INTERRUPTER RESISTANCE IN PRESCHOOL CHILDREN: CLINICAL UTILITY IN ASTHMA MANAGEMENT

Boddi G.,[1] Tuccio A.,[1] Nanni S.,[1] Coccina F.,[1] Rossi E.,[2] Nistri E.,[2] Vascotto M.,[1] Balestri P.[1]

[1]U.O.C. Pediatria, Dipartimento Materno-Infantile, AOU Santa Maria alle Scotte, Siena, Italy
[2]Scuola di Specializzazione in Pediatria, Università degli Studi di Siena, Italy

Abstract. Asthma is the most common chronic disease affecting children in industrialized countries but it is greatly underdiagnosed in preschool children. In these patients, who are not able to collaborate in the execution of spirometry tests, it is possible to use interrupter resistance (Rint) technique. The aim of our study is to assess Rint utility in asthma management when integrated with clinical evaluation in preschool children. Data from 35 preschool children with recurrent wheezing and/or cough were collected. Case history, physical examination, in vitro and in vivo allergy testing were investigated. According to the presence or absence of symptoms in intercritical period they were divided into two groups, asymptomatic (A) and symptomatic (B). To assess respiratory function we used baseline and post-bronchodilator Rint. In group A (asymptomatic) baseline Rint was normal in 78,9% of children and increased in 21,1%. After bronchodilator (BD) administration there was a significant response in 52,6% of patients. In group B (symptomatic) baseline Rint was normal in 81,3% of children and increased in 18,7%. After bronchodilator administration there was a significant response in 56,3% of patients. Our results confirm that baseline Rint cannot be used to discriminate between healthy and sick children, therefore it is necessary to perform this test after administration of BD. In our patients, a significant response to BD permitted to objectify the discomfort of symptomatic children and to report a state of subclinical bronchial obstruction and/or bad perceptions of the severity of bronchospasm in asymptomatic ones, allowing to confirm previous therapeutic choices in some cases and to suggest different therapeutic strategies in others. Therefore, bronchodilator response measured by Rint should be systematically studied and further assessed in conjunction with clinical outcomes, in order to implement asthma management in children unable to produce reliable spirometry.

INTRODUCTION

Asthma is the most common chronic disease in children of industrialized countries [1]. GINA (Global Initiative for Asthma) guidelines defines asthma as a chronic inflammatory disorder of the airways in which the chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment [2]. Diagnosis in preschool children is greatly underestimated (prevalence 8.6%) because of high frequency of infections of respiratory tract and difficulties in performing spirometry tests. Therefore asthma should be suspected in every child with recurrent wheezing or cough [3]. In the diagnostic process of asthma in children case history, physical examination, *in vitro* and *in vivo* testing for allergies and determination of pulmonary function are needed. The most used measures for lung function evaluation are peak expiratory flow (PEF) and forced expiratory flow-volume curve [4]. In preschool children, unable to perform reliable spirometry tests, we can use interrupter resistance (Rint) technique. Rint is a non-invasive technique, easy and repeatable, with a good correlation with gold standard techniques and able to detect changes in airway caliber [5-6]. This technique needs a little cooperation from children who are only requested to breath quietly trough a mouthpiece. In the execution of Rint, while the child breathes in tidal volumes, the airflow is interrupted for 100 milliseconds and during this occlusion, alveolar and mouth pressure rapidly equilibrate [7]. Rint is defined as the pressure dived by the air flow measured immediately before the interruption. Optimal control of symptoms in asthmatic children requires, according to GINA report 2011, continual clinical follow up and lung function valuation [2]. The aim of our study is to assess Rint utility in asthma management when integrated with clinical evaluation of preschool children.

METHODS

Data from children with recurrent wheezing and/or

Correspondence to:
Giulia Boddi
University of Siena. Polyclinic "Le Scotte". Viale Bracci, 53100 Siena, Italy.
Phone: +39.0577.586570.
E-mail: giulia.boddi@gmail.com

cough, referred to our allergology and bronchopneumology laboratory from 2009 to 2011, were collected. The patients were 35 preschool children (3-5 years), 22 boys and 13 girls, with a mean age 4,46 years.

All the patients were requested to answer some questions about case history with particular attention to wheezing features: starting age, number of episodes in the last year, wheezing frequency, number of episodes that required hospitalization, trigger factors. Clinical conditions in the intercritical period were investigated (daytime respiratory symptoms, changes in sleep pattern, interference with physical activity and need for bronchodilators) and according to these criteria children were divided into two groups, asymptomatic and symptomatic. Atopic status was documented by Skin Prick Test (SPT) for common allergens: dermatophagoides pteronissinus, dermatophagoides farinae, aspergillus, alternaria, derived epithelial cells of animals, grasses, olive tree, cypress, beech tree, ash tree, holm oak, plane tree, oak tree, birch tree, pellitory, ambrosia, and food allergens. Respiratory function was studied through baseline and post-bronchodilator (salbutamol 200 µg, short-acting β2-adrenergic receptor agonist) interrupter resistance (Rint) technique. Rint was performed using desktop spirometer COSMED Pony FX. In our study we used, as reference values, those "predicted" developed from the study of Lombardi [8], calculated through the following equation:

Predicted Rint=2,126878-(0,012538xheight in cm)

After the determination of that value, depending on the auxometric characteristics of each patient, we calculated the z-score (coinciding with the SD from predicted):

$$\text{z-score} = \frac{\text{measured Rint - predicted Rint}}{\text{RSD}}$$

with RSD= residual standard deviation=0,2038

Rint values with z-score >2 standard deviations (SD) were considered pathological. Bronchoreversibility was defined significant when the decrease in airway resistance was >0.25 kPa/Ls. To process the report the graph in Figure 1 was used.

RESULTS

Children included in our research were submitted to the study of airway resistance using the interrupter resistance technique (Rint). In the whole group, 20% of patients had increased baseline Rint, while the remaining 80% had values within the normal range. After bronchodilator administration, the percentage of children with significant response was 54.2%, of which 63.2% with normal baseline Rint and 36.8% with increased baseline Rint.

Children were divided in two groups: group A (asymptomatic)=19 (54.3%) and group B (symptomatic)=16 (45.7%) (Table 1).

In group A, basal respiratory resistance was increased in 21.1% of patients while the remaining 78.9% had values within the normal range (Table 2). After administration of bronchodilator, 52.6% had a significant response (Table 3). A patient with normal baseline Rint did not cooperate in bronchoreversibility test. All the patients with increased baseline Rint had significant response to β2-agonist (100%), 6 of 15 patients with normal baseline Rint had significant response (40%).

In group B, baseline Rint was increased in 18.7% of patients and normal in 81.3% (Table 2). After administration of bronchodilator, Rint was significant in 56.3% of patients (Table 3). All the children (100%) with increased baseline Rint and 46% of those who have normal baseline airway resistance significantly responded to salbutamol.

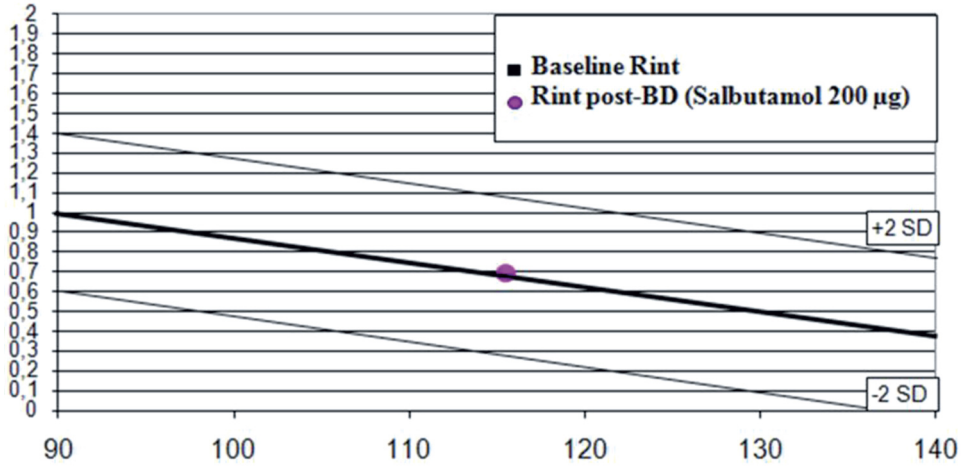

Figure 1. Graph used to process baseline and post-bronchodilator Rint data.

DISCUSSION

In our case series baseline Rint showed increased airway resistance in 21,1% among asymptomatic children and in 18,7% among symptomatic ones, whereas it was normal in 78,8% of asymptomatic and in 81,3% of symptomatic children.

Our data confirm the literature [9-12]: in fact, according to the large interindividual variability of Rint detected in healthy subjects and the overlapping of values between healthy and asthmatic children, the only measurement of airway resistance in basal conditions does not discriminate between healthy and wheezer children. Therefore, to increase the diagnostic effectiveness of this method, it is appropriate to perform the bronchoreversibility test. In our small case series, a positive response to β2-agonist showed no differences between symptomatic (56,3%) and asymptomatic patients (52,6%): these data are probably influenced by the small amount of the sample and by the fact that more than a half of asymptomatic children, susceptible to β2-agonist and with high percentage of wheezing related to airway infections, performed Rint in September (a short distance from respiratory viral infections which can influence the bronchoreversibility).

Moreover, some children with symptomatic intercritical period but refractory to salbutamol, reported recurrent cough. This was immediately treated with repeated inhalation of β2-agonist, and this may had affected the response to bronchodilator (for instance, children must have stopped therapy at least 8 hours before the test). In this preschool population the positive measurement of baseline and post-bronchodilator Rint permitted to objectify the discomfort of symptomatic children and to report a state of subclinical bronchial obstruction and/or bad perceptions of the severity of bronchospasm in asymptomatic ones. Conversely, a negative result allowed a misinterpretation of the clinical symptoms of symptomatic children or to confirm a good respiratory performance in asymptomatic ones.

Table 1. Clinical features of children included in groups A and B.

	Group A (Asymptomatic *n*=19)	**Group B (Symptomatic *n*=16)**
Parental asthma	6 (31%)	7 (43.7%)
Atopic dermatitis	9 (47.3%)	9 (56.2%)
Positive spt	10 (52.6%)	9 (56.2%)
Symptoms and airway infections	12 (63.2%)	5 (31.2%)

Table 2. Baseline Rint in asymptomatic (A) and symptomatic (B) children.

Airway resistance in baseline rint	**Group A (Asymptomatic *n*=19)**	**Group B (Symptomatic *n*=16)**
Normal	21,1%	18,7%
Increased	78,9%	81,3%

Table 3. Rint after bronchodilator administration in asymptomatic (A) and symptomatic (B) children.

Rint after β2-agonist	**Gruppo A* (Asymptomatic *n*=19)**	**Gruppo B (Symptomatic *n*=16)**
Significant	52,6%	56,3%
Non significant	42,1%	43,7%

The evaluation of airways resistances, however, plays an important role in management of the wheezer child, allowing, in some cases, to validate the previous therapeutic choice and in others to suggest a different therapeutic approach. As stated in the study of Beydon, in a large proportion of the population of asthmatic children, Rint correlates with spirometric indexes (FEV_1, FEV_1/FVC, $FEF_{25-75\%}$), but has poor sensitivity to detect baseline obstruction, while has good sensitivity and specificity to detect bronchoreversibility [12]. Therefore, bronchodilator response measured by Rint should be systematically studied and further assessed in conjunction with clinical outcomes, in order to implement asthma management in children unable to produce reliable spirometry.

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