# Interrupter resistance changes in children with bronchiolitis

#### Ozge Yilmaz<sup>1</sup>, Ayhan Sogut<sup>1</sup>, Senem Alkan<sup>2</sup>, Hasan Yuksel<sup>1</sup>

1. Celal Bayar University Medical Faculty, Dept of Pediatric Allergy and Pulmonology, Manisa, Turkey, 2. Celal Bayar University Medical Faculty, Dept of Pediatrics, Manisa, Turkey

Contact: Ozge Yilmaz, MD, Uncubozkoy Mah. Altin Site B Blok No:6, Manisa, Turkiye Email: oyilmaz\_76@hotmail.com

#### **Abstract**

**Introduction:** Determination of lung function in children younger than three years with bronchiolitis may aid in treatment; however, technical difficulties such as requirement of sedation and lack in standardization limit clinical use. **Objectives:** Aim of this study was to evaluate lung function changes using the interrupter technique in unsedated wheezing children younger than 3 years during and after acute bronchiolitis. **Methods:** Children with acute bronchiolitis younger than three years age were enrolled in this cohort study. Number of previous bronchiolitis episodes, severity of pulmonary findings, duration of acute bronchiolitis findings before presentation, requirement for hospitalization were recorded during initial enrollment. Duration of the current bronchiolitis was recorded. Interrupter resistance (Rint) measurements were performed on all children during and after bronchiolitis, using a face mask. Results: Mean  $(\pm SD)$  age of the children enrolled was 9.4  $\pm$ 2.9 months. Mean bronchiolitis score was 5.6  $\pm$ 1.4 at presentation. Mean duration of acute bronchiolitis before and after presentation were 10.1  $\pm$ 13.0 and 5.1  $\pm$ 2.3 days, respectively. There was a significant decrease in expiratory Rint values after clinical bronchiolitis findings terminated [1.08 (0.45) vs 0.80 (0.33) kPa.L-1.s, p=0.009]. Flow had not changed significantly while mouth pressure had decreased (p=0.96 and p=0.01, respectively). **Conclusion:** Interrupter technique measurements showed higher resistance during acute bronchiolitis in children, which decreased after acute findings, disappeared. Rint may be used as a method to detect the change in airway function in unsedated children younger than three years in ambulatory conditions, despite some limitations of standardization in this age group. **Keywords:** Bronchiolitis, airway

#### Introduction

Wheezing is a common disease entity in preschool children and increases risk for future childhood asthma<sup>1-3</sup>. Association between childhood asthma and severe bronchiolitis is reported commonly, but the pathophysiology underlying this is not completely clear and understanding lung physiology and respiratory mechanics in this age group may provide important clues about this 1,3,4. Measurement of airway resistance during tidal breathing using sudden and rapid airflow interruptions allows evaluation of lung function in preschool children who can not perform the voluntary maneuvers required for spirometry<sup>4,5,6</sup>. Although different methods used by different laboratories make it difficult for comparison of results, this is a promising technique with good reproductibility in preschool children<sup>4,7</sup>. Most of the previous studies have used the "classical" interrupter resistance technique which is defined as mouth pressure divided by the airflow measured immediately before interruption<sup>4,7</sup>. American Thoracic Society/European Respiratory Society recommendations have been recently published for lung function measurements in preschool children, including the interrupter technique<sup>4</sup>.

resistance, interrupter, Rint

#### Rezumat

#### Modificări ale rezistenței la flux la copiii cu bronșiolită

Introducere: Determinarea funcției pulmonare la copii mai mici de trei ani cu bronșiolită poate fi de ajutor în tratamentul acesteia; cu toate acestea, dificultățile tehnice, cum ar fi nevoia de sedare și lipsa de standardizare, limitează utilizarea clinică. Obiective: Scopul acestui studiu a fost evaluarea modificărilor funcției pulmonare folosind tehnica de măsurare a rezistenței la flux cu întrerupere (Rint) la copii mai mici de 3 ani, nesedați, cu wheezing, în timpul și după bronsiolită. **Metodă:** În acest studiu de cohortă au fost înrolați copii cu bronșiolită acută mai mici de trei ani. Numărul de episoade anterioare de bronșiolită, severitatea modificărilor pulmonare, durata bronșiolitei acute înainte de prezentare și necesitatea de internare au fost înregistrate în timpul înrolării inițiale. A fost notată durata episodului curent de bronșiolită. Măsurătorile Rint au fost efectuate la toți copiii în timpul și după bronșiolită folosind o mască facială. Rezultate: Vârsta medie (±SD) a copiilor înrolați a fost  $9.4 \pm 2.9$  luni. Scorul mediu de bronsiolită a fost  $5.6 \pm 1.4$ la prezentare. Durata medie a bronșiolitei acute înainte și după prezentare a fost  $10,1 \pm 13$  și respectiv  $5,1 \pm 2,3$  zile. A fost o scădere semnificativă a valorilor Rint expirator după terminarea manifestărilor clinice ale bronșiolitei [1,08 (0,45) vs. 0,8 (0,33) kPa.L-1.s, p=0,009]. Fluxul nu s-a schimbat semnificativ în timp ce presiunea la nivelul gurii a scăzut (p=0,96 și respectiv p=0,01). **Concluzie:** Măsurătorile tehnicii cu întrerupere la copii au arătat rezistențe mari în timpul bronșiolitei acute, care au scăzut după ce manifestările clinice acute au dispărut. Rint poate fi utilizată ca o metodă de detecție a schimbărilor funcției respiratorii la copii nesedați, mai mici de trei ani, în condiții ambulatorii, în ciuda unor limitări ale standardizării în acest grup de vârstă. Cuvinte-cheie: bronsiolită, rezistenta

căilor aeriene, întrerupere, Rint

Despite the important information that may be provided by infant lung function testing in young children, just a few studies have assessed the interrupter technique in infants and toddlers because of sedation and standardization problems  $^{5,8,9}$ . However, assessment of lung function changes in bronchiolitis cases may provide clues to pathophysiological aspect and aid in therapeutic planning.

The aim of this study was to evaluate the changes in respiratory resistance using the interrupter technique (Rint) in non-sedated wheezing children aged below 3 years during and after an acute wheezing episode.

#### Materials and method

#### Subjects

Wheezy children aged younger than three years presenting with an acute episode of wheezing to the Department of Pediatric Allergy and Pulmonology were enrolled in this study consecutively. Diagnosis of wheezing child was based on history of recurrent wheezing and expiratory obstruction documented by a physician. Children with any other risk factors such as cystic fibrosis and bronchiolitis obliterans were excluded from the study population.

#### Study design and ethical approval

This was a cohort study in which all children enrolled were followed up until current wheezing episode terminated. The study was approved by the Institutional Ethical Board of our institution and informed consent was obtained from the parents of children enrolled.

#### Data collection

Disease characteristics including the number of previous wheezing episodes, severity of pulmonary findings, duration of current wheezing episode before presentation, requirement for hospitalization were recorded during the initial enrollment. All children were followed up until current wheezing episode terminated. Duration of the current respiratory findings was recorded. Rint measurements were performed on all children at the beginning and end of the study.

#### Measurement of interrupter resistance

Interrupter resistance (Rint) was measured using PONY Fx spirometer with the Rint unit (Cosmed, Italy) which back-extrapolates to 15 ms<sup>4,5</sup>. An oronasal mask (Datex Ohmeda, Helsinki Finland) was adapted to the original Rint unit since the study was carried on children aged below three years who can not hold the mouthpiece. Nasal obstruction was not performed.

The tests were performed in a quiet room with stable room temperature. Expiratory measurements were taken while the child was sitting quietly on the parents lap. Cheeks were not supported and sedation was not given for ethical reasons.

Measurements were performed until three technically acceptable measurements were achieved and these were recorded <sup>10</sup>. Mean of these three measurements were taken into the statistical analysis. The parameters that are expressed by the Pony Fx include Rint, Flow, mouth pressure (Pmo)<sup>11</sup>.

#### Bronchiolitis severity score

Bronchiolitis severity score was determined according to cardiac and respiratory rate, wheezing, presence of cyanosis and peripheral oxygen saturation as previously described $^3$ . The score ranged between values of 5 to 15 which increased as the severity increased.

#### Statistical analysis

Statistical analyses were performed by SPSS 13.0 (Chicago IL) computer program. Nonparametric tests were used in the analysis because the values were widely distributed. Wilcoxon signed rank test was used to compare Rint parameters during and after bronchiolitis. Spearman's correlation analysis was performed to assess correlation between Rint parameters and disease severity parameters like acute bronchiolitis severity score, duration of current wheezing findings and the duration of current wheezing episode findings after the first Rint measurement. Rint parameters were also compared between children with family history of atopy and asthma and the ones without a positive history using the Mann Whitney U test. P values <0.05 were accepted as statistically significant.

#### Results

#### Subject characteristics

Mean ( $\pm$ SD) age of the thirty children (20 male, 10 female) enrolled in the study was 9.4  $\pm$ 2.9 months. Family history of atopy or asthma was present in 36.7% of the cases. Mean (SD) age at the first wheezing episode was 5.1  $\pm$ 2.4 months.

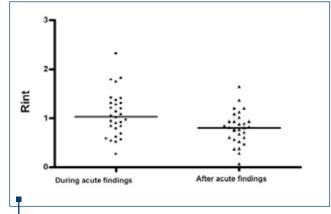
Table I

Expiratory Lung Function Results During and After Acute Bronchiolitis Findings (n=30)

	During acute bronchiolitis	After acute bronchiolits	P**
Rint*	1.08 (0.45)	0.81 (0.33)	0.009
Flow*	70.33 (23.70)	70.87 (19.45)	0.957
Pmo*	0.08 (0.04)	0.06 (0.03)	0.010

<sup>\*</sup>Mean (standard deviation)

<sup>\*\*</sup>Mann Whitney u test



**Figure 1.** Distribution of Rint values during and after acute bronchiolitis findings

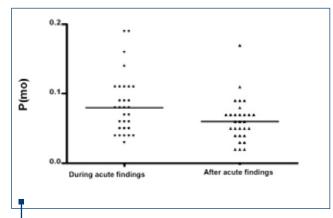
Mean (SD) bronchiolitis score was  $5.6 \pm 1.4$  at presentation. Mean (SD) duration of current wheezing episode before and after presentation were 10.1 (13.0) and 5.1 (2.3) days, respectively.

### Comparison of Rint values during and after bronchiolitis

There was a significant decrease in the Rint values after the wheezing episode terminated [mean (SD) 1.08 (0.45) vs 0.80 (0.33) kPa.L<sup>-1</sup>.s, p=0.009] (Table I, Fig 1). Flow had not changed significantly while Pmo had decreased significantly (p=0.96 and p=0.01 respectively) (Table I, Figure 2).

#### Correlation of Rint values with clinical severity

There was no significant correlation between Rint values and the bronchiolitis severity score (rho=-0.06) (Fig 3). Simi-



**Figure 2.** Distribution of P(mo) during and after acute bronchiolitis findings

Table II

Expiratory lung function results during acute bronchiolitis period in children with and without history of atopy or asthma in the family

	Family History		
	Present	Absent	P**
Rint*	1.07 (0.39)	1.09 (0.49)	0.98
Flow*	74.4 (25.1)	67.9 (23.2)	0.39
Pmo*	0.09 (0.05)	0.08 (0.04)	0.42

<sup>\*</sup>Mean(standard deviation)

<sup>\*\*</sup>Mann Whitney u test

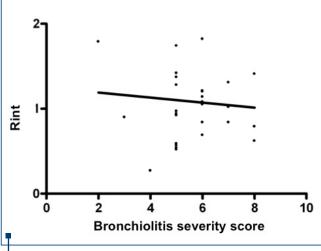


Figure 3. Correlation of Rint and bronchiolitis severity score

larly flow or Pmo did not correlate with bronchiolitis severity score either (rho=-0.08 and -0.11 respectively). Duration of current wheezing episode before presentation was not significantly correlated with Rint, flow or Pmo (rho = 0.09, -0.04 and 0.09 respectively). Number of previous wheezing episodes was not correlated with any of the lung function values (rho<0.20 for all).

Lung function values were not significantly different between children with and without history of atopy or asthma in the family (p>0.05 for all, Table II).

#### Discussion

The results of our study demonstrated that airway resistance is significantly higher during an acute wheezing episode in preschool wheezing children. Moreover, we have shown that the change in airway difference may be demonstrated in children younger than three years age without medical sedation and using an oro-nasal facemask. This finding may be important in incorporation of infant pulmonary function testing into routine clinical care for follow-up of wheezing in children.

It is widely accepted that origins of adult respiratory diseases lie in the childhood period and that lung function deficits and airway remodeling is already established in preschools years<sup>9, 12</sup>. Similarly, pulmonary functions of the preschool years predict those during adulthood <sup>9</sup>. Pulmonary

function tests that do not require active cooperation of the child has been demonstrated to be acceptable for preschool children<sup>13</sup>. These techniques that include the interrupter technique may allow for pulmonary function follow up for this age group who can not cooperate to perform forced expiratory maneuvers<sup>7,8,13</sup>. Many of the lung function tests in infants have been performed after sedation but feasibility of the interrupter technique in spontaneously breathing non-sedated infants has been shown in a previous study<sup>5,14</sup>. Therefore, the aim of this study was to evaluate the change in airway resistance using expiratory Rint measurements in non-sedated wheezing children below three years age during and after an acute wheezing episode.

Previous studies have reported significantly higher resistance and significantly higher change in resistance with bronchodilator in children with asthma when compared with healthy control<sup>13</sup>. Moreover, in sedated infants aged less than 18 months, Rint values were found to be significantly correlated with respiratory system resistance by single breath occlusion method<sup>15</sup>. Therefore, resistance can be used as an indicator of bronchial responsiveness to bronchodilator or other therapy<sup>13, 16</sup>. Similar to these previous studies we detected a significant decrease in airway resistance after the wheezing episode terminated compared to the values during wheezing.

Many risk factors have been suggested to play a role in development of asthma in children, including: male sex, atopic sensitization, family history of atopy and/or asthma and socioeconomic factors<sup>17, 18, 19</sup>. Therefore, airway resistance measurements were compared among children with and without family history of atopy or asthma as one of these risk factors but significant difference was not demonstrated. Similarly, clinical severity was not found to be associated with resistance measurements.

Moreover, inability to block nasal passage and need to use oronasal masks for children aged below 2 years is expected to cause upper airway influence on the airway resistance results. However, nasal obstruction in this age group without sedating the child would have agitated the child and preclude the use to the technique. A previous study on a similar age group as has used face mask over the mouth and nose and demonstrated that the results were correlated with respiratory system resistance by single breath occlusion method<sup>18</sup>. Another study has demonstrated that use of mask or mouthpiece for interrupter measurements causes a difference in the results but they have suggested that both measurements can be used<sup>7,20</sup>. Additionally another study using face-mask has shown that interrupter technique is feasible but considering that the mask type used influences the results. Therefore, a single mask type was used for all measurements in our study<sup>14</sup>. Moreover, in a previous study performed on children aged above three years using a mouthpiece, it was demonstrated that upper airway did not change airway resistance measurements much<sup>21</sup>. However, still this latter study used a mouthpiece therefore can't preclude influence of nasal resistance<sup>21</sup>. Therefore, we think that this limitation needs to be incorporated in daily use and interpretation of Rocc in very young children aged below two years age and can be overcome by using a standard technique and mask for each measurement.

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Another issue that has been discussed previously was the use of mean or median values in the interrupter technique and the use of expiratory or inspiratory measurements<sup>22</sup>. It has been demonstrated that use of inspiratory and expiratory resistance does not make a statistically significant difference therefore we preferred to record expiratory values considering that clinical findings are more prominent during expiration in acute bronchiolitis<sup>22</sup>. Mostly median values of the measurements have been recommended to be used but it has been reported that there is no significant difference between mean and median in the interrupter technique<sup>4,22</sup>. Since we recorded only technically acceptable measurements we preferred to use the mean values of three measurements for each patient.

The main limitations of the study include lack of standards for healthy children aged below 2 years of age, which precluded us from making conclusions about the airway resistance in wheezy children compared to healthy peers. Therefore, the children were compared with their own values during and after acute bronchiolitis.

#### Conclusion

In conclusion, airway resistance measured by interrupter technique during acute wheezing episodes in children younger than three years age decreases after the episode terminates. Therefore, this may be used as a method that can detect this change in airway function in non-sedated children younger than three years age in ambulatory conditions, despite some limitations of standardization.

## References

- 1. Singh AM, Moore PE, Gern JE, et al. Bronchiolitis to asthma: a review and call for studies of gene-virus interactions in asthma causation. *Am J Respir Crit Care Med* 2007; 175: 108-119.
- 2. Oh JW. Respiratory viral infections and early asthma in childhood. *Allergol Int* 2006; 55: 369-372.
- 3. Gern JE. Viral respiratory infection and the link to asthma. *Pediatr Infect Dis J* 2008: 27: S97-103.
- 4. Beydon N, Davis SD, Lombardi E, et al. An official American Thoracic Society/European Respiratory Society statement: pulmonary function testing in preschool children. *Am J Respir Crit Care Med.* 2007; 175: 1304-1345.
- Kooi EM, Schokker S, van der Molen T, et al. Airway resistance measurements in pre-school children with asthmatic symptoms: the interrupter technique. Respir Med 2006; 100: 955-964.
- 6. Merkus PJ, Mijnsbergen JY, Hop WC, et al. Interrupter resistance in preschool children: measurement characteristics and reference values. *Am J Respir Crit Care Med* 2001; 163: 1350-1355.
- 7. Child F. The measurement of airways resistance using the interrupter technique (Rint). *Paediatr Respir Rev* 2005; 6: 273-277.
- 8. Papadopoulos NG, Moustaki M, Tsolia M, et al. Association of rhinovirus infection with increased disease severity in acute bronchiolitis. *Am J Respir Crit Care Med* 2002; 165: 1285-1289.
- 9. Martinez FD. The origins of asthma and chronic obstructive pulmonary disease in early life. *Proc Am Thorac Soc* 2009; 6: 272-277.
- 10. Arets HG, Brackel HJ, van der Ent CK. Applicability of interrupter resistance measurements using the MicroRint in daily practice. *Respir Med* 2003:97:366-74.
- Adams AM, Olden C, Wertheim D, et al. Measurement and repeatability of interrupter resistance in unsedated newborn infants. *Pediatr Pulmonol* 2009:44:1168-73

- 12. Jartti T, Mäkelä MJ, Vanto T, et al. The link between bronchiolitis and asthma. *Infect Dis Clin North Am* 2005; 19: 667-689.
- 13. Beydon N, Pin I, Matran R, et al. Pulmonary function tests in preschool children with asthma. *Am J Respir Crit Care Med* 2003; 168: 640-644.
- 14. Hall GL, Wildhaber JH, Cernelc M,et al. Evaluation of the interrupter technique in healthy, unsedated infants. *Eur Respir J* 2001; 18: 982-928.
- 15. Chavasse RJ, Bastian-Lee Y, Seddon P. Comparison of resistance measured by the interrupter technique and by passive mechanics in sedated infants. *Eur Respir J* 2001: 18: 330-334.
- Pao CS, McKenzie SA. Randomized controlled trial of fluticasone in preschool children with intermittent wheeze. Am J Respir Crit Care Med 2002; 166: 945-949
- 17. Sterling YM, El-Dahr JM. Wheezing and asthma in early childhood: an update. *Pediatr Nurs* 2006; 32: 27-31.
- 18. Morgan WJ, Stern DA, Sherrill DL, et al. Outcome of Asthma and Wheezing in the First 6 Years of Life: Follow-up through Adolescence. *Am J Respir Crit Care Med* 2005; 172: 1253-1258.
- 19. Yuksel H, Sakar A, Dinç G, et al. The frequency of wheezing phenotypes and risk factors for persistence in aegean region of Turkey. *J Asthma* 2007; 44: 89-93.
- 20. Child F, Clayton S, Davies S, et al. How should airways resistance be measured in young children: mask or mouthpiece? *Eur Respir J* 2001; 17: 1244-1249
- 21. Lombardi E, Sly PD, Concutelli G,et al. Reference values of interrupter respiratory resistance in healthy preschool white children. *Thorax* 2001; 56: 691-695
- 22. Adams AM, Olden C, Wertheim D, et al. Measurement and repeatability of interrupter resistance in unsedated newborn infants. *Pediatr Pulmonol* 2009; 44: 1168-73