and R20 (R5−R20), (4) reactance at 5 Hz (X5), (5) reactance area (AX) and (6) resonant frequency of reactance (Fres). Because low oscillation frequencies can transmit more distally in the lungs than high frequencies, R5 reflects the respiratory system resistance, while R20 reflects the central airways resistance. R5−20 is an index of the peripheral airways. X5 represents the peripheral elastic resistance. AX reflects the elastic properties of the lung. As with low-frequency reactance, it provides important information about small airway obstruction. Finally, Fres is the oscillation frequency when the reactance is zero.

The usefulness of IOS has been examined in different respiratory diseases, including asthma [35]. The greatest advantage is the ability to monitor the course of the disease [36] and to assess therapy response [37][38], which is most notable in children because patient cooperation is only minimally required [39] and measurements are reproducable [40].

One of the main advantages of IOS, compared to other lung function tests, is that measurements of respiratory mechanics are as easy to take in preschool children as in schoolchildren and adolescents. In fact, in 2006, Tomalak et al. [41] demonstrated that all oscillometric resistances (at 5, 20 and 35 Hz) correlated significantly with plethysmographic airway resistance (Raw) in a group of 334 children aged 5–18 years. Furthermore, the strongest correlation was seen for R5 (r = 0.64) [41].

The strong relationship between oscillometric and pletismographic measurements allows to compare different populations and changes in respiratory function over the years in both physiological and pathophysiological conditions. In fact, in 2008, Nowowiejska et al. [42] studied 626 healthy polish children aged 3.1–18.9 years (278 boys and 348 girls) in order to define equations describing normal values of oscillatory parameters. The authors found that body height was the best predictor and resistance was best described with an exponential model, while reactances with a linear model, with correlation coefficient r reaching the value of 0.9. Furthermore, oscillometric resistances decreased with height, while reactances increased [42].

2.3. Exhaled Nitric Oxide

Measurement of exhaled nitric oxide (FeNO) through the mouth nitric oxide is a technique now used in children [43]. In the pediatric population, 20 parts per billion (ppb) is the cut point for low FeNO value, while an elevated FeNO value is above 35 ppb; finally, values between 20 and 35 ppb are considered indeterminant [44]. This procedure is an attractive additional tool in children because it does not involve any forced mechanics and is relatively simple to accomplish. The clinical use of FeNO in the pediatric population is still under investigation [45][46][47]. Recently, Lo et al. investigated the prevalence of abnormal FeNO values in 612 children aged 5–16 years with an existing asthma diagnosis or receiving asthma drugs [48]. A total of 36% of patients showed FeNO ≥35 ppb and 41.8% reported poor control [48]. More recently, Lo et al. demonstrated that high FeNO levels predicted asthma exacerbations during follow-up in a cohort of 460 children aged 5–16 years [49]. To date, there is evidence to conditionally recommend the use of FeNO as an additional tool for evaluating the treatment of asthma patients [44].

Limiting the contribution of respiratory function tests for diagnosing and monitoring adolescent asthma is the current COVID-19 pandemic context. Nevertheless, the possibility of carrying out oscillometric measurements and FeNO tests, with smaller devices compared to body plethysmographs, with the operator placed behind the child during breathing maneuvers, and with reduced acquisition times, could cushion the negative impact of new pandemic rises on the daily practice of pulmonary function laboratories [50].

3. Impact of Asthma on Quality of Life in Adolescents

Adolescence represents a critical developmental period as the individual loses the characteristics of childhood to fast reach psychic maturity [51]. Furthermore, the process of acceptance and internalization is much more complex than any other moment in life, making the adolescent more vulnerable to stress, which has a strong negative impact on the management of chronic diseases such as bronchial asthma [52]. As early as 2007, de Benedictis and Bush recognized that adolescents with asthma have specific needs and problems and should take separate attention [53]. In fact, while young children are completely dependent on their parents regarding their asthma care [54], and adults are capable of managing their own chronic illness effectively, adolescents find themselves somewhere in between [55].

These problems can include low levels of disease knowledge [56], denial of symptoms, non-adherence to asthma medications [57][58], unfruitful preventive asthma medication use [59], poor relationship between adolescents and their families [53] and a higher risk of morbidity, mortality and severe exacerbations [60].

Furthermore, growing evidence highlights the role of bronchial asthma in school absenteeism [61][62][63], its detrimental effect on at-school productivity (presenteeism) [63][64][65] and friend relations [66][67].

A negative effect on QoL is the inevitable and foreseeable consequence of these problems [68][69].

Growing scientific literature on the importance of QoL in pathologies has unveiled heterogeneity of the conceptualization, definition and operationalization [70]. This influences the interpretation of the increasing quality of life studies, even for asthmatic patients [71].

Table 1 shows studies published over the past 10 years exploring the QoL of asthmatic adolescents from 10 to 19 years of age.

Table 1. Studies focused on QoL in adolescent asthmatics (in the 10- to 19-year age bracket).

Author	Year	Country	Definition of QoL	Study Design	Number of Patients	Instrument
Dinglasan et al. [56]	2022	Malaysia	-	Cross-sectional	214	PAQLQ
Cekic et al. [72]	2022	Turkey	-	Cross-sectional	125	EUROHIS-QOL 8
Dut et al. [73]	2021	Turkey	-	Cross-sectional	122	PAQLQ BSI
Lang et al. [69]	2015	USA	-	Cross-sectional	58	PAQLQ, PACQLQ
Halterman et al. [74]	2011	USA	-	Prospective cohort	28	PAQLQ, PACQLQ

PAQLQ: Pediatric Asthma Quality of Life Questionnaire. BSI: Brief symptom inventory. PACQLQ: Pediatric Asthma Caregiver's Quality of Life Questionnaire.

Feinstein already observed over 30 years that QoL is often used as a generic term [75]. Exploratory tools such as dedicated questionnaires frequently replace a lacking explicit definition of QoL. As noted by Costa et al., these "patient-reported outcomes" are equally used as an umbrella term as they specify the data source, the patient, but do not explicitly specify outcomes [71].

The impact of asthma on individuals varies greatly from person to person according to their unique circumstances. According to Falvo, the impact is dependent on the individuals' pre-illness personality, severity of the illness, the meaning the individual attaches to the illness, current living circumstances and the availability of family and social support [76]. Additionally, asthma not only significantly affects patients' lives but also that of their friends, family, colleagues and the community [54].

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