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ORIGINAL ARTICLE

Utility of bronchodilator response for asthma diagnosis in Latino preschoolers

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Abstract
Background: Asthma diagnosis in preschoolers is mostly based on clinical evidence, but a bronchodilator response could be used to help confirm the diagnosis. The objective of this study is to evaluate the utility of bronchodilator response for asthma diagnosis in preschoolers by using spirometry standardised for this specific age group.
Methods: A standardised spirometry was performed before and after 200 mcg of salbutamol in 64 asthmatics and 32 healthy control preschoolers in a case-control design study.
Results: The mean age of the population was 4.1 years (3–5.9 years) and 60% were females. Almost 95% of asthmatics and controls could perform an acceptable spirometry, but more asthmatics than controls reached forced expiratory volume in one second (FEV_1) (57% vs. 23%, $p = 0.033$), independent of age. Basal flows and FEV_1 were significantly lower in asthmatics than in controls, but no difference was found between groups in forced vital capacity (FVC) and FEV in 0.5 s ($FEV_{0.5}$). Using receiver operating characteristic (ROC) curves, the variable with higher power to discriminate asthmatics from healthy controls was a bronchodilator response (% of change from basal above the coefficient of repeatability) of 25% in forced expiratory flow between 25% and 75% (FEF_{25-75}) with 41% sensitivity, 80% specificity. The higher positive likelihood ratio for asthma equalled three for a bronchodilator response of 11% in $FEV_{0.5}$ (sensitivity 30%, specificity 90%).
Conclusions: In this sample of Chilean preschoolers, spirometry had a very high performance and bronchodilator response was very specific but had low sensitivity to confirm asthma diagnosis.

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Introduction

Although the diagnosis of asthma in children is mainly clinical, confirming it by post-bronchodilator reversibility reassures the diagnosis and is useful for evaluating response to therapy.[1–3] Measuring lung function in children generally entails two main alternatives: techniques requiring little collaboration (e.g. measuring airway resistance by impulse oscillometry (IOS), plethysmography or resistance by the interrupter technique (Rint)); or by spirometry. Performing the first techniques usually requires specialised pulmonary function laboratories with costly equipment, sometimes yielding results that are difficult to interpret.[4] In contrast, spirometry, the most commonly used test in schoolchildren and adults across the globe, is generally available in lung function laboratories, and is easy to interpret.

Chile has a public health system named FONASA, funded mostly by the goverment, and which is used by 80% of the population. The remaining 20% belong to a private health institution named ISAPRE, providing financial services and health insurance, whose costs are mostly assumed by the patient. Since 2005 in Chile legislation has been established with explicit guarantees in health (GES) and constitutes a set of benefits guaranteed by law for persons affiliated to FONASA and ISAPRE. Patients who suffer from any disease included in the GES (e.g. asthma) are entitled to early diagnosis, treatment and follow-up by medical specialists, with zero-cost or a low amount by the patient co-payment. Therefore, if the physician suspected asthma, he/she may request a spirometry. On the other hand, spirometers and physiotherapists and technologists trained to carry out spirometry are widely available at primary care centres across the country, as well as in hospitals and private practice. The organisation of the Chilean health system allows spirometry to be widely available and accessible around all the country.

In the last 15 years, many studies have been carried out to standardise spirometry in preschoolers.[4–10] An important feature of preschool spirometry is that forced expiratory volume in 0.5 s ($FEV_{0.5}$) is more appropriate than FEV in one second (FEV_1) to interpret their results because FEV_1 is difficult to obtain and its meaning differs from older children and adults.[4,7] Some studies determined the value of measured bronchodilator response to short beta-2 agonists (e.g. salbutamol) for asthma diagnosis in all ages, using different techniques with diverse results.[11–16] However, the studies that included preschooler spirometry reported only FEV_1[12–15] and in two of them, spirometry was performed using standardised criteria for adults.[12,15]

The objective of the present study was to evaluate the utility of measured bronchodilator response to short beta-2 agonists for asthma diagnosis in Chilean preschoolers using spirometry standardised for this specific age group.

Materials and methods

A case-control study was performed in asthmatic preschoolers matched by age, gender and height to healthy controls. Asthmatic children were selected by two paediatric pulmonologists for the study (ML, IC) according to Global Initiative for Asthma (GINA) guidelines.[1] Asthmatic children had, at least once a month, one wheezing episode, atopic eczema or parents with asthma, eczema or allergic rhinitis diagnosis. In all of them clinical improvement was demonstrated with short-acting bronchodilators and inhaled corticosteroids (ICS). Preschoolers with moderate to severe persistent asthma presenting at the asthma clinic at the Hospital Padre Hurtado, Santiago, Chile were consecutively included in the study. All asthmatics were on ICS, mean doses of 400 mcg/d of budesonide or equivalent for at least three months prior to entering the study. Using a previously validated questionnaire to rule out asthma and other chronic respiratory conditions, healthy preschoolers (controls) were selected from eight random preschool day care institutions from the Santiago Metropolitan Region. Three hundred questionnaires were sent to parents or guardians of those preschoolers. After one week, 216 (72%) questionnaires were returned, of which 143/216 (66%) had complete information and signed informed consent forms for participation in the study. This protocol was approved by the Hospital's Ethics Committee.

Demographic data including information about the neonatal period, tobacco exposure, type of heating used in the home, and history of personal and parental atopy (rhinitis and dermatitis) were collected from asthmatics and controls. Exclusion criteria of the study were prematurity, low weight for gestational age, undernourishment, cardiac or other chronic pulmonary conditions, and parental or guardian failure to sign the informed consent form. Also, children with acute respiratory infection in the preceding seven days were excluded.

All participants (asthmatics and controls) performed pre- and post-salbutamol spirometry (Jaeger MasterScreen® IOS, Würzburg, Germany). Two puffs (200mcg total dosis) of salbutamol (Aerolin®, GSK, Aranda de Duero, Spain) were administrated with three minutes of separation in between puffs and using a mouthpiece chamber (Volumatic®, Glaxo Wellcome GmbH & Co. Bad Oldesloe, Germany). The use of short acting and long acting beta-2 agonists were stopped in asthmatics at least six and 12 h, respectively, before performing spirometry. The spirometer was calibrated daily using a 2 L syringe.

Weight and height measurements were taken before spirometry, which was performed according to American Thoracic Society/European Respiratory Society guidelines for preschoolers.[4] None of the participants had performed a spirometry before. Children belonging to the control group attended the lung function laboratory in groups of five and accompanied by an assistant. They came together to the laboratory, and after a demonstration and verbal explanation by the operator, began to test the child who voluntarily offered. This allowed all the children to try to do spirometry with great enthusiasm, imitating and competing with their peers. Asthmatic preschoolers performed spirometry accompanied only by a parent. Each child did all possible expiratory force curves over a 15-min period, without a nasal clip and standing up. Sometimes, according to operator criteria, animation programmes included in the software (e.g. candles, balloons) were used. All of the spirometry was conducted by one research coordinator (RM) for the study.

We considered acceptable spirometric curves as those with evident PEF, without abrupt end of flow > 10% of PEF, with expiratory time > 0.5 s and without evidence of cough