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Review

Impulse oscillometry in the assessment of asthmatic children and adolescents: from a narrative to a systematic review

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EDUCATIONAL AIMS

The reader will come to appreciate:

- That impulse oscillometry [IOS] may have utility in children who are unable to perform spirometry.
- Reactance may be a better parameter than FEV1 in the assessment of peripheral airway function.
- Both spirometry and IOS may support, but will not replace, the role of the clinician in the diagnosis of asthma in children.

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SUMMARY

Diagnosis and management of asthma often relies mostly on symptoms because spirometry is not always reliable in some age groups, such as preschoolers. It is unclear whether impulse oscillometry (IOS) can supplement or replace spirometry. Available reports suggest that IOS has been applied with success in asthmatic children and adolescents to assess exacerbations, level of control, severity and response to treatment in the short and long term. Very few studies using adequate sample sizes and methods have been performed comparing the accuracy of IOS to spirometry for the diagnosis of asthma. Our systematic review found only four studies that met the eligibility criteria. However, no meta-analysis was possible with the available data. Consequently, this review helps to identify research gaps involving IOS, highlighting opportunities for future studies.

INTRODUCTION

The first step toward the effective treatment and management of asthma is a proper diagnosis [1]. In fact, the assessment of asthma is still based mostly on symptoms because the measurement of pulmonary function is not always reliable, particularly in extreme age groups, such as preschool children and the elderly [2,3].

There is no gold standard method or tool to monitor the pulmonary function. Currently, spirometry is a widely used technique. As it requires forced expiratory maneuvers, the accuracy and reproducibility of spirometry depend on the patient's cognitive level and effort [4]. When spirometry is not performed properly, it becomes almost meaningless [5]. A recent study suggested that spirometry can be supplemented by impulse oscillometry (IOS), particularly when the expiration curves obtained by spirometry are irregular [6].

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Abbreviations: AX, area of reactance; $FEF_{25-75\%}$, forced expiratory flow at 25-75%; FEV_1, forced expiratory volume in first second; FEV_1/FVC, Tiffeneau index; FVC, forced vital capacity; Fres, resonant frequency; IOS, impulse oscillometry; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, International prospective register of systematic reviews; QUADAS, Quality Assessment of Diagnostic Accuracy Studies; R5, resistance at 5 Hz; R10, resistance at 10 Hz; R20, resistance at 20 Hz; R35, resistance at 35 Hz; ROC, Receiver Operating Characteristic; SIGN, Scottish Intercollegiate Guidelines Network; X5, reactance at 5 Hz.

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IOS is a simple method, which demands minimal co-operation and allows an evaluation of pulmonary function through the measurements of reactance and resistance of the airways [7]. Reactance and resistance are parameters of IOS that reflect different pathophysiological features of asthma. Reactance at 5 Hz (X5) and area of reactance (AX) reflect changes of the degree of obstruction in the peripheral airways. In contrast, resistance at 5 Hz (R5) reflects obstructive phenomena in both large and small airways. On the other hand, resistance at 20 Hz (R20) represents the resistance of large airways. The resistance of the small airways can be calculated by subtracting R20 from R5 [7]. The alterations in small airways are used for diagnosing asthma in its very early stages [8,9]. These aspects make IOS suitable to be used in children, especially in pre-schoolers [10].

Although it is tempting to look favourably upon IOS as an additional test to be used when spirometry is not performed properly, it is still unclear if IOS has sufficient sensitivity and specificity [11]. As IOS is not as popular as spirometry, a deeper knowledge about the properties of IOS can improve understanding of the technique, minimize the number of incorrect diagnoses and improve in the management of asthma.

Since aspects related to the equipment, procedures, applications and limitations of spirometry and IOS are well described in the literature [12,13], this review was intended to briefly revise some noteworthy aspects of IOS before providing a systematic review comparing studies that have demonstrated the sensitivity and specificity of IOS and spirometry for diagnosing asthma in children and adolescents.

IOS BEYOND ASTHMA DIAGNOSIS: DISEASE MANAGEMENT

Short to long term monitoring with objective methods of assessment is recognized as a critical aspect of asthma management. This is especially important when tracking the effects of therapy in both clinical research and day to day practice.

Asthma exacerbations

IOS may be used to evaluate respiratory function during an asthma exacerbation. Batmaz et al. evaluated 35 children with asthma exacerbations, 107 children with stable asthma and 103 healthy children, aged 6-17 years. In this study, all IOS and spirometric parameters were able to discriminate asthmatic children (both acute and stable) and healthy controls. Moreover, AX had the highest area under curve (AUC) for all comparisons between the three groups. The parameter AX distinguished acute and stable asthmatics with 85% sensitivity and 79.2% specificity. The results suggested that the parameters related to small airways are more significantly able to discriminate between groups. This emphasises the importance of assessing the relationship between the peripheral airways and asthma exacerbations [14].

IOS has also been used to predict the risk of exacerbation in asthmatic children. Schulze et al. evaluated 75 children with intermittent asthma, aged 4-7 years [15]. At visit 1, baseline measurements were performed, including spirometry, IOS and methacholine challenge testing. The patients were tracked for 1 year by phone calls asking about exacerbation symptoms. R5, X5 e R5-R20 were the most accurate parameters to predict the risk of a moderate exacerbation (AUC = 0.78, 0.70 and 0.77, respectively). On the other hand, single parameters such as forced expiratory volume in 1 second (FEV_1), FEV_1/FVC ratio and PD_{20}methacholine did not differentiate between the groups with exacerbations and those without exacerbations. Interestingly, in the logistic regression analysis, the combination of R5, FEV_1 and PD_{20}methacholine demonstrated the best accuracy (87%) to predict the risk of a moderate exacerbation. The results suggested that in mild asthmatics, FEV_1 alone might not be sensitive enough to detect moderate exacerbations. Additionally, even during symptom-free intervals, impaired peripheral airways (R5-R20 and X5) are present in children with intermittent asthma, and these children experienced exacerbations during infections [15].

Early response to treatment

In general terms, published reports indicate that IOS can detect airways changes, especially in peripheral airways, even after a short period of treatment. Following medication administration, IOS can detect changes in the airways of asthmatic children. The response to short-acting beta 2-agonists evaluated by IOS was investigated in several studies [10,16–18]. After administration of terbutaline, R5 and X5 improved significantly in asthmatics, while healthy children had a significant improvement only in R5 [16]. Significant differences also were observed in R5, X5, AX, FEV_1, forced vital capacity (FVC) and forced expiratory flow at 25-75% ($FEF_{25-75\%}$) after administration of salbutamol [17]. Song et al. showed significant differences in R5, resistance at 10 Hz (R10), R20 and resistance at 35 Hz (R35), but spirometry values did not show statistically significant differences between asthmatic children and control subjects in the bronchodilator response [10]. Olaguíbel et al. studied the effect of placebo and salbutamol in asthmatic children. They verified improvement in R5, R20, X5 and FEV_1, but R5 had the highest sensitivity to salbutamol inhalation [18].

The effect of antileukotrienes on the IOS and spirometric parameters was investigated in an open label study. Forty-six children with mild asthma were randomized to receive montelukast or no preventive treatment over 4 weeks. In the montelukast group there was a significant improvement in all IOS parameters (R5, R20, R5-R20, X5 and resonant frequency - Fres), especially in X5. There was a trend for improvement also in spirometric parameters, especially for $FEF_{25-75\%}$, although this did not reach statistical significance. The decrease of airways resistance by therapy with montelukast was found in the whole airway, but it was more pronounced in the peripheral airways [19].

Nielsen and Bisgaard studied 38 children, aged 2-5 years with moderately severe asthma in a randomized, double-blind, placebo-controlled study involving 8 weeks of treatment with budesonide. X5 and R5 were measured using the IOS technique. At the endpoint, X5 and R5 were significantly improved with budesonide and deteriorated during placebo administration [20].

Asthma severity and phenotypes

IOS can discriminate intermittent to persistent asthma in children. Shin et al. assessed 162 children aged 2-5 years diagnosed with asthma. Asthma severity was classified as intermittent, mild persistent or moderate-severe persistent. All children were assessed by IOS. The results showed a significant difference in X5 between intermittent and mild persistent asthma and between intermittent and moderate-severe persistent asthma. Taken together, changes in R5 and R5-R20 were useful in discriminating between children with asthma symptoms and controls [21].

IOS can also help with differentiating asthma phenotypes. In a prospective birth cohort study, children and adolescents performed spirometry at 8 and 16 years and IOS at 16 years of age. Children were categorized in the following groups: never asthma, early transient asthma (asthma in subjects aged up to 4 years), early persistent (asthma in the first 4 years and asthma at 16 years) and late onset asthma (no asthma at ages 1, 2, or 4, but asthma at age 16). At 16 years of age, all asthma groups were associated with lower FEV_1, FEV_1/FVC, and $FEF_{50\%}$ values in comparison to the never asthma group. All estimated mean values for R5 and R20 were significantly lower in the reference group than in any other